Universitat Ramon Llull

DOCTORAL THESIS

Title Development and validation of the HarsMeth NP methodology for the assessment of chemical reaction hazards.

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"To be thus is nothing,
but to be safely thus"

William Shakespeare
(Macbeth, Act III, Scene I)

To my family

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ABSTRACT

The aim of this work is focused on the development, testing and improvement of a methodology for the assessment of thermal hazards of chemical reactions, mainly oriented to be used at small and medium enterprises. The methodology consists on a checklist based system to identify thermal hazards, including tools easy to be followed by non experts in the field of safety. The origins of the development are two already existing tools known as HarsMeth and Check Cards for Runaway. Different approaches have been followed in order to come up with a reliable assessment tool. In the first place, the two mentioned methodologies were tested at different companies working on fine chemical production, which gave the possibility to determine strengths and weaknesses for both methodologies, and to profit from the identified strengths to combine them to create one single tool called HarsMeth version 2. Later, this version was thoroughly tested at two different companies to improve it, by detecting flaws and expanding the checklists in order to cover as many issues as possible in the assessment. Further work performed aimed at the development of tools for the theoretical estimation of reaction enthalpies and for the identification of thermal hazards in process equipment. A final version of the methodology was produced, called HarsMeth New Process, structured to perform the hazard assessment at every step followed in the development of a chemical process, starting from the design of the chemical reaction at the laboratory, followed by the study of stability and compatibility of the reactants involved, the bench scale analysis of the synthesis path chosen, the scale up of the process and the determination of the necessary safety measures for the implementation of the process at industrial scale in accordance with the hazards identified. Another strategy followed in order to improve the methodology has been to analyse the chemical accidents reported to the MARS database in order to establish lessons learned from such accidents, and to identify what topics of the methodology could have helped to prevent the accidents and to emphasize what aspects of chemical safety need to be taken into account by the process industries.

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1.- INTRODUCTION

Accidents in chemical industrial plants represent a high potential threat because of the dangerous substances that are usually handled and the conditions of the processes performed at these installations. These conditions often involve mixing of hazardous chemicals in large vessels at severe temperature and pressure values, kept under control by both human and technical measures. The failure of those measures or an incorrect design of process and equipment parameters may lead to a loss of control in the process, which can generate a runaway reaction.

Many accidents involving chemical substances have generated human and / or environmental disasters in the past, not to mention the continuous concern of the population regarding the safety of industrial facilities. Particularly tragic was the accident that occurred in 1984 in Bhopal, India, where over 20000 people were killed or seriously injured (Gupta, 2007). Another important accident was the one that happened at Seveso, Italy, in 1976, which triggered the European Commission Directive 82/501/EEC (Council Directive, 1982) commonly referred to as the Seveso Directive. This Directive was renewed in 1996 with the so called Seveso II Directive, or Directive 96/82/EC (Council Directive, 1996) in order to clarify some of its contents, and later amended in 2003 (Directive, 2003) as a result of other accidents like the ones occurred in Enschede, The Netherlands, in 2000, or in Toulouse, France, in 2001.

The Seveso II Directive states in its Annex I the criteria under which it is determined whether an establishment falls under the regulation or not, based on the type and quantities of the substances handled. For those sites that are concerned by the regulation, the Directive states in its Article 9 that a hazard identification of the processes carried out at the establishment must be performed, as well as providing the necessary safety measures to prevent an accident from occurring.

Several systems to perform hazard analysis of chemical processes have been developed in the last decades (CCPS, 1985; Khan and Abbasi, 1998). Checklists are the simplest method available, and different versions have been widely used by the chemical industry in the past years. Structured and organized checklist systems for hazard identification of chemical processes date from as early as the mid 1960's (The Dow Chemical Company, 1964), and have been broadly developed ever since (Lees, 2005). They consist on a set of questions that engineers or operators must answer in order to verify that no safety requirement is neglected. In general, checklists are a good method to be used by untrained personnel and are not time consuming. On the other hand, it can provide limited information if answers are restricted to 'Yes' or 'No', it can focus on a single item at a time, and its effectiveness is limited to the ability and experience of the person preparing it, with a significant probability of some item being neglected.

A very popular tool for hazard identification is Hazop (Hazard and Operability). This method was initiated at ICI in 1974 and further developed and described by Kletz (1992). The basis of Hazop studies is a systematic analysis of design and operation documents by a group of experts, in which the use of guide words (e.g. more, none, less and so on) are applied on the different process parameters (e.g. flow, temperature, concentration and so on) to analyse the effects that such variations will have on the evolution of a process. Hazop can be performed with the aid of PI&Ds (Piping and Instrumentation Diagrams) or flow sheets of the process applied to different units of a plant.

Since Hazop is based on the variations of normal process conditions, it assumes that those conditions are correctly designed, so it cannot identify hazards related to design failures. Furthermore, it is also extremely dependent on the expertise of the users, and it requires large inputs of time and expert manpower. But in spite of those limitations, it is still nowadays one of the preferred systems for hazard identification because it helps to prioritise hazards, it gives ideas on mitigation measures and it can be performed either at design stage or during operation stage, as well as providing a basis for subsequent steps in the risk management program (Khan and Abbasi, 1998).

Fault Tree Analysis (FTA) is an analytical tool that uses deductive reasoning to determine the occurrence of an undesired event. FTA was first conceived in 1961 by the Bell Telephone Laboratories in connection with a US Air Force contract to study the Minuteman Missile launch control system. In the following years it was reviewed extensively (Lee *et al*. 1985). FTA, along with component failure data and human reliability data, can enable the determination of the frequency of occurrence of an accidental event. However, the accuracy of prediction is limited and it depends upon the reliability and failure data of components of the fault tree. Besides, it requires considerable time and effort by a skilled team of analysts.

Failure Mode Effect Analysis (FMEA) consists on an examination of individual components such as pumps, pipes, valves and so on to identify the likely failures which could have undesired effects on system operation. FMEA was originally developed in the mid 1970’s by the USA Department of Navy (MIL, 1974); it is a qualitative inductive method and it is relatively easy to apply. It is assisted by the preparation of a list of expected failure modes. It is an efficient method of analysing elements which can cause failure of the whole plant, but it is less suitable when complex logic is required to describe system failures. It is unable to deal with the interaction among different components and it needs a highly expert team with sufficient experience and time to carry out the study.

‘What if’ analysis (CCPS, 1985) is a technique that involves asking a series of questions beginning with ‘what if’ as a means of identifying hazards. These questions address different possible failure situations of plant equipment. The result is a qualitative tabular summary of identified hazards, with questions that can be used throughout the life of a project. On the other hand, it requires a team of experts to perform the study, and the results will be extremely dependant on the experience and intuition of the study team.

Another available system to analyse hazards are the Hazard Indices. These provide a measure of hazards in different contexts. The most widely used is the Dow Index, originally published in 1964 by the Dow Chemical Company for fire and explosion hazards. The procedure is to calculate the fire and explosion index (F&EI) following a structured system taking into consideration general and specific process factors and exposure estimations, and to use these to determine fire protection measures and, in combination with a damage factor, to derive the base to determine a Maximum Probable Property Damage (MPPD) and the Business Interruption (BI) loss.

The Mond Index is an extension of the Dow Index. It is intended to quantify fire, explosion and toxicity hazards, and was originally described by Lewis (1979) at the Mond division of ICI. It involves making an initial assessment of hazard in a manner similar to that used in the Dow Index, but taking into account additional hazard considerations.

The Instantaneous Fractional Annual Loss (IFAL) Index was developed by the Insurance Technical Bureau (1981) initially for insurance assessment purposes.

The procedure for calculation of the Index involves considering the plant as a set of blocks and examining each major item of process equipment in turn to assess its contribution to the index, considering fire and explosion issues. It is more complex than the previous indices since it requires computational calculations.

In the recent past, different index based systems have been developed in order to quantify the safety of industrial installations (Heikkilä, 1999; Khan and Amyotte, 2004; Chen and Yang, 2004). Usually these approaches try to quantify the overall risk through the combination of different factors, which are rated according to predefined scales or ‘weighting’ systems. These methods are usually derived from the indexes mentioned earlier (Dow, Mond, IFAL), and they consider the damage potential related to different sections of an establishment, according to plant and process characteristics, and taking into consideration the available hazard control measures.

However, in spite of the fact that the previously described methods have been available and used by process industries for a long time, accidents are still happening in the European chemical industry. One reason for this fact could be that most part of the chemical production in Europe is performed by Small and Medium Enterprises (SMEs) (Nomen *et al*., 2002) with less time, human and economic resources than big companies to perform extensive and sophisticated hazard analysis of their processes. In this sense, the development of simple tools that can be easy to use by non experts in the field of safety could be of interest for the small chemical companies in Europe. As it has been mentioned in the previous description of available hazard assessment methods, checklists are the only system that do not require either long time or high degree of expertise for their completion. In this sense, it is considered that the development of a checklist system specific to identify chemical reactive hazards could be of great help for the European process industries. These system should try to eliminate the flaws pointed out for checklists as a tool for hazard identification, basically the limitation of the ‘Yes’ and ‘No’ answers, the requirement to focus on one item at a time, and the necessity to rely on the expertise of the person preparing the checklist.

As it has been mentioned, accidents in European chemical industries are still happening nowadays. Recent studies (Sales *et al*., 2007a) show that in the period from 1994 to 2004, 301 Major Accidents happened in European process plants generating 153 fatalities. This study has been based on the accidents reported to the Major Accident Reporting System (MARS, 2007), established in 1984 and managed by the Major Accident Hazards Bureau (MAHB) of the Joint Research Centre of the European Commission, so it must be taken into consideration that those accidents are exclusively major accidents as described in Annex VI of the Seveso II Directive, which specifies the criteria under which an accident must be reported by Competent Authorities of the different Member States of the European Commission to MAHB.

MARS is a distributed information network (Mushtaq *et al*., 2003), consisting of 27 local databases on an MS-Windows platform in each Member State of the European Union and a central version at the European Commission's Joint Research Centre in Ispra, Italy. The main scope of MARS (Mushtaq and Christou, 2004) is to fulfil the requirements of the Seveso II Directive, which under its articles 14, 15, 19 and 20 describes the tasks that have to be performed by the Member States in case of a major accident. These tasks basically concern the responsibilities regarding the collection and submission of information relating to the circumstances of the accident and to ensuring the availability and analysis of the information in order to prevent major accidents from recurring.

The information contained in the accidents reported to the MARS database is divided into different sections and type of information. Two reporting forms have been established: the "short report" is intended for immediate notification of an accident, and the "full report" is prepared when the accident has been fully investigated, and the causes, the evolution of the accident, and the consequences are fully understood. Next to those two forms, a report profile stores the necessary administrative information, regarding issues like the name of the company, the date of the accident or the Member State reporting the accident. Only the information contained in the “short report” is available to the general public, while the contents of the “full report” and the report profile are kept confidential for internal use of the Commission and the Member States.

The “short report” gives essential information concerning the accident, including both selection boxes and free-text format, under the following headings:

- accident type
- substances directly involved
- immediate sources of accident
- immediate causes
- immediate effects
- emergency measures taken
- immediate lessons learned

The “full report” is much more analytical, and it involves more work in its preparation. While there are always free-text fields available to describe facts connected with an accident, different selection lists have been generated by definition of descriptive codes, so the accidents can be classified under common patterns. There are almost 200 different headings (data variables), for example:

- type of accident
- industry where accident occurred
- activity being carried out
- components directly involved
- causative factors (immediate and underlying)
- ecological systems affected
- emergency measures taken

The analysis of past accidents can be a useful tool to establish causes and to learn lessons that can help to better understand what went wrong for an accident to occur (Gustin, 2002). This is a task in which MAHB has been particularly active in the recent past (Drogaris, 1993; Kirchsteiger, 1999; Christou, 1999 Mushtaq *et al.*, 2003) with the information contained in the MARS database, in an attempt to help organizations to learn from past mistakes, in order to improve their future hazard assessment systems.

Taking into consideration the fact that SMEs require assistance in the hazard assessment of their chemical processes, and that there seems to be a deficiency, either at disseminating the available methods or regarding their application, a large group of chemical companies (both small and big ones), universities and research centres created HarsNet in October 1998, under the initiative and the co-ordination of the PQAT research group of the Institut Químic de Sarrià – Universitat Ramon Llull (Nomen *et al*., 2002). The acronym HarsNet stands for “Thematic Network on Hazard Assessment of highly Reactive Systems”. HarsNet was not a research project, but a thematic network partially funded by the European Commission, included in the Industrial and Materials Technologies Programme (Brite EuRam). Its aim was the creation of an extensive forum within which universities, research centres and industries could collaborate to improve dissemination of the fundamental knowledge that can be used for hazard assessment of reactive systems, in order to improve the global safety of the chemical industry and to reduce long term costs in the Research and Development (R&D) phase. A total of 33 partners from 11 countries in the European Union took part in HarsNet, being the participation of the chemical industry in the network of about 58% of the consortium. HarsNet was active until September 2002.

The main objectives of HarsNet were a consequence of the urgent need to introduce hazard assessment techniques for reactive chemicals into the normal working procedures of small and medium enterprises. One of the aims of this network was to contribute to the design of intrinsically safe processes, giving precedence to prevention in front of protection, and reducing the probability of the runaway to a minimum. New guidelines should be produced including a step-by-step assessment procedure based on literature surveys, simple predictive calculations and laboratory based testing in easily available equipment. Such procedures should be designed to detect the situation in which more sophisticated tests should be performed by external laboratories or specialised experts.

The work developed by the HarsNet team was subdivided in the following tasks.

- *Task 1*: also named HarsNet forum, it contained two sub tasks named HarsBase, a database on available calorimetry techniques and equipment, and HarsBook, a guide for experts in the field of chemical hazard assessment which was published by Dechema at the end of HarsNet (HarsBook, 2003). This task contemplated all the work and exchanges of information done inside the network.

- *Task 2:* it was created for supporting the SMEs and it had three sub tasks; HarsMeth, a short cut method for hazard assessment, HarsRes, which collected the different research activities of the consortium, and HarsSMEs, which joined the most important objective of the network, the interaction with the European chemical industry.

- *Task 3:* this task contemplated the dissemination of the results to the whole interested society, and again was divided into three sub tasks, named HarsWeb, HarsEdu (focusing on academic requirements for safety engineers) and HarsNet publications. A global task for co-ordinating and managing the network ran from its beginning.

All information about the HarsNet group and its research are available nowadays through the HarsNet internet website (HarsNet, 2007).

The participation of big chemical companies in HarsNet gave the opportunity to the consortium to learn what techniques for hazard assessment are used in such companies, in order to understand how their philosophy can be introduced into the policy of SMEs. Even though big companies use a wide variety of the previously described tools, the checklists used by “Ciba Speciality Chemicals” (1998) and “The Dow Chemical Company” (2000) were analysed.

The Ciba Risk Analysis is subdivided in two parts: a set of forms, generated with the purpose of guiding a team through all steps of a risk assessment and also to document the findings at each step in a standardised way, and a guidance document that gives the necessary instructions to fill up the forms and the theoretical basis of the main aspects analysed.

This tool is very exhaustive and it was clear from the start that it would have been too difficult for many SMEs to collect all the data required. However, it provided interesting ideas from the point of view of considering each synthesis step at a time when making the analysis, and keeping separated data collection sheets. In fact one of the problems of small and medium enterprises is to find all necessary data for a safety analysis, and most of the time understanding where data have been noted is problematic. Therefore, it was thought that definitions of what is the basic set of data and where it has to be written would have been important. The use of a compatibility chart is also a very easy approach, although not very quick, to consider all possible interactions between the chemicals involved in the process.

The checklist part of the safety analysis performed in the Dow Chemical Company was studied with the same intent. In this tool, many aspects of the process are analysed, such as data on reactive chemicals, raw materials, construction and maintenance materials, reactive conditions, catalysts and inhibitors, control systems, waste handling, storage, training and failure scenarios. Specific questions for each aspect are defined. As in the case of the Ciba tool, the approach to the safety analysis was very interesting, but some questions were too complex to be easily answered. Moreover, the amount of information and the level of control needed to fill up the checklists turned out to be too demanding for the resources of a SME.

From this early study of existing methodologies, the HarsNet group decided that the checklists method would have been the most simple way to obtain a tool sufficiently easy to understand and quick to perform to comply with the needs of SMEs. In this way, the knowledge of experts on safety analysis, the literature search and the help given by existing methodologies could be used in order to develop a hazard assessment tool oriented to SMEs.

As it has been mentioned, HarsMeth was one of the tasks of the HarsNet project. Its aim was to produce and to check a methodology for the hazard assessment of chemical processes. It should offer assistance for the safety analysis of batch as well as semi-batch processes in an easy structured way by using basic rules and methods designed as an interface between experts and SMEs. The main part of the first draft version of HarsMeth represented a short cut procedure for the safety assessment of chemical processes working as an interactive online tool. Next to it, a document containing different checklists was available. The assessment was based on safety data entered by the user and it gave general indications concerning hazardous process conditions.

All the questions were subdivided in different checklists concerning the different aspects of the process considered. The intent of this structure is to consider as many different factors that form the basis of process safety as possible. Three principles are considered fundamental for process safety:

- *Good Engineering Design:* unless good basic chemical engineering standards are met, no amount of additional data or analysis will redeem the situation.
- *Good Process Design:* if a process cannot meet the requirements of quality, yield and throughput, it will be constantly changed and updated to meet demand, and this updating could lead to unsafe conditions unless strict control of the process changes is maintained.
- *Good Basic Data:* about the materials used and about the process. It is imperative that the fundamental thermo-kinetics of the desired process and any side reactions or decompositions are determined and understood, as well as physical data on raw materials, intermediates and final products.

These elements must be brought together in a systematic manner by means of a risk analysis. After that, measures can be put in place to control the risks to an acceptable level or, better, to eliminate it. Then all these elements can be Planned, Organized, Controlled, Monitored, Audited, Reviewed and Spot-checked (POCMARS) by a Management System. In order to assist companies in the assessment of all these elements, five checklists are included: the Good Engineering Design, the Good Process Design, the Good Basic Data, The Risk Analysis and the Good Management System checklist. A scheme of this structure is shown in Figure 1.1.

The Good Basic Data checklist is based on a shortcut methodology which intends to obtain the necessary data to carry out the analysis, with the minimum time, money and human investment possible. Four checklists were provided in order to obtain the proper data depending on the kind of process considered, batch, semi-batch, new or existing, as shown in Figure 1.2.

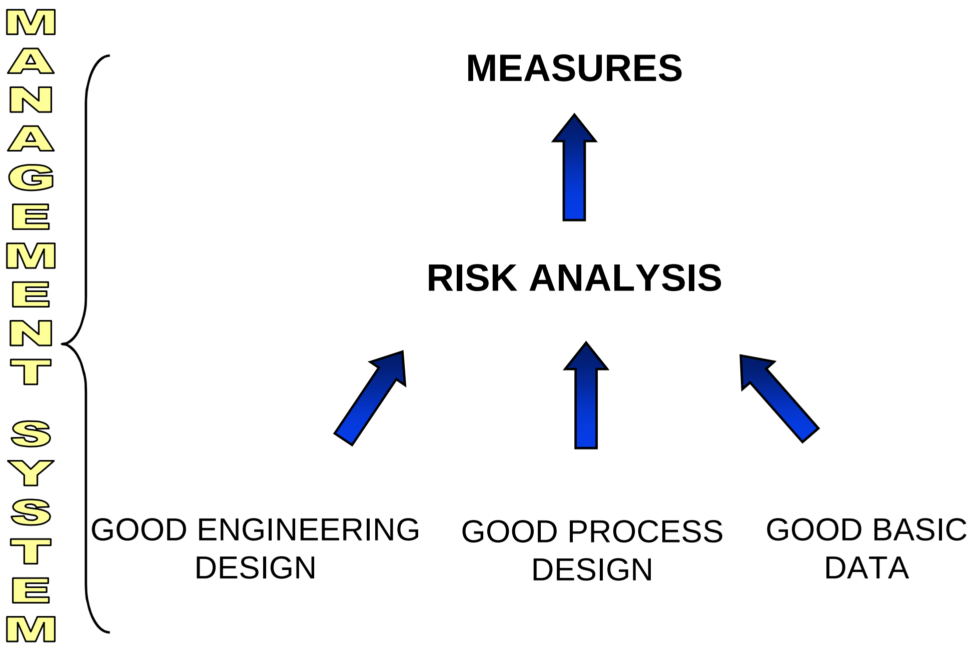

Figure 1.1. - HarsMeth original Structure.

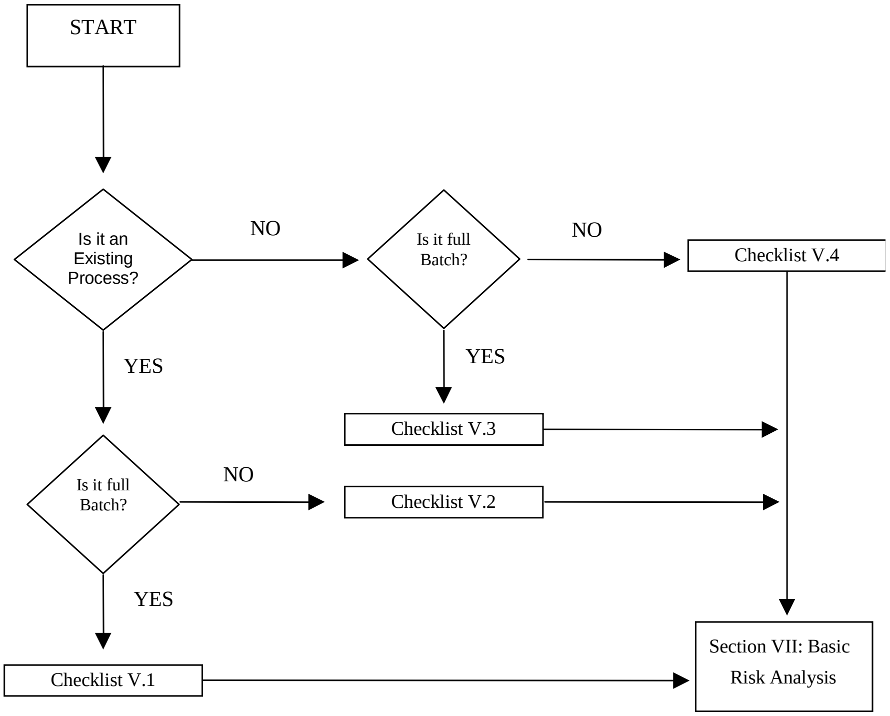

Figure 1.2. - Short cut methodology for HarsMeth.

Once the proper checklist has been filled up, the answers obtained have to be evaluated. It is necessary to determine, according to the answers provided, which issues regarding the process are likely to trigger a runaway. Clearly the details of the runaway theory are not provided in the methodology since it is intended to be used by non experts in the field of chemical safety. Instead, simple tools are proposed in HarsMeth in order to facilitate the user the comprehension of the thermal hazards associated to a chemical process.

A runaway reaction is usually considered as an unexpected and undesired event, in which the progressive generation of heat from a chemical process occurs due to the rate of heat production being greater than the rate of heat removal (Barton and Rogers, 1997). This means that the plant equipment is unable to eliminate all the heat generated by an exothermic reaction, leading to higher temperatures than those for which the process was designed.

Under a runaway scenario, some chemical systems are likely to accelerate even more the rate of heat production, in a runaway loop as shown in Figure 1.3. This effect can trigger secondary undesired reactions or even the decomposition of the reaction mass, which can generate uncontrolled amounts of gas, increasing the pressure inside the reactor vessel up to extremely high values. The ultimate consequence of this situation can be the explosion of the vessel if it is not mechanically prepared to withstand the pressure generated.

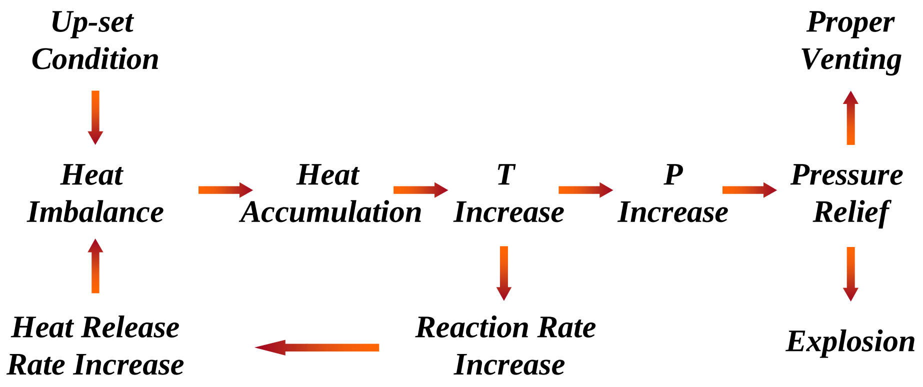

Figure 1.3. - The Runaway loop.

Runaway reactions represent a specific hazardous situation due to the fact that these events usually start at a slow path and remain unnoticed for a while, but since the rate of heat generation increases exponentially, they can suddenly accelerate the temperature increase, so when the runaway is detected, little time is left for process operators to react and try to regain control of the situation (Barton and Rogers, 1997). According to these authors, the causes for runaway reaction accidents are mainly found on the lack of knowledge of process chemistry and thermochemistry, inadequate engineering design for heat transfer, inadequate control systems and safety back-up systems, and absence of operational procedures, including training.

However, it is clear that a hazardous chemical scenario does not necessarily come from a reactive step. The presence of unstable substances in a chemical establishment, even in storage facilities, is likely to generate an accident if the conditions under which those substances are handled are not kept under strict control. Some hazards related to unstable substances can be decomposition of thermally unstable substances generating large amounts of pressure or release of toxic substances, unexpected mixing of incompatible substances generating a runaway, or the generation of a fire if flammable reactants are involved.

Considering a simplified approach for the heat balance of a chemical reactor (Stoessel, 1993), two terms can be considered; the heat production due to the reaction and the heat removal by heat exchange with the cooling system. The heat production, or heat release rate of a reaction (Eq. 1.1), is proportional to the rate of the reaction (Eq. 1.2), to the enthalpy of the reaction and to the volume of the reaction mixture. The model, as originally developed by Semenov (1928), assumes a zero order reaction that follows Arrhenius law, which means that the rate of reaction increases exponentially with temperature.

$$\frac{dQ}{dt}_{\text{release}} = V \cdot \left(-\Delta H_r\right) \cdot r \qquad \text{[Eq. 1.1]}$$

$$r = k_0 \cdot C_A^n \cdot e^{-\frac{E_A}{R \cdot T}} \qquad \text{[Eq. 1.2]}$$

where:

V	is the volume of the reaction mixture	[m^{-3}]
ΔH_r	is the reaction enthalpy	[$J \cdot mol^{-1}$]
k_0	is the pre-exponential factor, units depending on reaction order (n)	
C_A^n	is the concentration of reactant A	[$mol \cdot m^{-3}$]^n
E_A	is the activation energy	[$J \cdot mol^{-1}$]
R	is the universal gas constant	[$J \cdot mol^{-1} \cdot K^{-1}$]
T	is the temperature	[K]

On the other hand, the heat removal rate of a reactor by heat exchange with the cooling system (Eq. 1.3) is proportional to the temperature difference between the reaction mixture and the cooling system, to the heat exchange area and to the heat transfer coefficient. It is therefore a linear function of temperature.

$$\frac{dQ}{dt}_{remove} = U \cdot A \cdot (T_r - T_c) \qquad \text{[Eq. 1.3]}$$

where:

U	is the heat transfer coefficient	$[J \cdot s^{-1} \cdot m^{-2} \cdot K^{-1}]$
A	is the heat transfer area	$[m^{-2}]$
T_r	is the process temperature	[K]
T_c	is the temperature of the cooling system	[K]

If the heat removal from an exothermic reaction fails, the evolution of the process may vary greatly. This situation is shown in Figure 1.4, as developed by Semenov (1928).

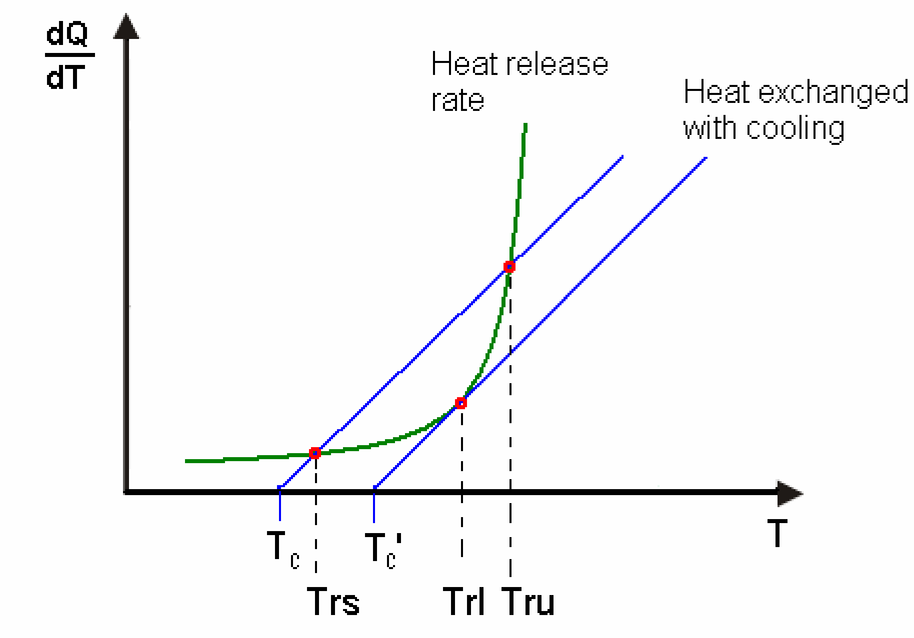

Figure 1.4. - Semenov heat balance diagram

This diagram represents the evolution of heat versus temperature, reflecting the exponential increase of the heat released by the reaction with the reaction temperature, and the linear dependence of the heat exchanged with the cooling temperature. If a deviation occurs in reaction temperature working at the stable point (Trs), the system will eventually return to that position, since the cooling power will be greater than the heat generated by the reaction. However, at the unstable point (Tru), any oscillation above reaction temperature will lead to a runaway. The limit point (Trl) defines the maximum temperature for coolant that allows the process to be run under safe conditions.

The analysis of the situation of any batch or semi-batch chemical reactor depending on the evolution of the situations described in Figure 1.4 can be done by means of a runaway scenario as proposed by Gygax (1988), as shown in Figure 1.5.

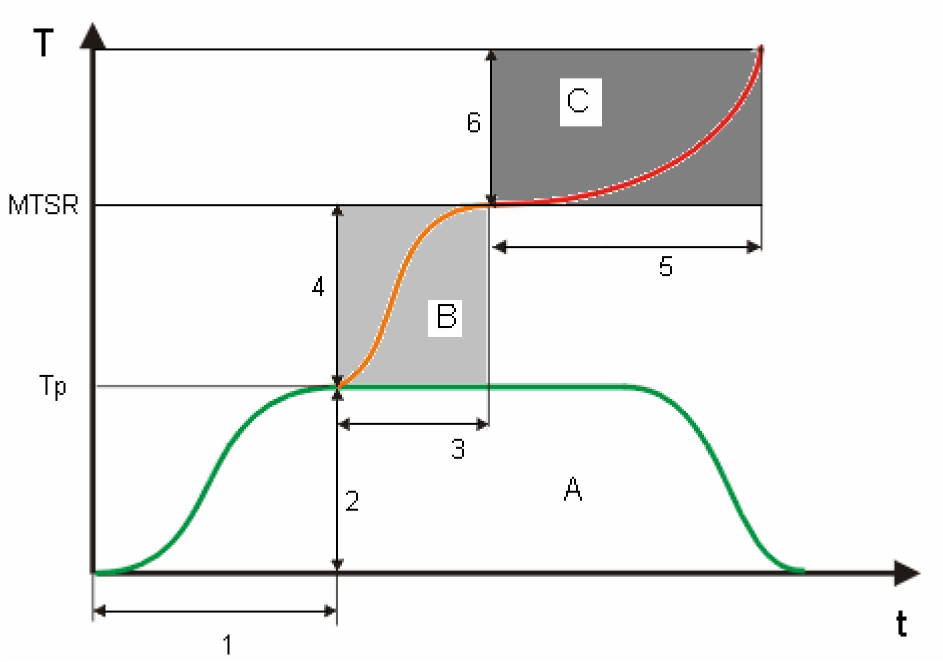

Figure 1.5. - Schematic presentation of a cooling failure scenario.

This Temperature vs. Time diagram shows how the loss of control of the desired synthesis reaction leads to a temperature level above the normal process temperature and therefore may trigger a secondary reaction. The main features included in the Gygax diagram are:

- A = desired reaction B = loss of cooling C = runaway
- 1: time to cooling failure.
- 2: temperature increase under normal operating conditions.
- 3: time to reach the maximum temperature due to synthetic reaction.
- 4: temperature increase due to loss of cooling.
- 5: time to maximum rate under adiabatic conditions, TMR_{ad}.
- 6: temperature increase due to secondary reactions.

The parameter MTSR shown in Figure 1.5 stands for to the Maximum Temperature attainable by the synthesis reaction, and it corresponds to the process temperature plus the adiabatic temperature increase (i.e., the temperature increase that occurs due to a failure scenario as seen in Figure 1.5)., according to Eq 1.4.

$$MTSR = T_P + \Delta T_{Ad} \cdot Y = T_p + \frac{Q_R}{c_P} \cdot Y \qquad \text{[Eq. 1.4]}$$

where:

ΔT_{ad} is the adiabatic temperature rise [K]
c_P is the specific heat of the reaction mixture [J kg^{-1} K^{-1})]
Q_R is the energy of reaction [J kg^{-1}]
Y is the degree of accumulated reactants (Y=1-conversion)

MTSR should be calculated in the worst case scenario of the considered process. Whereas in the batch case MTSR corresponds always to the maximum adiabatic temperature increase, for the semi-batch case three scenarios can be considered (Serra *et al*., 1997):

- *Batch:* all reactants are mixed at the beginning of the process, adiabatic conditions are assumed.
- *Stop:* dosing is stopped after a cooling failure. Only the actual accumulation is considered at each time.
- *Non-stop:* dosing is not stopped when adiabatic conditions are established. Actual accumulation and remaining heat of reaction should be considered.

The Time to Maximum Rate is the time taken for a material to self-heat to the maximum rate of decomposition from a specific temperature (normally the MTSR), under adiabatic conditions, and it can be determined according to Eq. 1.5. It should not be mistaken with the adiabatic induction time, which is considered as the time interval, starting at a normal operating situation, after which a runaway shows its maximum effects under adiabatic conditions.

$$\mathrm{TMR}_{ad} = \frac{c_P R T_0^2}{q_0 E_a} \qquad \text{[Eq. 1.5]}$$

where:

c_P is the specific heat of the reaction mixture	[J kg^{-1} K^{-1}]
R is the universal gas constant	[J mol^{-1} K^{-1}]
T_0 is the initial temperature of the runaway	[K]
q_0 is the heat output at T_0	[W kg^{-1}]
E_a is the activation energy	[J mol^{-1}]

This formula is established for zero-order reactions, but it can also be used for other reactions if the influence of concentration on reaction rate can be neglected (Stoessel, 1993).

It is helpful for the evaluation of the runaway scenario to discuss some temperature levels and their interactions. This procedure is known as the Stoessel (1993) method. This is a useful system to perform a preliminary evaluation of the thermal hazards of a chemical process, and it is based on the possible different positions of four temperature levels relative to each other, and the classification of the process under certain levels of criticality. The Stoessel diagram is shown in Figure 1.6.

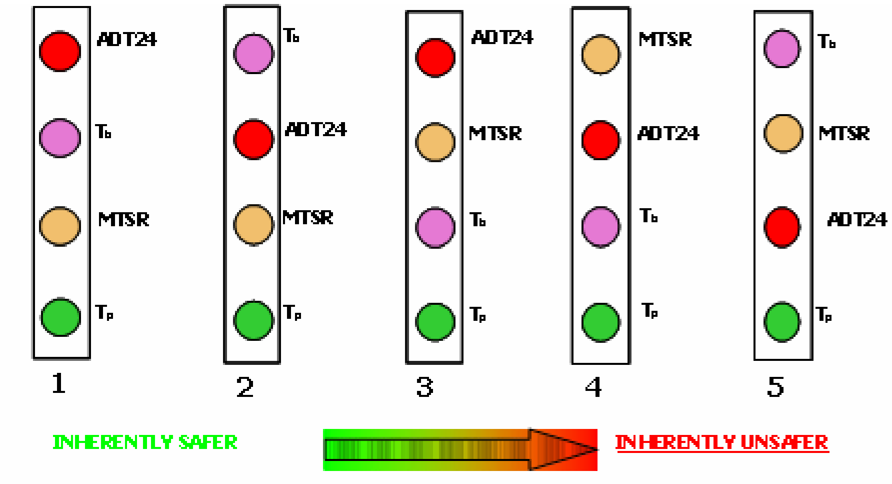

Figure 1.6. - Scenarios with increasing criticality according to Stoessel.

The temperature values considered by Stoessel are:

- The process temperature, T_P.
- The temperature to be reached under upset conditions, MTSR.
- The boiling point of the reaction mass T_b.
- A safety maximum temperature value considered, ADT24.

ADT24 is considered as the temperature limit before a decomposition process falls out of control. It corresponds to the temperature at which the adiabatic induction time is less than 24 hours. This parameter can be determined by means of adiabatic calorimetry.

The descriptions of the 5 scenarios described by Stoessel are the following:

- *Case 1:* in a case one scenario, neither the boiling point of the mixture nor the dangerous region in which the decomposition reaction becomes effective within a critical time is ever reached. Such processes may be regarded as inherently safe with respect to the process deviation evaluated.

- *Case 2:* also in the second case, which differs from the first by the absence of the boiling point barrier between MTSR and ADT24, the process may be regarded as safe.

- *Case 3:* in the third case, the boiling point with its latent heat of evaporation may be looked upon as a safety barrier, provided the condenser is adequately designed. However, it must be considered that for some mixtures, evaporation of solvent during some time can reduce the ADT24 value of the mixture. If the process is performed in a closed system, the apparatus must be designed for the maximum expectable overpressure or be equipped with a pressure relief device.

- *Case 4:* scenarios with case four characteristics must be evaluated as to whether or not the evaporation capacity provides sufficient safety. If this is not the case, additional organizational or technical measures have to be implemented. Should the operation be performed in a closed system, then the temperature corresponding to the set pressure of the relief valve may not be much higher than the level of T_b.

- *Case 5:* the fifth case must in any case be rated as problematic. Plant and / or process modifications usually cannot be avoided in such situations.

The combination of the expertise of the HarsNet members with easy to understand methods like the Gygax and Stoessel diagrams resulted in the first draft of the HarsMeth methodology, known as HarsMeth version 1. The next step was to test this draft version at different SMEs involved in the HarsNet network to obtain their feedback, check their needs and determine how the methodology could be improved to help them in the hazard assessment of their chemical reactions.

Another research activity launched by the PQAT research group was the ART project (Thermal Risk Audit), with the financial support of the "Generalitat de Catalunya". As a part of this project, another methodology called 'Check Cards for Runaway' (Pey, 1999) was developed at the TNO (Apledoorn, The Netherlands) in collaboration with IQS. The main target was to obtain a simple tool for industrial inspectors in The Netherlands to quickly evaluate the safety level of a chemical plant liable to suffer a runaway reaction, with the possibility to be used also for the assessment of the process engineering during the design stage.

The first part of this methodology (Nomen *et al*., 2004b) is to define which data are required to assess each potential hazard. Once the data are defined, the necessary tests are selected and run. For this purpose, a set of Data Collection Cards, divided in different tables to introduce data are provided, including a chemical compatibility chart. The tool is based on the definition of possible critical factors that may generate a runaway during a chemical process. Different sets of questions were developed in order to try to identify hazards that can appear related to each factor. Critical factors considered in the CCR methodology are:

- Wrong Chemicals
- Auto catalytic Reactions
- Segregation
- Accumulation
- Temperature Hazard

The methodology is divided into three sections, depending on the stage of the analysis of the process:

- *Storage:* considering hazards of stored substances.
- *Physical processes:* considering physical changes in substances and mixtures. This introduces the issue of assessing chemical hazards at process equipment different from the chemical reactor.
- *Reaction:* covering the reaction step of a process, where both physical and chemical changes take place.

The tool is designed in a card-shape system that enables the user to keep track of the information provided and of the results of the analysis.

A preliminary analysis of both methodologies (HarsMeth v1 and CCRs) was done at IQS (Ghinaglia, 2002). This analysis revealed some deficiencies in both tools regarding the ease of use and understanding of the terms involved. It became clear that testing both methodologies with different chemical SMEs could be a good step towards producing a reliable and easy to use assessment methodology for chemical hazards.

Thus, the main objectives of this PhD work are:

To analyse the information contained in the MARS database regarding chemical accidents in European industries, in an attempt to learn lessons from previous incidents and to extract information as to what are the key issues to take into consideration when trying to prevent such accidents.

To develop a tool for the hazard assessment of chemical processes specifically designed for SMEs. This tool will consist on a checklist based methodology that will be generated from the synthesis of the HarsMeth v1 and the CCRs methods already existing. It will also include the expertise of the HarsNet group and it will be tested at different SMEs, with the objective to reduce the dependence of the quality of checklists on the ability of the person preparing it. An attempt to eliminate the rigidity of the ‘yes’ and ‘no’ answers for checklists will also be made.

The tool will be focused on thermal hazards of chemical reactors, eliminating or better assuming the weakness of the checklist system to assess one item at a time by concentrating the key target of the analysis. The possibility to expand its philosophy to chemical hazards in other process equipment apart from the chemical reactor itself will also be taken into consideration.

2.- RESULTS AND DISCUSSION

2.1.- Analysis of chemical accidents in Europe and lessons learned

The final scope of a methodology for the hazard assessment of chemical reactions is to avoid accidents in the process industries. In this sense, it is of great importance to know and to understand why and how accidents in chemical plants have occurred in the past. Indeed it is also interesting to know what has been the evolution of the number and severity of the chemical accidents that have taken place in Europe in the recent past, in order to determine tendencies and to understand the true needs in the field of accident prevention.

The Major Accident Reporting System (MARS) contains 588 reports at the time of the present work. 301 accidents were reported by EU 15 Member States during the period between 1994 and 2004 (Sales *et al.*, 2007a). The evolution of these accidents per year is shown in Figure 2.1.

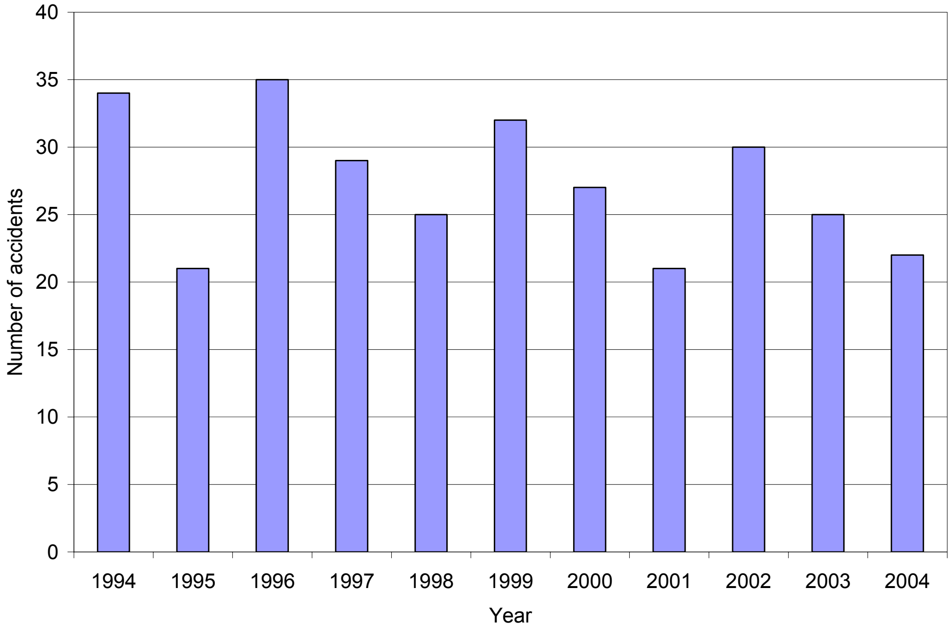

Figure 2.1. - Number of major accidents per year for the period 1994-2004 in EU 15 countries reported to MARS.

From the previous figure, it can be seen that there is a tendency which indicates that the number of major accidents is being reduced. Moreover, there seems to be a trend starting from the year 1996. According to that trend, accidents could be grouped in periods of three years. In each group, the number of accidents decreases, but at the beginning of the next cycle (1999, 2002) there is an abrupt increase in the number of accidents. However, an overall decrease in the number of accidents seems to be hinted comparing the first (1996-1999-2002), second (1997-2000-2003) and third (1998-2001-2004) respective years of each cycle. The only exception is found in the year 2004, in which there was one more major accident reported compared to the year 2001.

Figure 2.2 shows the number of accidents that reported at least one fatality and the number of fatalities generated by the accidents, compared to the total number of accidents reported as shown in Figure 2.1. A total of 63 accidents had one or more fatalities, whereas 153 people died as a consequence of those accidents.

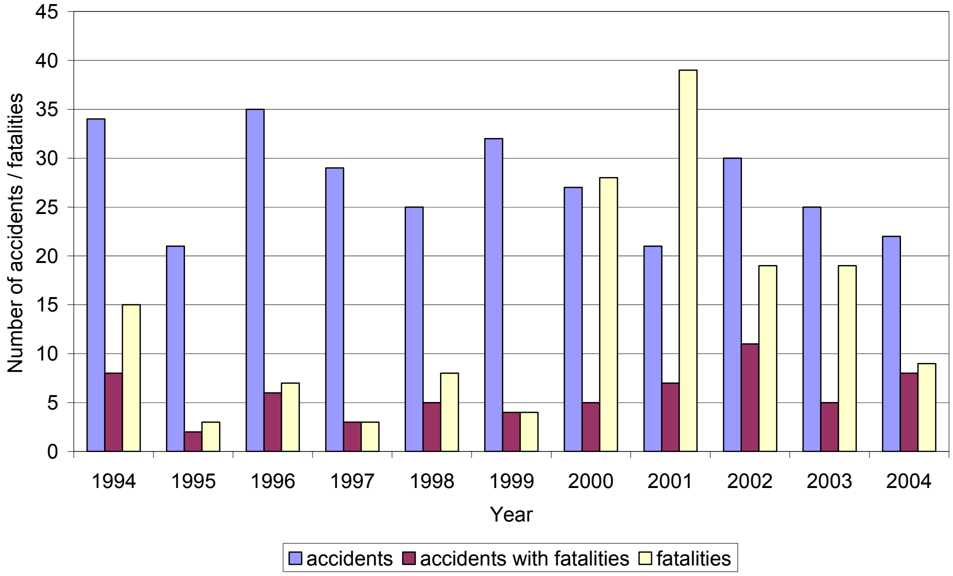

Figure 2.2. - Comparison of the number of accidents, number of accidents with fatalities and number of fatalities.

It can be seen that from the year 2000 there has been an increase in the number of fatalities. The high numbers of fatalities shown for the years 2000 and 2001 correspond in great measure to the accidents that happened in Enschede (The Netherlands) and in Toulouse (France), which were key events for the launching the amendment of the Seveso II Directive in 2003. It can also be seen that the number of fatalities in the years 2002 and 2003 were higher than in any of the other years of the 1990’s. The number of accidents reporting fatalities increased constantly for the period 1999 and 2002, being this last one the year with more accidents with fatalities, a total of 11, for the whole period analysed.

These figures show that despite the progressive reduction in the number of major accidents, the consequences generated by such events that are still happening in process industries are serious enough to continue the efforts of improving safety in European process plants. The next step is to try to obtain as much information as possible from the data included in the reports from the MARS database and to determine how similar events can be avoided in the future.

Many of the accidents reported to MARS involve chemical reactions either intended or unintended. An analysis of such accidents has been performed in order to identify the causes, both technical and organizational that led to the occurrence of those accidents (Sales *et al.*, 2007b). This kind of analysis gives the possibility to learn lessons with the objective to improve safety conditions throughout the European process industries. Moreover, it can be a valuable aid to improve hazard assessment methodologies in order to identify gaps and to test the reliability of such tools.

The criteria to select the cases to analyse for this work was based on the interaction of two or more chemical substances that created or could have created a dangerous situation, or the incorrect handling of some specific substances, considered as potentially dangerous given their chemical properties. This includes not only the study of runaway events that take place during a chemical reaction, but also those chemical accidents that involve other zones of an industrial establishment, such as storage facilities, transfer systems, or other equipment related to a process. A total of 132 accidents of the total 588 reports included in the database have been identified and analysed; a list of these accidents can be found in Appendix 2.1, with brief indications of the chemicals involved and the main causes identified for each accident.

Even though MARS includes accidents that happened as early as 1980, it was not until the early 1990´s that the reporting system was standardised in an attempt to improve the quality of the reports. Therefore, the quality of the information provided is quite heterogeneous; some cases include very detailed explanations of the accidents, but unfortunately, in some cases, the information provided is quite scarce. For this reason, some accidents that matched the selection criteria have not been included in the analysis, given the difficulty to extract reliable conclusions as to the causes or consequences of the accidents.

2.1.1.- Location and severity of the accidents

At a first stage, the accidents have been classified according to the location within the establishment where they have taken place. Figure 2.3 shows the different process areas for which the accidents were reported.

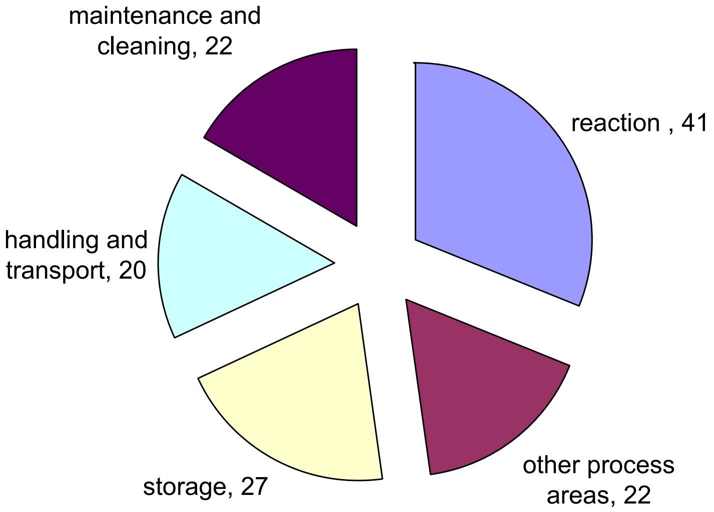

Figure 2.3. - Number of accidents that occurred in different areas of industrial establishments.

As it can be seen in Figure 2.3, the majority of accidents involving chemical interactions occur during the reaction stage. However, the number of accidents that occurred elsewhere in an establishment is significant enough to understand that chemical reactivity is an issue that must be taken into consideration at any stage of a process. Figure 2.4 further analyses the 22 accidents identified in “other process areas” (from Figure 2.3), involving specific plant equipment.

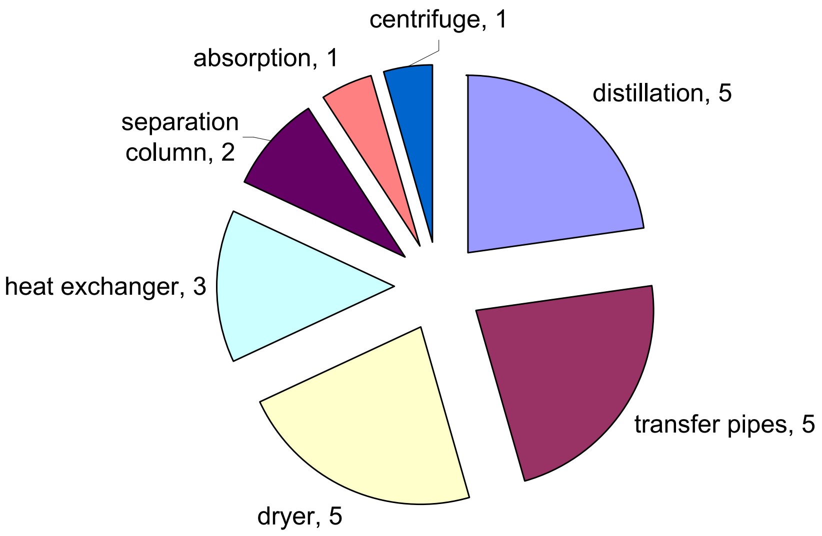

Figure 2.4. - Number of accidents identified in the “other process areas” category, involving specific equipment.

The numbers shown in Figure 2.4 demonstrate that chemical accidents can occur at a wide variety of plant equipment during the development of a chemical process. When performing hazard analysis for unit operations, some hazards can be identified due to the severe temperature conditions under which some substances are handled, but reactivity hazards are frequently ignored since no chemical reaction is expected at the equipment detailed in Figure 2.4.

It is relevant to identify the process areas or equipment that present a higher number of accidents and their severity. Table 2.1 presents the numbers of fatalities, injuries, and number of accidents involving a fatality or an injury in each of the process areas presented in Figure 2.3. Table 2.2 gives percentages of fatalities and injuries per accident, as well as the percentage of accidents that generated human fatalities or injuries.

Process area	Number of accidents	Accidents with fatalities	Accidents with injuries	Number of fatalities	Number of injuries
Reaction	41	7	25	10	275
Other process areas	22	3	11	4	171
Storage	27	2	15	2	168
Handling and transport	20	1	14	1	148
Maintenance and cleaning	22	12	17	31	100

Table 2.1. - Severity of the accidents involved in each process area.

Process area	Fatalities per accident	Injuries per accident	% of accident with fatalities	% of accident with injuries
Reaction	0.24	6.71	17.07	60.98
Other process areas	0.18	7.77	13.64	50.00
Storage	0.07	6.22	7.41	55.56
Handling and transport	0.05	7.40	5.00	70.00
Maintenance and cleaning	1.41	4.55	54.55	77.27

Table 2.2. - Ratios and percentages of the severity of the accidents related to process areas.

From the numbers shown in the previous tables, three classifications of industrial operations can be established in terms of severity of consequences:

- *Storage and handling operations:* this is the category with the lowest number of fatalities per accident. There are two reasons for this figure. Firstly, accidents at storage facilities can happen at times when there is no personnel present near the equipment involved in the failure. Secondly, accidents involving handling operations can result in the release of toxic material due to spills, loose joints, and so on. This effect is usually less likely to be lethal than a fire or an explosion (Sales *et al.*, 2007a), mainly because usually there is time for the employees to evacuate the facility once the release has been identified. However, the number of accidents (47) in this category and the amount of injuries (6.72 per accident) are strong enough reasons to take chemical accidents very seriously at storage facilities, not to mention the economic loss usually involved.

- *Reaction and other process areas:* in this category the severity of the accidents is slightly higher than in the previous one, mainly due to the fact that usually there are employees in charge of the operations in the vicinity of the equipment involved in the accident. In these situations, physical and chemical interactions are expected and usually possible failure scenarios have been identified in a risk analysis. In these cases the implementation of mitigation measures is usually more extended to take these interactions into account in order to reduce the severity of the accidents.
- *Maintenance and cleaning operations:* it is in these situations where accidents are the most severe. It has to be remarked that more than half of the accidents studied under this category (54.55%) resulted in human fatalities, and that there was an average of 1.41 deaths per accident studied. The reason for these elevated numbers is mainly that usually these accidents take place during manual operations being performed close to the equipment that is involved in the accident. Also, employees may not be trained in the specific hazards involved, therefore being unaware of the risks and without knowledge of how to react.

2.1.2.- Identification and classification of the causes of accidents

In terms of learning lessons the most valuable data on accidents is the information on their causes. The selection fields in the “Full report” of the MARS reports are useful for statistical and trend analysis, and in order to facilitate this effectively, predefined selection lists have been produced by expert technical working groups, for inputting data in the majority of the fields, including the causes of accidents (Mushtaq *et al.*, 2003). Out of the 132 accidents analysed, 95 include the “Full report”. A further examination of the information contained in the “Short Report” of the remaining 37 accidents has been performed; this has given the possibility to relate the information to the classification system used in the “Full report”. Table 2.3 shows the results obtained for technical and physical causes, while Table 2.4 presents the number of cases in which human and organizational causes were involved.

TECHNICAL AND PHYSICAL CAUSES	Number of instances	%
Unexpected reaction / phase transition	30	22.9
Runaway reaction	21	16
Component / machinery failure / malfunction	13	9.9
Vessel / container / containment equipment failure	12	9.2
Electrostatic accumulation	9	6.9
Instrument / control / monitoring device failure	7	5.3
Loss of process control	6	4.6
Corrosion / fatigue	6	4.6
Blockage	4	3.1
Utilities failure (electricity, gas, water, steam air, etc.)	4	3.1
Natural event (weather, temperature, earthquake, etc)	3	2.3
Other	3	2.3
Transport accident	1	0.8

Table 2.3. - Number of reports analysed involving technical and physical causes.

HUMAN AND ORGANIZATIONAL CAUSES	Number of instances	%
Process analysis (inadequate, incorrect)	53	40.5
Organized procedures (none, inadequate, inappropriate, unclear)	49	37.4
Design of plant / equipment / system (inadequate, inappropriate)	42	32.1
Operator error	36	27.5
Training / instruction (none, inadequate, inappropriate)	26	19.8
Management organization inadequate	13	9.9
Management attitude problem	9	6.9
Supervision (none, inadequate, inappropriate)	7	5.3
Maintenance / repair (none, inadequate, inappropriate)	7	5.3
Testing / inspecting / recording (none, inadequate, inappropriate)	5	3.8
User unfriendliness (apparatus, system, etc.)	3	2.3
Staffing (inadequate, inappropriate)	2	1.5
Manufacture / construction (inadequate, inappropriate)	2	1.5
Installation (inadequate, inappropriate)	2	1.5
Isolation of equipment / system (none, inadequate, inappropriate)	2	1.5
Other	2	1.5

Table 2.4. - Number of reports analysed involving human and organizational causes.

It should be kept in mind that many accidents have multiple causes. It can be seen that the most common causes of failure are those issues related to inadequate or inappropriate organized procedures, process analysis, equipment design, training and human error. The safety management system, which includes organized procedures and training, is of special importance in order to promote an appropriate safety culture inside the establishment. In some cases the hazards related to a chemical process are unknown to, or underestimated by those operators that must carry out the process in the plant.

2.1.3.- Lessons learned from chemical reactive accidents

Taking into consideration all the information contained in the MARS reports and the analysis of the causes that has been described previously, different lessons can be generated. The most common issues involve deficiencies in the process analysis, the design and / or implementation of safety measures, or the development of operational procedures.

Process analysis

Process conditions must be studied in order to identify possible hazards related to a process. From the accidents analysed, it is clear that special attention must be given to the following issues.

- Identification of properties of the substances involved in the process related to chemical or physical stability, including safety margins for temperature, humidity, storage time, and so on.
- Identification of incompatibility of the mixtures that could be generated (intentionally or unintentionally) in the chemical establishment. Compatibility with auxiliary and construction materials must also be studied.
- Identification of those physical and chemical parameters (temperature, pH, reaction time, or any other critical process condition), the variation of which could lead to a loss of control of a chemical reaction or other process operations.

- Identification of possible protective measures (e.g. inhibition, extra cooling, containment, venting or quenching) that could be taken in order to stop a runaway event.
- Identification of possible physical consequences (toxic release, explosion and / or fire) that could be originated as a result of a runaway.

Safety measures and control systems

It must be ensured that any parameter identified as critical for the safety of the process will always be kept under safe conditions no matter what deviation may occur. If a loss of control is still regarded as possible, the necessary safety barriers to avoid a hazardous situation or to mitigate its consequences must be put in place. Some of the actions that can be taken are listed below:

- Whenever a hazardous substance has been identified, it should be replaced, if possible, with a less hazardous one, or at least its use should be minimized.
- For storage and transport, the control and monitoring of critical parameters of unstable substances must be made available. These may include, among others, temperature and humidity control, and verification of storage periods.
- Measures must be introduced to ensure that incompatible substances will not come into contact at any stage of the process.
- When using flammable materials, if their use cannot be avoided, two conditions are of great importance. First, to avoid oxidant atmospheres that may trigger an explosion; this can be achieved by the use of inert gases like nitrogen. Second, to avoid ignition sources such as static electricity, hot surfaces, or sparks originating from other operations such as welding works.
- For reaction and process operations, sensors to monitor the evolution of critical safety parameters identified during process analysis should be incorporated into the plant equipment. These sensors should be interlocked with the equipment devices (such as cooling system, reactant dosing devices, agitation system, and so on), so that the control system can act to restore appropriate process conditions.

- The correct functioning of the control system must always be guaranteed, for this reason redundant control systems should be provided whenever necessary. These must also be effective and reliable when called upon.
- If a loss of process control should happen, it must always be possible to stop the activity. For this reason, reactors and other process vessels should be provided with systems to “kill” a reactive process, such as introduction of inhibitors, addition of solvent to quench a reaction, or transfer of reaction mass to catchment tanks.
- The implementation of mitigation measures should also be considered in case the risk analysis has identified the potential for an accident to occur, even if it is considered unlikely. Some possibilities would include the use of water curtains or foam sprays to dilute toxic releases, relief valves or rupture discs or other devices to deal with pressure increases in order to avoid explosions, and fire containment and extinguishing systems.
- It must be guaranteed that, in case they should be necessary, safety measures are always effective and correctly designed. For this, the analysis of a possible runaway event must be highly accurate. Also, it must be granted that supply lines such as electrical power, cooling circuits, air, steam or nitrogen feeds will always be operational.

Organizational measures

The development of a safety management system is indispensable in order to spread an appropriate safety culture in a chemical establishment. Some of the lessons learned regarding the management system are presented:

- Preparation of training systems is of primary importance. Workers must be aware at any point of the hazards involved in chemical processes. This training must be extended to any temporary worker even if they are present in the establishment for a short time. Training procedures should include case studies, describing possible effects of chemical accidents.
- Detailed maintenance and cleaning procedures must be implemented. These have to take into account the incompatibility of substances used for these

operations. Also, an effective system of work permits must be used to ensure safe conditions when such works are to be performed.

- Emergency plan systems must include the activation of defence systems, evacuation routes, identification of personnel on site during an accident, correct alarm systems, and so on.
- Appropriate operating procedures must be provided, according to the process analysis. After evaluating the hazards of a chemical process, the appropriate methods to perform common operations should be decided. Some examples are:
    - Implement correct labelling rules and procedures, including verification, to avoid mishandling of chemicals.
    - Provide description of requirements for safe handling of chemicals for transport and loading operations. This should include personal protection measures and equipment (isolation, connections, and so on).
    - Ensure fluent communication throughout a process.
    - Ensure appropriate supervision of hazardous activities.

The previous lessons learned, obtained through the analysis of past accidents in chemical industries, should be evaluated by any company working in the production of potentially hazardous chemical processes, and adapted to the safety management systems whenever it is considered appropriate. It must be taken into consideration that even the conclusions from this analysis related to technical issues, like process analysis or the determination of safety measures are strongly related to organizational and management issues. As it has been mentioned, it must be a policy for chemical companies to implement an appropriate safety culture throughout the whole plant, related to every stage of the development of a process, to ensure that all the necessary aspects related to chemical safety have been correctly covered. Learning from past accidents occurred in plants or processes similar to those performed at existing chemical plants, and introducing the lessons learned from such accidents into the safety procedures of the company should be a first and valuable step.

2.2.- Development of the HarsMeth methodology

2.2.1.- Development of HarsMeth v2

The analysis of past accidents and the establishment of general lessons learned, derived after analysing the causes that led to those accidents, provides a valuable first step in the objective of understanding the key issues that need to be covered when performing a hazard assessment of chemical processes. In other words, the analysis described previously can be a good system to lay the base of the contents of a hazard assessment methodology. It must be considered that, as it has been stated previously, usually the most common cause for an accident is the lack of knowledge of operators or management staff of the hazards involved in the process, either from a technical point of view or from an organizational perspective, so it is clear that efforts have to be made to highlight those hidden hazards and “bring them to the surface”, especially when a process is performed at small and medium enterprises with fewer resources and expertise on safety issues.

The objective of this work is to produce a hazard assessment tool based on the existing methodologies HarsMeth and CCRs, as well as from the conclusions of the accidents analysis. With this goal, it is necessary to determine the strengths and weaknesses for each one of those methodologies. For this reason, it was decided within the HarsNet group to test them at different SMEs. Five Spanish enterprises working in fine chemicals production in the Barcelona area were visited and they were asked to try to use HarsMeth and the CCRs methodologies. Usually, they use multi-purpose plants, where different processes can be carried out at different periods of time without significant changes in plant design. The variability of production is one of the reasons that make it difficult to perform a complete safety analysis for each process with the resources typically available at these SMEs.

The meetings with these companies were structured as workshops in which a number of persons involved in the process were invited at the same table. During the first meeting, the HarsMeth methodology and the CCRs were presented. The SMEs were asked to choose one process as a case study for these methodologies to understand how they work and to detect possible changes to be introduced. During further meetings (from three to five depending on the case), both methodologies were applied to the process chosen by the SME, together with the personnel from the company. People participating in the workshops were asked to explain the deficiencies they encountered while applying both methodologies, also what features should be included in a hazard assessment tool according to their experience and needs. Next, the feedback obtained was presented, structured according to the weaknesses and strengths identified by the personnel of the 5 companies that participated at this stage of the project. The versions used of HarsMeth and CCRs can be found in Appendices 3.1 and 3.2 respectively.

2.2.1.1.- HarsMeth weaknesses

Each checklist included in HarsMeth was analysed and a number of weaknesses were identified. The most significant difficulties pointed out are described next:

1.- The Good Basic Data section is not useful

The first general conclusion obtained from the meetings is that the chapter “Good Basic Data” of HarsMeth is not always useful. The problem is found in the lack of resources necessary to calculate the required parameters. Indeed, this chapter only gives an indication of what information should be provided. Calorimetric studies usually come from university laboratories or research centres, not from inside of the SME. This can lead to a low level of understanding of the parameters involved in the safety of the process. An improvement of the basic knowledge on the interpretation of the results of the most relevant thermal analysis and calorimetry techniques would be necessary for engineers and operators of chemical SMEs.

HarsMeth suggests the use of historical data when no experimental results are available. In many cases this cannot be considered an appropriate procedure to induce safety conclusions. The fact that a process never registered any accident does not mean that it is safe nor does it imply that safety is ensured just by maintaining the same conditions as in previous operations.

2.- “All answers should be YES” is a limiting condition

The main characteristic of the first two checklists (“Good Engineering Design” and “Good Process Design”) is that all the questions need a “yes” answer to avoid a hazard to be generated, as stated in the methodology. The questions are quite generic in order to try to take into account as many cases as possible. This aspect turned out to be a disadvantage, because in some cases the question was not applicable. As a consequence, it was not possible to answer “yes” to all the questions, but this did not necessarily generate a problem from the safety point of view.

For example

- Question 1.13 in the Good Engineering Design checklist regarding critical liquid levels: in one case, the answer to all the questions was “no” because these liquid levels in vessels were not considered critical for the safety analysis.

3,- A place where to justify the given answers is missing

Apart from the possibility of answering “no” or “not applicable” in some cases, a field where to add explanations about the non-applicability or about the way how problems have been solved should be added. This would be useful for the person that is using the methodology, who needs to deeply analyse the question in order to give an explanation of his / her answer. Moreover, this practice will become a way to collect information about the process and its characteristics, and a useful base of knowledge for following safety analysis.

For example:

- Questions 1.4, 1.5 and 1.6 in the Good Engineering Design checklist regarding addition of reactants: most of the time, the addition is not automatic but it is controlled by an operator. As a consequence, the shut-off valve can be turned on only manually. Therefore, it cannot be automatically linked to a temperature or an “agitation status” indicator. It would be better to ask about “system” and not about “shut-off valve”, in order to consider the possibility of manual control.

Moreover, the “temperature high and low” indicators are not always necessary; therefore, the question is not always applicable.

- Questions 1.8 and 1.12 in the Good Engineering Design checklist, regarding computer control: computer control is not frequently used in Small and Medium Enterprises.

4.- Some questions are too generic and do not help in identifying possible safety hazards

If the intent of the methodology is to help to reduce the possible lack of knowledge in SMEs, the questions should help to identify the possible causes of a hazard. For example, the knowledge of experts can be used to define not only the situation in which a hazard can occur, but also at which equipment it is more probable that it can take place.

For example:

- Question 1.1 in the Good Engineering Design checklist, regarding critical instruments: this question should include a list of critical instruments related to the installation and to the different processes (e.g. security valves, rupture discs, controlled gas output to the atmosphere).
- Question 1.2 and 1.3 in the Good Engineering Design checklist regarding calibration and maintenance: it is not necessary to make a distinction between instruments related or not to safety, since when dealing with maintenance practically everything is related to safety.
- Question 1.2 in the Operational Risk Analysis checklist, regarding charging with partly used drums: it should be asked if the charged quantities are adjusted for critical reactants or raw materials.
- Question 1.6 in the Operational Risk Analysis checklist, regarding the criticality of addition rate: the possibility of making the addition slowly (as some SMEs use to do) should be added, as an indication in the case of “yes” answer.
- Management System checklist: all the items included are put forward using the verb “should”. It would be better to use “have to”. In this way it would be more clear that the presented requirements are essential for the safety management

and that the company needs to comply with all of them. Besides, the limits of the adopted policy should be specified with more detail and a section concerning the application of the policy is missing.

5.- Some questions are not clear, or they are difficult to understand

In some cases, it was not exactly specified what was actually asked or in which conditions it had to be calculated.

For example:

- Question 1.9 in the Good Engineering Design checklist, dealing with heat generation: it should be specified whether the heat generated should be considered under normal conditions or under uncontrolled conditions.
- Question 2.5 in the Good Process Design checklist, regarding compatibility: in the proposed form, this question is considered a trap, since the use of the word “unaffected” can easily lead to confusion.
- Question 2.10 in the Good Process Design checklist, regarding accumulation: it is not clear if this question is referred to normal operation conditions or to upset conditions. Moreover, no indication is given as to when to consider accumulation as high or low.
- Question 2.5 in the Existing Semi-batch Process checklist, dealing with accumulation: the meaning of the word “dramatically” cannot be easily established.
- Question 1.8 in the Operational Risk Analysis checklist, about temperature control in the reactor: it is not clear to which conditions the question is referred, i.e. during the reaction or at the end of it.

6.- Some checklists cannot be filled in taking into account the whole process

All the questions included in the “Shortcut method” need to be related to a specific step of the reaction, because the conditions may change depending on the stage of the process that is being analysed and different results regarding safety could be given.

7.- Some of the limits defined may not be acceptable in some cases

Some of the values given in order to evaluate possible changes in the behaviour of the process are not always coherent with those used by the SMEs.

For example:

- Question 2.3 in the Good Process Design checklist, regarding temperature variations: deviations of ± 10°C cannot be evaluated as small in some cases. It would be better to eliminate the word “small” and use a percentage of temperature variation instead of the ±10°C margin.
- Question 2.3 in the Good Process Design checklist, regarding yield: in discontinuous processes the average yield is often under 90%. For this reason, it would be more useful to ask if the reaction is being carried out at the maximum possible chemical yield.
- Question 1.14 in the Management System checklist: as most of the productions take less than five years to be completed, it would be useful to define the frequency (in months) of revision of the risk analysis.

8.- Some questions are missing, others are unnecessary, others are placed in the wrong checklist

For example:

- Question 1.10, 1.11 and 1.12 in the Good Engineering Design checklist, related to permit to works and management of change: they should be moved to the Management System checklist.
- Question 1.16 in the Good Engineering Design checklist regarding overpressure: a question about “blow up” and where it discharges should be added.
- Question 2.7 in the Existing Semi-batch Process checklist, regarding changes in process conditions: according to SMEs experts, these conditions can be changed only in exceptional cases, and if so, the process has to be considered

as a different one. Moreover, this question should be moved to the Management System checklist.

- Good Process Design checklist: in the opinion of most SMEs, it would be useful to add questions about the physical state of raw materials and to specify to which conditions the questions are referred to.

9.- Some values asked are too difficult to know by SMEs

TMRad is generally an unknown value and it is asked in all the checklists of the "Shortcut method" in the Good Basic Data section. Likewise, the ADT24 asked in the Stoessel thermal evaluation is a value that is hardly used in the SMEs. Most of the times, the knowledge of the process was not deep enough to allow them to answer the questions about the effects of temperature changes on the adiabatic temperature rise or on the heat of reaction as asked, for instance, in the New Semi-batch Process checklist. For the same reason, the percentage of accumulation which is asked in the same checklist is usually not known.

In any case, a first general lesson that can be derived from the work developed with the 5 companies, is that the level of knowledge regarding safety parameters of chemical reactions is not always as good as it would be desirable, especially if it is compared to the knowledge of such variations in other process parameters.

For example:

- Question 2.3 in the Good Process Design checklist, regarding temperature variations: it happened in some cases that the engineers from the SMEs knew exactly what would be the consequences of variations in the temperature margins from the point of view of quality, yield and so on, even with details regarding the physical state of the product (e.g. colour, viscosity or polymorphic form), but the consequences from the safety point of view would remain unknown or doubtful.

10.- Some aspects that are important for the safety evaluation are missing

For some of the SMEs visited, it would be useful to consider also the following aspects:

- Human error and personnel training.
- Services failure.
- Where and how to perform an emergency stop.
- Physical properties and quality of raw materials.

2.2.1.2.- HarsMeth strengths

1.- Useful methodology especially for non experts in safety analysis

One of the aims of this tool was to help those enterprises for which performing a complete safety analysis would need too many human and economic resources. In this sense, although it may be not complete, the first version of HarsMeth gives the possibility to analyse the chemical process hazards even in case of few human resources. As it has been mentioned, the checklist method is the best tool for this purpose. According to its flexibility of use, it gives the possibility of improving the efficiency of the methodology by using the experience of those that are making the analysis in order to increase the effectiveness of the questions. Another advantage of the checklist method is its simple applicability. The ease-to-use is one of the main targets that can be achieved by means of this tool. For this reason, in this case the feedback received has been very positive and important for further developments.

2.- The methodology is useful in order to let the workgroup think

Another important advantage of this methodology is to help people in the SMEs to consider possible hazard sources that normally are not taken into account. The formula of applying HarsMeth by a group of personnel from different areas of the SME gives the possibility to improve the knowledge of the process of the whole group, taking advantage of the heterogeneous know-how of the process that each member of the group can supply. The discussions that arose during the application of the methodology were a very positive result, since it turned out that one of the main problems of SMEs is the lack of exchange of information between different departments involved in the process. This exercise can be very helpful for the engineers of SMEs to fully understand every detail related to the safety of the chemical reactions performed in the plant.

For example:

- Question 1.10 in the Good Engineering Design checklist, regarding permit to work systems: most of the SMEs use a batch card, in which information about causes of malfunctions and possible accidents are not included, but it was generally agreed that they should be taken into consideration.
- Question 1.11 in the Management System checklist, about systems to ensure operability of safety measures: this is not a frequent practice, but almost all the SMEs found it a good way to improve safety in the process.
- Question 1.13 in the Management System checklist, dealing with periodical reviews of safety: in most cases, a yearly review of the safety of the process is not performed but almost everybody thinks that it would be very useful.

3.- The Stoessel method is quick and gives an idea of the criticality of the process

This way of evaluating the criticality of the process was very appreciated by the SMEs because of its simple applicability. One problem was found, however, in the calculation of ADT24: if another safety value could be used instead of it as a decomposition temperature of the reaction mass, this method would be very useful.

4.- The Management System checklist was considered adequate

This checklist gives the possibility to organize and standardize the safety policy of the company. It was considered quite exhaustive and easy to apply.

As a summary, it can be stated that, according to the feedback received from the SMEs, the two first checklists in HarsMeth needed to be fully revised, considering both their comprehensibility and the effectiveness of the questions. The “Shortcut method” was found not adequate in order to analyse the hazards of chemical reactions. Moreover, it was considered not clear the reason why the questions have to be different when analysing new or existing processes.

Other findings were that the Operational Risk Analysis checklist was missing some aspects that are considered important from the safety point of view. Moreover, something needed to be changed in the structure of the methodology, to make it possible to justify those cases in which a question is not applicable. In this way, the identification of the hazardous aspects would be easier, considering only those situations that really require special attention.

2.2.1.3.- Check Cards for Runaway weaknesses

As it was done with HarsMeth, a series of deficiencies where detected for this tool during the meetings with the SMEs. The main results are described next.

1.- The use of empirical values can represent a risk and should be used with care

As seen for the *HarsMeth* methodology, the use of empirical values can lead to errors if used for safety purposes. For example, the calculation of the heat of reaction by means of bond energies as suggested by the HarsNet group (HarsBook, 2003) is reliable only for simple reactions, but for complex ones the results can be significantly different from the experimental values.

2.- Some data are not easy to obtain

Some of the data included in the two tables of the Data Collection Cards were not easy to calculate, such as:

- Phase stability *vs*. T and P
- Total adiabatic temperature rise
- Thermal activity at temperature at which the substance should be stored, $T_{STORAGE}$
- Thermal activity at the end of the reaction step

Some of them were considered unnecessary for the evaluation (e.g. phase stability *vs*. T or P, or thermal activity). Since the other ones were considered necessary for the analysis, it was clear that a basic calorimetric study was unavoidable in order to assess the hazards of chemical reactions. Moreover, in some cases it is difficult to take into account all the substances and the mixtures involved in the process, and to fill in the tables with all of them. A selection among those that are considered possible sources of hazards should be done.

3.- The filling in of all the tables can be time consuming and difficult

The amount of information required in order to perform the analysis needs to be as little as possible. For some of the SMEs the two tables were too long and too difficult to fill in. Moreover, the way to calculate some of the parameters and their meaning for the hazard analysis was not explained enough in the methodology.

4.- The separate answer forms generates confusion

The fact of having a sheet for the answers separated from the questionnaire can lead to confusion. The “tree structure” was found useful and clear, but the questions and the answer should be combined in a single form.

5.- Some questions can be considered general for the whole process

The questions concerning the critical factor “Mistaken Chemicals” in the Process section can be asked only once during the analysis of the process instead of doing it for each considered step, since the answers received would be the same for each process step.

6.- Some of the questions can be answered only from a general point of view

In some cases, the behaviour of the reaction mass under certain conditions is known only from the qualitative point of view.

For example:

- Question 6 in the Reaction section, regarding the dosing rate: most of the times only the “order of magnitude” of the maximum dosing rate is known. And, in some cases, the minimum dosing rate should be considered too.
- Question 8 in the Reaction section, regarding accumulation: the way the accumulation can be affected by a variation of the temperature of the reaction mass is known, but many times only in a qualitative way.

7.- Some questions need to be more clearly explained and some aspects are not analysed deeply enough

For example:

- Question 1 in the Reaction section, related to formation of dangerous mixtures: it would be useful to consider also the solvents as chemicals involved in a possible dangerous mix formation.
- Question 2 in the Reaction section, dealing with solvents: the flammable behaviour of the solvents should also be considered.
- Question 10 in the Reaction section, dealing with cooling: it is not clear if “cooling system” means the general capacity of the plant or the cooling system of the considered reactor. Moreover, the reasons why the capacity of the cooling system of the reactor may decrease should be analysed too. This question asks whether the system works at 80% of its maximum capacity. It should be discussed why this is considered an appropriate value. Ideally, under this situation there is a margin for the cooling system to increase its capacity in case a runaway occurs, and there should be a need for more cooling. But the safety margin depends on the dimensioning of the runaway, which will be different for different reactions, and an extra 20% of cooling capacity may not be enough to regain control of the reaction in every situation.
- Question 13 in the Reaction section, dealing with interlocks: It should be specified that, in case of manual control, the operator can act as an interlock between the failure of the cooling system and dosing stop. The training of the operators needs to be checked in this case.

- Process section: some questions concerning the inerting, by-products and residues treatment should also be considered.
- Question 4.1 in the Process section, regarding homogeneous temperature distribution: as the non homogeneous distribution can be hardly checked by the temperature control, it would be better to ask if there is a way to avoid hot spots from being generated.

8.- The ADT24 is a difficult value to obtain

As it has been mentioned, The ADT24 is a value that SMEs hardly ever use. The reason is that it is quite difficult to determine. Only when adiabatic calorimetry experiments have been performed by external laboratories this value is available, and even then the knowledge that personnel from the SMEs have of it is quite limited.

2.2.1.4.- Check Cards for Runaway strengths

1.- The Reaction section is adequate for identifying hazards

The analysis made in the Reaction section was considered quite complete, and the structure used to detect the hazard turned out to be useful and easy to follow.

2.- Almost all the questions can be answered with the knowledge of the SMEs

As with HarsMeth, It was found very useful the possibility to take advantage of the know-how of the people applying the methodology, in order to obtain the necessary knowledge of the process. Most of the times, they know very well the behaviour of the process, but they are not able to calculate some specific data. The structure adopted to perform the analysis permits to use this “practice” knowledge in order to detect possible hazards.

3.- The compatibility chart included is very useful and it is a tool that usually SMEs do not know

Although it can take quite a long time to fill it completely, the compatibility chart is an important tool to analyse the behaviour of substances and mixtures. It is structured in a way that is clear and easy to understand. The possibility to use the information included in the general compatibility chart helps in those cases where the knowledge of the chemical behaviour of the substance is missing. In any case, it should be used with care, considering that general information cannot be exhaustive and that some interaction could be ignored by the method.

4.- The methodology is useful in order to let the workgroup think about safety

As seen for the *HarsMeth* methodology, the CCRs helps to consider the possible hazard causes that normally are not taken into account. For example, in one of the considered processes, a possible cause of dangerous mix formation was detected because of the absence of a pre-charge zone nearby the reactor. In another case, the use of partially used bags or drums was detected as another possible cause of this kind of hazard. Another fundamental aspect in order to avoid mistakes in the process is the necessity of training carefully and controlling the operators: in some cases, deficiencies were found in the way the company normally checks the work done by an operator. A possible solution is to nominate a supervisor responsible for a specific part of the process.

This methodology was not as easy to use as HarsMeth. On the other hand, it gave better results than HarsMeth in the detection of possible hazards, especially for those hazards related to the chemical reaction. Some of the SMEs estimated that it required too many resources to be used.

2.2.1.5.- Synthesis of the two methodologies

Once the feedback described above was collected, a way to respond to the needs of SMEs had to be developed. It was quite clear that both methodologies needed to be reviewed, and that some changes had to be introduced. In particular, some of the

SMEs found the HarsMeth method more useful and complete than the CCRs method, while some others thought the opposite, depending on what they usually consider more important to assess the safety of a process (e.g. the design and the engineering of the process or the way it is actually carried out in the plant). Analysing the comments received from the SMEs, especially the weak points, it turned out that both tools could be considered complementary: those points that are detected as weaknesses in one of them can be adequately improved by means of the strengths of the other methodology. Thus, while HarsMeth was considered more complete as an overall assessment tool and easier to follow, the CCRs proved to be more efficient to identify the specific hazards of chemical reactions. For this reason, it was decided to combine both tools and to produce a new methodology for the assessment of chemical reactive hazards.

The adopted strategy was to try to take advantage of the structure of the HarsMeth methodology and to implement the CCRs as a part of it. The reason is that the HarsMeth tool was identified as the more complete of the two, while the CCRs turned out to be more specifically focused on the way the reaction is carried out. As a result, HarsMeth can be completed with some checklists specific for the process evolution that will substitute the “Short-cut method”. They are included as a new chapter, called “Good Process Practice”.

The new methodology developed, which was called “HarsMeth version 2” (Nomen *et al.*, 2004a), can be found in Appendix 2.2. It is structured as shown in Figure 2.5.

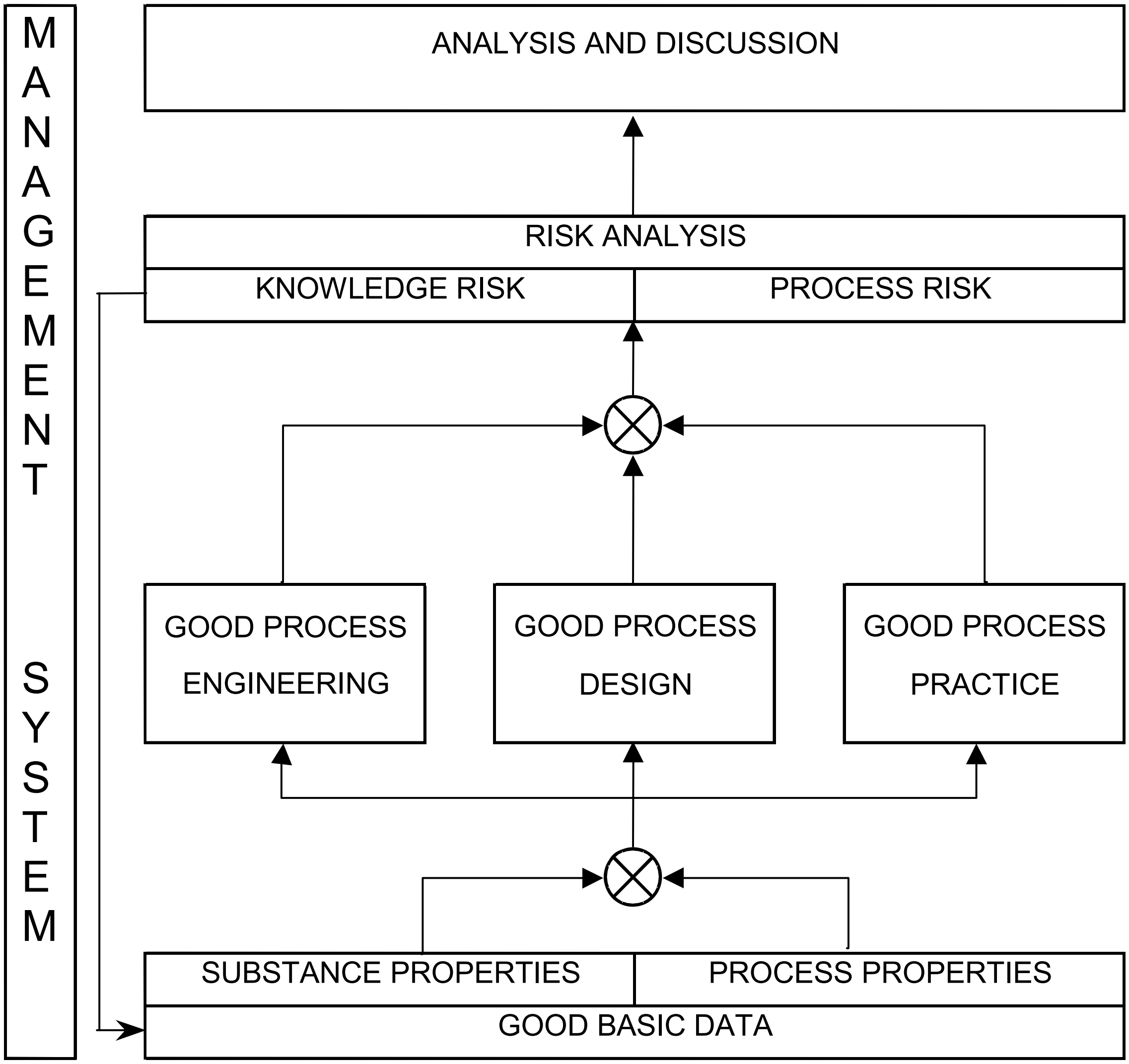

Figure 2.5. - Structure of HarsMeth version 2.

With this kind of structure, the basic data necessary to perform the analysis is collected at the beginning of the analysis. Then, the checklists are presented. They are subdivided in three groups and each group analyses a different aspect of the process. The “Good Process Engineering” and the “Good Process Design” checklists are those already included in the HarsMeth methodology. Some changes have been introduced in order to respond to the needs of the SMEs, as described in the analysis of the feedback received. The “Good Process Practice” checklist derives from the CCRs questions. As in the CCRs, each step has to be referred to one specific process area (Storage, Process or Reaction) and then the adequate list of questions has to be followed. As it was done with the first two checklists, some changes have been introduced following the feedback received from the SMEs.

Data tables

The way data are collected in the CCRs method is considered suitable in order to keep all the data together and available in one document. These data tables can improve the Good Basic Data chapter in HarsMeth. The subdivision in substances and process properties introduced in the CCRs methodology is maintained. The compatibility chart specific can be included in this chapter, seeing that it is an important instrument for the safety analysis and much appreciated by the SMEs. As it was established from the feedback collected, some of the data may not be necessary for the safety analysis. However it was decided not to eliminate any field from the tables at this stage of the development of the methodology. Figures 2.6 and 2.7 show the data collection tables included in HarsMeth v.2 for substances and process conditions respectively.

Substances and Mixtures	Chemical composition and CAS number	Purity	Phase			Report of handling conditions	Specific heat	Thermal activity at $T_{STORAGE}$	Detonation and deflagration sensitivity
			G	L	S				

Figure 2.6. - Data collection table for substances and mixtures included in HarsMeth v2.

STEP	T	P	Substances	Specific heat	Heat of reaction	MTSR	Kinetic behaviour	Adiabatic temperature rise	Thermal activity at the end of the step	MAXTSAFE

Figure 2.7. - Data collection table for process conditions included in HarsMeth v2.

Determination of MaxTsafe

As it has been mentioned in the analysis of the weaknesses of HarsMeth and the CCRs, the use of the ADT24 value proposed in the Stoessel methodology as a temperature safety limit is not considered to be appropriate by SMEs since it is a parameter that they are not familiar with. For this reason, it was decided to include in the new methodology another way to establish a maximum safety temperature barrier, known as MaxTsafe, which could require less safety knowledge and less complicated techniques. Hence, if adiabatic calorimetry is not available, MaxTsafe (Serra *et al*., 1999) can be obtained by means of a dynamic differential scanning calorimetry register of the reaction mass, with a heating rate of 5 K/min. The value can be determined, at a first step, as the temperature of the first exothermal peak less 70 °C. Then it has to be compared with the MTSR. In case the difference between the two values was greater than 50 °C ($|MTSR – (T_{peak} – 70\ °C)| > 50\ °C$), then the determination of MaxTsafe can be considered correct. If this is not the case, then it is necessary to perform an isothermal DSC[1] at MTSR, followed by a dynamic register to understand the mutual position of MTSR and MaxTsafe and to decide to which criticality level the process has to be referred. Four different circumstances could occur:

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[1] When performing an isothermal DSC, it can be considered that a 12 hours experiment should be long enough.

- If MTSR>T_{peak}-70, the isothermal register does not reveal any significant change of the reaction mass, and the dynamic register is equivalent to the first DSC performed, then it can be concluded that MaxTsafe>T_{peak}-70 and therefore MaxTsafe>MTSR.
- If MTSR>T_{peak}-70, the isothermal register does reveal significant change of the mass reaction (low velocity of the exothermal phenomena at the process temperature can be a problem for detection), and the dynamic register is not equivalent to the first DSC performed, then the approximation MaxTsafe=T_{peak}-70 can be considered correct.
- If MTSR<T_{peak}-70, the isothermal register does not reveal any significant change of the mass reaction, and the dynamic register is equivalent to the first DSC performed, then the approximation MaxTsafe=T_{peak}-70 can be considered correct.
- If MTSR<T_{peak}-70, the isothermal register does reveal significant change of the mass reaction, and the dynamic register is not equivalent to the first DSC performed, then it can be concluded that MaxTsafe<T_{peak}-70 and therefore MaxTsafe<MTSR.

Another value frequently used in the literature that can be estimated by means of a DSC register is the T_{onset}, which corresponds to the temperature at which exothermic activity is first detected. However, this possibility was not consider as a reliable value as a safety barrier temperature in the analysis of the criticality of a chemical reaction (Serra *et al.,* 1999), because this parameter is strongly dependent on the sensitivity of the apparatus, on the behaviour of the considered reaction and on the way the value is calculated, making it unreliable.

Restructure of the existing checklists

The structure from the CCRs methodology was used to rearrange the checklists for “Good Process Engineering” and “Good Process Design” included in HarsMeth. In this way, the detection of possible hazards follows a path that was found to be very effective during the meetings with the SMEs. The separation between questions and answers forms from the CCRs is changed in order to add the answer field in the same place of the questions, as generally required. This way, the analysis becomes easier to understand and to keep track of it. The questions are structured so that at the end of each branch of questions only three possibilities remain: a justification of the given answer if the result is that no hazard can be generated from the parameter asked in the question, a review of the existing safety measures in case a hazard is identified, or a check request in case the answer is unknown.

The implementation of the “tree structure” requires a radical change in the way the questions are asked. The path followed by the CCRs is considered more effective, so the questions were changed in order to analyse, in the first place, whether the hazardous situation can occur, and then, to consider if enough measures are implemented to control it. As a result, the questions in the new methodology are rewritten so that the “tree structure” used in the CCRs is combined with the requirement of comprehensibility pointed out during the meetings. The questions are structured in such a way that, at the end, three possible levels of answers are available. These possible answers are classified as follows:

- *Justify your answer*. This answer will be given in case a specific parameter is regarded as safe, and no hazard will be generated from the item analysed. In such case, a written justification is required in order to explain the reason for this consideration.

- *Review your safety measures*. It means that a hazard may be derived from the parameter studied. In this case, either the process development should be modified, or the plant set-up must be adapted to reduce, mitigate or prevent such hazard, and its possible effects.

- *Check it!* This indicates that the answer to the question put forward is unknown. In this case the user should stop completing the questionnaires and seek the answer to the question.

Figure 2.8 shows an example of the type of questions given in the new methodology.

4	***Is showing any of the substances involved (or a mixture of them) an autocatalytic or radical chain reactive behaviour?***			
	YES	*Is it controlled?*		
		YES	*How is it controlled?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
5	***Is there the possibility of crystallisation or formation of a segregated phase in the reaction mixture (especially on cool down operations and at minimum jacket temperature)?***			
	YES	*Can it affect thermal behaviour of the reaction mass or T control, or is the phase thermally unstable?*		
		YES	*Are there measures to manage or prevent it (mixing, separation, re-homogenisation, etc)?*	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
6	***Is the maximum dosing rate known?***			
	YES	*Does it exceed the maximum safe dosing rate?*		
		YES	REVIEW REACTOR SETUP	
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
	NO	CHECK IT!		

Figure 2.8. - Example of the structure of the questions included in HarsMeth v2.

The questions included in the HarsMeth “Operational Risk Analysis” that were considered relevant were relocated in the other checklists. Hazards are classified in two categories, knowledge and process hazards. The knowledge hazard comes from unknown chemical or physical values of substances or mixtures. All these cases lead to a ”Check It” at the end of a branch of a set of questions as seen in Figure 2.8. If a risk of this kind is detected, the unknown values need to be determined before going on with the analysis. On the other hand, process hazards are a consequence of the industrial activity itself. The number of occurrences of this kind of hazard encountered gives an idea of the level of safety of the process. This kind of hazards leads to a “Review your safety measures” at the end of the tree of questions.

Evaluation in steps

As it has been seen from the feedback obtained, some of the questions included in HarsMeth could not be answered taking into account the whole process. Maintaining the subdivision in steps adopted for the CCRs methodology in the new chapter “Good Process Practice”, those questions that have been found to be problematic during the testing sessions can be moved to the adequate checklist (Storage, Process or Reaction) and be analysed considering single step conditions.

Once a hazard of any kind has been identified, prevention or protection measures have to be put in place. Even though some general ideas or guidelines are given, these measures should come from operators and engineers of the SME carrying out the analysis. The philosophy of HarsMeth at this stage of development of the tool is that engineers and operators from SMEs are the best experts in the process, the plant and the company's capabilities. The experience of the people working on the process can be used to define which measures can be better applied to each single case. It must be remarked that one of the objectives of this tool is to make people think about the safety of the process. Moreover, during the meetings it was found to be quite difficult to define safety measures applicable to every kind of process. So, specific sessions using adequate methodologies for problem solving might be planned according to the results produced by the hazard analysis. Nevertheless, very basic guidance regarding possible measures to eliminate some of the hazards identified developed by the HarsNet group was included in HarsMeth v2.

2.2.2.- Validation of HarsMeth v2

To assure the reliability of the new version of HarsMeth developed, it was decided that it was necessary to test the methodology in the day to day work routine at a chemical industry, applying it to as many different situations as possible. In order to fulfil this goal, the methodology was applied during one year at the pharmaceutical company C1, its name being omitted due to a confidentiality agreement between the company and IQS. The intention was to improve the methodology with the experience acquired during the application of the tool and from the feedback received from the company C1, by eliminating possible vagueness that still remained from the previous revision, completing it with the addition of new questions taking into account new hazards and adapting it to the actual way of development of a chemical process in order to fulfil the real needs of the SMEs.

The approach used in order to improve HarsMeth v2 was firstly to observe and analyse the different working procedures used to perform a chemical process in the plant, at the facilities that the company C1 has in the surroundings of the Barcelona area, especially the safety policies followed and safety measures used. All the information required to complete the questionnaires was asked during this stage to the personnel in charge of the different operations. Besides, different calorimetric experiments have been performed, which will be described later, in order to determine the criticality of a specific chemical process performed at the company C1 (*cfr*. page 132) according to the requirements of the methodology. Once the criticality of the process studied was determined by means of the necessary experiments, a critical review of the checklists included in HarsMeth v2 was performed, in a similar procedure to the one described previously for the first version of HarsMeth and the CCRs.

From the experience gained during the observation step, together with the experience of operators and engineers from the company, it was possible to state the different weaknesses and strengths of HarsMeth v2 that were identified at this stage (Romero, 2004).

2.2.2.1.- HarsMeth v2 weaknesses

1.- Some questions are too generic and others present available answers which are too general and limited

In order to ensure a reliable identification of the hazards related to a chemical reaction, the questions put forward in the methodology must be clear and should not generate any doubt as to under which conditions they should be applicable.

For example:

- In the Good Basic Data section, when the compatibility chart is filled in, there should be an indication as to extend the analysis to any possible mixture that could be formed unexpectedly between process substances and auxiliary services (e.g. water or fluids for heating and cooling).
- Question 2.2 in the Good Process Design checklist, regarding quality and yield: it should be specified at what stage of process development (laboratory scale, pilot plant scale) should yield results at industrial scale be compared with and evaluated.

- Question 3.2 in the Good Process Practice checklist, in the storage section: Depending on the type of substance, the specific hazards and the amounts involved, the use of inhibitors may or may not be necessary. In fact, it is possible to keep autocatalytic substances in small containers (e.g. 5 L) with no inhibitor control, according to operators from the company C1. In this case the methodology would identify a hazard when the situation should actually be regarded as safe.
- Question 5.11 in the Good Process Practice checklist, in the reaction section, dealing with temperature control when the reaction is ended: at the company C1 the procedure used is to control temperature unless the situation is considered to be safe. Strictly, the given answer when completing the methodology will give, in the majority of cases, “Review your safety measures”, even if the situation is considered as safe at a given temperature. For this reason, it is considered that this question should come after a comparison of the temperature evolution after completion of the reaction and the temperature at which it is considered that the reactor can be left without temperature control.

2.- Some values or conditions asked are too difficult to know, or the way to determine them is not clear enough

For example

- In the section corresponding to the analysis of a runaway scenario, it is specified that the MTSR parameter should be calculated in different possible scenarios (i.e. batch or semi-batch), however it is not specified how this parameter can be calculated. Moreover the knowledge of processes from SMEs in most cases is not deep enough to allow them to calculate this parameter because of the lack of resources or procedures to estimate it.
- In the section of Good Basic Data: there are no specifications as to how to obtain the required data on thermal activity at the temperature of storage, nor regarding to the sensitivity of a substance to detonation or deflagration.

3.- The conditions to evaluate the answers to the questions are sometimes not appropriate for hazard analysis

In some cases, HarsMeth v2 asks for an evaluation during normal process conditions, but it would be more interesting to assume upset conditions in order to identify unexpected situations. It is clear that an appropriate process design must ensure safe conditions during normal operation.

For example:

- Question 2.3 in the Good Process Design checklist, dealing with cooling capacity: it is clear that the cooling system must be designed to remove the heat generated by the reaction in normal conditions. However, the really interesting question is whether the cooling system is prepared to eliminate the heat generated in a possible malfunction scenario in order to avoid a runaway reaction. As it was pointed out in the previous analysis that led to the development of HarsMeth v2, this type of questions generate an internal discussion about the evolution of a possible runaway scenario, the available intervention measures and the readiness or adequate infrastructures available in the plant (e.g. cooling systems), which could create a synergy in the development of the process.
- In the Good Basic Data tables, in the column referred to the thermal activity at the storage temperature: it is clear that it is necessary to know the thermal behaviour of a substance at normal conditions, but it would also be necessary to know the stability of substances or mixtures at extreme conditions, like the MTSR, or under conditions such as, for instance, a fire at the storage facility that would increase the temperature in the containers.

4.- Some aspects that are considered relevant for the safety evaluation are not included

For example:

- The Good Process Practice checklist should include hazards related to transportation or wrong handling of containers. Besides, indications on the hazards of picking substances from the wrong container due to incorrect labelling should also be considered.

- The Good Process Engineering checklist does not cover issues such as wrong temperature measurements, wrong venting systems design or two phase flows.

5.- Some information is repeated as the user proceeds to complete the methodology

The structure given in HarsMeth v2 can generate sometimes a considerable amount of checklists containing the same information, which can lead to excessive time, fatigue by the person or persons completing the assessment and neglecting key items in the analysis. Moreover, the fact of including generic checklists applied for different reactions, storage and unit operations performed at one single process makes it difficult to come up with a specific checklist for a stage or set of stages that would require a more careful assessment, with the risk of leaving out some important hazards unnoticed.

6.- The level of safety of the process is not specified after completing the methodology

Once HarsMeth v2 has been applied to a process, the result is a set of hazards and parameters that may be unknown, as well as a classification according to the Stoessel method, but it is not clear whether there are enough safety measures available in case of a runaway.

These drawbacks have been addressed by suggesting some modifications to the methodology (review of existing questions, new questions added and changes in the structure) to improve the reliability of the tool.

2.2.2.2.- HarsMeth v2 strengths

1.- Useful methodology for companies with few resources to perform a complete risk analysis; easy to follow and to understand

One of the main objectives of the methodology is to help SMEs with few resources (either human, time or economic) in performing a hazard analysis and to offer them a useful tool in the field of safety. In this sense, even though the methodology may not be complete at this stage, and it cannot replace a complete and thorough risk analysis, it gives the possibility to perform a preliminary hazard assessment.

Another objective of the methodology is to be easy to apply and to make it available to be used by personnel with little experience in the field of process safety. Again the Stoessel evaluation of the criticality of a chemical reaction is much appreciated by the engineers and operators from the company, since it is very intuitive and provides a first idea on whether the chemical reaction will need further safety measures to be performed at plant scale.

2.- The methodology allows identifying a great variety of possible hazards and critical elements for the process from the thermal point of view

Even though HarsMeth v2 only takes into consideration the hazards originated by thermal conditions, the tool includes a wide number of possible hazard sources in a chemical process. The fact that this is a specific methodology to identify thermal hazards gives the SMEs the opportunity to learn and to gain experience in this kind of hazard analysis; another advantage that was pointed out previously is that the methodology is a useful tool to help the personnel of the SME to think about the safety of the process while it is being used. This feature proved to be very useful when it was applied at the company C1. This also gives the possibility in the future to introduce more complex systems that could perform a more complete risk analysis.

3.- The flexibility of the tool allows its use at any point of the development of a process and to extend it in the future

The division of the HarsMeth v2 in different sections with separated checklists gives the opportunity to complete each one of those sections independently. This is considered to be especially interesting in order to evaluate the safety at different stages of the development of the process (e.g. initial synthesis investigation, scale-up procedures and so on). This feature makes it also easy to introduce more items in the future, either with general questions for the different checklists or with particular issues that might be of specific interest for the SME using the tool, company C1 in this case.

2.2.2.3.- Proposal for a new draft version of HarsMeth

In the first place, the Safety Management System checklist should be expanded, adding new sections regarding the training plan for operators and description of the emergency plan procedures. This new questions were a direct input from the experience of the personnel in charge of developing and putting the emergency plan into practice, and they indicate some basics requirements under an emergency situation. Other questions should be included in this checklist taking into account the possible hazards that may arise due to the loss or poor communication or transfer of documentation between different departments in the company while performing the process. Finally, a system to collect information from near misses or historical failures occurred in the plant should be provided in order to keep track of those events and to learn lessons to avoid similar situations in the future; it was detected that a considerable number of possible malfunction scenarios, written in the text description of the methodology, were usually neglected or ignored in the checklists.

After revising HarsMeth v2 and applying it into different processes performed at the company C1, it was stated that, following the method of application of the different checklists, an important number of completed questionnaires contained, in many cases, the same information. This was mainly due to the fact that for one single process, different reactive stages can be involved, as well as a great number of process operations (like distillation, drying or filtering) that caused an excessive and repetitive information being generated, increasing the time necessary to complete the methodology. This makes it more difficult to extract possible conclusions, since it can lead to an excessive fatigue in the person or persons completing the methodology. In order to solve this problem a new division was proposed in each checklist of the Good Process Practice section (Reaction, Process and Storage), which is explained next:

- The “Reaction” checklist was proposed to be divided in two parts: first, a “General Reaction” checklist, which would contain the common hazards that could arise from the general procedures of performing chemical reactions like connections between agitation and dosing or general procedures that could lead to the formation of hazardous mixtures. Next, a “Specific Reaction” checklist, which will contain the intrinsic hazards to the particular reaction analysed like the solvents used, accumulation, temperature control, and so on. Therefore the “General Reaction” checklist must be completed once for all the process and the “Specific Reaction” checklist must be completed for each reaction step in the whole process.
- The “Storage” checklist should also be divided in two parts: a “General Storage” checklist, which will be applied to the general storage facility of the plant, defined as the place where all the substances are stored for an indeterminate period of time, and that should be completed in a prefixed time frequency, and a “Specific Storage” checklist for reactants and products, which is to be applied to the place where these are stored for a brief period of time (before starting the reaction or when they are generated).
- Finally, the “Process” checklist was considered to be too generic, and it was suggested that its structure should be modified completely. A new “General Process” checklist was created, which would be completed once for the whole process, and a series of “Specific Process” checklists, referring each one to one of the common operations done in the process apart from the chemical reaction steps, to be completed every time that one of these operations is performed in the process. The “Specific Process” checklists generated in this first approach are Addition / Dosing of substances, Distillation / Reflux and Extraction / Drying / Centrifugation. These checklists were considered as preliminary versions of a system that should be further developed in

successive improvements of the methodology to cover all the unit operations that could be involved in a chemical process.

The new schema proposed at this stage of the development of HarsMeth for the "Good Process Practice" section is presented in Figure 2.9.

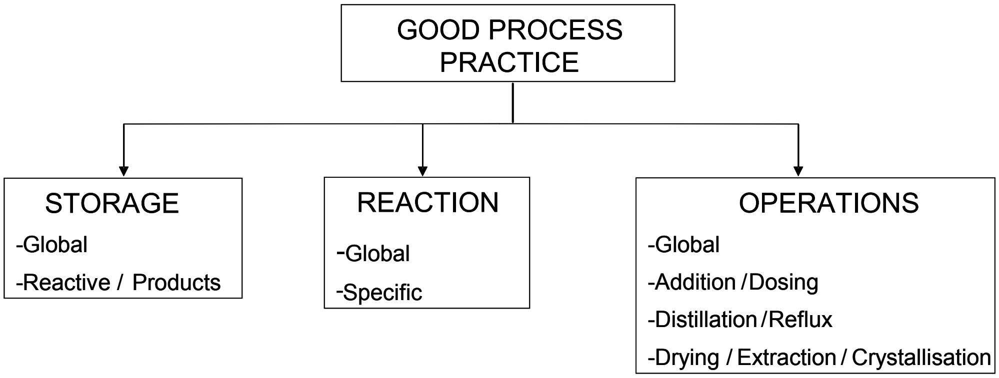

Figure 2.9. - New schema proposed for the "Good Process Practice" section of HarsMeth v2.

All these modifications were adopted by the company C1, and the version HarsMeth v2 with the mentioned changes is a key tool for this company nowadays to perform hazard analysis of their chemical processes. The new checklists generated can be found in Appendix 2.3.

2.2.3.- Development of a system to identify chemical reactive hazards in unit operations equipment

As it has been described, all the effort in the development of HarsMeth has been related so far to the identification of chemical hazards in the reaction stage, as well as during the storage of hazardous materials. Some questions have been included referring to physical processes, but it was stated at all stages of the validation of the tool that this section should be extended further, in order to identify chemical reactive hazards in other process or plant equipment different from the chemical reactor itself.

With the intention to fulfil this requirement, HarsMeth was again tested at a chemical company during several months. The company C2, its name being omitted due to a confidentiality agreement signed between the company and IQS, is another enterprise specialized in fine chemicals production. The intention this time was to focus on specific unit operations involved in the processes performed at the plant of the company C2 in the surroundings of Barcelona and to prepare specific checklists according to the hazards involved in those operations. The checklists for process operations developed at the company C1 as described in Figure 2.9 were used as a starting point, using the same philosophy in presenting the questions as for the other checklists of HarsMeth v2. Specifically, checklists were developed for the following unit operations (Roma, 2006).

- Charging / Reaction
- Addition / Dosing
- Distillation / Reflux
- Precipitation
- Centrifugation
- Filtration / Mass transfer
- Extraction / Decanting / pH fixing
- Drying
- Micronization / Grinding

All these checklists can be found in Appendix 2.4. Again, the strategy to develop these questionnaires was the analysis of the operations performed in the plant, with the help of operators and engineers from the company C2, and to decide which were the specific hazards related to each one of the operations studied.

Nevertheless, it is clear that this strategy can give limited results, since it is restricted to the experience gained by working with processes performed by one chemical company. Therefore it becomes necessary to develop a more generic system to identify all the possible reactive hazards that can be generated during every single physical operation that is used in the chemical industries these days. A method for this purpose was developed under the umbrella of the Safety to Safety (S2S) network. S2S was another European Commission sponsored network, coordinated by the PQAT research group of IQS that aimed at improving the safety of SMEs that perform chemical processes. The project deliverables were knowledge bases, training modules and assessment tools on areas like toxicity, fires & explosions and reaction hazards among others. Those deliverables are freely available through the S2S website (S2S, 2007). The project has been active during the period 2002 – 2006, and it included most of the partners that were involved in HarsNet.

As it has been described earlier (*cfr*. page34), nearly 70% of the reactive chemical incidents take place in equipment or units other than the chemical reactor itself. When analysing such incidents in terms of causal effects it can be concluded that the inadequate recognition of reactive hazards is one of the main causes that lead to the occurrence of those accidents. This is usually due to the fact that the equipment types and process steps are diverse. The diversity makes it difficult to detect patterns and to transfer the knowledge to operators and engineers. For this reason, a teaching concept should be developed based on commonality.

A training and assessment tool for unexpected reactors (Weve *et al*., 2007) has been developed by the S2S network, which includes the following features:

- A training concept that helps to recognize how deviations from design intention will result in reaction hazards.
- A method to generate general mechanisms for such deviations and to input them as user specific questions, known as ‘decisive questions’.
- A database containing the above knowledge in tables that was built from a limited number of incidents.
- A spreadsheet containing the logic programmed as Microsoft Excel$^{®}$ macros to access the database.

All these items are described and developed next.

For a reaction[2] to occur at any part of a chemical plant, a combination of 3 factors needs to be fulfilled:

- Concentration of reactants.
- Temperature of reactants.
- Time for reaction.

This can be described in a triangle similar to the fire triangle (Amyotte, 2003) as seen in Figure 2.10.

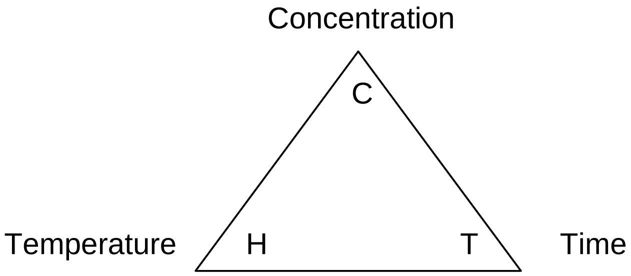

Figure 2.10. - The reaction triangle.

The reason why these three factors are chosen is that they also represent the most important degrees of freedom in process operation and design. As with the fire triangle, a reaction requires an appropriate combination of these three factors: reducing the contribution of concentration, temperature or residence time within the triangle will reduce the possibility of a reaction to take place.

There are some special reactions that need a catalyst or high interfacial area between phases (V/L, L/L, S/L or V/S) in order to obtain sufficient reaction speed. These factors should be added to the Time-corner, in the sense that they 'help' the time factor. They both determine the speed of the reaction and can be varied independently of the concentration and temperature. More so, they are frequently

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[2] The method implies the assumption of simple reactions such as $A+B \rightarrow C$ and $A \rightarrow C+D$

used to reduce the time for reactions to complete and could rightfully take the place in the reaction triangle. The Time corner could then be replaced by the TIC corner (Time/Interface/Catalyst).

In order to better understand the idea behind the reaction triangle and how it can be linked to process equipment, a series of examples can be introduced:

Example 1: A reactor is evidently equipment located near the middle of the triangle.

Example 2: A feed pre-heater in a process with a fast reaction, for instance, can be considered as equipment on the temperature-time side of the triangle. This means that it is supposed to heat a substance to reaction conditions, and it cannot avoid substantial residence time (typically 1-5% of the reactor time), so it should have a low concentration of one of two reactants to prevent unintended reactions. So, what is needed to turn this equipment into an unintended reactor? The answer would be to increase the missing axis of the triangle, which is concentration. This situation would be generated by an unexpected event, maybe backflow from the reactor, maybe product residues from another process step in a multipurpose plant.

Example 3: A centrifugal pump for a thermally unstable liquid can be designed to operate in the concentration corner of the triangle. Then, two things are needed to turn the pump into an unexpected reactor: temperature and time. This situation can be achieved by a blocked inlet or outlet (time) and a pump motor that keeps running and generates heat (temperature).

Like the feed pre-heater and the pump, all unit operations have been conceptualized with a specific task and are used with assumptions on their capabilities. Conceptually they can all be positioned on the sides of the reaction triangle, and they will not pose hazards unless they move towards the middle. There are several ways in which equipment can vary their position in the reaction triangle: there are outside / process failures (like backflow), equipment failure modes (e.g. pipe bundles in heaters leak and foul) and equipment inherent side effects (e.g. pumps generate heat). Some of the equipment effects are specific to the product or process properties. For example, if a thermally unstable product is involved, it will reduce the temperature margin for safety operation; a heater or a system using an evaporative coolant / diluent can evaporate a product and therefore bring the equipment closer to the concentration corner of the triangle.

Like the fire triangle, the main factors that contribute to the hazard are easily recognized and provide a simple concept to learn. Unlike the fire triangle which serves as a tool to solve a single situation, the reaction triangle is meant as a complete description of the process. It helps understanding of how the process design aims to avoid reaction hazards and how deviations can overcome the design intentions.

The goal of the method is therefore to provide a system that will allow the user to identify the possible ways in which the equipment used in an installation could ‘move’ process streams with their properties over the triangle map, hence generating a possible hazardous situation.

General Mechanisms for Reaction Hazards

A non-reactor equipment item has the potential to move its process stream from a side of the reaction triangle towards the centre, thereby creating a reaction hazard. This potential is not always recognised. However, the mechanisms involved in the movement can be generalized. The benefit of generalization is that the knowledge can be applied in a wider range of cases than that from which the generalization derived. This is especially important when analysing incidents, where there is a desire to derive as much learning as possible from a few cases. Generalizations require deep understanding of the physics and the design intent, skills that are not usually accessible in the team that performs the risk analysis. Once they have been developed they can be applied by people with less experience.

The generalized mechanisms developed for the preparation of the assessment tool have been divided in three classes:

- *Failure*: equipment specific failure is also related to the way the equipment is designed to accomplish its design intent. As an example, all coolers need a cooling medium, which may mix with the process fluid through leakage.
- *Side effects*: equipment inherent side effects are related to the way the equipment is designed to accomplish its design intent. For instance, a pump can also be considered a small mixer. Normally these side effects will focus on physical phenomena such as phase behaviour, friction, turbulence, dynamics, stability and driving forces like gravity, heat and pressure.
- *External causes*: mechanisms that are not caused by the equipment themselves but by general events in the process. As an example, solar radiation may sometimes heat a drum up to a decomposition reaction temperature.

Mechanisms can be developed from scratch using theoretical and practical knowledge of equipment and chemistry behaviour but it is also possible to develop them based on an incident. The mechanism will subsequently be tested for its potential to occur in other equipment. Sometimes it is found that the mechanism itself involves specific physical and chemical properties of the process or process materials. An example is shock-sensitivity.

Example 4: decomposition reactions can be triggered by the presence of rust in the bottom of a distillation column. The following generalizations can be derived from this example:

- Triangle generalization: it was a move towards the time (Time / Interface / Catalyst) corner.
- Physical generalization: particles can accumulate by settling out in a stagnant zone with a low liquid velocity. The mechanism can therefore be expected in vessels, tanks and heat exchangers.
- Process generalisation: There are many process materials that are incompatible with rust and may decompose.
- Failure generalization: carbon steel being a common construction material, rust formation should be expected.

Generating the 'Decisive Question'

It is clear that having a set of generalized mechanisms involved in potential hazards does not constitute a training / assessment tool in itself, especially if a combination of general mechanisms and factors is needed to pose a hazard. There are two problems that need to be addressed, the delivery of the information and the accuracy of the method. In the proposed method, both problems are handled through the so called 'User Specific Decisive Question'.

Since the objective of the tool is to train people in recognizing reactive hazards, the entire mechanism will be split in just two parts: a condition and a consequence.

> IF condition THEN consequence

The user will have to supply the 'condition' by answering a final Decisive Question in order to learn the 'consequence' of the potential hazard. This forces the user into an active role and regulates the flow of information. To stimulate thinking, the Decisive Question should preferably suggest to the mechanism involved. To limit the amount of information, the user first selects from a list what equipment and process properties he / she wants to consider.

Looking at example 4 (*cfr.* page 78), if the user has selected the process property that rust may catalyse reactions and that there is a tank, then the following question will be generated:

> Can the equipment upstream form rust (e.g. it is made from carbon steel)?

If the answer is positive, the consequence will be displayed as:

> This equipment can accumulate rust and provide both a high temperature and a sufficiently long residence time and therefore has a potential for a reactive hazard.

The set of generalized mechanisms for a standard set of equipment and process properties are broad enough to describe most potential hazards, but would generate too many false positives (identifying a potential hazard where the likelihood is very low). The risk of many false positives is that the attention of the user is diverted from the more realistic potential hazards. The accuracy can be improved by asking the user to supply additional information on the likelihood themselves. The information can come from the process design and control, construction materials, and so on, and essentially it moves a conditional aspect from the entire mechanism into the Decisive Question.

Looking at example 3 (*cfr.* page 76), if the user has selected a pump and a thermally unstable product, then the potential hazard can be described in the general mechanism as:

IF product=unstable AND equipment=pump
  THEN potential-hazard=”If the flow can be blocked then the temperature rise due to dissipation of heat may be sufficiently high to initiate a decomposition reaction.”

With a User-specific, Decisive Question “Is it possible to block flow through this equipment?” The user provides the unknown likelihood and the potential hazard becomes more relevant:

IF product=unstable AND equipment=pump AND condition=TRUE
  THEN potential-hazard=”The temperature rise due to dissipation of heat during blocked flow may be sufficiently high to initiate a decomposition reaction.”

Building a database from incidents

A knowledge database was build using different sets of incident sources, both from open literature and proprietary information. The main source of information used has been the IChemE Accident database (IChemE, 2007). A query was performed on the database as to identify incidents with unwanted chemical reactions as triggering causes of the events and yielded a total of 631 cases for analysis. From the public information of the accidents reported to the MARS database (MARS, 2007) 68 useful cases were identified. Incident descriptions and summaries were interpreted and generalized using the concepts described previously. Some cases are also used as examples in the tool.

The resulting database consists of tables for 16 equipment types, 7 process properties, 22 User Specific Decisive Questions, 25 general mechanisms and 61 incident examples. Matrices are used to assign process properties to general mechanisms and to equipment Matrices and Decisive Questions to General Mechanisms. The complete tables are downloadable from the S2S website (S2S, 2007).

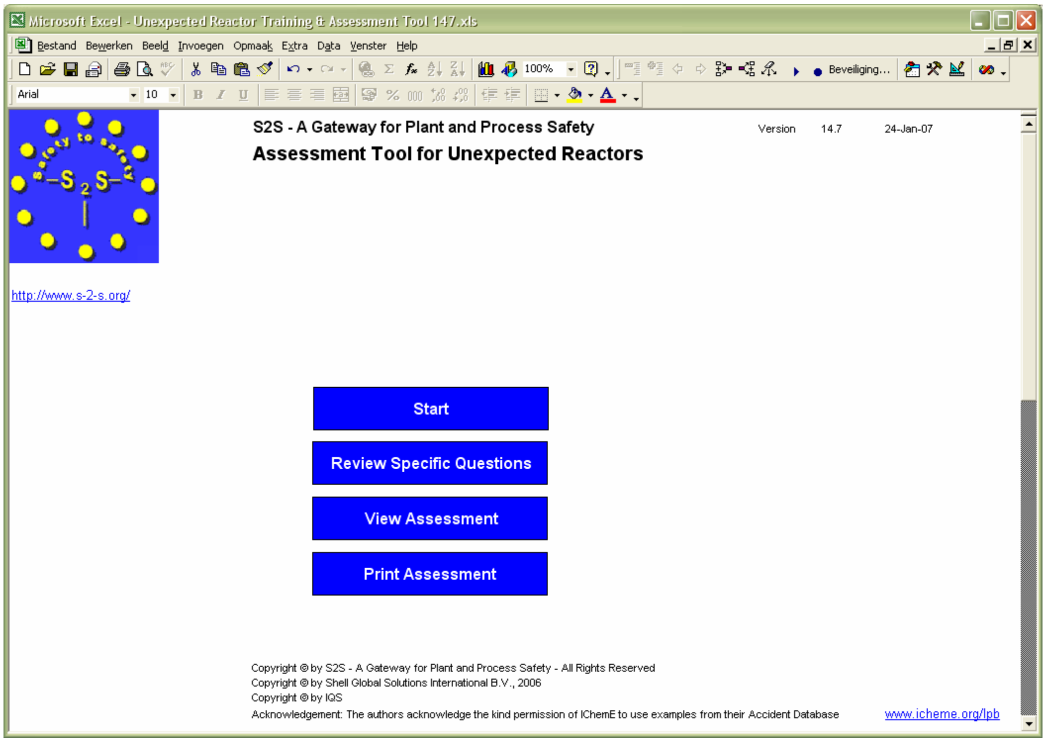
Implementation of the assessment tool

The S2S training & assessment tool for unexpected reactors has been implemented as a Microsoft Excel® Worksheet included in the S2S website (S2S, 2007), and it is included in the CD attached in this PhD work. It can be run either on-line at the S2S web portal or downloaded for use off-line. The tool has the following functionality:

- Simple user interface including time-stamped print.
- Executing the knowledge contained in the database.
- The knowledge database can be viewed / modified by specialists.
- Language portability.

The tool requirements are limited to Excel® 2000 with macros enabled option.

The tool developed is started from the S2S website by double-clicking on the corresponding link. This will automatically launch Excel® to display & run the tool as shown in Figure 2.11. The User interface is a main screen with access to the main functions: Help, Assessment & Print. The Assessment itself cycles through the screens and displays tables to complete and results to view & print. The macros are triggered by jumping to the next or previous page. Thus the list of Decisive Questions and Mechanisms is adjusted dynamically to changes in the user response.



S2S - A Gateway for Plant and Process Safety

Assessment Tool for Unexpected Reactors

Version 14.7 24-Jan-07

http://www.s-2-s.org/

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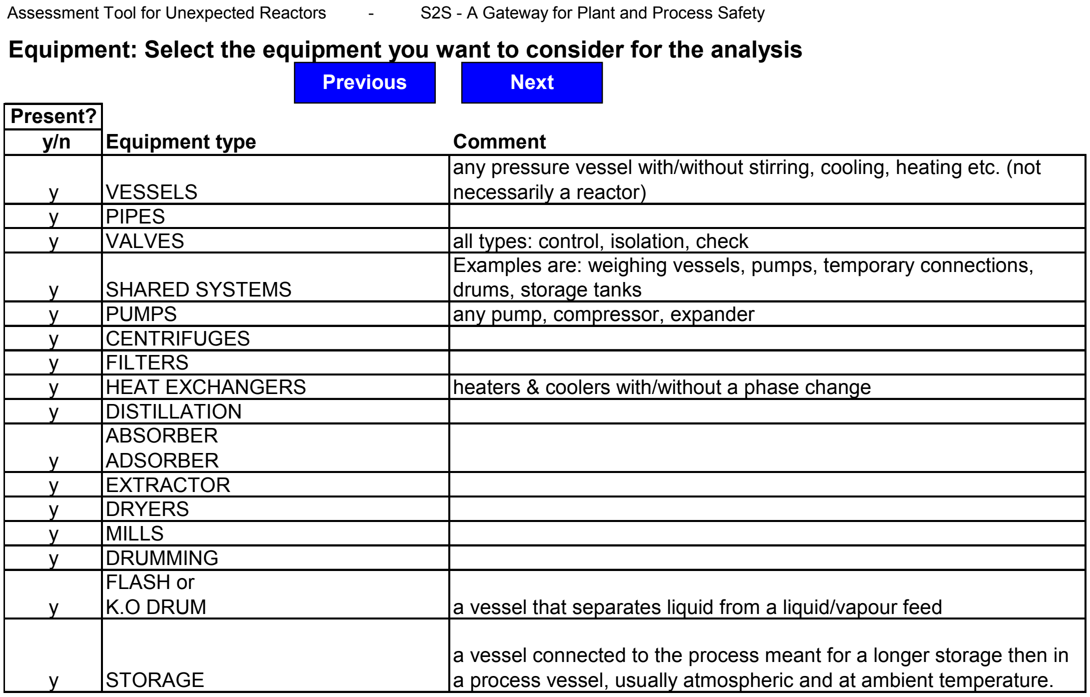
Figure 2.11. - First page of the S2S training & assessment tool for unexpected reactors.

The knowledge of the database is executed using Visual Basic Macros to perform the following logic steps.

1) Display an ‘Equipment Table’ (see Figure 2.12) and a ‘Process Properties Table’ (see Figure 2.13) in which the user selects which equipment and process properties combinations are to be assessed.
2) It pre-selects possible mechanisms from the ‘Equipment-Mechanism Matrix’.
3) Using the ‘Mechanism-Properties Matrix’, it removes mechanisms that need a process property that was not selected.
4) For the remaining possible mechanisms, it builds a list of ‘Decisive Questions’ from the ‘Mechanism-Question Matrix’.
5) A ‘Decisive Questions’ list is displayed, which the user must answer with Yes or No. In order to facilitate the visualization of the hazards that the tool intends to identify, different examples based on real accidents triggered by such hazards are available for each of the Decisive Questions generated.

6) For each positively answered Decisive Questions, a table listing the relevant mechanisms will be displayed as well as the equipment, process properties and mechanism type that are involved in the mechanism.

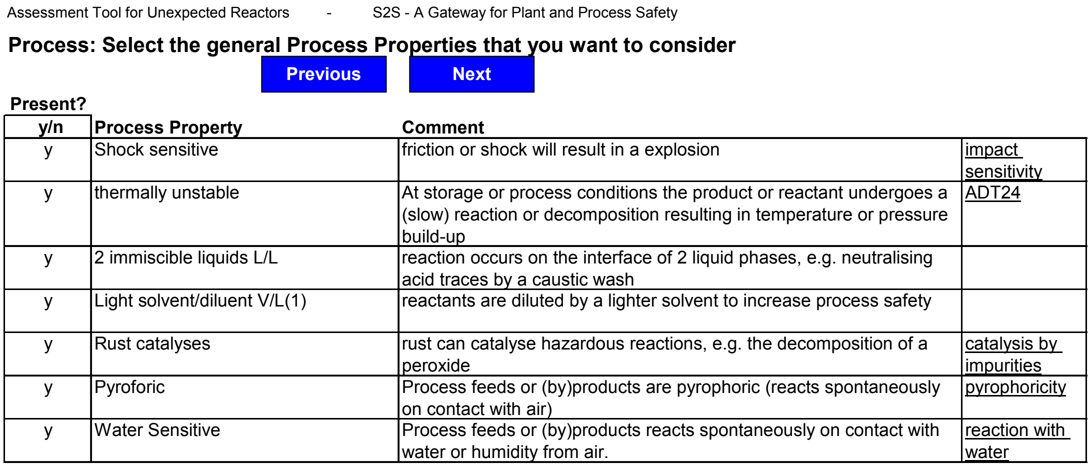


Assessment Tool for Unexpected Reactors - S2S - A Gateway for Plant and Process Safety

Equipment: Select the equipment you want to consider for the analysis

Present? y/n	Equipment type	Comment
y	VESSELS	any pressure vessel with/without stirring, cooling, heating etc. (not necessarily a reactor)
y	PIPES	
y	VALVES	all types: control, isolation, check
y	SHARED SYSTEMS	Examples are: weighing vessels, pumps, temporary connections, drums, storage tanks
y	PUMPS	any pump, compressor, expander
y	CENTRIFUGES	
y	FILTERS	
y	HEAT EXCHANGERS	heaters & coolers with/without a phase change
y	DISTILLATION	
y	ABSORBER ADSORBER	
y	EXTRACTOR	
y	DRYERS	
y	MILLS	
y	DRUMMING	
y	FLASH or K.O DRUM	a vessel that separates liquid from a liquid/vapour feed
y	STORAGE	a vessel connected to the process meant for a longer storage then in a process vessel, usually atmospheric and at ambient temperature.

Figure 2.12. - Equipment table included in the S2S assessment tool for unexpected reactors.



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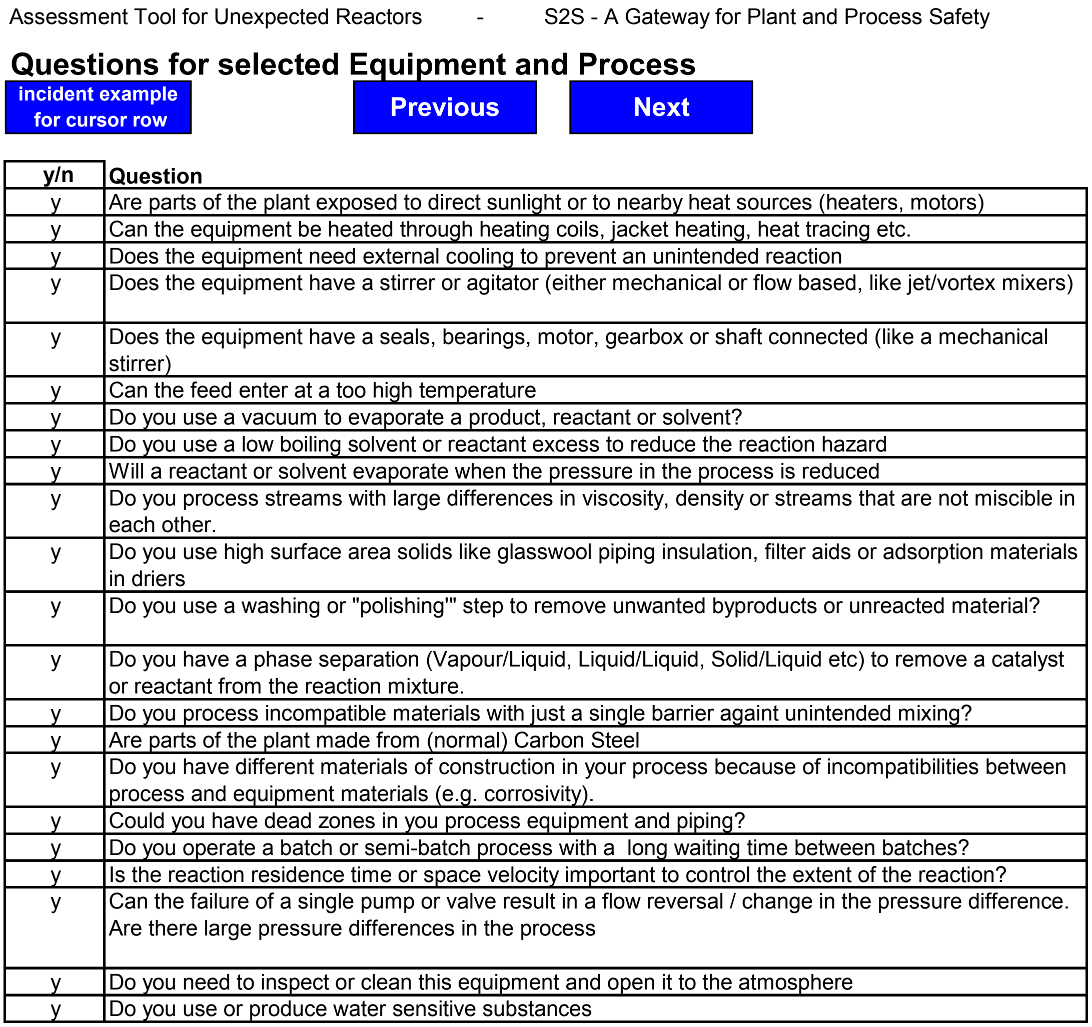
Process: Select the general Process Properties that you want to consider

Present? y/n	Process Property	Comment	
y	Shock sensitive	friction or shock will result in a explosion	impact sensitivity
y	thermally unstable	At storage or process conditions the product or reactant undergoes a (slow) reaction or decomposition resulting in temperature or pressure build-up	ADT24
y	2 immiscible liquids L/L	reaction occurs on the interface of 2 liquid phases, e.g. neutralising acid traces by a caustic wash	
y	Light solvent/diluent V/L(1)	reactants are diluted by a lighter solvent to increase process safety	
y	Rust catalyses	rust can catalyse hazardous reactions, e.g. the decomposition of a peroxide	catalysis by impurities
y	Pyroforic	Process feeds or (by)products are pyrophoric (reacts spontaneously on contact with air)	pyrophoricity
y	Water Sensitive	Process feeds or (by)products reacts spontaneously on contact with water or humidity from air.	reaction with water

Figure 2.13. - Process Properties table included in the S2S assessment tool for unexpected reactors.

Figure 2.14 shows all the possible Decisive Questions included in the tool. This page includes examples describing how the question posed is related to past accidents that are included either in the IChemE database or in the MARS database. The user can visualize the description of such accidents by placing the cursor on the question of interest.



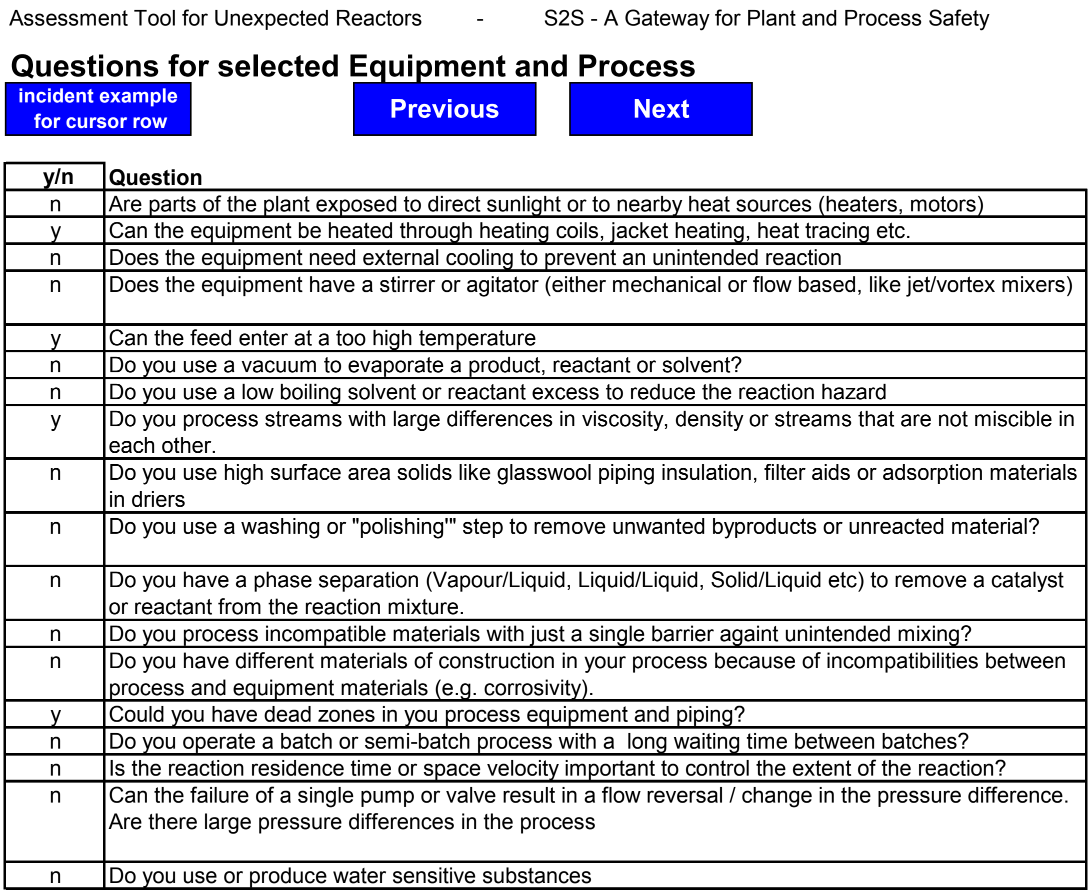
Assessment Tool for Unexpected Reactors - S2S - A Gateway for Plant and Process Safety

Questions for selected Equipment and Process

y/n	Question
y	Are parts of the plant exposed to direct sunlight or to nearby heat sources (heaters, motors)
y	Can the equipment be heated through heating coils, jacket heating, heat tracing etc.
y	Does the equipment need external cooling to prevent an unintended reaction
y	Does the equipment have a stirrer or agitator (either mechanical or flow based, like jet/vortex mixers)
y	Does the equipment have a seals, bearings, motor, gearbox or shaft connected (like a mechanical stirrer)
y	Can the feed enter at a too high temperature
y	Do you use a vacuum to evaporate a product, reactant or solvent?
y	Do you use a low boiling solvent or reactant excess to reduce the reaction hazard
y	Will a reactant or solvent evaporate when the pressure in the process is reduced
y	Do you process streams with large differences in viscosity, density or streams that are not miscible in each other.
y	Do you use high surface area solids like glasswool piping insulation, filter aids or adsorption materials in driers
y	Do you use a washing or "polishing'" step to remove unwanted byproducts or unreacted material?
y	Do you have a phase separation (Vapour/Liquid, Liquid/Liquid, Solid/Liquid etc) to remove a catalyst or reactant from the reaction mixture.
y	Do you process incompatible materials with just a single barrier againt unintended mixing?
y	Are parts of the plant made from (normal) Carbon Steel
y	Do you have different materials of construction in your process because of incompatibilities between process and equipment materials (e.g. corrosivity).
y	Could you have dead zones in you process equipment and piping?
y	Do you operate a batch or semi-batch process with a long waiting time between batches?
y	Is the reaction residence time or space velocity important to control the extent of the reaction?
y	Can the failure of a single pump or valve result in a flow reversal / change in the pressure difference. Are there large pressure differences in the process
y	Do you need to inspect or clean this equipment and open it to the atmosphere
y	Do you use or produce water sensitive substances

Figure 2.14. - Decisive Questions included in the S2S assessment tool for unexpected reactors.

In order to better illustrate the functioning of the tool, let us assume a case in which the user has selected the presence of vessels, pipes, valves, pumps, heat exchangers, distillation and dryers as equipment present in the plant, as well as the handling of thermally unstable, immiscible liquids and water reactive substances. In such a case, the list of Decisive Questions generated would be the one shown in Figure 2.15.



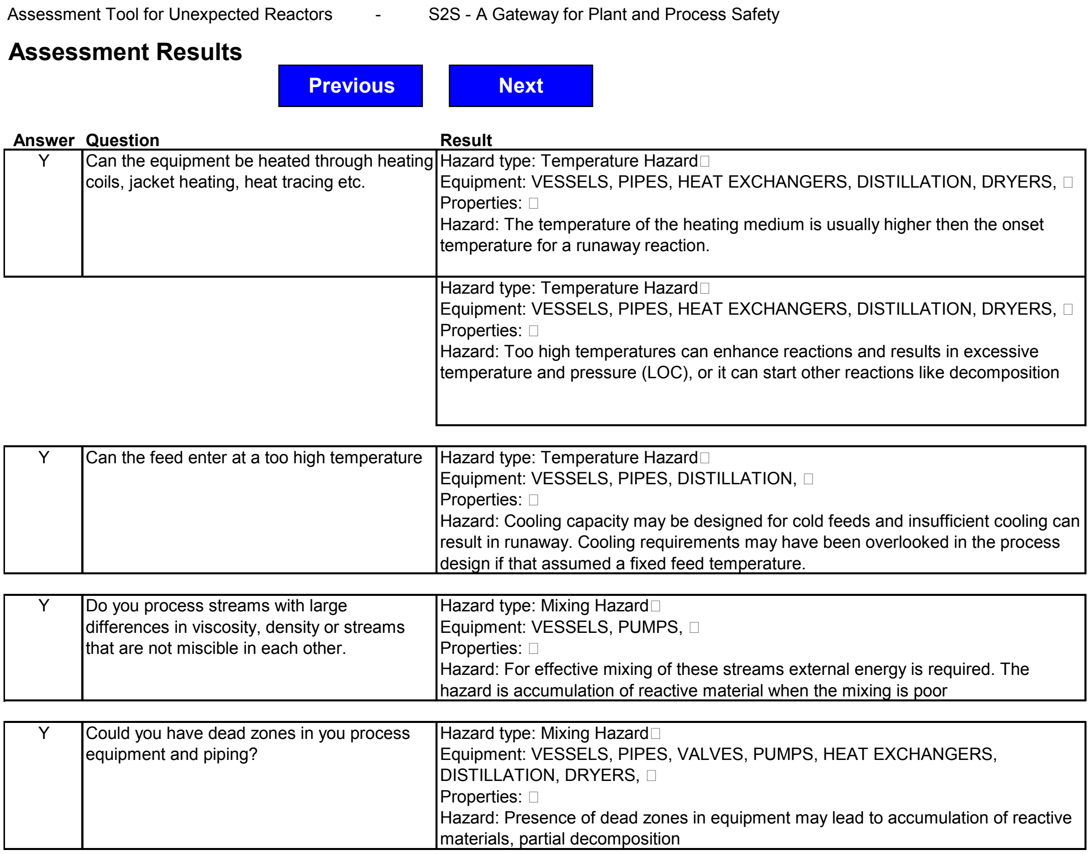
Assessment Tool for Unexpected Reactors - S2S - A Gateway for Plant and Process Safety

Questions for selected Equipment and Process

y/n	Question
n	Are parts of the plant exposed to direct sunlight or to nearby heat sources (heaters, motors)
y	Can the equipment be heated through heating coils, jacket heating, heat tracing etc.
n	Does the equipment need external cooling to prevent an unintended reaction
n	Does the equipment have a stirrer or agitator (either mechanical or flow based, like jet/vortex mixers)
y	Can the feed enter at a too high temperature
n	Do you use a vacuum to evaporate a product, reactant or solvent?
n	Do you use a low boiling solvent or reactant excess to reduce the reaction hazard
y	Do you process streams with large differences in viscosity, density or streams that are not miscible in each other.
n	Do you use high surface area solids like glasswool piping insulation, filter aids or adsorption materials in driers
n	Do you use a washing or "polishing'" step to remove unwanted byproducts or unreacted material?
n	Do you have a phase separation (Vapour/Liquid, Liquid/Liquid, Solid/Liquid etc) to remove a catalyst or reactant from the reaction mixture.
n	Do you process incompatible materials with just a single barrier againt unintended mixing?
n	Do you have different materials of construction in your process because of incompatibilities between process and equipment materials (e.g. corrosivity).
y	Could you have dead zones in you process equipment and piping?
n	Do you operate a batch or semi-batch process with a long waiting time between batches?
n	Is the reaction residence time or space velocity important to control the extent of the reaction?
n	Can the failure of a single pump or valve result in a flow reversal / change in the pressure difference. Are there large pressure differences in the process
n	Do you use or produce water sensitive substances

Figure 2.15. - Decisive Questions generated for a limited number of inputs selected by the user.

This list is shorter than the one shown in Figure 2.14 since the system has eliminated some of the questions considered as not relevant depending on the inputs selected by the user. Now, let us assume that, after carefully considering the questions put forward, the user has decided that the only questions that truly concern the situation at his / her plant are the possibility of heating through coils, a too high temperature of feeds, differences in viscosity and the presence of dead zones, as shown in the selection column in Figure 2.15. In this case, the result of the assessment would be given as shown in Figure 2.16.



Assessment Tool for Unexpected Reactors - S2S - A Gateway for Plant and Process Safety

Assessment Results

Answer	Question	Result
Y	Can the equipment be heated through heating coils, jacket heating, heat tracing etc.	Hazard type: Temperature Hazard□ Equipment: VESSELS, PIPES, HEAT EXCHANGERS, DISTILLATION, DRYERS, □ Properties: □ Hazard: The temperature of the heating medium is usually higher then the onset temperature for a runaway reaction.
		Hazard type: Temperature Hazard□ Equipment: VESSELS, PIPES, HEAT EXCHANGERS, DISTILLATION, DRYERS, □ Properties: □ Hazard: Too high temperatures can enhance reactions and results in excessive temperature and pressure (LOC), or it can start other reactions like decomposition
Y	Can the feed enter at a too high temperature	Hazard type: Temperature Hazard□ Equipment: VESSELS, PIPES, DISTILLATION, □ Properties: □ Hazard: Cooling capacity may be designed for cold feeds and insufficient cooling can result in runaway. Cooling requirements may have been overlooked in the process design if that assumed a fixed feed temperature.
Y	Do you process streams with large differences in viscosity, density or streams that are not miscible in each other.	Hazard type: Mixing Hazard□ Equipment: VESSELS, PUMPS, □ Properties: □ Hazard: For effective mixing of these streams external energy is required. The hazard is accumulation of reactive material when the mixing is poor
Y	Could you have dead zones in you process equipment and piping?	Hazard type: Mixing Hazard□ Equipment: VESSELS, PIPES, VALVES, PUMPS, HEAT EXCHANGERS, DISTILLATION, DRYERS, □ Properties: □ Hazard: Presence of dead zones in equipment may lead to accumulation of reactive materials, partial decomposition

Figure 2.16. - Results of the assessment generated for a limited number of inputs selected by the user.

As it can be seen in Figure 2.16, the results to the questions considered include descriptions of what the hazard related to the specific question would be, and the equipment that may be related to such a hazard.

The database can be customized to change the language of the assessment and to change the knowledge database (modify or extend equipment, process properties, mechanisms and so on). The Excel® sheet can be switched between a protected runtime (=user) mode and an unprotected maintenance mode. The switch is possible with two buttons that are located two pages down on the start screen. After the modifications, the Excel® sheet can be saved under a new name.

The language of the tool can be changed by replacing the English texts in the Excel® tables. Furthermore, a new Assessment Case can be defined for a new potential reactive hazard. The user must provide definitions for new elements to be included in the tables, along with their relevant combinations for the new cases. This is done by completing the 2 matrices that define the equipment and process properties for which the mechanism is valid: in the Equipment-Mechanism matrix, all Equipment that can exhibit the mechanism is defined by a 1; in the Property-Mechanism matrix, all Process Properties that are essential to exhibit the mechanism are defined by a 1. Table 2.5 shows the required information for each of the elements of a new Assessment Case.

Assessment Element	Information Required
Equipment	A short (2 words maximum) description of the type, plus a help sentence explaining details of the equipment where confusion might exist.
Process type	A short (2 words maximum) description of the type, plus a help sentence clarifying details of the Process, plus a multi-character abbreviation identification
Mechanism	A paragraph explaining how external causes, equipment failure or equipment side effects can cause a movement in the reaction triangle and hence pose a hazard, plus a mechanism type number indicating the type of movement done in the reaction triangle, plus a Decisive Question number that needs to be answered affirmative in order to make the hazard relevant.
Decisive Question	A question that can be answered by yes or no and, if answered positively, displays to the user the mechanism of the hazard.

Table 2.5. - Summary of necessary information to create a new Assessment Case.

When developing an Assessment Case, an effort should be made to identify all equipment that could have a similar mechanism and reconsider modification of Mechanism & Decisive Questions in order to combine them in a more general mechanism. The advantage of fewer mechanisms is fewer questions for the same number of equipment-mechanisms. The disadvantage of too little general mechanisms is that the abstraction level increases and that the hazards may become too general.

2.2.4.- Development and validation of HarsMeth NP

At this point of the development of the HarsMeth methodology, the strategy followed so far was deeply analysed. It has become clear that testing HarsMeth at different SMEs is a very useful system to identify a great number of possible hazardous sources at establishments working with fine chemicals production. The possibility given to some companies to work during several months with the tool has helped them to improve the knowledge of safety issues of their engineers and operators, and indeed the improvements in the checklists developed are currently being used by both the companies C1 and C2 for the hazard assessment of their processes, which also leads to an improvement of their safety procedures. Moreover, it has been proved that it is relatively easy for any company to extend the methodology with any particular issue relevant to that company by adding more questions, using the philosophy of completion of the checklists included in HarsMeth v2.

However, implementing all the suggestions given by these companies into further versions of HarsMeth also presents some drawbacks. Clearly those companies become experts in the use of HarsMeth after a long period of time working with it, so it is relatively easy for them to understand why the different changes are introduced. It must be kept in mind that the objective is to obtain a methodology that is easy to use by all the SMEs working in chemical production. As it has been mentioned, developing the methodology with the results obtained at one company may limit the hazard identification to those items that are particularly critical to the processes developed at that company. Besides, the questions proposed are usually put forward in a way that fits better the internal working procedures of the company introducing such questions.

Different suggestions have been described so far in order to expand the methodology with further questions, checklists and so on, to an extent in which it is possible to redefine the objective of developing a tool for a preliminary hazard assessment, to create a system that gives the possibility to perform, if not a complete safety analysis, at least a well structured procedure to identify the main chemical reactive hazards of a process at each stage of the development of the process. In order to achieve this goal, it is clear that a new structure is required, so that the methodology can be applied at any SME, and not only to those that are already familiar with HarsMeth.

2.2.4.1.- Development of the structure of HarsMeth NP

The structure of the checklists included in HarsMeth v2 combined the identification of hazards with the suggestion of possible safety measures, so the questions were rather extensive. They can be appropriate for a small number of issues, but as the methodology grows it can become tedious and confusing since the questions occupy a lot of space. So the intention at this point was to separate the hazard identification from the suggestion of possible actions to deal with the hazards, which enables the user to perform the analysis at different stages of the process, so the necessary safety measures will be pointed out as a consequence of the hazards identified, stressing only those measures that are really necessary. On the other hand, it is also necessary to include guidance on how to obtain some of the data required in the methodology, since this is a point that has often been required by the SMEs working with HarsMeth.

The distribution of questions in checklists considering engineering, design or practice of the process as shown in Figure 2.5 (*cfr.* page 58), turned to be somehow confusing, as sometimes it became difficult to decide under which section a specific question should be included, especially since a high number of questions were suggested after testing the tool at different SMEs. Even though the information and the questions in the tool were considered useful, it became necessary to rearrange the information included in HarsMeth v2.

There are different approaches that can be followed to perform a hazard assessment of chemical processes. However, there are some concepts that should always be present in a reliable decision making tool (Steinbach, 1999). These concepts are:

- Definition of process and plant characteristics.
- Identification of hazards at normal operating conditions.
- Identification of possible process deviations and hazards associated to them.
- Evaluation of plant conditions in order to carry out the process within safety margins (related to the hazards previously identified).
- Determination of necessity to modify process or plant conditions.

Besides, it must be a company policy to register the results, to keep these results available for engineers or operators who carry out the process, and to review this procedure from time to time, or whenever a significant change is introduced in the process or in the plant. A good example of the strategy to follow is the PHASE method (Steinbach, 1999), shown in Figure 2.17.

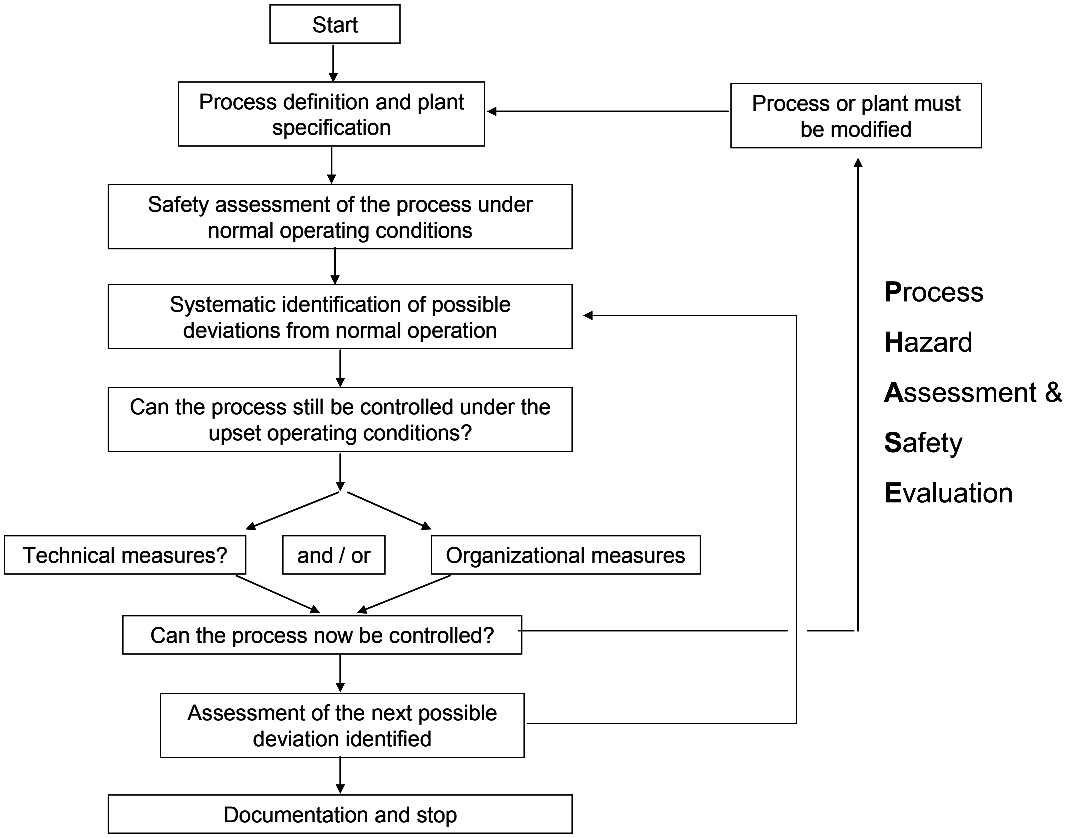


Figure 2.17. - Procedure for process safety evaluation.

Such concepts have been implemented in the HarsMeth methodology in an attempt to cover the different stages in the development of a process, generating a new version of the tool called HarsMeth NP (Nomen *et al*., 2007), and it can be found in Appendix 1. NP stands for New Process, stressing the idea that a good hazard assessment should start at the earliest stages of Research & Development, covering different aspects as the industrial process is developed. The structure and main information included in this new version is shown in Figure 2.18.

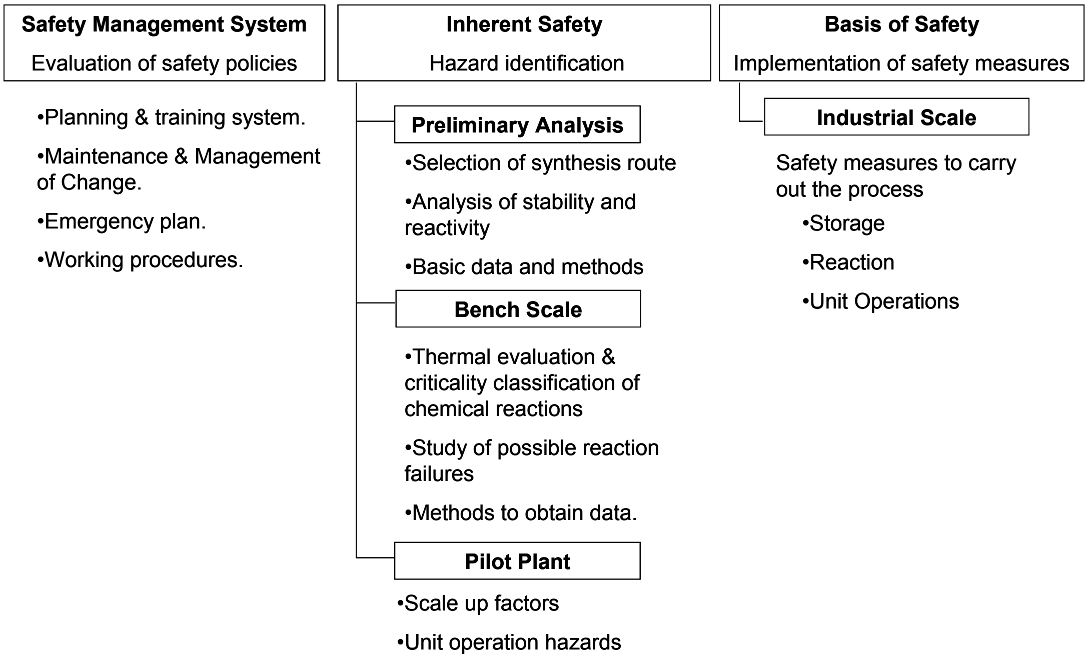


Figure 2.18. - Structure of HarsMeth NP.

HarsMeth NP is based in three concepts:

- Inherent Safety. A system is considered to be inherently safe if it remains in a non-hazardous situation after the occurrence of unintended deviations from normal operating conditions (Kletz, 1985). Even though it is impossible to achieve a 100% inherently safe process, the intention is to determine all the possible sources of hazards from the safety point of view previously to the plant development of the process. In order to achieve an inherently safe process, the main need is to be able to perform thorough hazard identification. To achieve this, the process is analysed at three different stages.

    - *Preliminary stage.* All the different possible synthetic routes for a reaction are studied, and different screening tests are performed to have a general idea of the hazards of each route.
    - *Bench scale stage.* A reduced number of possible synthetic paths can be studied here. Each one of them has to be deeply studied, considering normal and all kind of possible failure conditions.

    - *Pilot Plant Scale.* One single process should be studied here. Emphasis must be placed on correctly dimensioning the equipment to be used at industrial scale. Hazard assessment of unit operations that are going to be used in plant should be performed here.

- Basis of Safety. It includes the implementation of preventive or mitigation measures, besides process control requirements, that a process needs to be carried out safely. For each process, they will depend on the hazards defined in the previous section. In case those hazards cannot be completely removed, measures must be included at the industrial production stage to ensure the reduction of likelihood or effects in case an incident occurs.

- Safety Management System. Differentiated from the previous points, it is independent of the chemical process to be developed. It deals with the safety policies of the company, with a special focus on how routine operations are carried out at the chemical plant. The objective is to differentiate the inherent safety, or better said, the inherent hazards related to the chemistry itself, and the added on hazards that can come from incorrect working procedures or company organization, since a hazard will be easier to keep under control if its origin is correctly understood.

The hazard identification is performed through a set of checklists that cover all the aspects that may have an influence in the safety of a chemical process. It is intended that, by answering those questions, all the possible hazards that may arise from a process developed at industrial scale can be determined. There are 5 checklists included in HarsMeth NP, one for each section included in the methodology. It is suggested that those checklists should be filled in the following order:

1. Safety Management System.
2. Preliminary Reaction Analysis.
3. Bench Scale Analysis.
4. Pilot Plant Analysis.
5. Industrial Scale Analysis.

While checklists number 1 and 5 are simply an inventory of suggested issues, which the user must indicate whether they have been considered or not, the questions in the checklists 2, 3, and 4 are structured in such a way, that only three levels of answers are available, following the same system that was developed in HarsMeth v2 (*cfr.* page 62), including the possibility to provide a comment to support the answer. Any question that leads to a “Review your Safety Measures” type of reply in any of those checklists will have a corresponding evaluation in the Industrial Scale checklist, proposing measures to avoid the hazard or to mitigate the consequences of any incident derived from such hazard. All the information contained in these checklists is derived from the contents included in the previous versions of the methodology. Next, those sections are explained further.

Safety Management System

This section has not been excessively modified from the different revisions of HarsMeth. Basically it contains a selected list of items that a chemical company should check in order to avoid chemical accidents generated by a deficient Safety Management System. The information contained is distributed in the following sections.

- Planning & Safety training
- Maintenance & Management of change
- Emergency plan
- Operational Practice System

The Operational Practice System section corresponds mainly to the Good Process Practice checklist included in HarsMeth v2. This section refers to common routine operations performed during chemical processes that can trigger a hazard, which are more related to management issues than to the hazardous nature of chemical substances or reactions (e.g. systems to ensure that the appropriate chemicals are selected, details of working procedures and permits, and so on).

Even though HarsMeth NP is considered a technical guide for hazard assessment, it is clear that some basic management requirements should be met from the safety point of view. While the issues included in HarsMeth NP are considered a minimum safety provision, a more complete safety management assessment tool has been developed by the S2S network, which can be found at the S2S website (S2S, 2007). HarsMeth NP strongly suggests the use of this tool for a more complete assessment of the Safety Management System of a chemical company.

Preliminary Reaction Analysis

It should be considered that the safety analysis of a chemical process must begin at the earliest stage of the development of the process. At this stage, different paths to obtain a desired product could be put forward, where different combinations of reactants, solvents, catalysts, products and by-products can be involved. It is usually unavailable to perform a rigorous safety study on every single combination. Furthermore, other parameters different from safety can be of importance in the election, such as cost, yield, quality or environmental policies. Nevertheless, an orientation on the possible hazards to each possible synthesis path must be given in order to take a decision on the choice of a chemical route. Basically, the information to be given for each combination of reactants is divided in two groups.

- Chemical stability of reactants and products.
- Reactivity and Compatibility of chemicals.

This section contains some of the data tables included in the Good Basic Data section of HarsMeth v2, as well as a checklist to identify specifically hazardous properties of substances and mixtures such as flammability, shock sensitivity and dangerous incompatibilities. Different available techniques (both theoretical and experimental) that can help to determine every single parameter required are described, focusing on those that are considered to be reasonably simple and not excessively costly. Among these techniques are included:

- Different literature surveys and available safety indexes.
- Theoretical methods for determination of formation enthalpies by use of Benson groups, as will be described later (*cfr*. page 148).
- Experimental techniques such as Dewar calorimetry and DSC.
- Chemical compatibility tables and available software.

General descriptions on how and when to use these techniques are also provided, as well as further references in order to obtain more information.

Bench Scale Analysis

The Bench Scale Analysis section introduces the user of HarsMeth NP into the basics of thermal evaluation of chemical reactions. A brief explanation of the theory of runaway reactions is provided, together with a description of some of the most common hazards related to chemical processes, such as accumulation, segregated phases or formation of hot spots in the reaction mixture, and the failures that can generate such hazards (e.g. loss of cooling power or excessive dosing speed). This section includes also descriptions of the Gygax and Stoessel diagrams, as well as the parameters required in each one of those tools, with descriptions of the main techniques available in order to obtain those parameters, which are reaction calorimetry and adiabatic calorimetry (DSC is already presented in the previous section). Since the use of adiabatic calorimetry is rarely available in most SMEs, alternatives to the use of this analysis have to be provided. For this reason, the procedure for the calculation of MaxTsafe previously described (*cfr.* page 60) is also given.

This section includes some of the tables provided in the Good Basic Data section from HarsMeth v2, as well as some checklists to identify the critical parameters from the safety point of view of a chemical reaction, such as dosing system, agitation, temperature control and so on. Finally, further references to obtain more information on the topics covered are also provided.

Pilot Plant Analysis

This section was not considered in previous versions of HarsMeth, but it was thought to be necessary during the testing phase of the methodology. Indeed there are different hazards associated with changing of scale procedures during the development of chemical processes that must be taken into account. Some explanations of those hazards, related to topics like mass transfer, heat transfer, momentum transfer and kinetics are provided, together with a checklist to identify those hazards.

Furthermore, the Decisive Questions developed for the S2S training and assessment tool for unexpected reactors (*cfr*. page 84) have been implemented in a HarsMeth NP checklist as the strategy to follow in order to identify hazards related to unexpected chemical behaviour during unit operations in chemical processes. The knowledge developed during the testing of HarsMeth at the companies C1 and C2 has also been used. Descriptions of each of the questions put forward in this checklist are also provided in order to help the user to understand the scenarios that should be identified in this section.

Industrial Scale Analysis

The last section included in HarsMeth NP aims to determine the basis of safety required to perform the chemical process safely at an industrial scale. This section describes commonly available alternatives to control any possible failure in the process, according to the hazards identified in the previous sections of HarsMeth NP. Simple suggestions are given, since the idea is still that the user should come up with the best solution for the process, seeking further advice if necessary. Topics like time factor or systems to stop reaction (e.g. quenching or the use of inhibitors) and process control systems (e.g. interlocks between reactor equipment) as well as pressure relief systems are described. Nevertheless, the objective should always be to avoid hazards as much as possible rather than providing numerous safety measures at this stage, as it is stressed in the methodology.

This section includes a checklist which contains a selection of items that should be considered in case a specific hazard is identified. The checklist is divided into the following topics:

- Stability and compatibility
- Reaction
- Unit operations
- Process and plant design

The stability and compatibility section in this checklist should be considered for the whole plant, but especially in the storage area where there is supposed to be a limited handling of the chemical substances. The process and plant design section contains very basic requirements from the point of view of engineering design. Clearly it will be difficult to run a process under safety conditions unless specific quality standards in process and plant design are met. However, it must be stressed that these considerations fall out of the scope of the methodology, as so does the identification of other type of hazards that should always be taken into consideration when running a chemical process, such as dust explosions or toxic effects.

The result of the new structure introduced in HarsMeth NP is a better organized system to follow a process from the R&D stage until the implementation in plant scale, even though it can also be applied to already existing processes. The method includes simpler questions, better targeted to identify the specific hazards at the correct moment, keeping only track of those that are really related to the process, which allows the user to come up with specific safety measures appropriate for the hazards identified. When applying HarsMeth NP to a process, the user should not move to another checklist until all the aspects required in the previous one have been filled correctly and fully understood. This means that in case the answer to one question is unknown, it should be checked before going any further. This way, it is assured that the process development is stopped at the earlier stages, instead of carrying it on industrial scale with uncertainties in the safety issues involved. Moreover, it is advised that the user should seek further information before actually performing any experimental test based on the information included in HarsMeth NP.

2.2.4.2.- Application of HarsMeth NP to the hazard analysis of a chemical process

In order to test the efficiency of HarsMeth NP, the tool has been used to analyse the hazards of a real process tested in the laboratory for its implementation at industrial scale (Nomen *et al.*, 2007). The process chosen is the production of macrocyclic peroxides from catalytical oxidation of cyclohexanone with hydrogen peroxide as seen in Figure 2.19. This reaction is the first step in the production of macrocyclic lactones, and it should be followed by decomposition (thermal or photochemical) of the obtained peroxides to yield the desired final product.

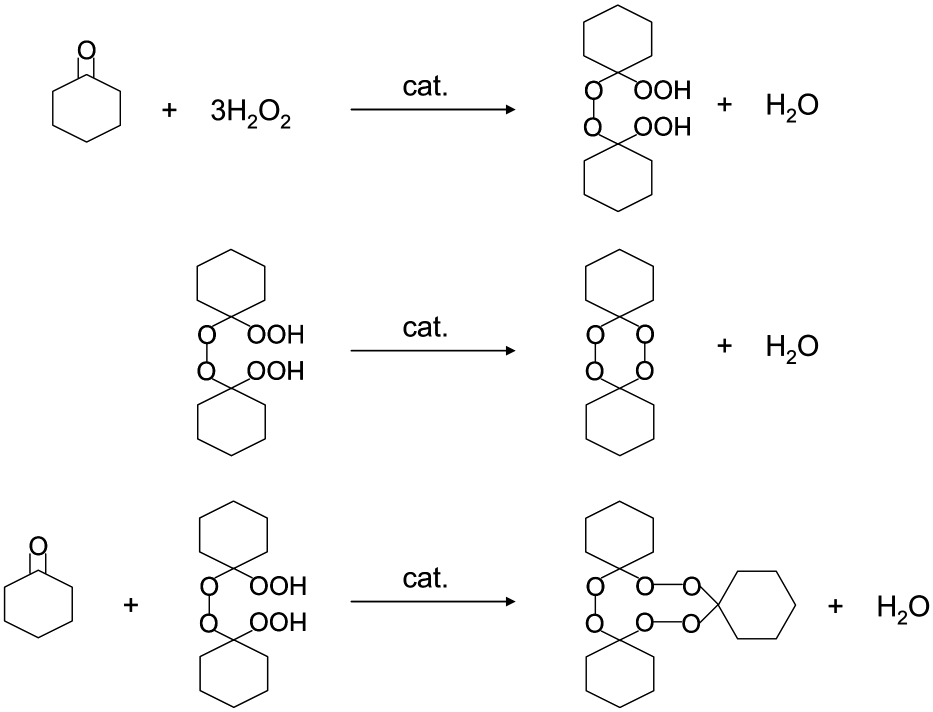


Figure 2.19. - Reaction scheme for the oxidation of cyclohexanone by hydrogen peroxide to obtain cyclohexanone diperoxide or triperoxide.

In the past, this reaction was performed using perchloric acid as a catalyst (Story *et al.*, 1968), which is strongly toxic and hazardous. More recent research on the synthesis (Avilés, 2004) has replaced it by a safer substance, the phosphotungstic acid hydrate. Moreover, the hydrogen peroxide concentration has been reduced to 35% in comparison to 90% proposed by previous authors (Sanderson, *et al.*, 1975).

The reaction conditions were roughly optimised concerning reaction temperature, reaction time, molar relation of the reactants and amount of catalyst.

Preliminary Safety Analysis

The first step when applying HarsMeth NP would be to complete the Safety Management System section. However, in this case this checklist is left out of the analysis since it is more related to company issues and falls out of the scientific scope of the study of the chemical reaction itself. Therefore, the analysis begins with the preliminary evaluation of different synthesis paths proposed to obtain the desired product (Avilés, 2004). All the synthesis routes studied are based on the reaction between cyclohexanone and hydrogen peroxide with the following specifications:

1. Hydrogen peroxide 90% and perchloric acid as catalyser.
2. Hydrogen peroxide 35% and sulphuric acid as catalyser.
3. Hydrogen peroxide 35% and phosphotungstic acid hydrate as catalyser.

For each possible synthesis route, reactants must be analysed and a table with their main characteristics must be filled in. Table 2.6 shows a summary of those tables. Next, for each one of the substances shown in Table 2.6, a checklist is filled in order to identify possible stability hazards. This checklist must be filled with the help either of bibliographic references (material safety data sheets, handbooks, reliable indexes, and so on) as suggested in the methodology. Table 2.7 summarizes the results obtained for all the substances involved in the three possible synthesis paths studied.

Substances and mixtures	Chemical composition	CAS num.	Purity	Phase			Handling conditions	Thermal activity at Tstorage
				G	L	S		
Cyclohexanone (CYC)	$C_6H_{10}O$	108-94-1	-		X		Reacts with oxidants	Stored in cooled facilities; flash point=43 °C
Hydrogen peroxide	H_2O_2	7722-84-1	90% / 35%		X		Decomposes dramatically on warming; avoid contact with metals dust and alkaline	To be stored tightly closed in a well-ventilated place below 25 °C
Sulphuric acid	H_2SO_4	7664-93-9	-		X		Reacts with moisture, water and metals	Stable
Perchloric acid	$HClO_4$	7601-90-3	-		X		Reacts with wide variety of substances	Stable
Phosphotungstic acid hydrate (PAH)	$HPW_{12}O_{40}*nH_2O$	12501-23-4	-			X	Toxic, non flammable, corrosive	No thermal decomposition reported in references over 1000 °C

Table 2.6. - Summary of the information required for each substance at the Preliminary Reaction Analysis section of HarsMeth NP.

Is any of the substances considered to be potentially as:	CYC	H_2O_2	$HClO_4$	H_2SO_4	PAH
Susceptible of decomposition with time	NO	NO	NO	NO	NO
Thermally unstable	YES	YES	NO	NO	NO
Self reacting / autocatalytic / polymerizing	NO	NO	NO	NO	NO
Water reactive	NO	NO	YES	YES	NO
Oxidizer	NO	YES	YES	YES	NO
Reducer	YES	NO	NO	NO	NO
Flammable	YES	NO	NO	NO	NO
Corrosive	NO	YES	YES	YES	YES
Pyrophoric	NO	NO	NO	NO	NO
Shock sensitive	NO	NO	NO	NO	NO
Explosive	YES	YES	NO	NO	NO
Toxic	YES	YES	YES	YES	YES

Table 2.7. - Compilation of the possible hazards associated to the different chemical substances involved in the different synthesis paths.

Some of the answers in Table 2.7 may be dependant on the environment and conditions at which each substance may be used or stored. For this reason, it is important to write a justification in the space provided for each question. For instance, it is reported by Avilés (2004) that, since it contains a large number of water molecules of crystallisation (up to 29), phosphotungstic acid dehydrates 23 molecules of water around 100 ºC and the remaining 6 around 200 ºC, but without thermal decomposition reported up to 1000ºC.

The following step is to analyse the compatibility between the different combinations of chemicals for each synthesis route. Another checklist is provided in HarsMeth NP for this objective, asking whether the combination of two substances may pose a hazard, related to the possible generation of heat, fire or hazardous substances. A chemical compatibility chart based on the risk of combining different functional groups is appended in the methodology as a help for the user, but other available methods are also indicated.

It is stressed in the methodology that other materials different from the listed chemical substances should be included in the compatibility analyses. HarsMeth NP advices to include water and iron (as the most common construction material), but the user should include any other auxiliary materials (oils, cooling fluids) if it is considered that they may pose a hazard if they come in touch with chemical reactants.

The main conclusions from the compatibility analysis for the three synthesis paths are:

- Cyclohexanone and hydrogen peroxide are likely to react with violence generating heat (including also the effects of the desired reaction), fire or even explosion hazards.
- Hydrogen peroxide will react with water, metals and organic substances. The liberation of oxygen during the decomposition reaction will increase the explosive range of possible unexpected reactions.
- Sulphuric acid is also likely to react with water, most common metals and organic materials, releasing hydrogen and increasing flammability and explosion hazards.

- Perchloric acid is incompatible with a wide variety of substances, including both organic and inorganic. Its reaction with wood, paper and other cellulose products may lead to explosion.
- Phosphotungstic acid hydrate is a less reactive substance. It may generate a reactive hazard if exposed to strong bases, alkali or other more active metals, metal oxides and strong reducing agents.

Finally, a comparison of the hazards identified for the three synthesis paths must be given in order to select one of them for a deeper hazard analysis. This comparison can be seen in Table 2.8.

Chemical synthesis path ID	**Stability and reactivity hazards**	**Other aspects**
1 H_2O_2 90%; $HClO_4$	Hazardous catalyst and concentration of H_2O_2	Low selectivity & yield
2 H_2O_2 35% H_2SO_4	Lower H_2O_2 concentration, less hazardous catalyser	Low selectivity & yield
3 H_2O_2 35% PAH	Lower H_2O_2 concentration, less hazardous catalyst	Improved selectivity & yield

Table 2.8. - Summary of the hazards identified for the three synthesis paths studied.

It must be stated that at this stage of the analysis, other parameters different from safety issues may be considered in the final decision as to which should be the synthesis route chosen. A chemical path that provides poor results in yield will not be interesting from an industrial point of view. In any case it is clear that, given similar results in yield, the safer option should always be preferred. Previous works with this synthesis (Avilés, 2004) have compared the results of the three synthesis paths, showing that the use of phosphotungstic acid hydrate is safer because of the lower concentration of peroxide and the characteristics of the catalyst, and it also gives better results regarding selectivity and yield. Therefore, it is the route selected to continue the analysis with HarsMeth NP.

It has been demonstrated (Avilés, 2004) that the reaction generates the best yield results when it is performed using 0.05 g of phosphotungstic acid per gram of cyclohexanone as catalyst and 35% hydrogen peroxide as the oxidising agent in 10% excess, temperature 65 ºC and 2 hours of reaction, with molar cyclohexanone / hydrogen peroxide relation of 0.9. The reaction is performed in semi-batch mode, dosing the H_2O_2 on a reactor containing cyclohexanone and phosphotungstic acid in stoichiometric quantities.

A safety study of the reaction conditions and their possible variations in case of a loss of control of the process has also been performed (Avilés, 2004). This study has been done by means of different experiments involving reaction calorimetry and differential scanning calorimetry techniques, and it intends to determine the necessary safety measures or precautions that would be required to prevent or mitigate a runaway scenario if the reaction has to be performed safely at an industrial scale. The main results from the experiments performed are given in Tables 2.9 and 2.10 (Avilés, 2004).

Step description	**Quantity of heat released / $J*g^{-1}$**	**Heat release rate / $W*kg^{-1}$**	**Quantity of gas generated / L per g H_2O_2**	**Gas generation rate / $L*h^{-1}$ per g H_2O_2**
Dosing of H_2O_2	969.2	264.3	$0.12*10^{-3}$	$83.6*10^{-3}$

Table 2.9. - Values for heat and gas generation for the synthesis studied.

Process T / °C	**Heat of reaction / $J*g^{-1}$**	**Specific heat / $J*kg^{-1}*K^{-1}$ (3)**	**Adiabatic T rise / °C**	**MTSR / °C**	**Boiling T / °C**	**MaxTsafe / °C**	**TMR / min**
65	969.2	2000	215	280	116	70	19

Table 2.10. - Thermal values for the assessment of a possible runaway scenario for the synthesis studied.

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[3] The specific heat of the mixture changes during the reaction from a value of 1961 $J*(kg*K)^{-1}$ to 3335 $J*(kg*K)^{-1}$. For this reason, a conservative value of 2000 $J*(kg*K)^{-1}$ has been applied for calculations.

In order to better illustrate the results given in Table 2.10, it is interesting to view the Gygax diagram corresponding to this reaction, which is shown in Figure 2.20. According to these results, the reaction analysed would be classified as level 5 in the Stoessel scale. This is considered the worst possible scenario because, in case of a loss of control in the reactor during normal operation (T=65 ^{o}C), the temperature evolution in the reactor will reach the MaxTsafe value before MTSR or Tb, hence leading to a runaway. This is represented in Figure 2.20 by the continuous line starting at 70 ^{o}C, generating an uncontrolled temperature increase, as opposed to the, in principle, safer evolution of the temperature leading to MTSR, represented by the discontinuous line, which will not happen under this situation. This scenario will initiate the decomposition of the reaction mass, which would eventually lead to an overpressure in the reactor.

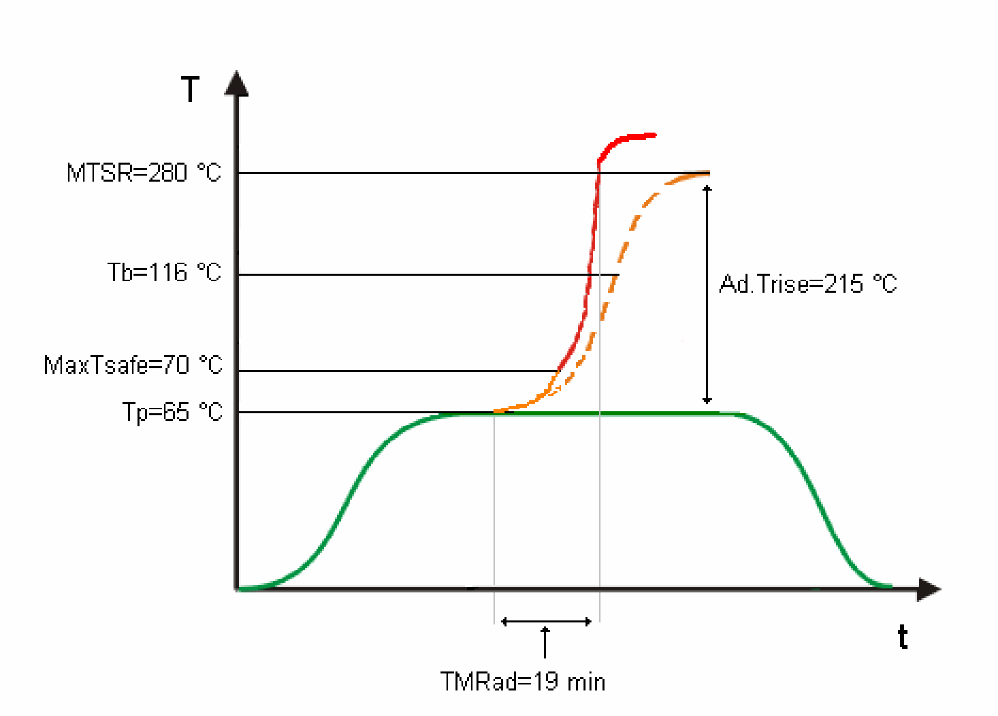

Figure 2.20. - Cooling failure scenario diagram for the reaction analysed.

Another parameter that gives an indication of how inherently safe or unsafe is a reaction, is the Time to Maximum Rate (TMR). This value refers to the time that the decomposition reactions will need under adiabatic conditions to reach a maximum temperature value. As it can be seen in Table 2.10, the value of TMR for the reaction

The analysis of the experimental values shown before already indicates that the reaction will be inherently unsafe. The first suggestion would be to modify process conditions. However, it has been seen previously that there are no other alternatives that allow the reaction to be performed safely in a profitable industrial process (at least in a discontinuous mode), so specific safety measures will have to be provided. Next, the different process conditions required to perform the chemical reaction (temperature, dosing, agitation and so on) are analysed to determine which one will require special attention in the industrial implementation of the process. Table 2.11 shows the checklist used in HarsMeth NP for this analysis and the answers for the studied reaction.

Can variations in the following parameters affect the normal evolution of the process?	
Process temperature / cooling failure?	YES; Safety measures or control systems will be required for this parameter
Catalyst concentration?	YES; Safety measures or control systems will be required for this parameter
Solvent concentration?	NO; No solvent is required for the reaction
Reactants concentration?	YES; Safety measures or control systems will be required for this parameter
pH?	YES; Safety measures or control systems will be required for this parameter
Reaction time / delayed reaction start?	YES; Safety measures or control systems will be required for this parameter
Dosing rate / dosing failure (including wrong order of addition)?	YES; Safety measures or control systems will be required for this parameter
Agitation speed / agitation failure?	YES; Safety measures or control systems will be required for this parameter
Contamination of reactants?	YES; Safety measures or control systems will be required for this parameter

Table 2.11- Analysis of the possible critical parameters for the synthesis studied.

As it can be seen, all the parameters considered in the methodology are regarded as potentially hazardous (except the solvent concentration). This is obviously related to the criticality level determined for the reaction as it has been previously stated.

HarsMeth NP requires at this point a description of the items identified as critical in the previous checklist. These descriptions are provided in Table 2.12.

Critical parameter	Comments
Temperature	If reactants are mixed at a too low temperature, the reaction rate might be very small, generating accumulation. If afterwards the reaction mixture is heated up to the reaction temperature the accumulated reactants might react very fast and lead to a runaway.
Temperature	If the cooling system fails, the heat of the primary reaction and the decomposition reactions cannot be removed properly. This will cause a high and possibly fast temperature increase, which might lead to a runaway.
Delayed start	Any unexpected delay in the reaction start may lead to the accumulation of reactants, which could result in a faster than expected exothermic process when the reaction starts.
Dosing	If the rate of addition compared with the rate of reaction is too high, quantities of the reactants can accumulate. The reaction can lead to a runaway like a batch reaction.
Agitation	If mass transfer is too slow, e.g. because of failure of the agitator in a semi-continuous process, an accumulation of reactants is possible. If the mass transfer is intensified later, e.g. by switching on the stirrer again, the accumulated substances can perform a fast reaction of the type of a thermal explosion.
Concentration	If the concentrations of the chemicals change significantly (e.g. concentration of hydrogen peroxide), the decomposition process might be much faster than found in the reactions so far evaluated. This might lead to a fast temperature rise, which can also lead to a runaway of the reaction.
Contamination / pH / catalyst concentration	The decomposition of hydrogen peroxide is strongly dependent on the presence of catalysts and on pH, so the variation of any of these will probably trigger a runaway. Contamination of hydrogen peroxide also contributes to a more rapid decomposition. Specifically the presence of metals and alkalis should be avoided.

Table 2.12. - Summary of the different critical parameters identified for the studied synthesis.

Once the critical parameters and main hazards for the process have been identified, the necessary safety measures must be put in place. Since HarsMeth NP is designed as a hazard assessment tool for any chemical process, it can only provide basic general guidance on appropriate safety measures for the identified hazards. The final decision on what specific solutions should be taken is left in the hands of the engineers and operators of the process, since they know better what the specific process conditions and resources of their company really are. In any case, the advice of a safety expert should be considered whenever necessary.

Following the analysis detailed previously, the main actions to be taken have to be selected by the person or persons using HarsMeth NP. Tables 2.13 and 2.14 show a summary of the main recommendations given by the methodology depending on the hazards identified in the Preliminary Reaction Analysis section and in the Bench Scale Analysis section respectively. It must be stressed once again that the reaction has been categorized as very hazardous, so the following measures have to be totally reliable.

Make sure that chemicals are stored and handled under compatibility criteria
Make sure to establish effective and easy to follow storing and labelling rules
Introduce measures to monitor and control the conditions of any parameter identified as critical (T, P, pH, concentration, physical characteristics of product…)
Introduce measures to detect long periods of storage (periodic sample analysis)
Avoid possible ignition sources
Avoid possible oxidant atmospheres (use of inert gases)
Introduce fire detection systems
Introduce fire protective systems
Introduce toxicity protective systems
Provide pressure relief systems for vessels
Consider the possibility of two-phase flow when designing relief systems

Table 2.13. - Safety measures recommended by HarsMeth NP related to the hazards identified in the Preliminary Reaction Analysis.

Make sure that cooling system is started before starting addition of reactants
Make sure that stirring system is started before starting addition of reactants
Introduce measures to ensure correct charging operations (appropriate chemicals, quantities, order…)
Introduce measures to follow state of product for any parameter identified as critical (T, P, viscosity, pH, concentration, physical characteristics of product…)
Prepare a dumping system in order to stop the reaction in case of a runaway
Prepare solvent for quenching (consider volume requirements for reactor) in case of a runaway
Include interlock between temperature measurement and quenching and / or dumping vessel valve
Include interlock between dosing valve and cooling system to stop dosing in case of cooling failure
Include interlock between temperature measurement and dosing valve in order to stop dosing in case of temperature value increases unexpectedly
Include interlock between temperature measurement and cooling system in order to increase cooling power if temperature value increases unexpectedly (example break of dosing valve).
Include interlock between stirring failure and dosing valve in order to stop dosing in case of loss of agitation
Improve agitation systems to avoid possible dead zones in vessels where reactants can accumulate
Include multiple temperature measurements in order to detect non homogeneous distributions of temperature
Include systems to restart agitation safely (speed control) in case of loss of agitation
Include multiple temperature measurements in order to detect non homogeneous distributions of temperature
Include a pressure relief system (bursting disk, relief valve, depressurisation, containment…)
Consider the possibility of two-phase flow when designing relief systems

Table 2.14. - Safety measures recommended by HarsMeth NP related to the hazards identified in the Bench Scale Analysis.

It has to be stressed that the Pilot Plant Analysis section has not been completed since it would require an analysis of the subsequent treatment of the obtained products which is not available at the present time. However, the strategy to complete the checklist would be the same as for the Preliminary Analysis and Bench Scale Analysis, followed by a determination of the appropriate safety measures for the change of scale and for each of the unit operations required. Nevertheless, considering the high number of safety measures suggested should bring to consideration the possibility of changing the process conditions. Changing from a semi-batch process to the use of a continuous reactor should be analysed, as is stressed in HarsMeth NP as a part of the attempt to achieve an inherently safe process. Indeed the work performed by Avilés (2004) gives details on the specifications that a continuous reactor should meet in order to perform the industrial production of macrocylic peroxides in a safe way.

As it can be seen, the new version of HarsMeth provides a more coherent way to perform the analysis of a chemical process under development. In fact, it can be considered as a more complete analysis of the hazards involved in the process than what could be achieved with HarsMeth v2. Besides, even though HarsMeth NP has been designed to perform the hazard analysis of a new process, it can be easily applied to already existing processes by studying the specific hazards at each section of the methodology, starting with the safety management system, and following with the stability and compatibility hazards, reaction hazards, change of scale hazards and implementation of safety measures. However it would be very problematic to analyse a new process with the structure of HarsMeth v2, especially considering the proposals for enlargement of that version of the methodology. The level of accuracy of the analysis, however, will depend on the safety knowledge of the user and the resources available, which will have to be considered when evaluating the results.

The main goal of this tool is to guide SMEs in a preliminary hazard assessment of their processes, even though the degree of detail achieved in this version is very high, considering the topics covered and the information provided. In fact, the methodology can also be very helpful for big chemical companies as a preliminary assessment tool or as a back up system to support management in the decision making process regarding their safety assessments. Basic tools and methods to avoid expensive experiments during the hazard assessment are described in HarsMeth NP (such as the Benson groups theory for determination of reaction enthalpies or the use of Dewar Calorimetry), but it must be stressed that if the results obtained with these methods are unclear or the reaction is regarded as potentially hazardous, then more detailed calorimetry tests will be required.

2.2.4.3.- Application of HarsMeth NP as a tool for accident analysis

A good validation exercise in order to test the efficiency of HarsMeth NP is to profit from the accident analysis described previously and try to match the identified causes that triggered those accidents with the topics covered by the methodology. With this goal, a further revision of the chemical accidents reported to the MARS database shown in Appendix 2.1 has been performed.

Apart from the selection fields described in Tables 2.3 and 2.4 (*cfr.* page 38), the MARS reports contain text descriptions of the evolution of the events, which many times provide more detailed information than the one that can be extracted from the classification fields in order to find which were the direct and underlying causes that led to the accidents. An exhaustive analysis of each case description has been performed in order to extract as much information as possible from each one of the cases studied.

Many of the causes described in the MARS reports can be linked to the issues covered by HarsMeth NP. In order to test the reliability of the methodology, the causes identified for the accidents have been grouped under different categories of topics covered by HarsMeth NP (Sales *et al.*, 2007d). A table has been produced for each category, indicating the number of accidents in which a common failure was identified as a cause for the accident. The results are presented with some examples from the list of accidents analysed given in Appendix 2.1, to illustrate how the use of the methodology may have helped to identify the hazards that eventually generated the accidents.

Incorrect operations

The development of appropriate procedures detailing how to perform chemical operations in a safe manner is of great importance for any chemical company. Especially, the issue of appropriate work permits is essential. These work permits must ensure correct plant and process conditions by means of accurate and detailed instructions on how to carry out a process, in order to enable any activity to be performed safely. There exist, however, a number of specific “incorrect” operations that have been found to be repeated frequently as potential sources of accidents, often involving situations that could have been easily avoided by means of a correct process analysis. Some of these situations are presented in Table 2.15.

INCORRECT OPERATIONS	Number of instances
Incorrect chemicals used	15
Bad connections	12
Incorrect treatment of waste streams	7
Corrosion / fatigue	6
Introduction of chemicals in vessels already in use	6
Incorrect handling of chemicals	4
Failure of utilities supply	4

Table 2.15. - Incorrect operations detailed in HarsMeth NP identified as sources of the accidents studied.

These situations should be preventable by the implementation of appropriate operating procedures detailing how to perform any operation when hazardous chemicals are involved. Such procedures should reduce the possibility of using incorrect substances or mistaken vessels by introducing adequate verification systems.

Waste products should be treated with extreme care, since the diverse nature of the substances involved can make it difficult to predict their behaviour. Mixing of waste streams should be avoided unless it can be ensured that the substances present are not going to create hazardous situations due to incompatibilities.

The failure of utilities supply should always be accounted for during process analysis. This includes electrical power supply, and auxiliary services such as nitrogen, water, or steam feeds. An interesting accident analysed is A-082. In this case, an accident occurred at some place in the installation, so it was decided to turn off the electricity supply. This decision affected other parts of the plant that were functioning normally, generating a second accident.

But the analysis of past accidents provides a great deal of information apart from that included in Table 2.15. For instance, three of the studied cases (A-084, A-118 and A-125) reported that similar incidents had happened at the establishment in the past. The study of past near misses was not included in previous versions of HarsMeth, but it is indeed a very valuable tool for hazard analysis, and it has been incorporated in the latest version of the methodology.

Stability and compatibility of substances and mixtures

It is obvious that many accidents involving chemicals occur because there is a lack of knowledge of the behaviour of certain substances under specific circumstances. From the analysis of the MARS data, at least 56 accidents have been identified that involved an incorrect process analysis related to the unexpected chemical behaviour of substances. Compatibility studies and stability tests of all the substances to be used should be performed. Also, possible mixtures that are not supposed to form, but might do due to unexpected situations, should be considered and accounted for. Some of the issues related to the stability and compatibility of substances, that have been found to contribute towards the studied accidents, are presented in Table 2.16.

STABILITY AND COMPATIBILITY CONDITIONS	Number of instances
Mixture of incompatible substances	28
Water reactive substances	20
Thermally unstable substances	9
Compatibility with construction materials / auxiliary services	8
Pyrophoric substances	6
Shock sensitive substances	5
Polymerizing substances	5

Table 2.16. - Stability and compatibility conditions detailed in HarsMeth NP identified as sources of the accidents studied.

Most of the cases involving the incorrect use of chemicals, or other causes described previously as incorrect operations (*cfr.* page 111) generally involve the mixing of incompatible chemicals. It is therefore important to know the compatibility of substances, to be able to establish correct procedures and training plans, so that these situations can be avoided and to be aware of safety procedures to be followed in case they should occur. For instance, case A-129 describes how an inexperienced worker erroneously mixed sodium dichloroisocyanurate and sulphuric acid (instead of the expected sodium sulphate) generating a toxic cloud of chlorine. The worker should have been made aware of the incompatibility of the mixed substances by means of appropriate operating instructions, and he should have been supervised while performing the activity.

When considering possible incompatibilities, it is particularly important to identify the effects of possible impurities. For example, case A-009 describes an explosion during a process involving distillation of nitroanthraquinone due to the catalytic effects of inorganic salt impurities present in the distillation mixture. The presence of these impurities remained unnoticed by plant personnel during the process.

It is interesting to highlight the number of cases involving water reactivity. This can be related to many issues. For example cleaning operations in which there have been failures to verify that the vessel to be cleaned did not contain a substance incompatible with water, as occurred in case A-041, where residues of sulphur chloride reacted with the cleaning water generating a toxic cloud. Also, weather effects can be of importance, since some substances react with ambient moisture. In accident A-003, ethylene oxide was released through a leak and reacted with moisture to form a polymer that auto-oxidized generating an explosion. Reactivity with water should always be taken into account, for example, in cases involving the transport of chemicals inside the installation. It is possible that a spill of a product containing a water reactive substance enters a drainage channel, bringing it into contact with water, or the break of a refrigerant system using water could bring into contact reactive materials. This occurred in cases A-080, where a faulty pipe junction released polychloroacetone, which entered the drainage system and reacted with water generating a toxic cloud, and A-010, where the cleaning of the cooling circuit generated a leak within the circuit, and the released water reacted with process $TiCl_4$ generating a violent explosion.

It is strongly recommended in the HarsMeth NP methodology that compatibility studies should be extended to any auxiliary services or utilities (nitrogen, air, oil, water, etc) used during the process, as well as construction materials. As an example of this possible source of accidents, in case A-002 a leak in a pipe released ethylene oxide, which reacted exothermically with the auxiliary equipment, generating an explosion. It is also interesting to consider the formation and behaviour of unexpected substances during a runaway reaction. For example, in case A-130, hydrogen chloride was formed; this generated corrosion on the reactor wall, which reduced the mechanical resistance of the vessel leading to an explosion at a lower pressure than would have been expected.

For particularly hazardous substances, specific tests should be conducted in order to determine the optimum process conditions, and measures should be put in place to guarantee that those conditions will always remain unaltered in case of process deviations, or that the system will be able to cope with those deviations.

Chemical reaction failures

When performing a chemical reaction, it must always be ensured that any hazard arising from a possible deviation from process conditions has been identified. Of the 132 accidents analysed, 41 occurred during a reaction stage. A study of the failures that initiated those 41 accidents is presented in Table 2.17.

FAILURE SOURCES	Number of instances
Dosing failure	12
Impurities / contamination of reaction mixture	8
Mischarging	7
Cooling failure	3
Agitation failure	3
Supply failure	3
Unknown	5

Table 2.17. - Failure situations for chemical reactions detailed in HarsMeth NP identified as sources of the accidents studied.

It can be seen that the most common failure in these cases involves the dosing system. An alteration in the quantity or the rate of dosing of reactants will modify the expected kinetics of the process. This can lead to the development of secondary reactions, the consequences of which are often unknown. This is particularly important, for example in polymerization reactions, which are amongst the most common type of reactive systems generating accidents (EPA, 1999). Of the 41 cases analysed that happened during chemical reactions, 13 were identified as polymerization processes, being the polyvinylchloride and the phenol-formaldehyde reactions the most common processes leading to accidents of this kind, with 5 and 3 cases respectively.

Failures in cooling systems, agitation, or any other auxiliary device, as well as the presence of impurities, can also alter the evolution of the reaction temperature, leading to possible secondary processes that may generate a sudden increase in the gas generation rate, hence increasing the pressure and generating an explosion hazard. The number of cases in which the causes of the runaway event were not identified reveals that chemical reactions are sometimes performed without the necessary awareness of the hazards involved. In fact, in some of the cases in which an item from Table 2.17 was identified as a source of an accident, it was also unknown that a failure in the reported device could generate the consequences that followed the accident. In these cases, a deficiency in process analysis should also be reported.

Determination of safety measures

The first action that has to be taken when a hazardous substance or mixture is identified should be to try to replace it by a less hazardous one, or to reduce its use as much as possible to make it inherently safer. If this is not possible, additional safety management or technical measures must be proposed and implemented. Table 2.18 lists some of the most common safety systems that could have helped prevent the accidents studied.

SAFETY MEASURES	Number of instances
Introduce measures to follow state of product	47
Use of pressure relief systems	39
Chemicals stored / handled under compatibility criteria	38
Avoid ignition sources	24
Use of inhibitors for substances or mixtures involved	19
Use of interlocks for reactor components	16
Introduce appropriate labelling rules	13
Use of inert gases	13

Table 2.18. - Safety measures specified in HarsMeth NP related to the accidents studied.

For those substances that are considered unstable under certain situations, it is necessary to include monitoring and control of critical properties. Among the most common of these properties are temperature, humidity, storage time, concentration, pH, and so on. Such control should be applied at storage facilities and to reaction processes whenever it is considered necessary. To illustrate the need of substance control, case A-111 describes an incorrect mixing operation due to erroneous pH control that generated an explosion during the charging of oxyethilenic tensioactives.

One important issue from the management point of view is to ensure correct labelling procedures, which can also be reinforced by double checks to avoid the use of mistaken chemicals. This is emphasized in case A-020, where a vessel typically used to store sodium hypochlorite was exceptionally loaded with hydrogen chloride, labelled and put aside for some time. Due to weather effects the label became detached, so when the vessel was refilled with hypochlorite, nobody remembered that it still contained the acid, which subsequently resulted in an explosion.

If a pressure increase inside a vessel is considered a possible consequence from an accident scenario, it is clear that a pressure relief system should be provided. At the same time, if it is known that the decomposition of a substance or a runaway event can be controlled by emergency cooling systems, or by the use of inhibitor substances, these options should always be available. Of the 41 cases associated with chemical accidents reported in MARS, 9 cases state that a safety system was implemented but did not respond adequately. This fact suggests either a failure in the design of equipment, or the underestimation of the possible consequences of a runaway event. For example in accident A-130, which has already been highlighted, hydrogen chloride formed during a runaway scenario corroded the reactor wall, attacking the construction material of the vessel. This affected the mechanical resistance of the reactor, so the pressure that it could withstand was less than the design for the pressure relief system, which failed, generating a violent explosion. It is also interesting that extra cooling was provided as a safety measure but it did not avert the accident. This shows that even though sometimes a hazard can be identified, there can be a failure in the appropriate design or maintenance of safety devices (Sales *et al.*, 2007c).

Moreover, in the case of chemical reactions, the determination of critical parameters during the safety analyses should determine a series of interlocks to be included in the reactor vessel. Devices such as cooling, dosing, or agitation systems, which are commonly known critical equipment for safety as can be seen by the results presented in Table 2.17 (*cfr.* page115), should be linked to temperature control systems and other devices in order to stop the reaction in case of a runaway. This can be done by stopping the dosing of reactants when an unexpected temperature rise is detected, increasing cooling power, or introducing inhibitors in the vessel. Furthermore, it should be a policy to provide redundant control systems and safety measures for critical parameters identified in the hazard assessment.

It is clear that the selection of safety measures must be in accordance with the nature of the hazard identified as a possible source of an accident. To demonstrate this, in case A-117, two substances were supposed to be mixed in a container, without any particular hazard identified in the operation. In one occasion there was an explosion in the vessel under normal process conditions. Further investigations revealed that one of the reactants had been supplied out of specification. For this case, it is not absolutely necessary to provide the vessel with a pressure relief system, even though an explosion did occur; instead, appropriate procedures to check the conditions of supplied chemicals should be put in place to prevent similar accidents occurring in the future.

Case studies

In order to better understand the analysis performed, some case studies extracted from the MARS database are described in detail. These cases have been selected because they present an accurate and detailed description of the circumstances that led to the accidents, and they are considered to be representative of the whole set of accidents analysed, since they share many causes with the rest of the events studied and have similar circumstances that led to the accidents being realised. Moreover, they are considered to be particularly illustrative as to show how the use of HarsMeth NP might have helped to prevent the accidents. Some of the following accidents happened during a reaction step, but others occurred elsewhere in the chemical plants (e.g. distillation, pipelines, storage), stressing the idea that chemical reactivity must be kept under control anywhere in an industrial establishment. For each case, the code of the accident corresponding to the list shown in Appendix 2.1 is given.

Case 1: A-131

In a reactor for the production of ortho-nitroanisol (a substance used for painting material and pigments production), methanol and ortho-nitrochlorobenzene were mixed. The vessel was shut down and nitrogen impressed. Then, without the stirring apparatus connected, the reactor was heated at the established reaction temperature and caustic soda was pumped in. After waiting of the prescribed reaction time, it was observed that the stirring apparatus did not run. At that point an operator controller switched it on. This accelerated the running exothermic reaction, with a temperature rise from 95 to 115 degrees Celsius. The reactor pressure rose from 9 to 16 bar. The safety valves opened, and about 40% of the reaction mixture, approximately 10 tons, was released. During normal process, the products from the reaction are ortho-nitroanisol, common salt and water. Due to the alteration in the process, other products like dichlorazobenzene and dichlorazoxibenzene were generated. The released reaction mixture was dispersed over an inhabited area of 25-30 ha, where more than 2000 people lived, covering it with a yellow sediment. In total about 100 people in the following days suffered from head aches, irritation of the breath ways and mucous membrane, and received on demand ambulatory care.

After the accident, the following measures were established by the company:

- Improvement of the training / instruction of the personnel.
- Better knowledge of the chemistry of the reaction.
- Improvement of the operating procedures (particularly with reference to the filling of the reactor and the checks to be carried out on the recipe).
- Re-design the sizing of vents and safety valves.

The key factor involved in this accident was, as stated in the lessons learned, the lack of knowledge of the chemistry of the reaction. The hazard of agitation failure during an exothermic reaction and restart of the agitation after the reactants have been mixed and heated is well known (Barton and Rogers, 1997), and it is described in HarsMeth NP as a common source of hazards for these kinds of reactions.

It must be highlighted that the failure in performing a hazard analysis was the main cause leading to the accident, and that all the other items mentioned in the description of the accident or the lessons learned are secondary. Obviously if the hazard is unknown, it cannot be included in the operating procedures or training programmes for operators. Besides, the effect of such a hazard on the evolution of the reaction is unknown, so the consequences of the accident, as mentioned in the description, were totally unexpected. Furthermore, the safety systems put in place, as mentioned in the lessons learned, where not effective. But before thinking about including safety measures in the reactor set up, it is necessary to perform a thorough process analysis of the reaction and of all the possible failure modes in order to identify the possible consequences of an accident.

Case 2: A-130

The accident occurred during the polymerization of vinylchloride in an organic chemical industry for latex production in a reactor heated with steam at a temperature of 165-175 °C. Due to a human error, a mixture of PVC-latex with insufficient ammonia was used. Ammonia is used in latex production as a stabilizer agent to prevent polymerization and to act as pH modifier. Since the reaction was carried out without an adequate addition of ammonia, the normal small hydrogen chloride production to be expected during the process could not be compensated. Hence, the excess of hydrogen chloride destabilized the suspension of PVC-latex which coagulated. The coagulation of the latex caused the mixer failure but there was no indication of it. Consequently, a local overheating resulted and decomposition of PVC occurred because the steam temperature (165-175 °C) was higher than the PVC decomposition temperature (144 °C). Being the PVC decomposition exothermic, the heat caused an expansion of coagulated latex which clogged the piping system including the inlet to the bursting disc and to the safety valve. The uncompensated hydrogen chloride started to react with the material of the reactor (stainless steel was not resistant against hydrogen chloride at high temperatures). Even though the steam supply had been stopped and the external cooling started (activated by the release of hot gases from the reactor), the vessel burst because the wall thickness was reduced from 9.8 mm to 2 mm. Activation of the sprinkler system enhanced reactor cooling and diluted the hydrogen chloride vapours.

After the accident, the following lessons learned were established by the company:

- Substitution of the plasticizing agent and use of steam with a maximum temperature of 127 °C (latex starts decomposing at 140 °C).
- Installation of a double signalling device on the mixer for the detection of malfunctions.
- Interlock of the steam supply to the mixer so that the steam supply will be automatically shut off in the case of agitator failure.
- Installation of two independent temperature sensors. The steam supply will be automatically shut off if any of the sensors indicates a temperature above 100 °C or when there is a substantial difference in indications of the two sensors.
- Installation of a level switch, which will automatically shut off the steam supply when a high level in the reactor is reached.
- Installation of a pressure switch (set at 1 bar overpressure) which will automatically shut off the steam supply when a high pressure is reached.
- All these steam shut off actions to be coupled to an alarm signal in control room.
- During the process the pH to be monitored through regular sampling; the possibility of continuous pH-monitoring to be investigated.

This is an interesting case of a runaway reaction in which the addition of a wrong quantity of one of the reactants generates a hazardous situation and eventually a runaway. The lessons learned reported for this case give specific details on issues that are covered in HarsMeth NP. First of all, the company decided to modify the process substances and conditions by replacing PVC as plasticizing agent and reducing the steam temperature below latex decomposition point. Then, a set of safety measures such as double signals, interlocks and sensor redundancy were introduced in the reactor setup (which is important considering that the failure of mixing was not registered during the accident), as well as monitoring of critical parameters for safety such as pH.

However, there are no indications in the MARS record about improving working procedures to avoid introducing wrong quantities of a reactant during the process. This topic is covered in the Safety Management System checklist of HarsMeth NP, and it was actually the main cause that triggered the runaway. If it is not taken care of, a similar accident could happen again in the future even if the process conditions are changed. The MARS report states that the use of a too low quantity of ammonia was due to a human error, without giving any more details. Appropriate working procedures such as weighing systems or double checks before loading should have been used, as well as specific training programs detailing the hazards of process variations such as the use of a too low quantity of stabilising agent.

Case 3: A-120

The accident occurred during the distillation of crude ortho-nitrobenzaldehyde. Six months prior to the final processing the material was oxidized with nitric acid and the products set aside. This led to the formation of appreciable amounts of thermally unstable ortho-nitrobenzylnitrate being formed. This was not recognized, and resulted in an earlier exothermic reaction and more vigorous acceleration of decomposition processes than had been anticipated. However, immediately prior to distillation, a sample of the crude product was tested using the differential scanning calorimetry method to determine the temperature at which an exothermic reaction would begin. The crude had been washed with water, toluene and caustic soda prior to testing but the test equipment differed from that specified, and the condensation of water within the equipment masked the identification of an exothermic reaction in the sample. With the information from the test indicating that there was no exothermic process likely at (or around) the operating temperature, the process of distillation of the bulk material was started. At about 140 °C an exothermic reaction occurred rapidly reducing the vacuum in the system to a positive pressure with a final violent runaway resulting in deflagration. The vessel (although equipped with a high-temperature alarm set at 140 °C, a high-temperature trip of the steam supply set at 150 °C and a second trip set at 170 °C activating the dumping of the heavy hydrocarbons) could not cope with this speed of reaction and did not prevent the runaway. It is thought that the automatic dumping system did not operate.

After the accident, the company decided not to process the substance involved in the accident any further and to review all the management system and control of processes.

This case shows the importance of the reliability of tests performed to determine the thermal stability of substances handled in a chemical establishment. This issue was not sufficiently stressed in previous versions of HarsMeth. The fact that past accidents have been reported in which failures during this kind of testing have been identified as a cause of the accidents, enforces the necessity of a hazard assessment tool to give some guidance or references to this matter, as has been included in HarsMeth NP. In this particular case, the failure to identify the exact temperature for decomposition led to an incorrect process analysis and to a failure in the design of safety measures, as the provided system of alarms and trips was not effective when the runaway took place.

Case 4: A-103

In a facility for chlorination used in the production of dimethyl-phosphorochloridothioate (MP-2) and diethyl-phosphorochloridothioate (EP-2), a new reactor for production of MP-2 was used for the first time. Similar equipment was already in use at the same establishment, but the new reactor was microprocessor controlled, especially for controlling the chlorine addition rate and the cooling in order to maintain the process conditions (30 °C and atmospheric pressure) because the chlorination of dimethyl-phosphorodithiotic acid (MP-1) to MP-2 is exothermic.

During commissioning, the temperature controller was blocked while testing the microprocessor and the connection was not re-established before starting operation. The production started at noon and the operators did not pay attention to the temperature that was recorded. Owing to a high chlorine addition rate and no cooling, the temperature rose to be in excess of 120 °C about 2 hours after starting production. The solvent (naphtha) evaporated and a sudden fast decomposition occurred. The reactor was equipped with a venting system and a relief pipe provided with a rupture disc but the relief capacity of the system was however insufficient compared to the amount of gases released during the fast decomposition of the substances. The result of the accident was the fracture of the rupture disc, deformation of the reactor lid and the elongation of the bolts of the lid. Flammable gases were released through the venting system and through the open reactor lid into process hall. The vapour cloud was ignited when it reached the control room causing an explosion. On the basis of the deformations of the reactor and of the building, the company estimated that the pressure in the reactor reached values of 25-35 bar and that the overpressure in the building reached values of 100-150 mbar.

After this accident, the following lessons learned were provided as reported to MARS:

- The buildings, the process and control equipment will be rebuilt and modified.
- The emergency shut-down system to be independent from the unit (operation) control system.
- Redundancy in the control system to be provided.
- Process supervision (warning / alarm) signals to be improved.
- Temperature and chlorine addition rate control systems to be improved.
- Safety management system to be improved.
- Man-machine communication system to be improved.
- The control room structure should be strengthened and direct access from the production hall to it had to be eliminated.

The lessons learned given for this case, even though are appropriate, are a bit too generic and do not analyse in depth the causes of the accident, which can be derived from the accident description. In the first place, there was a deficiency in the working procedures for the testing of the microprocessor. Besides, a lack of supervision and training of operators was probably involved in the failure of not re-establishing of the connection after testing.

The fact that there was a relief system in place shows that the reaction was known to be potentially hazardous. However, its design was not appropriate for the consequences that could be generated from a loss of control of the reaction. Either the analysis of the runaway was not adequate or the dimensioning of the relief disc should have been improved for the situation of too high chlorine addition rate plus loss of cooling. A better solution is, however, to provide measures in order to avoid starting operation without the signal of the microprocessor being in place.

Case 5: A-085

Phosphorous trichloride was released from the bottom of an iron tank during the separation of the two layers formed by decanting and transferring the layers to storage tanks linked to the installation. The released liquid, having got in contact with the water on the ground, caused a primary exothermal reaction forming a hydrochloric acid cloud, and secondary reactions forming flammable products, followed by the ignition of such products. The response action for extinguishing the fire with water and foam caused the formation of more hydrochloric acid in significant quantities and the further increase of the toxic cloud which moved towards an inhabited area outside the establishment, but did not generate consequences among the population.

The MARS report states that the probable cause of the accident was the wrong positioning of the tank in respect to the withdrawal point for the transfer of the phosphorous trichloride to the plant, due to an error of an operator. The lessons learned reported are the following:

- Modifications have been made in order to improve the discharge system of the iron tanks.
- The accident demonstrates the need for a better training of the operators responsible for discharging operations.

However, there is also a need to improve the analysis of compatibility of the phosphorous trichloride. A process analysis detailing the reactivity of this substance with water (as suggested in HarsMeth NP) should have been performed. This would have revealed the need to improve the design and training for the discharge operation, as mentioned in the lessons learned, and would have also made the plant personnel aware of the hazards of discharging this substance in an area where it could easily come in contact with water.

Case 6: A-060

A tank containing benzoyl chloride was scheduled for emptying and cleaning operations. A few days before the accident occurred, it was impossible to empty the tank due to the presence of solid deposits of benzoic acid which had probably been formed by a slow decomposition reaction of the product. It was decided to dissolve the deposits by adding a solvent, and some tests were performed in the laboratory with methanol without any kind of reaction occurring. After a few minutes of pumping methanol into the tank, a small explosion caused by an overpressure in the tank took place and a gas cloud was released. Benzoyl chloride reacts with alcohols releasing hydrogen chloride. This is what occurred when methanol was added to the tank. The cloud formed in the accident reached some houses located 150 meters from the establishment. Some inhabitants suffered from severe eye irritation. The operators attempted to abate the cloud by setting up a water curtain and by spraying the tank.

The analysis of the accident report and the on-site investigation has shown the following failures that have to be dealt with in the future:

- Tests performed proved to be not sufficiently representative. Further tests performed after the accident showed an exothermic reactive behaviour of the mixture of methanol and benzoyl chloride above 30 °C.
- Absence of a management representative on the site and failure in managing the organization and decision chain with respect to the safety issues.
- Delayed instigation of the onsite contingency plan.
- Organizational failure of the operator in managing the immediate consequences of the accident.
- Overflow alarm of the tank not connected to the control room.
- Poor condition of the joint on the man-hole flange of the tank.
- Carrying out the emptying procedure presented a hazardous situation to the plant personnel and the environment consequent to a faulty hazard assessment. This led to the use of incompatible substances and an incorrect evaluation of the consequences of such an operation.
- Missing hazard labelling on the methanol container.

Again the issue of representative hazard tests is given as a cause for the accident. The lessons learned from this report give a very good and comprehensive description of the failures that led to this accident, mainly the lack of training, process analysis and appropriate procedures for cleaning operations, as well as failures in the inspection of the flange and connections of alarms.

Case 7: A-054

During delivery of sodium chlorite to a chemicals warehouse, a violent explosion occurred when two products were mixed. Some sodium chlorite had been put in a container holding ferric chloride, which is incompatible with the delivered substance. Subsequent explosions in other containers were generated, and a toxic chemical cloud was formed, consisting of chlorine and chlorine dioxide.

Even though the MARS record does not provide further information regarding the causes or the lessons learned from the accident, this is an obvious case in which it is clear that either the procedures for the operation were insufficient or they were not followed properly. There must be a system in place to verify the contents of a vessel before loading it with another chemical substance. Extending binary compatibility tests to all the possible chemical combinations of substances involved in a chemical plant, as suggested in HarsMeth NP, could help to raise awareness among process engineers and operators as to the possible hazards related to an unexpected chemical mixing.

Case 8, A-040

The accident occurred in one of the two hydrogen peroxide production units of a general chemical industry. Each production unit was composed of three sections: hydrogenation, oxidation and extraction. A pipeline containing hydrogen peroxide was ruptured due to the decomposition of this substance, leading to a release and subsequent fire of the decomposition products. The most probable cause for the decomposition of hydrogen peroxide was the presence of unstabilizing agents in suspension (metallic particles due to rust). An abrupt increase of temperature from 70 to 200 °C in less than 5 minutes was registered.

The initiating event was the failure of the automatic control devices together with a series of human errors during the attempt to repair them. Particularly, the safety procedures followed were not suitable for the event. Furthermore these procedures were not fully applied. Some valves, that could be manually closed, remained opened. As those valves were necessary for the isolation of the various sections of the production chain, the solution passed from the oxidation to the extraction step and back again via the pipeline. An overflowing of the fire extinction water to the natural environment was generated, due to the under-dimensioning of the containment basin designed for this purpose.

The activity of the destroyed production chain was suspended by the inspection authorities and a permission to restart the production will be given only by resubmission of a complete request for operating authorisation. This request has to contain a new safety report taking into account the results of the actual investigations. As far as the new start-up of the other production unit, the following measures were established by the authorities:

- Prevention of hydrogen peroxide back flow to the oxidation section.
- Improvement of the automatic control system.
- Improvement of operators training and improvement of written procedures.
- Increase of the retention basins capacity was required.

In this case, the accident report and the lessons learned focus on the improvement of training for operators, written procedures and prevention of backflow. However, it is also necessary to control the presence of impurities in the pipeline, how and where they can be generated. Then, it is also necessary to ensure that those impurities, if formed, will never become in touch with the hydrogen peroxide, for example, by introducing measures to avoid the backflow. Hydrogen peroxide is known for being extremely reactive with metals, which catalyses the decomposition of this substance very fast, so it is necessary to provide all the required measures to avoid this situation. Again, the use of HarsMeth NP could have helped to prevent the hazard.

Case 9: A-012

A welding process (manual electrode welding) took place on the outside wall of a storage tank which was two thirds filled with formaldehyde (37% solution). The welding operation over the level of the liquid phase in the storage tank overheated the gas causing the explosion of the air / formaldehyde mixture and the release of vapours into the environment. Inside the establishment 2 people were killed and 10 were injured by the explosion.

After the accident the following measures were established by the company.

- The storage temperature must be controlled.
- The revision of the fire and explosion certificate is necessary.
- Measures to match the state-of-the art in matters of safety have to be introduced.
- Welding works to be performed only under management supervision.
- Storage tanks have to be equipped with hermetic sealed pumps and leak proof fittings.

This accident shows the importance of a correct check of the chemical conditions in a vessel when reparation works have to be performed. In this case, the flammability of the mixture and the hazards of providing a heat source such as electrode welding should have been analysed. Supervision during maintenance operations is also essential. Both issues (analysis of flammable mixtures and correct supervision during routine operations) are clearly stated in HarsMeth NP.

Case 10: A-005

An inspection of the level measurement device of a titanium tetrachloride ($TiCl_4$) evaporator was being carried out. On disconnecting the signal wiring of the level measurement device, the process computer responded to this signal as empty and opened the control valve to fill the evaporator. The evaporator was not isolated prior to the start of the work, so it started to fill with $TiCl_4$, without anyone noticing. Meanwhile the work continued and the level measurement device was removed. At this moment the evaporator overflowed releasing $TiCl_4$ on the first and second level of the reactor building. The high level alarm was silenced by the panel operator. $TiCl_4$ produces hydrogen chloride and TiO_2 in contact with water (including air humidity), so rapidly a thick toxic white cloud was formed inside the reactor building. Two contractors working on the first floor could not locate an emergency ladder. Both were new to the installation and were trapped with very little visibility due to the thick white cloud. Both were found dead by search parties afterwards.

The main lessons to be learned from this accident are:

- Work permit system has to be used strictly. The installation was not properly isolated prior to the work.
- Adequate training and supervision are necessary. This must include adequate information for contractor workers about safety in the installation, such us the use of safe evacuation routes.
- Contractors cannot be relied upon to inform their personnel about the on-site safety information; a strict control system is necessary.
- Improvement of control and alarm systems. There should be a clear difference between no signal and zero signals in the process computer. Also, an interlock system should be used to prevent overflow of the evaporator, and a better management of alarms should be introduced, to avoid neglecting critical alarms.
- A management crisis team is necessary to ensure communications with external emergency services. A prompt alert for these services is also necessary.

This case shows the importance of appropriate management for maintenance. As mentioned previously, procedures for correct inspection of plant equipment should have been put in place, especially those related to preparation of the equipment for maintenance. Furthermore, permit systems as well as training for contractors are essential to avoid similar situations.

As it can be seen from the descriptions of the previous case studies, chemical accidents can have a wide variety of direct or underlying causes. It is therefore necessary to try to take all the possible hazard sources into account in order to run chemical processes safely at industrial scale. The comparison of the causes of those accidents with the items covered in the HarsMeth NP methodology shows that in many cases the use of the methodology could have helped to identify the hazards that eventually led to the occurrence of the accidents.

2.3.- Calorimetry study

HarsMeth version 2 has been used in order to establish the criticality of one of the processes under development at the company C1, according to the information required in the methodology. Different experiments have been performed to determine the required values asked in HarsMeth v2 to perform the hazard assessment of the studied process.

Due to the confidentiality agreement signed between IQS and the company C1, in order to protect industrial property, only limited information regarding the chemical products involved in the analysis is given. Only reference codes can be given for the initial reactant (1474) and for the final desired product (1482). This limitation will not affect the essential information regarding the reactivity and hazards related to the process analysed.

The process chosen for the study is related to the synthesis of a pharmaceutical compound produced at the installations of the company C1. The process involves four reactive steps according to the following schema shown in Figure 2.21.

1. 1474 + MeONa	R-SO$_3$-R’	EQR.01
2. R-SO$_3$-R’ + R’’-SH	R-S-R’’ + R-SO$_3$H	EQR.02
3. R’-Cl + MeONa	R’-OCH$_3$ + NaCl	EQR.03
4. R-OCH$_3$ + H$_2$O$_2$	1482	EQR.04

Figure 2.21. - Synthesis path for the production of the pharmaceutical compound 1482 according to the chemical recipe provided by the company C1.

In order to determine the safety parameters required in HarsMeth v2, different experimental techniques are available. Reaction calorimetry is perhaps the most common method to determine the heat of a reaction (HarsBook, 2003). This technique has some disadvantages, mainly the higher cost compared to other methods like differential scanning calorimetry, or the lower sensibility compared to microcalorimetry. Besides, it can provide little information regarding undesired secondary reactions generated in the course of a runaway, even though some calorimeters provide the option of inducing such conditions by operating in pseudo-adiabatic mode. In spite of these disadvantages, reaction calorimetry is a much appreciated technique in the measurement of the heat of chemical reactions.

Reaction calorimetry is not only a key technique for risk assessment of chemical processes, but also an effective tool to determine the dimension of cooling systems for chemical reactors. In a final stage, the combination of reaction calorimetry with commonly available laboratory equipment can provide direct and accurate measures of the quantity and rate of gas generation during the desired reaction, so it is an appropriate tool for scale-up and optimization of processes. A wide variety of reaction calorimeters is available nowadays. They differ basically in the approach used for the measurement of the heat flux generated or absorbed by the reaction, and innovative methods to develop new calorimeters in order to improve the determination of the parameters involved in the heat balance of chemical reactions are constantly being developed (Sempere *et al.*, 2003). Comparisons of the strengths and weaknesses of each type of existing calorimeters can be found in the literature (HarsBook, 2003).

The best technique to obtain data from runaway reactions is adiabatic calorimetry. The term adiabatic refers to a system condition in which no heat is exchanged between the system and its environment (HarsBook, 2003). This is the situation that better represents a runaway scenario, considering that the rate of heat production in the reaction vessel is so high that the cooling capacity cannot remove the heat generated. Adiabatic calorimetry experiments are particularly useful in order to determine values related to the decomposition of chemical mixtures, such as the adiabatic induction time, (i.e. the time the system needs under adiabatic conditions to reach the point of highest temperature gradient), or the time to maximum rate of heat generation, TMRad. Another important feature is that it can also determine the gas generation rate in a decomposition process, giving accurate values for the pressure that can be reached during a runaway reaction. It must always be kept in mind that pressure increase is the final hazard in a runaway, since it is this phenomenon that can lead to the explosion of a reactor. However, adiabatic calorimetry experiments are expensive and require a high degree of expertise to perform them and to analyse the data obtained. For this reason, it is a technique that is hardly ever used in SMEs, as has been repeatedly stated in the feedback received during the testing of HarsMeth.

A basic technique to determine the thermal stability of a substance is differential scanning calorimetry, or DSC (HarsBook, 2003). It involves the measurement of the heat released or absorbed by a sample in comparison to a reference while they are both subject to the same temperature regime. This is a simple and easy to use method which is usually available at the majority of the chemical companies. DSC can be used to determine heats of decomposition of substances and mixtures, and its main advantages are the short time necessary to perform an experiment and the use of small sample quantities. This fact reduces the possible hazards associated to the reactants used, but it forces to ensure that the sampling is representative of the mixtures analysed. Another disadvantage of this technique is the fact that there is no possibility of including an agitation system, so it is difficult to provide appropriate mixing, especially when heterogeneous reactions are involved. Therefore, even though it can determine the heat of a reaction, the results may not be as reliable as those obtained by reaction calorimetry. Besides, the construction material of the sample container must be carefully chosen, since it may affect the results obtained during the analysis.

2.3.1.- Reaction calorimetry results

The Reaction calorimeter RC1® of Mettler-Toledo has been used to perform the experiments for each one of the four reaction steps described in Figure 2.21 (*cfr*. page 132), in order to obtain the necessary parameters to establish the criticality of the reactions. This calorimeter uses the method of heat flow calorimetry. The basic equation of this type of reaction calorimetry is the heat balance of a stirred tank reactor, described by Eq. 2.1:

$$m_r c_{pr} \frac{dT_r}{dt} = UA\left(T_j - T_r\right) + \dot{Q}_r + \dot{Q}_{loss} + \dot{Q}_{dos} + \dot{Q}_{stirr} + \dot{Q}_c \qquad \text{[Eq. 2.1]}$$

where

U is the heat transfer coefficient

A is the heat transfer area

$\dot{Q}_r$ is the exothermic power of the chemical reaction

$\dot{Q}_{loss}$ is the power of heat loss to environment

$\dot{Q}_{dos}$ is the power of heat absorption / release by dosed substances

$\dot{Q}_{stirr}$ is the power introduced by the stirrer

$\dot{Q}_c$ is the power of the electrical (calibration) heater

The respective signs (+/-) are introduced into the values according to the direction of the heat flow. The specific heat of the reaction mixture c_{pr} and the global heat transfer coefficient U are determined by calibrations before and after the reaction. An interpolation is carried out between these values, the exact conditions of which are defined by the user. The power input of the stirrer $\dot{Q}_{stirr}$ is obtained by measuring the torque of the stirrer shaft. The heat loss $\dot{Q}_{loss}$ of the reactor is usually determined by calibrations, but the use of a thermostated lid accomplishes that it can be usually neglected. In case of dosing or removal of material to or from the reactor a convective term must be considered, with the heat value being described by Eq. 2.2:

$$\dot{Q}_{dos} = \dot{m}_d c_{pd} \left(T_d - T_r \right) \qquad \text{[Eq. 2.2]}$$

with T_d = Temperature of the dosed substance.

In perfect isothermal mode the control unit adjusts the jacket temperature in a way that the reaction temperature remains constant and thus the accumulation term is zero at all times. In adiabatic mode the control unit maintains the jacket temperature at any time just slightly above the reactor temperature to avoid heat flow to the jacket.

The results obtained for each one of the reaction steps involved are shown next:

RC results obtained for EQR.01

The first step of the synthesis studied corresponds to an acid-base reaction. The procedure followed to perform the reaction consists on charging the reactant 1474 in the reaction vessel, and then MeONa (at ambient temperature) is dosed during 32 minutes. The reaction is performed at a temperature of 4 °C. The power profile for this first step is shown in Figure 2.22.

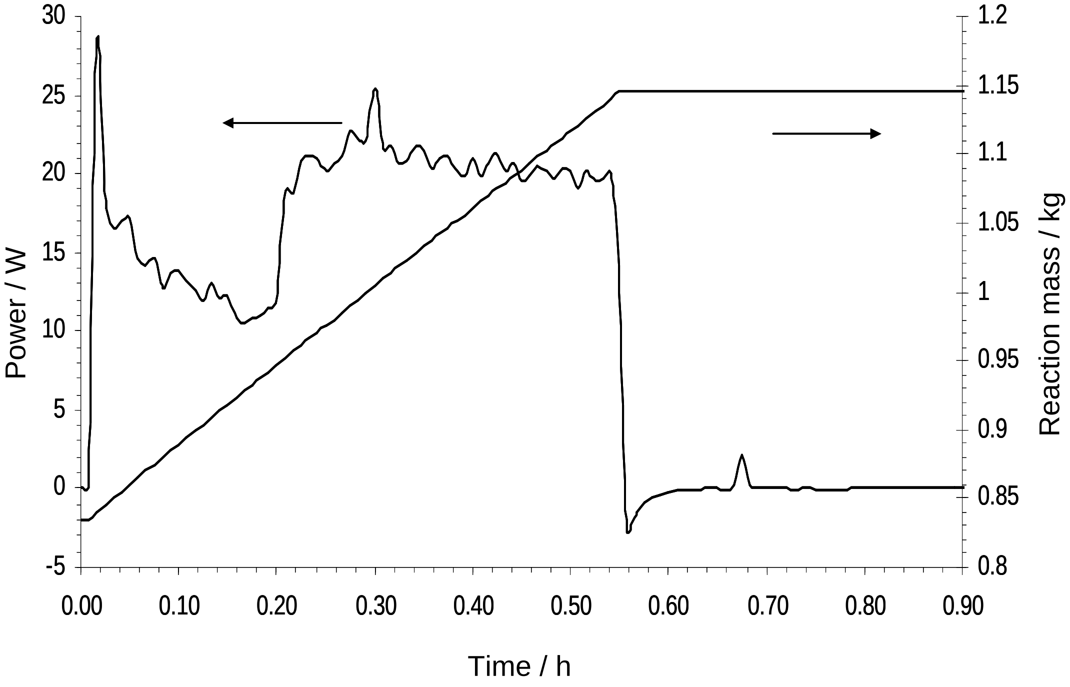

Figure 2.22. - Power profile for reaction EQR.01.

The main results obtained from this calorimetry test are given in Table 2.19.

Process stage	**Tr / °C**	**Reaction mass / kg**	**$\Delta_r H$ / kJ·kg^{-1} (4)**	**ΔTad / °C**
Charging of 1474	4	0.835	-	-
Dosing of MeONa	4	1.145	-30.95	17

Table 2.19 - Calorimetry results for reaction EQR.01.

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[4] kg of reaction mass

Two different zones can be seen in the power profile shown in Figure 2.22, which can be due to different physical-chemical mechanisms during the reaction. The first tendency corresponds to the time comprised between the beginning of dosing and the time when 32% of MeONa has been dosed. In this period, a peak of heat is generated (34 W per kg of reaction mass) and then the heat generation decreases progressively. At the end of this period, 23% of the total reaction heat has been generated. The second tendency corresponds to the time comprised between the 32% of MeONa dosed until the time when dosing has been completed. In this period, the heat generation is totally controlled by the dosing speed of MeONa.

The value for adiabatic temperature increase given in Table 2.19 is the highest value obtained, and it corresponds to the non-stop case (*cfr*. Introduction, page 22), in which it is considered that the dosing of MeONa would not be stopped under adiabatic conditions.

RC results obtained for EQR.02

The second reaction involved in the process is a sulphur alquilation. Figure 2.23 shows the power profile of this step.

The reaction is developed as follows: the reactant R-OSO_2-R' is charged in the reactor together with the solvent and the temperature of the reaction mass is set at 10 ^oC. Next, methanol is added, followed by the solid reactant R''-SH in the fastest possible way, after which the reaction mass is heated until 30 ^oC, and it is kept at that temperature during 2 hours. After that time, the reaction mass is ready to be discharged, after checking the conversion degree. The addition of solvent can be seen at t=1 min in Figure 2.23, while the addition of R'-SH corresponds to the period from t=6 min to t=21 min. All substances added to the reaction mass are at ambient temperature.

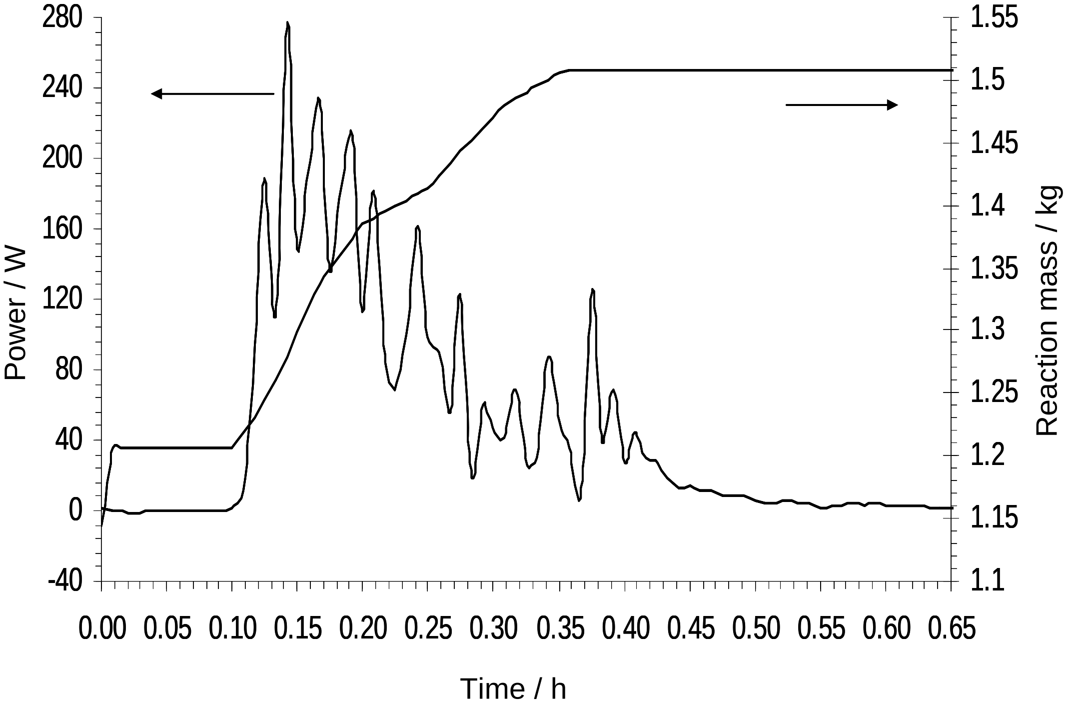

Figure 2.23. - Power profile for reaction EQR.02.

The main results obtained from this calorimetry test are given in Table 2.20.

Process stage	**Tr / °C**	**Reaction mass / kg**	**Δ_rH / kJ·kg^{-1} (5)**	**ΔTad / °C**
Charging of R-OSO$_2$-R’	10	1.143	-	-
Addition of solvent	10	1.207	-1.22	0.5
Addition of R’’-SH	10	1.507	-75.82	36

Table 2.20. - Calorimetry results for reaction EQR.02.

In this step, it has to be considered that the reactant R’’-SH should have been added instantaneously, but since it is a solid, it is added in the shortest possible time (15 minutes), since otherwise it would have blocked the addition tube of the reactor. It must be noted that at the company C1, the reaction is performed at plant scale by adding R’’-SH at once, which could lead to a further increase of the reaction temperature. But even in the worst possible situation (total adiabatic behaviour of the

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[5] kg of reaction mass

reaction mass) the maximum temperature that could be reached by the reaction mass would be around 50 ^{o}C, at which there is no further evolution of the reaction. The value for adiabatic temperature increase given in Table 2.20 is calculated for the batch case, in which it is considered that the reactant is added instantaneously under adiabatic conditions. Therefore, if the addition is performed keeping the cooling system active during the whole process, there should be no problem in keeping the heat generation under control.

RC results obtained for EQR.03

The third step studied is a nucleophilic substitution on an aromatic ring. The power profile for this reaction is shown in Figure 2.24.

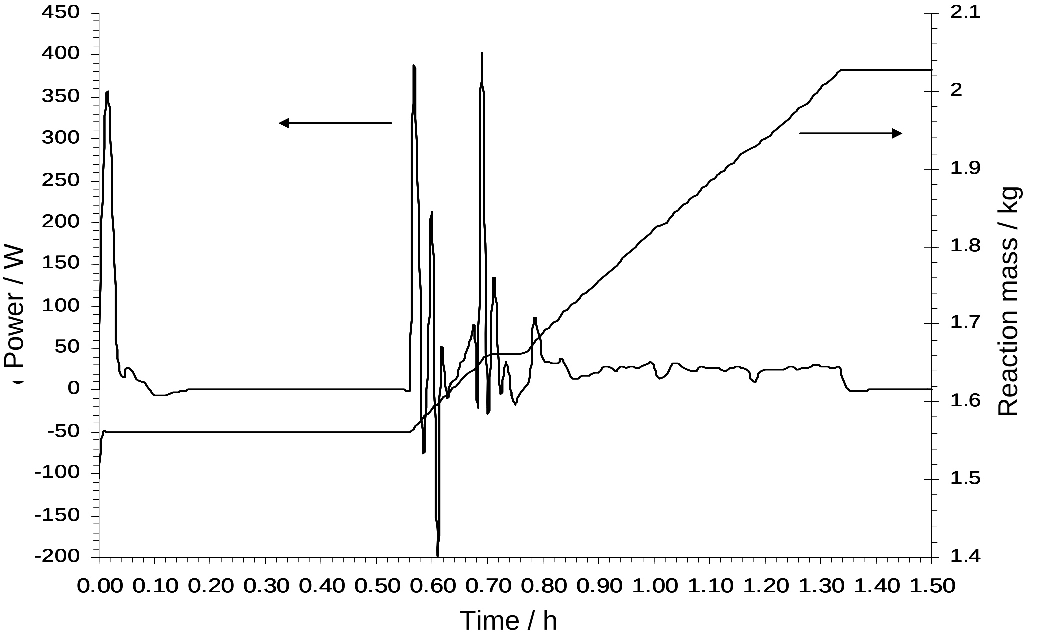

Figure 2.24. - Power profile for reaction EQR.03.

The procedure followed for this step is the following: first the reactant R-Cl is charged in the reactor, then the reaction mass is heated until 30 °C. The catalyser is added (t=0) and the limiting reactant MeONa is dosed during 24 minutes, both substances added at ambient temperature. In this case, however, due to a problem with the dosing pump (from t=43 min until t=46 min), the total time for dosing was 46 min (from t=34 min until t=80 min).

The second step for the reaction consists on heating the reaction mass until 60 °C and keeping this temperature for 30 minutes. Then the reaction mass is distilled at 67 °C until the distilled volume is 390 ml. At this point, the reaction is switched to reflux mode during 8 hours, according to the recipe for the reaction developed at the company C1.

The main results obtained from this calorimetry test are given in Table 2.21.

Process stage	**Tr / ^{o}C**	**Reaction mass / kg**	**Δ_rH / kJ·kg^{-1} (6)**	**ΔTad / ^{o}C**
Charging of R-Cl	30	1.503	-	-
Addition of catalyser	30	1.561	-13.22	6.3
Dosing of MeONa	30	2.027	-44.75	23
Tr set at 60 ^{o}C	60	2.027	-3.50	1.4

Table 2.21. - Calorimetry results for reaction EQR.03.

In this step, two different zones can be seen in the power profile shown in Figure 2.24, which can be due to different physical-chemical mechanisms during the reaction. The first tendency corresponds to the period comprised between the beginning of dosing and the time when 29% of MeONa has been dosed. In this period the heat of the reaction is generated in different peaks, with a maximum value of 245 W per kg of reaction mass. At the end of this period, 50% of the total heat of the reaction has been generated. The second tendency corresponds to the period comprised between the 29% of MeONa dosed until the time when dosing has been completed. In this period, the heat of reaction generated is totally controlled by the dosing speed of MeONa. In this step, 99% of the heat of reaction is generated during the dosing of MeONa.

The reaction takes place at the temperature of 30 ^{o}C during 30 minutes, and then the temperature is set at 60 ^{o}C. This generates an increase in the reaction speed, thus

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[6] kg of reaction mass

increasing the heat generated. However, after 15 minutes of reaching the new set temperature, no further heat generation is observed. It must also be noted that no heat is generated during the distillation procedure. This part of the reaction is not shown in Figure 2.24 for practical reasons.

The values for adiabatic temperature increase given in Table 2.21 correspond to the non-stop case for the dosing of MeONa, and to the batch case for the addition of the catalyser and temperature set at 60 ^{o}C.

RC results obtained for EQR.04

The final step for the synthesis of the product studied is the oxidation of the by-product obtained in the previous step with hydrogen peroxide at 35% solution. To perform this step, the reaction vessel is charged with the initial reactant, the reaction temperature is set at 2 ^{o}C and the hydrogen peroxide (at ambient temperature) is dosed during 90 minutes. Then the reaction is left at the set temperature during 5 hours. Figure 2.25 shows the power profile for this final reaction step.

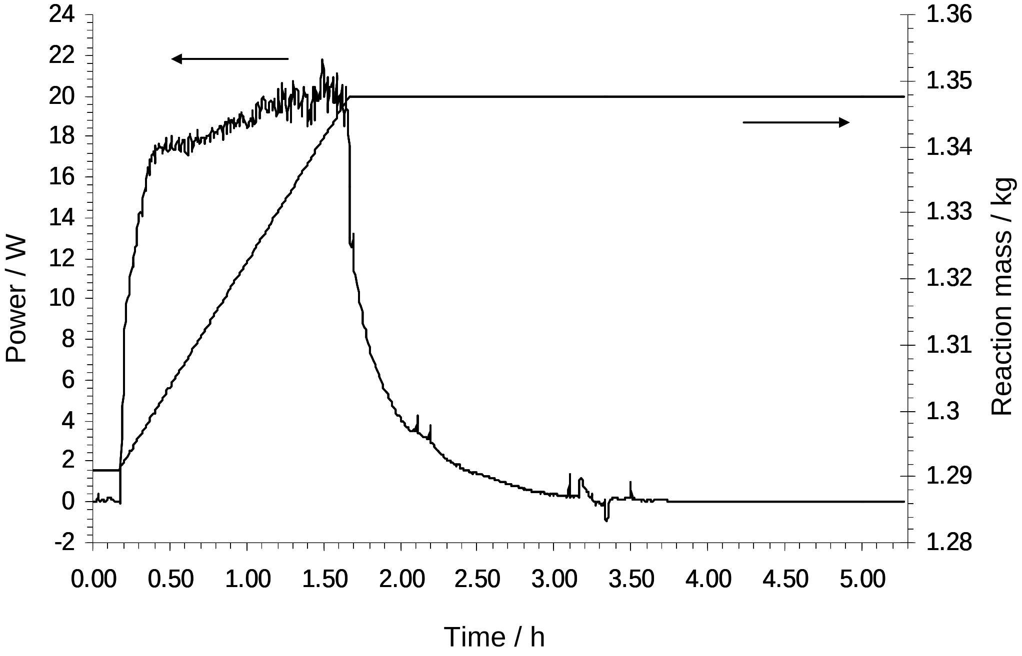

Figure 2.25. - Power profile for reaction EQR.04.

The main results obtained from this calorimetry test are given in Table 2.22.

Process stage	Tr / °C	Reaction mass / kg	$\Delta_r H$ / $kJ{\cdot}kg^{-1}$ [7]	ΔTad / °C
Charging of R-OCH_3	7	1.291	-	-
Dosing of H_2O_2	2	1.348	-82.70	35

Table 2.22. - Calorimetry results for reaction EQR.04.

From the power profile shown in Figure 2.25, it can be seen that there is an initial stage which corresponds to the period between the beginning of dosing and the time when 16 % of H_2O_2 has been dosed (which lasts around 15 minutes). In this period, the heat generation due to the reaction increases considerably. After this stage, it can be seen that the heat generation is nearly constant, even though it increases slightly until a maximum value of 16 W per kg of reaction mass.

The heat release during the dosing of the hydrogen peroxide solution is relatively high, taking into consideration the mass of the limiting reactant dosed. However, due to the dilution of the reactant in the reaction mass, the effect generated is significantly lower. The highest part of the heat is generated during the dosing time (when dosing is finished, 86% of the total heat has been released by the reaction), but it continues around two hours after dosing is complete.

2.3.2.- Differential scanning calorimetry results

The determination of the stability of the products obtained after each one of the reaction steps has been performed using differential scanning calorimetry (DSC). A series of DSC experiments has been conducted in a Mettler-Toledo DSC30® in order to determine the decomposition energies and their temperature regions.

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[7] kg of reaction mass

DSC results obtained for EQR.01

Table 2.23 shows the results obtained for the DSC experiments performed on the products of this reaction.

Experiment	**Reference**	**Tpeak / ºC**	**Qpeak / $W \cdot g^{-1}$**	**ΔrH / $J \cdot g^{-1}$**	**Tonset / ºC**
EQR.01 β: 5	8472	166	80.7E-03	-37.47	96
		287	0.14	-119.68	217

Table 2.23. - DSC results for reaction EQR.01.

Two exothermic phenomena are identified in this reaction step. The first one could be due to the thermal evolution of some of the reactants in excess, maybe MeONa, which under the studied process conditions has a significant importance starting at 96 ºC (Tonset in Table 2.23), which is a higher temperature than the one that could be reached if all the heat generated was accumulated in the reaction mass. The second peak observed in the DSC register probably corresponds to the decomposition of the final product.

DSC results obtained for EQR.02

Table 2.24 shows the results obtained for the DSC experiments performed on the products of this reaction.

Experiment	**Reference**	**Tpeak / ºC**	**Qpeak / $W \cdot g^{-1}$**	**ΔrH / $J \cdot g^{-1}$**	**Tonset / ºC**
EQR.02 β: 5	8473	222	0.27	-230.76	152

Table 2.24. - DSC results for reaction EQR.02.

The only exothermic peak that is observed for this DSC register probably corresponds to the decomposition of the final product, which under the studied process conditions has a significant importance starting at 151 ºC (Tonset in Table 2.24), which is a higher temperature than the one that would be reached if all the heat generated would be accumulated in the reaction mass.

DSC results obtained for EQR.03

Two DSC experiments were performed for this reaction. Table 2.25 shows the results obtained for these experiments.

Experiment	**Reference**	**Tpeak / ºC**	**Qpeak / $W{\cdot}g^{-1}$**	**ΔrH / $J{\cdot}g^{-1}$**	**Tonset / ºC**
EQR.03-1 β: 5	8475	152 277	0.10 0.21	-17.83 -36.29	82 207
EQR.03-2 / I+β: 5	8485	150 278	75.9E-03 0.21	-20.41 -34.48	80 208

Table 2.25. - DSC results for reaction EQR.03.

Experiment EQR.03-1 in Table 2.25 corresponds to the DSC register for the reaction mass at the end of this stage. Two exothermic phenomena are identified in this reaction step. The first one could be due to the thermal evolution of some of the reactants in excess, maybe MeONa, which under the studied process conditions has a significant importance starting at 80 ºC (Tonset in Table 2.25), which is a higher temperature than the one that could be reached if all the heat generated would be accumulated in the reaction mass. Again, the second peak observed in the DSC register probably corresponds to the decomposition of the final product.

A complementary register (EQR.03-2) is analysed for the reaction product at the end of the step, since the difference between the value for MaxTsafe and MTSR for this reaction stage is less than 50 ºC, MaxTsafe being calculated as the first Tpeak in Table 2.25 – 70 ºC, according to the strategy adopted for the determination of MaxTsafe (*cfr*. page 60) and established in 82 ºC. During the isothermal register (EQR.03-2 in Table 2.25), no exothermal activity is observed, and during the subsequent heating at 5 K/min the same phenomena are registered with the same magnitude as for the equivalent register (EQR.03-1 in Table 2.25). Therefore the value for MaxTsafe can be established in 82 ºC, determined following the previously mentioned procedure.

DSC results obtained for EQR.04

Four DSC experiments were performed for the final product of this reaction step. Table 2.26 shows the results obtained for these DSC experiments

Experiment	Reference	Tpeak / ºC	Qpeak / $W{\cdot}g^{-1}$	ΔrH / $J{\cdot}g^{-1}$	Tonset / ºC
EQR.04-1 β: 5	8489	200	51.5E-03	-9.58	130
		306	0.21	-59.13	236
EQR.04-2 (no inhibitor) β: 5	8490	128	0.15	-76.88	58
		303	0.18	-90.06	233
EQR.04-3 (inhibitor) β: 5	8491	127	99.9E-03	-52.31	57
		302	0.14	-53.84	232
EQR.04-4 (no inhibitor) I+β: 5	8498	130	0.13	-68.05	60
		299	0.16	-88.31	229

Table 2.26. - DSC results for reaction EQR.04.

Experiment EQR.04-1 in Table 2.26 corresponds to the DSC register for the reaction mass before dosing the hydrogen peroxide. Two exothermic phenomena are identified in this reaction step. The first one corresponds probably to the thermal evolution of some of the reactants of the process studied (it could be the decomposition of R-OCH_3), which under the studied process conditions has a significant importance starting at 130 ºC (Tonset in Table 2.26), which is a higher temperature than the one that would be reached if all the heat generated would accumulate in the reaction mass. The second peak observed in the DSC register probably corresponds to the combustion of methanol in gas phase, used as solvent in the reaction, which is known to behave as a gas above 240 ºC (Lide, 1993).

Register EQR.04-2 in Table 2.26 corresponds to the DSC register of the product obtained from the reaction. Again, two exothermic phenomena are identified in this register. The first one could correspond either to the thermal evolution of the product or to the excess of hydrogen peroxide, which under the studied process conditions could have a significant importance starting at 57 ºC (Tonset in Table 2.26); which is again higher than the temperature to be expected in case of accumulation of the heat generated in the reaction mass. As for the previous register, the second peak observed in the DSC experiment probably corresponds to the combustion of the solvent involved in the reaction.

A complementary register is analysed (EQR.04-3 in Table 2.26) in order to determine whether the first peak from the register EQR.04-2 corresponds to the hydrogen peroxide. With this purpose, sodium bisulphite is introduced in the sample in order to eliminate the excess of this reactant. It can be seen from Table 2.26 that both registers EQR.04-2 and EQR.04-03 present almost identical values for Tpeak and Qpeak, so it is concluded that the first peak observed in register EQR.04-2 cannot correspond to the hydrogen peroxide.

A first value for MaxTsafe has been calculated according to the strategy described previously (*cfr*. page 60), corresponding to 57 ºC. As for the previous reaction step, the difference between the value for MaxTsafe and MTSR for this reaction stage is less than 50 ºC. Therefore, it is necessary to analyse a complementary register for the reaction product at the end of the step. During the isothermal register (EQR.04-4 in Table 2.26), no exothermal activity is observed, registering the same phenomena with the same magnitude as for the equivalent register (EQR.04-2 in Table 2.26), during the subsequent heating at 5 K/min. Therefore the value of MaxTsafe can be determined in 57 ºC following the previously mentioned procedure.

2.3.3.- Criticality evaluation

According to the results obtained from the RC and DSC experiments described previously, it can be concluded that the first three reaction steps (EQR.01, EQR.02, and EQR.03) show a significant exothermic activity starting at higher temperatures than those corresponding to the process temperature, the boiling point of the reaction mass, which is 67 ºC corresponding to the boiling temperature of methanol, used as solvent (Lide, 1993), and the temperature that could be reached if the reaction was developed under adiabatic conditions in a closed system; as concerns the fourth reaction step (EQR.04), it can be concluded that it presents a significant exothermic activity starting at higher temperatures than those corresponding to the process temperature and the temperature that could be reached if the reaction was developed under adiabatic conditions in a closed system, but lower to the boiling point of the reaction, considered again as the boiling temperature of the solvent used.

According to the Stoessel classification proposed in HarsMeth v2 to determine the criticality of the studied reactions, as shown in Table 2.27, it can be concluded that the first three reaction steps correspond to a criticality value of 1, whereas the fourth stage corresponds to a criticality value of 2.

EQR.01		EQR.02		EQR.03		EQR.04	
Tp /ºC	10	Tp /ºC	25	Tp /ºC	30	Tp /ºC	2
MTSR /ºC	27	MTSR /ºC	61	MTSR /ºC	53	MTSR /ºC	37
Tb /ºC	67	Tb /ºC	67	Tb /ºC	67	Tb /ºC	67
MaxTsafe /ºC	96	MaxTsafe /ºC	152	MaxTsafe /ºC	82	MaxTsafe /ºC	57

Table 2.27. - Temperature values for the four reaction steps of the process analysed necessary to complete the Stoessel criticality evaluation.

According to these results it can be concluded that the four steps of the process carried on in the conditions tested in these experiments are inherently safe, provided that the following generic recommendations are met:

- The reactants and products used must be handled with care given their toxicity and flammability.
- It is necessary to work with the condenser turned on and connected to the reactor; besides, the reaction mass should be kept the least possible time under the reaction conditions.
- An appropriate agitation must be ensured throughout all the reaction steps of the process, since the reaction involves the use of solid reactants, to be sure that all solid substances are in suspension in the reaction mass.

2.4.- Development of strategies for the theoretical estimation of reaction enthalpies

The results obtained in the experiments performed during the validation of HarsMeth v2 at the company C1 give the opportunity to accurately determine the criticality of the process analysed. However, as it has also been mentioned several times during the discussion regarding the validation of HarsMeth with different SMEs, these companies are not always familiar with the equipment and experiments presented earlier. In fact, the reaction calorimetry experiments that have been described were performed at the IQS facilities. Even though DSC is a technique that is commonly applied in SMEs, it is not easy to find reaction calorimeters prepared to perform the experiments that would help to perform the necessary calculations required in the Stoessel method at these chemical companies. However, for a preliminary hazard assessment, it is usually appropriate to use data obtained during the course of process development together with calculated, estimated or literature data. Predictive techniques are therefore a necessary part of the tools used in the assessment of the overall energy release of a chemical reaction, even though it is important to note that the sole use of predictive techniques in a complete hazard evaluation is a dangerous approach to use.

In order to perform theoretical calculations of the heat of a reaction, a good initial estimate can be obtained by the difference between the heats of formation of the products and the reactants according to Hess Law, as seen in Eq. 2.3.

$$\Delta_r H = \sum \Delta_r H_{products} - \sum \Delta_r H_{reactants} \qquad \text{[Eq. 2.3]}$$

The precision of the results obtained depends on the accuracy of the determination of the heats of formation of the reactants and products and the level of completeness of the reaction, but it can be also affected by side reactions, changes of state or solution / dilution effects. According to the literature (HarsBook, 2003; Domalski and Hearing, 1993), the Benson method of group additivity (Benson, 1976) is probably the most widely used and practical method for estimating thermodynamic data of organic substances. This method estimates the heat of reaction with more precision and reliability than any other current theoretical method available. So, this method can be used to estimate heats of formation of complex molecules for which data are usually not available. In addition, the heats of reaction can be estimated by analogous reactions using simpler species, where the heats of formation of these species can also be estimated using the Benson method of group additivity.

The Benson method of group additivity introduced some improvements to the previous existing method, known as Average Bond Energy Summation (Benson, 1965). This improved method takes into account:

- The linking "envelope" effect to the main group / atom of the molecules considered
- The rings effect
- The isotopic effect (cis / trans, ortho / meta / para)
- The non-linking interactions

Previous studies (Frurip *et al*., 1995) have established that normally the uncertainty achieved by this method ranges between 9 to 13 kJ/mol for substances which contain the following atoms: C, H, N, O. On the other hand, the improved method is more complex to use and requires more data for parameterization, due to the higher number of groups used compared to the previous system. By means of this method, the gas-phase formation enthalpies of reactants and products or the reaction enthalpy can be calculated. Thus, the key point for an accurate estimation of the reaction enthalpy is the correct choice of the Benson Groups to be used.

Probably the more widely used computer program for the estimation of thermodynamic data is CHETAH® (ASTM, 1998), which possibly includes the most extensive available database of Benson groups. However, there are two important limitations to this method: the first one is the lack of accurate data for some organic functional groups which are present in the complex molecules commonly used in the fine chemical industries; the second limitation is the fact that the majority of the methods for thermodynamic data estimation are only for gas species, whereas usually, the organic reactions are carried out in the condensed phase. Thus, to take full advantage of the CHETAH® computer program, the adoption of an appropriate strategy in the definition of the calculations to be performed is essential in order to obtain the most accurate estimation.

To show some of the possible strategies that can be followed when a necessary group is missing, different calculations have been performed using the CHETAH® v.7.2 program, in order to estimate the reaction enthalpy for the reaction step EQR.02 of the process studied at the company C1, as shown in Eq. 2.4.

$$R-OSO_2-R'+R''-SH \rightarrow R-S-R''+R'-SO_3H \qquad \text{[Eq. 2.4]}$$

For the estimation of the heat of this reaction in gas phase, not all the necessary Benson groups were available in the current version of the computing program. In this reaction, the Benson groups which contain the molecular group SO_2, as the central group or as the "environment" (The central group is to the left of the hyphen in the notation used in CHETAH® and the environment is to the right of the hyphen), are absent in the current literature because of the problems associated with their experimental determination (Liebman, 1991).

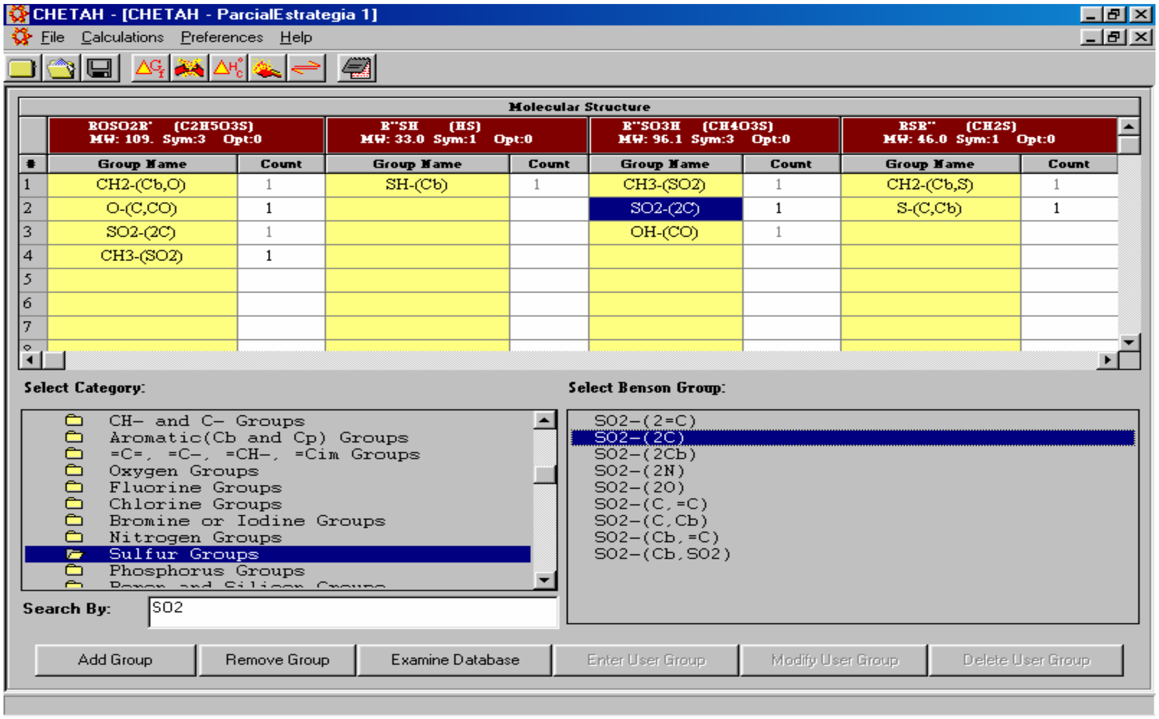
Different strategies tested for the determination of the reaction enthalpy are presented below (Nomen *et al.*, 2005):

Strategy one

It is recommended in the literature (Frurip *et al.*, 1995) that, when dealing with an absent group, this can be substituted by another one of "similar" nature. Substitutions in the "environment" are allowable, but the environmental changes should be as similar as possible to the environment. Substitutions in the central group are not allowed in this technique. This strategy is applied to the reaction studied as follows:

When the group SO_2 belongs to the environment, it can be replaced by the known and relatively "similar" group CO. The absent Benson groups [O-(C,SO_2)] and [OH-(SO_2)] have to be replaced by the known groups [O-(C,CO)] and [OH-(CO)]. When the group SO_2 is the central group (which cannot be substituted), the environment groups have to be replaced by known and “similar” Benson groups, while keeping the same central group. The absent Benson group [SO_2-(O,C)] is replaced by the known group [SO_2-(2C)]. Note that all the substitutions occur on the right-hand side of the hyphen in the modified notation which is the environment part of the group.

The introduction of the detailed groups of this strategy in the CHETAH® program is presented in Figure 2.26.



Molecular Structure

	ROSO2R' (C2H5O3S) MW: 109. Sym:3 Opt:0		R"SH (HS) MW: 33.0 Sym:1 Opt:0		R"SO3H (CH4O3S) MW: 96.1 Sym:3 Opt:0		RSR" (CH2S) MW: 46.0 Sym:1 Opt:0	
#	Group Name	Count	Group Name	Count	Group Name	Count	Group Name	Count
1	CH2-(Cb,O)	1	SH-(Cb)	1	CH3-(SO2)	1	CH2-(Cb,S)	1
2	O-(C,CO)	1			SO2-(2C)	1	S-(C,Cb)	1
3	SO2-(2C)	1			OH-(CO)	1		
4	CH3-(SO2)	1						
5								
6								
7								

Search By: SO2

Figure 2.26. - Strategy one followed for the estimation of reaction enthalpy for EQR.02, as introduced in the CHETAH® program.

Strategy two

The literature (Frurip *et al*., 1995) also suggests that the calculation can proceed by interpolation or extrapolation of known group values in a series of homologous groups in order to obtain a better accuracy of the estimated groups. It is important to realize that these operations should be performed in the “environment”. If that fails, an interpolation can be done in the central group, while keeping the environment constant, but with lower accuracy. Thus, interpolation or extrapolation in the environment is preferable because environmental group changes lead to values that are not very different and errors will be minimized, whereas central group changes lead to potentially larger errors.

Following this second strategy, the absent Benson group [SO_2-(O,C)] can be estimated by interpolation in the series [SO_2-(2C)] to [SO_2-(2O)] (shown in Table 2.28). From this result, together with a known value of the formation enthalpy of the gas molecule ($CH_3SO_2OCH_3$), which contains the last absent Benson group [O-(SO_2,C)], and the knowledge of all the other Benson groups contained in this molecule, it is possible to estimate the value of the last absent Benson group [O-(SO_2,C)] (as will be later discussed). However, this strategy can only be applied if the property of bonding addition is fulfilled and, according to the literature (Liebman, 1991), it is not the case in this example.

Known Groups	**$\Delta_f H$ / kJ·mol^{-1}**
SO_2-(2C)	-288
SO_2-(2O)	-417
Estimated Group	**$\Delta_f H$ / kJ·mol^{-1}**
SO_2-(C,O)	-353

Table 2.28. - Results from the estimation of the formation enthalpy of the SO_2-(C,O) group using strategy two.

Strategy three

Finally, given that the value of the formation enthalpy of methanesulphonic acid in the gas phase can be determined and the formation enthalpy of the compound CH_3SO_2OMe is known, it is possible to obtain the values of the necessary absent Benson groups ([SO_2-(O,C)] and [O-(SO_2,C)]) to calculate the reaction enthalpy of the reaction under study. Application of this strategy to the reaction considered is developed as follows:

- Because the value of the formation enthalpy of $PhSO_3H$ in the gas phase is known and using the specific relation shown in Eq. 2.6 (Liebman, 1991), (specific for a SO_2 group linked to benzene), it is possible to obtain the formation enthalpy in the gas phase of methanesulphonic acid.

$$\Delta H_f(g, CH_3SO_3H) = \Delta H_f(g, PhSO_3H) - 127.1 \quad kJ{\cdot}mol^{-1} \qquad \text{[Eq. 2.6]}$$

- From this value and the knowledge of all the other groups which form this molecule (extracted from CHETAH®), it is possible to obtain the value of the unknown Benson group [SO_2-(C,O)] (presented in Table 2.29).
- Finally, from this value and the formation enthalpy of CH_3SO_2OMe it is possible to determine the last unknown group [O-(SO_2,C)] (presented in Table 2.30).

Known Groups	**$\Delta_f H$ / kJ·mol^{-1}**
$PhSO_3H$, gas	-376
CH_3-(SO_2)	-42
HO-(SO_2)	-159
Estimation using Eq. 2.6	**$\Delta_f H$ / kJ·mol^{-1}**
$\Delta_f H$ (gas, $MeSO_3H$)	-503
Estimated Group	**$\Delta_f H$ / kJ·mol^{-1}**
SO_2-(C,O)	-302

Table 2.29. - Results from the estimation of the formation enthalpy of SO_2-(C,O) group using strategy three.

Known Groups	**$\Delta_f H$ / kJ·mol^{-1}**	
CH_3SO_2OMe, liq.	-564	
CH_3SO_3H	89[8]	
Estimation	**$\Delta_f H$ / kJ·mol^{-1}**	
CH_3SO_2OMe, gas	-475	
Known Groups	**$\Delta_f H$ / kJ·mol^{-1}**	
	Str. 2	Str. 3
CH_3-(SO_2)	-42	-42
CH_3-(O)	-42	-42
SO_2-(C,O)	-353	-302
Estimated Group	**$\Delta_f H$ / kJ·mol^{-1}**	
	Str. 2	Str. 3
O-(SO_2,C)	-38	-88

Table 2.30. - Results from the estimation of the formation enthalpy of O-(SO_2,C) group using strategies two and three.

All these values of formation enthalpy of Benson groups can be used to calculate the formation enthalpies in the gas phase of the reactants and products. Furthermore, these formation enthalpies can be used to calculate the reaction enthalpy (also in the gas phase) using Hess law. The values of the reaction enthalpy in the gas phase are corrected to obtain data under real process conditions, following the procedure described in Figure 2.27 (Romero, 2003). These values are shown in Table 2.31 for the different strategies used. These values are compared with the experimental result of the reaction enthalpy[9] (-133 ± 5% kJ·mol^{-1}) obtained using reaction calorimetry as has been described previously (See Table 2.20, *cfr.* page 138).

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[8] This value corresponds to the vaporization enthalpy of the group.

[9] The experimental value for reaction enthalpy has been converted to kJ per mol of limiting reactant in order to compare it with the results obtained in the CHETAH® program.

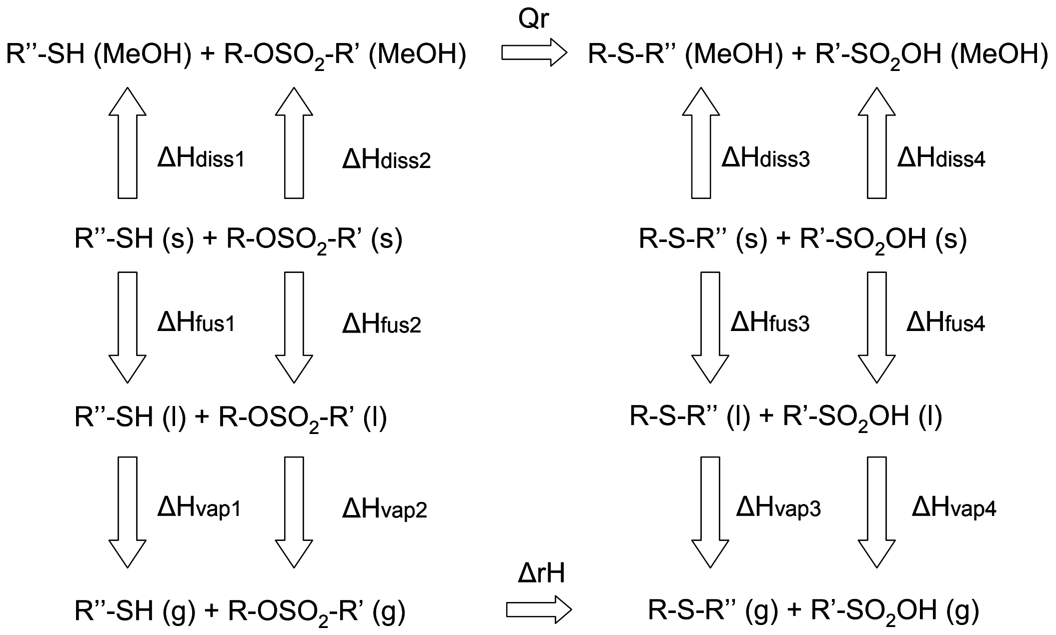

Figure 2.27. - Schema for the phase correction for the determination of the reaction enthalpy of EQR.02.

Strategy	Reaction Enthalpy / kJ*mol^{-1}	Estimation Error / %
one	-124	6.8
two	-182	37.0
three	-131.4	0.8

Table 2.31. - Results obtained for the theoretical estimation of the reaction enthalpy of reaction EQR.02 compared with the experimental result, referred to mol of limiting reactant.

The analysis of the results presented in Table 2.31 show that strategy one generates a good approximation to the experimental value (only 7% error), which is satisfactory for proceeding the next steps of the preliminary evaluation process of the reaction hazards. The accuracy of this estimation could come from the use of a similar functional group and the reliability of the data used to make this estimation. Strategy two generates an erroneous result (37% error), but since it is an error by excess, the results obtained remain on the conservative side, so the analysis would force to work on a safe scenario, provided it is reasonably practicable. This error could come from the application of one of the estimation rules, which cannot be done in this case, as it is suggested in the literature (Liebman, 1991). Strategy three generates the most precise data (1 % error). The low error is probably due to the reliability of the data used and the fact that, in this strategy, the central group remains constant. However, if the results obtained for the gas-phase reaction enthalpy are not corrected by the change of phase enthalpies, the error obtained would be greater (for example for strategy three the error would be around 80%).

3.- EXPERIMENTAL PART

The reaction calorimetry experiments have been performed with the RC1® reaction calorimeter by Mettler-Toledo at the PQAT research group from the Chemical Engineering Department of the Institut Químic de Sarrià. The reactor has been equipped during all the experiments with the following devices:

- Glass reactor AP01 with 2L capacity
- Thermostatic reactor cover MT01 using silicon oil as heating fluid
- Anchor type stirrer
- Pt 100 temperature probe
- 5 W Calibration probe
- Dosing pump Prominent gamma / 4
- Pt 100 dosing probe
- Mettler-Toledo Balance PM 4600
- Condenser covered with polyurethane with differential temperature measurement with the refrigerant fluid
- Thermostatic bath for the heating silicon for MT 01 cover, Julabo HC
- Thermostatic bath for the refrigerant fluid of the condenser, Julabo HC
- Periphery controllers Mettler-Toledo RD-10
- Dell Optiplex Personal Computer GXMT 5100

Experiments performed

The experiments that have been performed for the present work are shown in Table 3.1.

Code	Description
EQR.01	Calorimetry study for the process to obtain R-SO_3-R’
EQR.02	Calorimetry study for the process to obtain R-SO_3H
EQR.03	Calorimetry study for the process to obtain R’-OCH_3
EQR.04	Calorimetry study for the process to obtain 1482

Table 3.1. - Reaction calorimetry experiments performed

The quantities used for each of the reactants in 4 reaction steps, as well as the dosing times for each reaction are shown in Table 3.2. In order to comply with the confidentiality agreement signed between the company C1 and IQS, the names of the reactants are not given.

Experiment	Reactant	Quantity / g	t_{dos} / min
EQR.01	A	649.4	initial
EQR.01	B	186	initial
EQR.01	C	310.4	32
EQR.02	A	649.4	initial
EQR.02	E	319.1	initial
EQR.02	F	58	addition
EQR.02	G	465.6	24
EQR.03	A	649.4	initial
EQR.03	I	185.1	initial
EQR.03	J	63.4	addition
EQR.03	K	300	addition

Table 3.2 (1/2). - Reactant quantities and dosing times for the reaction calorimetry experiments performed

Experiment	Reactant	Quantity / g	t_{dos} / min
EQR.04	M	945.6	initial
EQR.04	N	200	initial
EQR.04	O	10	initial
EQR.04	P	12	initial
EQR.04	Q	124	initial
EQR.04	R	56.52	90

Table 3.2 (2/2). - Reactant quantities and dosing times for the reaction calorimetry experiments performed

RC1® configuration

The configuration of the RC1® calorimetry for the experiments is described next. For experiments EQR.01, EQR.02 and EQR.03 the configuration of the reactor is the same, and it is shown in Table 3.3. Table 3.4 shows the configuration used for experiment EQR.04.

P control: 6	R: 200 rpm	Tc necessary: -15 ºC
Cooling water flow for the condenser: 0.3 L / min Cooling water temperature for the condenser: 20 ºC Nitrogen to the reactor: yes Gas measuring device: no		

Table 3.3. - Specific RC1® Parameters for experiments EQR.01, EQR.02 and EQR.03

P control: 7	R: 175 rpm	Tc necessary: -15 ºC
Cooling water flow for the condenser: 0.3 L / min Cooling water temperature for the condenser: 20 ºC Nitrogen to the reactor: yes Gas measuring device: no		

Table 3.4. - Specific RC1® Parameters for experiment EQR.04

Table 3.5 shows the definition of analogical inputs for all the experiments

Input	Name	Type
A1/RD_2	T dos	Temperature
A2/RD_2	delta TC	Pressure
A3/RD_2	T amb	Temperature

Table 3.5. - Definition of analogical inputs for all the experiments

Table 3.6 shows the definition of control loops for all the experiments.

Name	Mode	Input	Output	Maximum deviation
L1/RD_2	Dos	B1/RD_2	C1/RD_2	0.1

Table 3.6. - Definition of control loops for all the experiments

Table 3.7 shows the definitions of safety limits for experiments EQR.01, EQR.02 and EQR.04, while Table 3.8 shows the same data for experiment EQR.04.

Variable	Minimum	Maximum
Tr	-	75
Tj	-	-
Tc	-	-
R	0 rpm	220 rpm
	Tsafe: 5 ºC	

Table 3.7. - Definition of safety limits for experiments EQR.01, EQR.02 and EQR.03

Variable	Minimum	Maximum
Tr	-12 ºC	40 ºC
Tj	-	-
Tc	-	-
R	0 rpm	220 rpm
	Tsafe: 5 ºC	

Table 3.8. - Definition of safety limits for experiment EQR.04

Previous operations

Once the experiments have been defined by introducing the previously mentioned parameters into the system, the necessary operations to carry out the experiments are performed, in the order specified in the RC1® manuals.

Tables 3.9, 3.10, 3.11 and 3.12 show the sequences of actions programmed in the RC1® for experiments EQR.01, EQR.02, EQR.03 and EQR.04 respectively.

#	Action	Duration	#	Action	Duration
1	Nitrogen connexion	X	14	Stabilization	10'
2	Addition A	1'	15	Dosing C	32'
3	Addition B	2'	16	Vv	1'
4	Addition A	1'	17	Stabilization	10'
5	R = 200 rpm	1'	18	Calibration	10'
6	Tr = 9 ºC	5'	19	Stabilization	10'
7	Vv	1'	20	Tr = 10 ºC	12'
8	Stabilization	10'	21	Stabilization	10'
9	Calibration	10'	22	Calibration	10'
10	Stabilization	10'	23	Stabilization	10'
11	Tr = 4 ºC	10'	24	Sample	1'
12	Stabilization	10'	25	Discharge	15'
13	Calibration	10'			

Table 3.9. - List of actions in the RC1® for experiment EQR.01

#	Action	Duration	#	Action	Duration
1	Nitrogen connexion	X	21	Stabilization	10'
2	Addition A	1'	22	Calibration	10'
3	Addition E	5'	23	Stabilization	10'
4	R = 200 rpm	1'	24	Tr = 60 ºC	30'
5	Tr = 25 ºC	5'	25	Stabilization	10'
6	Vv	1'	26	Calibration	10'
7	Stabilization	10'	27	Stabilization	10'
8	Calibration	10'	28	Vv	1'
9	Stabilization	10'	29	Mode Di ΔT=8	1'

Table 3.10 (1/2). - List of actions in the RC1® for experiment EQR.02

#	Action	Duration	#	Action	Duration
10	Tr = 30 ºC	10'	30	Distillation until V_D=390	
11	Stabilization	10'	31	Mode Reflux	1'
12	Calibration	10'	32	Stabilization	8h
13	Stabilization	10'	33	Calibration	10'
14	Addition F	1'	34	Stabilization	10'
15	Stabilization	10'	35	Di $\Delta T + 4$	X
16	Calibration	10'	36	Stabilization	10'
17	Stabilization	10'	37	Di $\Delta T - 4$	X
18	Vv	1'	38	Tr = 30ºC	20'
19	Dosing G	24'	39	Sample	1'
20	Vv	1'	40	Discharge	15'

Table 3.10 (2/2). - List of actions in the RC1® for experiment EQR.02

#	Action	Duration	#	Action	Duration
1	Nitrogen connexion	X	11	Tr = 10 ºC	10'
2	Addition A	1'	12	Stabilization	10'
3	Addition I	5'	13	Calibration	10'
4	Addition A	1'	14	Stabilization	10'
5	R = 200 rpm	1'	15	Addition J	1'
6	Tr = 15 ºC	5'	16	Addition K	5'
7	Vv	1'	17	Vv	1'
8	Stabilization	10'	18	Stabilization	10'
9	Calibration	10'	19	Calibration	10'
10	Stabilization	10'	20	Stabilization	10'

Table 3.11 (1/2). - List of actions in the RC1® for experiment EQR.03

#	Action	Duration	#	Action	Duration
21	Tr = 25 ºC	15'	28	Tr = 30 ºC	10'
22	Stabilization	120'	29	Stabilization	10'
23	Sample	1'	30	Calibration	10'
24	Vv	1'	31	Stabilization	10'
25	Stabilization	40'	32	Sample	1'
26	Calibration	10'	33	Discharge	15'
27	Stabilization	10'			

Table 3.11 (2/2). - List of actions in the RC1® for experiment EQR.03

#	Action	Duration	#	Action	Duration
1	Nitrogen connexion	X	13	Stabilization	10'
2	Addition M	2'	14	Tr = 2 ºC	10'
3	Addition N	2'	15	Stabilization	10'
4	Addition M	2'	16	Calibration	10'
5	Nitrogen connexion	1'	17	Stabilization	10'
6	Addition O + P + Q(1)	3'	18	Sample	1'
7	Nitrogen connexion	1'	19	Dosing R	90'
8	R = 175 rpm	1'	20	Vv	1'
9	Tr = 7 ºC	10'	21	Stabilization	50'
10	Vv	1'	22	Sample	1'
11	Stabilization	10'	23	Calibration	10'
12	Calibration	10'	24	Stabilization	10'

Table 3.12 (1/2). - List of actions in the RC1® for experiment EQR.04

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(1) Substances [O, P, Q] are introduced in the reactor by means of previously prepared solutions.

#	Action	Duration	#	Action	Duration
25	Tr = -3 ºC	10'	32	Tr = 2 ºC	10'
26	Stabilization	1h 30'	33	Stabilization	10'
27	Sample	1'	34	Calibration	10'
28	Stabilization	40'	35	Stabilization	10'
29	Vv	1'	36	Tr = 25 ºC	10'
30	Calibration	10'	37	Sample	1'
31	Stabilization	10'	38	Discharge	15'

Table 3.12 (1/2). - List of actions in the RC1® for experiment EQR.04

The main features of the DSC experiments performed are shown in Table 3.13.

Sample	Reference	Method	M / mg
End of reaction EQR.01	8472	High Pressure Crucible (40 mL) from 0 to 400ºC – 5K/min	8.646
End of reaction EQR.02	8475	High Pressure Crucible (40 mL) from 0 to 400ºC – 5K/min	5.451
End of reaction EQR.02	8485	High Pressure Crucible (40 mL) Isothermal at 52ºC during 12h + from 52 to 400ºC – 5K/min	5.595
End of reaction EQR.03	8473	High Pressure Crucible (40 mL) from 0 to 400ºC – 5K/min	8.300

Table 3.13 (1/2). – Description of DSC experiments performed.

Sample	Reference	Method	M / mg
Initial sample EQR.04	8489	High Pressure Crucible (40 mL) from -10 to 400ºC – 5K/min	5.770
End of reaction EQR.04 (without inhibitor)	8490	High Pressure Crucible (40 mL) from -10 to 400ºC – 5K/min	6.740
End of reaction EQR.04 (with inhibitor)	8491	High Pressure Crucible (40 mL) from -10 to 400ºC – 5K/min	6.774
End of reaction EQR.04 (without inhibitor)	8498	High Pressure Crucible (40 mL) Isothermal at 36ºC during 12h + from 36 to 400ºC – 5K/min	7.287

Table 3.13 (2/2). – Description of DSC experiments performed.

4.- CONCLUSIONS

A checklist based methodology for the assessment of the chemical reactive hazards involved in industrial processes has been developed and validated. The tool is especially designed to be used at small and medium enterprises working in the processing of chemical products. For this purpose several aspects have been reviewed:

- A first draft of a hazard assessment methodology for chemical reactions was created from the merging of two existing tools, HarsMeth and the Check Cards for Runaway. These methodologies were tested at 5 Spanish SMEs, and the strengths identified for each one were the basis for a new version of HarsMeth, called HarsMeth v2. Specific suggestions and findings from the collaboration with the companies were also included in the new tool.

- The new version HarsMeth v2 was extensively tested at two chemical companies. In one case, a real process was analysed following the suggestions of the methodology, and different calorimetry experiments were performed, establishing the degree of criticality of the process analysed as relatively low. The strengths and weaknesses of HarsMeth v2 were identified and further suggestions for the improvement of the methodology were put forward; in the other case, different industrial unit operations were analysed to prepare a set of checklists for the identification of chemical hazards involved in those operations.

- A systematic approach has been used to develop a tool for the identification of chemical reactive hazards in process equipment. The combination of simple reactivity concepts included in a user friendly Microsoft Excel® based system allows the user to perform an assessment of the hazards that may be encountered during different unit operations of an industrial process. Moreover, the experience gained in the use of the tool and the possibility to adapt it to new assessment cases gives the user the possibility to adapt it to the specific needs of a particular establishment.

- The final version of the methodology, known as HarsMeth NP, is designed to perform the hazard assessment on a step by step basis, in order to cover the common stages involved in the research and development phase of a new chemical synthesis. The objective is to identify possible sources of a chemical runaway as early as possible in the development of an industrial process, providing at the end a set of safety measures depending on the hazards identified. This version of the tool also provides extensive information and further references on simple to use strategies and experiments to help SMEs to complete their hazard assessments.

- HarsMeth NP has been tested with available information from a process developed at the PQAT research group at IQS. The checklists included in the methodology have been filled with the available data, which has made it possible to identify the hazards involved in the reaction, as well as the necessary safety measures in order to perform the process safely at industrial scale.

- An analysis of the chemical accidents included in the MARS database has been performed. Most of the reported causes that triggered the accidents are covered by HarsMeth NP, which proves that the methodology helps to visualize and obtain a better understanding of those topics, especially for those SMEs that have less resources or expertise in safety issues. The analysis of past accidents also helps to improve the methodology by identifying possible gaps in the tool.

- The main lessons to be learned from the accidents analysed have been established. Essentially these lessons can be grouped according to the same sections included in HarsMeth NP. In the first place, a true commitment of management staff is required in order to establish an appropriate safety culture in the company, which must be correctly explained, understood and applied by all personnel involved at any stage of the industrial activity. Next, a deep knowledge of the chemistry involved in a process is necessary, both from the point of view of the stability and compatibility of chemical products as well as from the critical parameters related to chemical reactions. Once this information has been collected, it is possible to design plant equipment according to the required parameters of the process. It must be assured that such equipment is suitably reliable, by applying maintenance and process control principles. In a last stage, safety measures must be put in place wherever necessary in order to cope with the consequences of a potential runaway scenario.

- In order to provide SMEs with simple tools to perform a hazard assessment, a system for the theoretical estimation of the reaction enthalpy of a chemical process has been developed. The Benson group theory has been applied and different strategies for the estimation in case of lack of information from one Benson group have been described. The results obtained have been compared with experimental values, obtaining in one of the strategies developed an error of 1%.

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6.- APPENDICES

The contents of the different appendices included in this PhD work are described next. The main achievement of this work, the final version of the HarsMeth methodology (HarsMeth New Process) is included in Appendix 1; in the second appendix, a series of intermediate achievements are included, like the list of chemical accidents analysed from the MARS database, or the provisional versions of HarsMeth developed during the course of this PhD. Even though these are somehow extensive, they are considered essential in order to better understand the evolution of the work that led to the final version of the methodology. Appendix 3 includes the methodologies that existed before starting the present work, and which were the origin of what the HarsMeth tool has become. They are included in the present work due to the continuous reference done to those methodologies during the description of the procedure developed to obtain the final version of HarsMeth. Finally, an Excel® sheet containing the S2S training & assessment tool for unexpected reactors can be found in the CD-Rom included with this PhD work.

Thus, the appendices are structured as follows.

- Appendix 1. HarsMeth New Process (NP).
- Appendix 2. Intermediate achievements.
    - Appendix 2.1. List of chemical accidents analysed from the MARS database.
    - Appendix 2.2 HarsMeth version 2
    - Appendix 2.3 Draft proposal for extension of HarsMeth version 2 developed at the Company C1.
    - Appendix 2.4. Checklists for hazard assessment of unit operations developed at the Company C2.
- Appendix 3. Preexisting methodologies.
    - Appendix 3.1. HarsMeth version 1
    - Appendix 3.2 Check Cards for Runaway

APPENDIX 1

HarsMeth NP (New Process)

A methodology for chemical process safety assessment for SMEs

TABLE OF CONTENTS

Preface

In the year 1998, a group of 35 European partners created ***HarsNet***, a thematic network on hazard assessment of highly reactive systems (Nomen *et al*., 2002), with the financial support of the European Commission. The aim of the implementation phase of ***HarsNet*** was the creation of an extensive forum within which universities, research centres and industries involved in the network collaborated to improve dissemination of the fundamental knowledge in the field of thermal hazard assessment of chemical processes. Preparation of short-cut, stepwise, methodologies that use simple, non expensive, techniques were in the focus of this project, in order to improve the global safety of the chemical industry. The activities of the network finished in the year 2002.

One task included in the ***HarsNet*** network was ***HarsMeth***. The objective of this task was to produce and to check a methodology for the hazard assessment of chemical processes, which could be applied by SMEs using commonly available equipment. This methodology, available at the ***HarsNet*** web page (Harsnet, 2007) provides assistance for the safety assessment of batch and semi-batch processes in an easy structured way by using basic rules and methods. ***HarsMeth*** was divided in two parts, one consisting on a short cut procedure that can be used as an interactive on-line tool, and a written guide containing different checklists to identify possible hazards in a chemical process.

In its initial stage, ***HarsMeth*** combined different short-cut methods already developed by some ***HarsNet*** partners (Nomen *et al*., 2004 (b); Ciba Speciality Chemicals, 1998; The Dow Chemical Company, 2000). All this elements were put together and combined to produce a first draft, which was improved through an intense interaction with different European SMEs working in the field of fine chemicals production. Co-operation between the network and more than 30 SMEs was generated during the last year of ***HarsNet***, and the feedback received was used to fit the work developed to the real needs of SMEs (Nomen *et al*., 2004 (a)).

The good acceptance and positive results obtained during the testing of ***HarsMeth*** suggested that further steps could be taken in the development of an integrated tool to help SMEs to perform hazard identification in their processes. The methodology was extensively tested at different chemical plants applying it at real production processes, in order to test its efficiency and to detect strengths, weaknesses and possible ways to improve it. Further revision of the method gave as a result the ***HarsMeth NP*** (New Process) version, structured to analyse specific hazards for each step involved in chemical production, from laboratory research to implementation of the process at plant scale. The method has been also improved under the umbrella of the Safety to Safety (S2S, 2007) network, involving most of the partners of ***HarsNet***, which has developed other assessment tools in specific areas such as explosions, fires, unexpected reactions in common plant equipment or safety management systems.

HarMeth is a guide for the safety assessment of chemical processes, and it is intended to identify the possible hazards that may be encountered during the performance of a chemical process. It consists on a set of checklists that cover all the steps involved in industrial production. Besides, it provides guidance on available techniques for determination of safety parameters of chemical reactions, and available measures in order to reduce probability and severity of an accident in process plants. It must be clear that ***HarsMeth NP*** does not intend to replace a complete risk assessment of external experts. Its aim is to highlight possible hazards and critical elements of the process to the user's attention. For this reason, the authors refuse any responsibility on any incident derived from the application of ***HarsMeth NP***, and it cannot serve as legal advice to any individual or entity. The initial target of this tool is small and medium enterprises working in chemical production, but this methodology can also be very useful as a preliminary guidance for international manufacturers with considerably big production plants. The wish to make this methodology applicable to as many companies as possible makes it impossible to include all aspects related to industrial safety, and only a brief inventory of items are included in each chapter. Some may find it too extensive, and others too elemental. The spirit of this work is that any non-expert in chemical safety can perform a preliminary analysis of a process, and through this, him or herself can determine what the safety requirements of a process are. The objective is to make people think on safety, given that it often happens that knowledge remains hidden under other aspects of process or plant specifications; the intention is therefore to “bring this knowledge to the surface”. In any case, the advice of safety experts should be sought anytime a doubt arises from the use of the methodology.

1. INTRODUCTION

Accidents in chemical plants represent a high potential threat because of the dangerous substances that are usually handled in that kind of installations. In a runaway situation the threat is even higher because the substances causing the accident are reacting during the event, many times in an unexpected way. This means that besides the release of dangerous chemical substances, a big release of energy will take place, for which the installation may not be prepared. Runaway reactions have been known for a long time, but they are still causing nowadays major accidents, the consequences of which are not only great economic losses, but also human lives and concern among the population. Recent studies (Sales *et al.*, 2007 (a)) show that in many cases there is a lack of knowledge of the chemistry involved in reactive processes. Furthermore, deficiencies in management of operations necessary to develop a chemical reaction are still present.

Many large companies are using robust hazard assessment methods (including sophisticated experimental techniques) and extensive management systems, to avoid chemical accidents and to reduce their severity in case they should occur. However, there is a failure to disseminate this best practice (including basic concepts and methodologies) to the large number of SMEs that are dedicated to the manufacture of fine and speciality chemicals in Europe. Moreover, the use of the expensive experimental techniques that are required for some studies limits their availability within many SMEs.

In any case, reaction hazard assessment should be an integral part of the earliest stages of good Research and Development with the objective of generating inherently safe designs of chemical processes. The experiments required can sometimes be quite inexpensive and easy to perform at a common chemistry laboratory, limiting the use of expensive testing and equipment to those cases where they are really necessary.

There are different approaches that can be followed when performing a hazard assessment. However, there are some concepts that should always be present in a reliable decision making tool. The concepts are listed below.

- Definition of process and plant characteristics.
- Identification of hazards at normal operating conditions.
- Identification of possible process deviations and hazards associated to them.
- Evaluation of plant conditions in order to carry out the process within safety margins (related to the hazards previously identified).
- Determination of the necessity to modify process or plant conditions.

Besides, it must be a company policy to register the results, to keep these results available to engineers or operators who carry out the process, and to review this procedure from time to time, or whenever a significant change is introduced in the process or in the plant.

A good example of the strategy to follow is the PHASE method (Steinbach, 1999), shown in Figure 1.

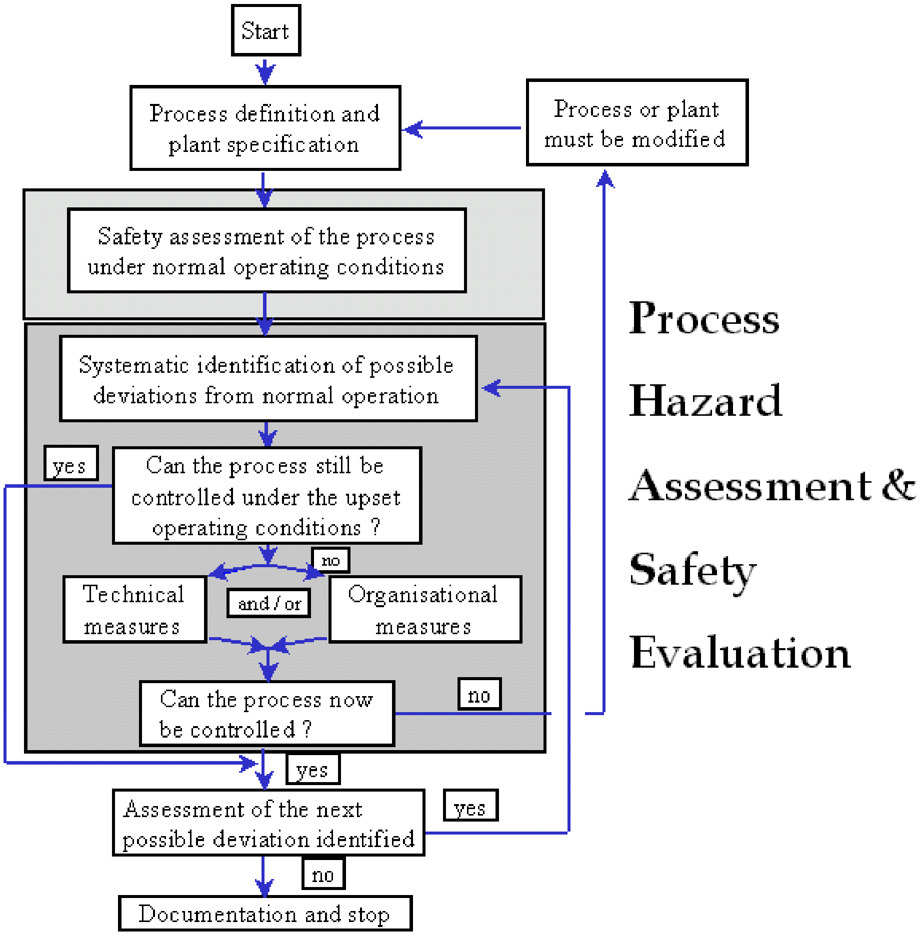

Figure 1. Procedure for safety investigations.

Such concepts have been implemented in the ***HarsMeth*** methodology in an attempt to cover the different stages in the development of a process (Figure 2).

HarsMeth NP is based in the three following concepts:

- <u>Inherent Safety</u>. A system is considered to be inherently safe if it remains in a non-hazardous situation after the occurrence of unintended deviations from normal operating conditions (Kletz, 1985). Even though it is impossible to achieve a 100% inherently safe process, the intention is to determine all the possible sources of trouble from the safety point of view previously to the plant development of the process. In order to achieve an inherently safe process, the main need is to be able to perform thorough hazard identification. To achieve this, the process is analysed in three different stages.

- *Preliminary stage.* All the different possible synthetic routes for a reaction are studied, and different screening tests are performed to have a general idea of the hazards of each route.
- *Bench scale stage.* A reduced number of possible synthetic paths can be studied here. Each one of them has to be deeply studied, considering normal and all kind of possible failure conditions.
- *Pilot Plant Scale.* One single process should be studied here. Emphasis must be placed on correctly dimensioning the equipment to be used at industrial scale. Hazard assessment of unit operations that are going to be used in plant should be performed here.

- Basis of Safety. It includes the implementation of preventive or mitigation measures, besides process control requirements, that a process needs to be carried out safely. For each process, it depends on the hazards defined in the previous section. In case those hazards cannot be completely removed, measures must be included at the industrial production stage to assure the reduction of likelihood or severity in case an incident occurs.

- Safety Management System. Differentiated from the previous points, it is independent of the chemical process to be developed. It deals with the safety policies of the company, with a special focus on how routine operations are carried out at the chemical plant. The objective is to differentiate the inherent safety, or better said, the inherent hazards related to the chemistry itself, and the added on hazards that can come from incorrect working procedures or company organisation, since a hazard will be easier to keep under control if its origin is correctly understood.

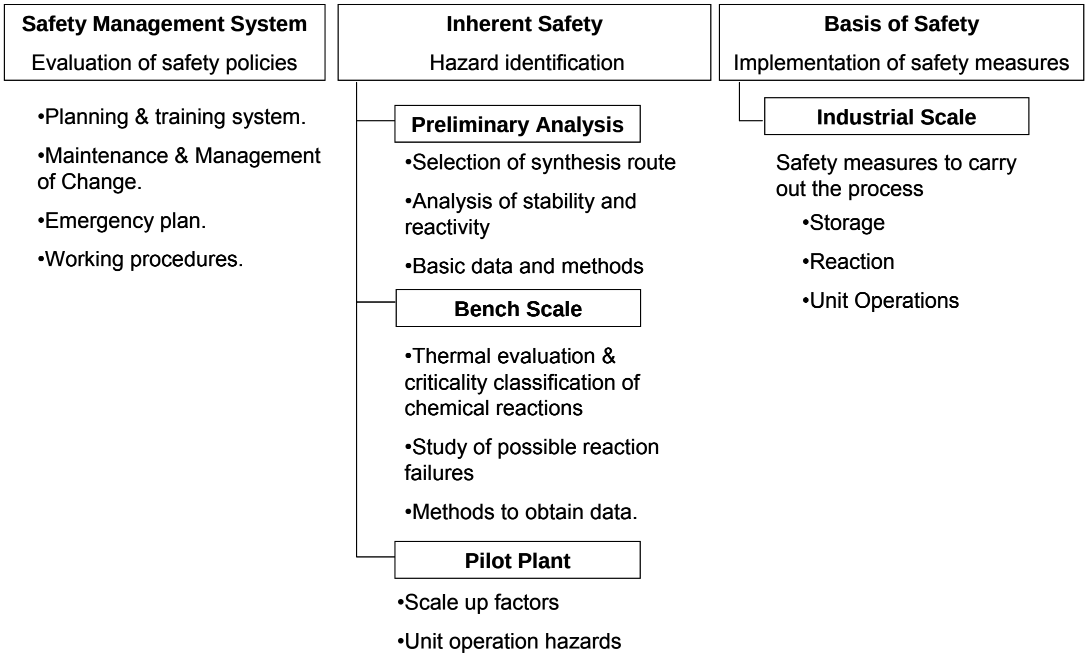

Figure 2. Structure of ***HarsMeth NP***.

The hazard identification is performed through a set of checklists that cover all the aspects that may have an influence in the safety of a chemical process. It is intended that, by answering those questions, all the possible hazards that may arise from a process developed at industrial scale can be determined.

There are 5 checklists included in ***HarsMeth NP***, one for each section included in the methodology. It is suggested that those checklists should be filled in the following order:

1. Safety Management System.
2. Preliminary Reaction Analysis.
3. Bench Scale Analysis.
4. Pilot Plant Analysis.
5. Industrial Scale Analysis.

While checklists number 1 and 5 are simply an inventory of suggested issues, which the user must indicate whether they have been considered or not, the questions in the checklists 2, 3, and 4 are structured in such a way, that three levels of answers are available. These possible answers are:

- *Justify your answer*. This answer will be given in case a specific parameter is regarded as safe. In such case, a written justification is required in order to explain the reason for this consideration.
- *Review your safety measures*. It means that a hazard may be derived from the parameter studied. In this case, either the process development should be modified, or the plant set-up must be adapted to reduce, mitigate or prevent such hazard, and its possible effects. Any answer of this type encountered in the preliminary scale, bench scale and pilot plant checklists, will have a corresponding evaluation in the Industrial Scale checklist, proposing measures to avoid the hazard or to mitigate the consequences of any incident derived from such hazard.
- *Check it!* This indicates that the answer to the question put forward is unknown. In this case the user of ***HarsMeth NP*** must stop completing the questionnaires and determine the answer to the question.

When applying ***HarsMeth NP*** to a process, the user should not move to another checklist until all the aspects required in the previous one have been filled correctly and fully understood. This means that in case the answer to one question is unknown, it should be checked before going any further. This way, it is assured that the process development is stopped at the earlier stages, instead of carrying it on industrial scale with uncertainties in the safety issues involved.

Along the methodology, some theoretical and experimental methods are proposed in order to determine and interpret the required information. However, it must be clear that any user should seek further information before actually performing any experimental test based on the information included in ***HarsMeth NP***, since the authors will accept no responsibilities on the possible consequences of such tests.

HarsMeth NP can be used by any engineer or operator with basic knowledge on chemical and process safety. The questionnaires can be filled individually or in groups, but it is strongly suggested that after it is completed, it is reviewed by another person or group, including the company's responsible for safety issues. Special emphasis on revision is encouraged in the validity of the *Justify your answer* type of answers.

One version of ***HarsMeth NP*** should be used for every new process carried out in the plant. Also, every time a process is modified significantly, the results obtained by ***HarsMeth NP*** should be verified. Even though some sections are considered independent of the chemical process studied (for example the Safety Management System) it should always be checked if any changes could modify in any way the answers given.

Finally, if more information on these issues is needed, one interesting source on the topic is another task developed by ***HarsNet*** called ***HarsBook*** (HarsBook, 2003). This task consists on a guide for experts and it describes the best methods currently available for predicting, assessing and minimising exothermic reaction hazards. It is structured in a way that covers all the steps related to a chemical process, from the research of information to the storage of unstable substances. Another useful source of information is the S2S web site (S2S, 2007), which includes other assessment and training tools for industrial hazards.

2. SAFETY MANAGEMENT SYSTEM

The ***HarsMeth*** methodology intends to cover all the stages of a process, from the laboratory research until the production at industrial scale. However, it is clear that there are some procedures inside the chemical company that should be common to all the processes that take place at the industrial installation. Even though the focus of ***HarsMeth NP*** is the assessment of chemical reaction hazards, some recommendations are put forward for an appropriate safety management system. A more complete safety management assessment tool has been developed by the S2S network, which can be found at the S2S web page (S2S, 2007). The user is encouraged to use this tool for a better understanding of management system requirements.

The Safety Management System should include standardized procedures in order to always carry out any kind of work in a safe way. It must involve the direction and all employees, and its specifications must be clear and easily available to anyone in the company. The elements covered in the following description do not form a rigid scheme, but are parts of an interdisciplinary flow of information combining elements common to all categories.

Planning & Safety training. Planning in chemical safety includes elaboration of safety practice procedures for the whole process, as well as nomination of people responsible for ensuring that those procedures are followed. Special care must be provided in training workers with all the necessary information to perform plant operations in a safe way, mainly those involving reactive systems.

Planning and training procedures should be subject to periodic revision and validation. It is the responsibility of the chemical company to establish a proper culture of safety in the establishment, where all workers (including those external to the chemical company) are always aware of the hazards related to the activities they perform.

Maintenance & Management of change. Many incidents involving chemical reactivity occur during non routine procedures such as maintenance work (Sales *et al.*, 2006 (b)). These activities must be correctly assessed by defining safety precautions to be applied. Appropriate supervision of maintenance activities must be provided. Also, a rigorous system to avoid hazards deriving from changes in plant or process conditions must be put forward.

Emergency plan. The actions to be taken in case of an emergency should occur must be clearly defined, explained, reviewed and practiced. It is important to assure that safe ways of stopping activities are provided and also that every worker (including external personnel) is aware of evacuation ways.

A correct management of the alarm system is also necessary. Different alarm systems should be used to identify critical parameters of the process in order to establish different actions to be taken in each case. Also, management should include proper supervision on each alarm included. If alarms are not clearly differentiated and identified, a critical signal could pass unnoticed and a hazardous situation may take place.

Operational Practice System. This section covers some routine actions to be taken during process operations. These are supposed to be performed in the same way no matter what the chemical process is. There should be specified procedures detailing how these should be carried out in order to avoid hazardous situations.

The permit to work is a protocol that assures that any work in the plant can be performed under safety conditions. This means, for instance, that welding operations should not be performed in a zone where flammable conditions might be present. It also implies that a procedure must be followed to assure that plant conditions allow the chemical process to be performed safely. For example, if an alarm, a probe or a safety measure has been deactivated for maintenance procedures, it should not be possible to reassume the process until it has been reconnected to the control system.

The management of waste streams must be carefully performed in order to avoid unexpected hazards. These streams usually involve mixtures of different substances, the properties of which many times remain unknown. Solvent recovery in process plants may involve mixtures of different reactants, intermediates or impurities, including thermally unstable products that can lead to accidents under certain conditions (Lunghi *et al*., 1998; Goulding, 1994)

The following checklist includes a relation of basic suggestions to cover the previous points. Since it is non dependent on the process, this checklist can be answered once for the whole plant, but the answers should be reviewed periodically.

I. SAFETY MANAGEMENT SYSTEM CHECKLIST

	Planning and Safety Training	OK
I.1	The company must comply with all the required legislation for safety issues	
I.2	There should be a written policy stating how chemical processes must be carried out under safety conditions	
I.3	Responsibilities of personnel involved in chemical processes should be clearly established	
I.4	All personnel involved in chemical processes should have access to the policies established	
I.5	A fluent system of communication between personnel and departments should be enhanced	
I.6	Periodic audits of processes and procedures should be performed in order to assure they follow safety policies	
I.7	There should be a clear procedure to train operators in the hazards involved in chemical processes	
I.8	External workers should be clearly informed about the safety requirements of each process	
I.9	Case studies, lessons learned from past accidents and historical data should be used in safety training	
I.10	Training procedures should be reviewed periodically in order to avoid overconfidence	
	Maintenance and Management of Change	OK
I.11	There should be a written procedure detailing how to perform maintenance of plant equipment	
I.12	Design and maximum values of critical parameters (P, T, V, etc.) should be documented for all equipment	
I.13	There should be a system to assure that all required safety measures are always in place and operational	
I.14	Maintenance procedures should include calibration systems for sensors	
I.15	Maintenance procedures should include studies of corrosion, equipment oxidation and fatigue of construction materials	
I.16	Maintenance procedures should include studies on compatibility of cleaning products with process reactants	
I.17	There should be a system to assure that all alarms are operational and well heard throughout the plant	
I.18	There should be a system to assure that workers are able to identify and differentiate the various existing alarms	
I.19	There should be a written procedure detailing how to perform cleaning operations in plant equipment	
I.20	There should be a system to assure appropriate supervision for maintenance and cleaning procedures	
I.21	There should be a written procedure detailing how to manage process and plant modifications	
I.22	The management of change system should include detailed procedures for renewal of documentation and software	
I.23	A quality control system should be implemented	

	Emergency plan	**OK**
I.24	All possible accident scenarios should be considered and their possible consequences evaluated	
I.25	There should be a written procedure detailing what actions must be taken in order to mitigate releases of loss of containments	
I.26	All safety systems necessary to mitigate a loss of containment should be implemented	
I.27	Near misses should be correctly reported and investigated	
I.28	There should be an emergency valve test to assure that all equipment is protected against overpressure	
I.29	There should be a written procedure detailing what actions should be taken by each worker in case of an emergency	
I.30	Personnel in charge of coordinating emergency situations should be nominated	
I.31	There should be emergency teams available, like fire brigades or medical aid	
I.32	A coordination system with local authorities in case of an emergency should be established	
I.33	There should be an organised system of alarms, differentiated and identifiable by every worker	
I.34	Emergency drills should be performed periodically	
I.35	Emergency drills should include activation of defence lines and establishment of meeting points	
I.36	The efficiency of emergency drills should be evaluated	
I.37	There should be a written procedure detailing how to stop an activity in case of an emergency	
I.38	There should be a written procedure detailing evacuation routes in case of an emergency	
	Operational practice system	**OK**
I.39	There should be a permit to work system in operation, specifying each task assigned to each worker involved in the process	
I.40	There should be a written procedure detailing correct plant conditions for start up and shut down of a process	
I.41	There should be a system to assure appropriate supervision for process operations	
	There should be an established procedure to avoid hazardous situations due to:	
I.42	Wrong chemicals used (i.e. wrong labelling, wrong pick up)	
I.43	Wrong quantities used	
I.44	Unavailability of chemicals (reactants, inhibitors…)	
I.45	Bad connections or piping	
I.46	Use of the same equipment for different processes (multi-purpose plants)	
I.47	New chemicals added in vessels already in use	
I.48	Transport or wrong manipulation	
I.49	Mixing of waste streams	
I.50	Failure of power supply and auxiliary services (N_2, air, water, oil, steam…)	

3. PRELIMINARY REACTION ANALYSIS

The safety analysis of a chemical process must begin at the earliest stage of the development of the process. When a new chemical product is to be produced at an industrial scale, a synthetic route has to be determined. This will be done by testing the chemical yield of different reactants in the laboratory. At this stage, different paths to obtain the desired product could be put forward, where different combinations of reactants, solvents, catalysts, products and by-products can be involved. It is usually unavailable to perform a rigorous safety study on every single combination. Furthermore, other parameters different from safety can be of importance in the election, such as cost, yield and quality, environmental policies, and so on.

Nevertheless, an orientation on the possible hazards to each possible synthesis path must be given in order to take a decision on the choice of a chemical route. Basically, the information to be given for each combination of reactants is divided into two groups.

- Chemical stability of reactants and products.
- Reactivity and Compatibility of chemicals.

There are some preliminary tests that can provide fair enough values on these safety issues, considering that further and deeper tests will be performed in following stages.

But before actually studying the hazards of chemical reactions, the concept of inherent safety must be introduced. This concept could be considered more like a philosophy that should be used during the whole life-cycle of industrial production.

3.1. Inherent Safety

The inherent safety approach for hazard assessment intends to ensure that a process will remain under safety margins of operability even if the process undergoes any deviations from the expected operation conditions. This implies that all the potential hazards have been identified, and process and plant designed in such a way that those hazards are eliminated introducing the necessary preventive measures. This can be achieved for example by changing reactants, reaction conditions, solvent, catalysts etc. (Rogers, 1991). The same is valid for any synthetic route or for the operation mode. Semi-batch processes should be preferred to batch, because the semi batch mode allows controlling the reaction through addition, besides fewer inventories have to be used for each reaction step. Likewise, if plant and organisational conditions allow it, changing to continuous production should be attempted.

Inherent safety was introduced by Kletz in 1985, and has been widely studied since that time. Four principles can be considered as the basis of the inherent safety concept.

- Minimise (or intensify). Use smaller quantities of hazardous substances in the process at any time.

- Substitute. Replace a material with a less hazardous substance or a hazardous reaction with a less hazardous one.

- Moderate (or attenuate). Use less hazardous conditions, a less hazardous form of material or facilities which reduce the impact of a release of hazardous material or energy.

- Simplify (or error tolerance). Design processes and equipment to eliminate opportunities for errors by identifying ways to eliminate excessive use of add-on safety features and protective devices.

Even though it is considered to be virtually impossible to completely eliminate all hazards, it should be a common practice in process development to apply inherent safety principles, under a basic general idea: to avoid a runaway rather than to mitigate its consequences.

3.2. Chemical Stability

The first thing that must be taken into account when considering the chemical products to use in a chemical reaction, is how stable this products are going to be. A good classification of stability hazards is provided by the CCPS (2001).

- Unstable: referred to chemicals that have tendency to break down (decompose) over time or when exposed to conditions such as heat, environmental conditions, shock, friction or a catalyst with the resulting decomposition products often being toxic or flammable. Decomposition can be rapid enough to give an explosive energy release and can generate enough heat and gases for fires or explosions to take place. Different types of unstable materials can be considered, such as:

    - Decomposing
    - Thermally sensitive
    - Shock sensitive
    - Explosive

- Polymerizing: tendency of some chemicals to self-react to form larger molecules, while possibly generating great amounts of heat or gases.

- Pyrophoric: a substance is considered pyrophoric if it ignites spontaneously when exposed to air.

- Peroxide former: any chemical that has the tendency to react with oxygen, such as from being exposed to air, to form unstable organic peroxides.

- Water reactive: a chemical that will react with water or moisture.

- Oxidizer: chemicals that give up oxygen easily or readily oxidize other materials.

- Reducer: chemicals that can reduce other materials generating dangerous amounts of heat.

- Toxic: property of a chemical to have poisonous effects after a certain time of exposure to a given concentration.

Even though there are currently no methods available for estimating the thermal stability of substances, a preliminary indication of this parameter can be found in the literature. However in the majority of cases some kind of experimental testing will be needed. Some first aid references and experimental techniques are outlined next.

a) Literature surveys

There are a great number of publications that can provide information on stability of chemical substances. Some classifications on the stability of functional groups can be helpful as a start (CCPS, 1995; Johnson *et al*., 2003; Barton and Rogers, 1997). Next some further literature references are cited

- *Material Safety Data Sheets (MSDS).* Suppliers of chemical reactants should always provide with MSDS, which should contain some section regarding Stability and Reactivity issues. Further Information on MSDS characteristics can be found at the S2S web site (S2S, 2007).

- *Bretherick's Reactive Chemical Hazards.* This work covers 4800 elements or compounds with an additional 5000 secondary entries involving two or more materials, with 30000 cross references, including case histories as examples (Bretherick, 1996).

- *Merck Index.* Commonly available encyclopedia for nearly 10000 chemicals, containing stability data for many materials (The Merck Index, 1983).

- *NFPA*. The compilation done by the US National Fire Protection Association includes different chapters such as hazardous chemical data, fire and explosion hazards, instability and reactivity hazards and a manual of hazardous chemical reactions (NFPA, 1991).

b) Experimental techniques

In order to perform preliminary tests to determine the stability of substances and mixtures, the following methods can be used.

- *Differential Thermal Analysis (DTA)*. Consists on the measurement of the change of the difference in temperature between the sample and a reference, while they are subject to a particular temperature regime. DTA measurements are useful to determine possible exothermic activity of a sample (HarsBook, 2003).

- *Differential Scanning Calorimetry (DSC)*. DSC involves measurement of the heat released or absorbed by the sample in comparison to a reference while they are both subject to the same temperature regime. DSC experiments provide information on thermal stability, such as the starting temperature of decomposition phenomena, or a possible autocatalytic behavior (HarsBook, 2003).

- *Flash point tests*. The flash point is the lowest temperature at which a substance can be ignited under certain conditions. There are a number of ASTM standard methods for these tests (D56, D1310, D93, D92, D3278) (ASTM, 2007)

- *Flammable limits*. Upper and lower concentrations of a substance in a mixture which can be ignited by an ignition source. The experimental procedure consists on a chamber into which different concentrations of the mixture are introduced and subject to a spark or hot wire to determine at which concentration the mixture ignites (The Dow Chemical Company, 1997).

- *CHETAH (Chemical Thermodynamic and Energy Release Program)*. This is a software program developed to screen mixtures of chemicals for their potential to undergo a violent decomposition leading to a deflagration or detonation. The program can determine whether the explosion potential of the material is high, medium or low (HarsBook, 2003; CHETAH, 1998).

- *Drop weight test*. This test gives an idea on how shock sensitive a substance is. It measures the susceptibility of a chemical to decompose explosively when subjected to the impact produced by dropping a weight onto a small sample on a metal cup. Results are not absolute and depend on the conditions of the test, but can be valid as a first guidance (The Dow Chemical Company, 1997).

- *Confinement cap test*. This test is used to determine the detonability of a material using a blasting cap as an initiator. The blasting cap is ignited to set up a shockwave in the sample test in less than 1 millisecond. If the material detonates, it will add energy to the system, which will split the aluminum tube in which it is confined. The amount of splitting can be compared to known explosive materials (The Dow Chemical Company, 1997).

- *Explosibility test*. A simple test to determine the possibility of delagration is to drop a few milligrams of the substance onto a hotplate or to heat it on a spatula. Rapid decomposition or burning suggests that the substance is capable of deflagration (Barton and Rogers, 1997).

- *Dust explosions*. A particularly hazardous operation is the handling of dust solids. Some preliminary tests can be performed, such as the so called 20 liter sphere test (Steinbach, 1999). A preliminary estimation can be done regarding the particle size of the material handled. The smaller the particle size, the greater the hazard will be(The Dow Chemical Company, 1994).

- *Pyrophoric*. A simple observation test can be performed, dropping a small amount of substance from a height about 1 meter and seeing whether it ignites or not during dropping (powders) or after some time (liquids). Test requires several repetitions for confirmation of results (CCPS, 1995).

- *Water reactive*. A simple test consists on introducing a small sample in a flask containing water. The flask is connected to a gas volume metering device, in order to determine the amount and rate of gas generated. Such gas must be tested afterwards for flammability (CCPS, 1995).

- *Oxidizer*. The first step should be to calculate the oxygen balance. This is the amount of oxygen, expressed as weight percent, liberated as a result of complete conversion of the material to relatively simple oxidized molecules. Further testing can be done mixing the substance with a combustible material in different concentrations, arranging different strips of the mixture which are later ignited. The burning time is measured and can be interpreted as a function of the oxidizing properties of the substance (CCPS, 1995).

- *Toxicity*. Unfortunately there are no techniques that can be used to test toxicity outside a specialized laboratory. Typical experiments here are performed with animals exposed to different concentrations of the selected material. However, a preliminary bibliographic search can be done, either on MSDS or in different web sites like NIOSH.

3.3. Reactivity and Compatibility

Once the thermal behaviour of each substance is determined, it is also necessary to determine possible hazards arising from the interaction of the different chemicals involved. Here compatibility charts must be elaborated that clearly specify any possible hazardous consequence of mixing two chemicals at any step of the process. There exist some previously developed methods, outlining the following:

- <u>Compatibility Charts</u>. There are different methods to determine the possible effects of the interaction between binary combinations of chemicals. A compatibility chart developed by the US Environmental Protection Agency is included (see annex I). This takes into consideration the effects of reactive functional groups. Substances must be classified according to the functional group that is considered more reactive, and then the possible effects of the different combinations of chemicals that can interact must be considered (EPA, 1980).

- Reactivity Worksheet. The Chemical Reactivity Worksheet is a free available software developed by the US National Oceanic and Atmospheric Administration (NOAA, 2004). It is a very helpful tool for the determination of hazardous chemicals interactions. It includes:
    - *a reactivity database*. This database contains information for more than 6,000 common hazardous chemicals. The database includes information about the special hazards of each chemical and about whether a chemical reacts with air, water, or other materials.
    - *a way to virtually mix chemicals*. Consisting of a program to find out what possible hazards could occur from accidental mixing.

When performing compatibility studies, the following issues must be considered.

1) Compatibility must be studied in front of any binary combination of chemicals involved in the process, independently of whether they must be mixed together during the industrial process. This procedure considers the possibility of using mistaken chemicals at any point of the process, or the possibility of mixing due to accidents at storage facilities or during transportation operations.
2) Construction materials should be considered in front of any reactant. Particularly any metal container that could act as a catalyzer of possible side reactions (or any other material that is known to be incompatible). In fact, when using catalyzers it must be assured all binary combinations plus the possible catalyzers are studied.
3) Finally, it must also be studied the possible interaction of any auxiliary material (nitrogen, oil, refrigerant fluids, cleaning or maintenance materials) with reactants and products. Special care must be taken with water, even if it is not directly involved in the process, since it can always be present due to weather effects.

Regarding the reactivity of the desired process, the first consideration must be the amount and rate of heat generation by the synthesis reaction. Even though this will be deeply studied in following sections, a rough estimation can be performed with commonly available equipment. Besides, a first approximation on the amounts of gas that the reaction is going generate must be given in order to have an idea on the amount of pressure that can be generated during the reaction. Following, a list of simple techniques for preliminary results is given.

- CHETAH. Although its chief aim is to predict deflagration/detonation potential from molecular structure, it can also be used to estimate heats of reaction, heats of combustion or heat capacities. Calculations are done using the Benson Group theory, and results can vary regarding how these groups are introduced in the program (Nomen *et al*., 2005), so the reaction conditions must be clearly defined.

- DSC. DSC is a useful technique to determine thermal stability, but it can give more information than DTA. For example, it is a very good method to determine the specific heat of a mixture, which is important for a complete thermal evaluation of a process (HarsBook, 2003).

- Mixing calorimetry and gas evolution tests. At least one mixing calorimetry test must be performed for every possible synthetic route. These tests must include all the chemicals involved (reactants, catalysts and solvents) and follow the conditions indicated in the synthesis path (temperature, pH an do on). They can be performed using commonly available laboratory material on a small scale. The use of a gas buret to collect the reaction products can give an indication of the gas generation (The Dow Chemical Company, 1997).

- Dewar calorimetry. The use of a stainless steel Dewar flask is the best way to simulate the loss of control of a reaction in the laboratory, but it can be replaced by any vacuum bottle equipped with thermocouples, in order to determine the temperature evolution of the reaction in absence of heat exchange. For pressure data, experiments should only be performed using the stainless steel vessel with a pressure gauge and assuring appropriate protective measures for personnel (HarsBook, 2003).

It must be noted that the techniques mentioned in this section can only be taken as preliminary references. It is strongly recommended the search of further information before performing any of these tests in the lab. Interesting sources for more information can be the American Society for Testing and Materials (ASTM, 2007) or the European Chemicals Bureau (http://ecb.jrc.it). This has been developed by the European Commission, and it includes a selection of standardized methods for testing physical and chemical properties, classification and labeling databases, legislation issues, and other interesting information.

The following section includes a table that must be used to specify the substances and mixtures used in the process; next, a checklist can be found that includes the basic hazards that should be identified at this stage of the process. One version of this checklist should be completed for each one of the possible synthesis paths considered so far, and results should be recorded and kept always present for further developments of the analysis. At the end of the checklist, a summary table can be found where the results of the analysis for each case should be compared. This table should also include non-safety related issues, in order to be able to perform a better comparison between all the possible paths, so that the analysis can be used as a trust worthy decision making tool.

II. PRELIMINARY REACTION ANALYSIS CHECKLIST

Substances and mixtures data:

Synthesis path ID(1):									
Substances and mixtures(2)	Chemical composition	CAS number	Identification number(3)	Purity(4)	Phase			Handling conditions(5)	Thermal activity at Tstorage(6)
					G	L	S		

NOTES:

1. One copy of this table should be filled for every possible synthetic route.
2. Consider all the possible phases that a substance can be present in the process (storage, reaction steps, etc).
3. Use any internal identification reference for substances.
4. Degree of purity as specified in each process.
5. Inhibitors, triggering agents, chemical substances able to influence the rate of reaction, etc.
6. Stable or unstable, considering the maximum storage period.

	Is any of the substances considered to be potentially as:		
II.1	**Susceptible of decomposition with time?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.2	**Thermally unstable?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.3	**Self reacting / autocatalytic / Polymerizing?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.4	**Water reactive?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.5	**Oxidizer?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.6	**Reducer?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.7	**Flammable?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.8	**Corrosive?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.9	**Pyrophoric (spontaneously combustible)?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.10	**Shock sensitive?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.11	**Explosive?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.12	**Toxic?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

	Can mixing of two substances generate a hazardous amount and/or rate production of:		
II.13	**Heat?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.14	**Fire?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.15	**Known hazardous substances (peroxides, azides,…)?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.16	**Toxic substance formation?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.17	**Flammable substance formation?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.18	**Explosive substance formation?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.19	**Corrosive substance formation?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.20	**Violent Polymerization?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

	Do preliminary tests suggest potentially dangerous:		
II.21	**Quantity and rate of heat production?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.22	**Quantity and rate of gas generation?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

Use the following table to indicate the substances or mixtures identified as hazardous, and the specific hazard associated to them.

1. Decomposition.
2. Autocatalytic.
3. Fire and Flammability.
4. Toxic.
5. Corrosive.
6. Explosion or gas generation.

Assure that compatibility tests include construction materials and auxiliary services

Substance or mixture	Hazard Identified

Use the following table to indicate which synthesis path has yielded hazardous values for any of the items reviewed in this section (stability, compatibility, heat and gas generation…). Include also possible comments regarding other aspects of the synthesis studied not specifically related to safety (yield, reaction time, purity of final product, reactant consumption, wastes generated, possible economic profit and so on).

Chemical synthesis path ID	Stability hazards	Reactivity hazards	Heat and gas generation hazards	Other aspects

4. BENCH SCALE ANALYSIS

Once a synthetic route has been chosen as the best way to carry out the industrial production of the desired chemical compound, it must be thoroughly studied in the laboratory. Apart from the production tests carried out by synthesis chemists, the chemical reaction hazards must be studied. When doing so, not only the expected conditions of the process must be considered, but also scenarios that may occur due to any deviation from the normal evolution of the synthesis reaction.

4.1. Thermal Evaluation of Chemical Reactions

It is clear that the evolution of the temperature through the whole process must be well known after the study of the process on a laboratory scale. Thermal evaluation is the way to know the expected thermal behaviour (under normal or abnormal conditions) of a chemical synthesis. Even though this guide does not intend to cover to all extent the theory of chemical reaction engineering, the following concepts when studying reaction hazards must be taken into account.

- <u>Thermodynamics.</u> The magnitude of the energetic change associated with the chemical reaction.

- <u>Kinetics.</u> The rate of the energetic change (heat release rate).

The importance of the temperature evaluation resides in the fact that generally the rate of a chemical reaction is governed by temperature in an exponential equation known as Arrhenius law (Barton and Rogers, 1997), whereas the cooling capacity of a typical reaction vessel is linearly proportional to the reaction temperature, in a relation that involves the heat transfer coefficient and the surface area between the reactor and the cooling device. If the evolution with temperature of both tendencies is compared (Figure 3), a differentiation between a stable and an unstable zone can be made (CCPS, 1995).

A runaway reaction is usually considered as an unexpected and undesired situation, in which the progressive generation of heat from a chemical process occurs due to the rate of heat production being greater than the rate of heat removal (Chilworth, 2001). It must be noted, however, that not always a runaway has to be hazardous. A temperature increase does not necessarily have to generate a safety problem. The problem comes when side effects are generated by this temperature increase, mainly being decomposition processes or secondary unexpected reactions that can lead to uncontrolled gas generation and consequently to dramatic pressure raises that can provoke the explosion of reaction vessels. Depending on the characteristics of gas generation in a runaway scenario, reaction systems can be classified as gassy, vapor-pressure and hybrid, depending on whether the pressure rise comes as an effect of permanent gas generation, increased evaporation of reactants, or a combination of both factors (Barton and Rogers, 1997).

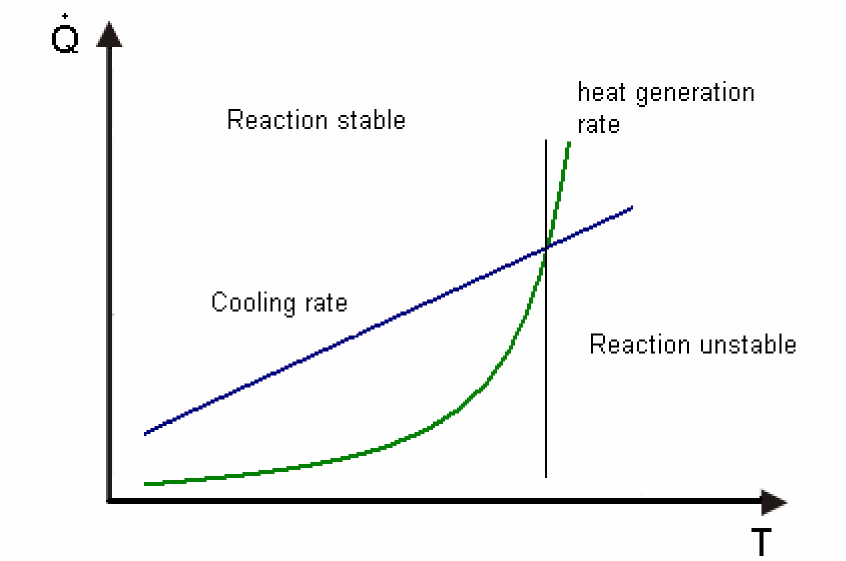

Figure 3. Comparison of typical evolution of heat generation ($\dot{Q}$) as a function of temperature for an Arrhenius type reaction, and the cooling system of a reaction vessel.

The first step must be a thorough study of the desired reaction in order to check that no hazard arises under normal operating conditions. Probably the preliminary tests described in the previous chapter have already proved this, but laboratory experiments should now determine the design of the cooling system, agitation, and other devices necessary to carry out the reaction safely.

There are many factors that can alter the course of a chemical reaction produced at industrial scale, mainly due to equipment malfunction during the process. It has already been outlined in the Safety Management System how some actions (use of mistaken chemicals, and so on) can generate an accident, but also malfunctioning of reaction equipment can lead to hazardous situations. Some of these hazards can be.

- Accumulation. It is a build up of non reacted chemicals inside the reaction vessel. This problem arises when the concentration of the controlling reactant in the bulk reaches a too high value, then the reaction is triggered too fast and high exothermal behaviour appears. Some causes that may lead to an increase in accumulation are:
  - *Inappropriate dosing speed.* A failure in the dosing system will alter the expected kinetics of the reaction, which will generate an increase in the concentration of non reacted chemicals.
  - *Agitation failure.* This will lead to an improper mixing. Reactants will not be put in contact, so the concentration of non reacted chemicals will increase
  - *Too low temperature.* A temperature drop can slow the rate of reaction generating an increase in accumulation.
  - *Impurities.* Any unwanted chemical present in the reaction mixture might inhibit the reaction making it slower.

- Segregated phases. The formation of a segregated phase in the reaction mixture can lead to an unstable situation because such phase can be thermally unstable or can change the properties of the reaction mixture. Moreover, it can jam measurement devices like level, temperature or pressure probes (Nomen *et al*., 2004 (b)). Failures in agitation or too low temperatures are typical causes that can lead to generation of segregated phases. A scenario that must be particularly studied is the case of an unexpected stop of the stirrer. If a segregated phase is formed and the agitation is restarted, a great amount of heat can be suddenly released.

- Hot spots. It is a too high local temperature. They are especially critical if the reaction mixture contains detonating, deflagrating or self-igniting substances, since it could trigger an explosion. This hazard is usually originated by insufficient stirring (Nomen *et al*., 2004 (b)).

In order to identify when it is likely that a runaway can take place in a chemical reaction, some experimental determinations have to be made, regarding the possible levels of temperature that can be reached during the reaction. There are two simple methods that can be helpful for this determination, the Gygax and Stoessel methods.

a) The Gygax diagram

The Gygax (1988) diagram is a plot of Temperature Vs Time, which represents a cooling failure or a runaway situation (see Figure 4).

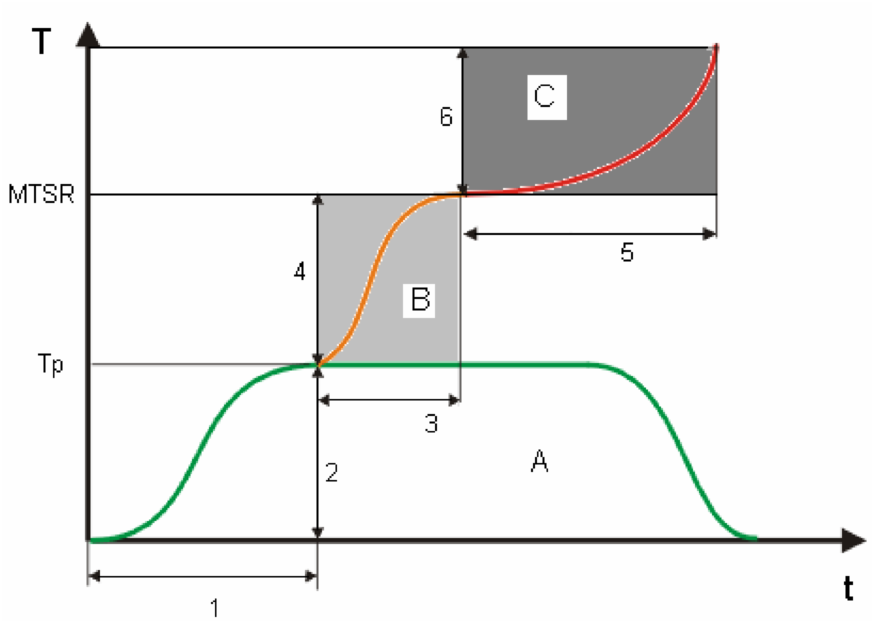

Figure 4. Schematic presentation of a cooling failure scenario.

The main features included in the Gygax diagram are:

- A = desired reaction B = loss of cooling C = runaway
- 1: time to cooling failure
- 2: temperature increase under normal operating conditions
- 3: time to reach the maximum temperature due to synthetic reaction
- 4: temperature increase due to loss of cooling
- 5: time to maximum rate under adiabatic conditions
- 6: temperature increase due to secondary reactions

It is helpful for the evaluation of the cooling failure scenario to discuss four temperature levels and their interactions. This procedure is known as the Stoeesel method.

b) The Stoessel diagram

The methodology developed by Stoessel (1993) is a useful system to perform a preliminary evaluation of the thermal risk that a chemical process might generate. It is based on the possible different positions of the temperature levels described above relative to each other, and the classification of the process under certain levels of criticality. The Stoessel diagram is shown in Figure 5.

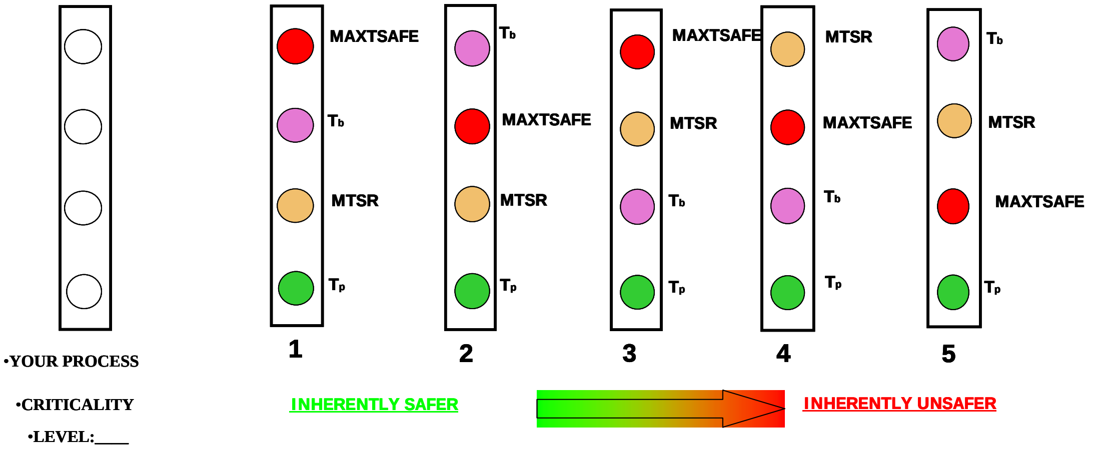

Figure 5. Scenarios with increasing criticality according to Stoessel.

The temperature values considered by Stoessel are:

- The process temperature, **T_P.**
- The temperature to be reached under upset conditions, **MTSR**.
- The boiling point of the reaction mass **T_b.**
- A safety maximum temperature value considered, **MAXTSAFE**.

The descriptions of the 5 scenarios described by Stoessel are the following:

- <u>Case 1:</u> in a case one scenario, neither the boiling point of the mixture nor the dangerous region in which the decomposition reaction becomes effective within a critical time is ever reached. Such processes may be regarded as inherently safe with respect to the process deviation evaluated.

- <u>Case 2:</u> also in the second case, which differs from the first by the absence of the boiling point barrier between MTSR and MAXTSAFE, the process may be regarded as safe.

- <u>Case 3:</u> in the third case, the boiling point with its latent heat of evaporation may be looked upon as a safety barrier, provided the condenser is adequately designed. However, it must be considered that for some mixtures, evaporation of solvent during some time can reduce the MAXTSAFE value of the mixture. If the process is performed in a closed system, the apparatus must be designed for the maximum expectable overpressure or be equipped with a pressure relief device.

- <u>Case 4:</u> scenarios with case four characteristics must be evaluated as to whether or not the evaporation capacity provides sufficient safety. If this is not the case, additional organizational or technical measures have to be implemented. Should the operation be performed in a closed system, then the temperature corresponding to the relief valve's set pressure may not be much higher than the level of T_b.

- <u>Case 5:</u> the fifth case must in any case be rated problematic. Plant and/or process modifications usually cannot be avoided in such situations.

Whenever a possible runaway reaction is identified, it must be studied what possible actions can be taken in order to regain control of the process. Such actions generally include extra cooling, inhibition of the reaction, or introduction of relief systems in the reactor vessel. The chapter Industrial Scale Analysis deals with possible safety measures to carry out a process safely at plant scale.

Along with uncontrolled gas generation leading to extremely high pressure values, possible hazardous effects of chemical substances generated during a runaway situation must be taken into consideration. This hazard is known to have generated accidents, as in the case of a reaction in which an unexpected generation of hydrogen chloride during a runaway corroded the metal reaction vessel, reducing its mechanical resistance. The consequence of this was that the design of the pressure relief system became incorrect, generating an explosion in the vessel at a lower pressure than expected (Sales *et. al*, 2007).

4.2. Test Methods for Runaway Assessment

In order to obtain accurate values for MTSR and MAXTSAFE, some calorimetric experiments must be performed. There are two main calorimetry techniques.

a) Reaction Calorimetry

This is the main technique to determine the heat of reaction, which is the total quantity of thermal energy liberated or absorbed during a chemical reaction. The heat release rate, or power released by the reaction can be determined as a difference between terms included in the heat balance (HarsBook, 2003). One of the values that can be calculated by this technique is the adiabatic temperature increase[1], which together with the process temperature provides the MTSR value.

MTSR should be calculated in the worst case scenario of the considered process. Whereas in the batch case MTSR corresponds always to the maximum adiabatic temperature increase, for the semi-batch case three scenarios can be considered (Serra *et al*., 1997):

- *batch*: all reactants are mixed at the beginning of the process, adiabatic conditions are assumed.
- *stop*: dosing is stopped after a cooling failure. Only the actual accumulation is considered at each time.
- *non-stop*: dosing is not stopped when adiabatic conditions are established. Actual accumulation and remaining heat of reaction should be considered.

Reaction calorimetry is not only a key technique for risk assessment of chemical process, but also an effective tool to determine the dimension of cooling systems for the reactor. In a final stage, the combination of reaction calorimetry equipment with commonly available laboratory equipment can provide direct and accurate measures of the quantity and rate of gas generation during the desired reaction. The different existing calorimeters have been widely studied and compared so far (HarsBook, 2003).

b) Adiabatic calorimetry

The term adiabatic refers to a system condition in which no heat is exchanged between the system and its environment. This is the situation that better represents a runaway scenario, considering that the rate of heat production in the reaction vessel is so high that the cooling capacity cannot remove the heat generated.

Adiabatic calorimetry experiments are particularly useful in order to determine values related to the decomposition of chemical mixtures, such as the adiabatic induction

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[1] Adiabatic temperature increase is the temperature rise that will take place in case the system loses its capacity to exchange heat with its environment, e.g. a cooling failure. It can be calculated as the ratio between the reaction enthalpy and the heat capacity of the mixture.

time[2], decomposition temperature gradients or time to maximum rate of heat generation (TMRad). Another important feature is that it can also determine the gas generation rate in a decomposition process, giving accurate values for the pressure that can be reached during a runaway reaction. It must always be kept in mind that pressure increase is the final hazard in a runaway, since it is this phenomenon that can lead to the explosion of a reactor.

MAXTSAFE, considered as the temperature limit before a decomposition process falls out of control, can be determined by adiabatic calorimetry as the temperature at which the adiabatic induction time of a possible decomposition reaction falls below a specific limit value, **ADT24** (adiabatic induction time less than 24 hours). If adiabatic calorimetry data is not available, MAXTSAFE can be obtained by means of a dynamic DSC register of the reaction mass, with a heating rate of 5 K/min, following the detailed procedure:

- The value of MAXTSAFE can be determined, at a first step, as the temperature at the first exothermal peak less 70 K. This safety reference is more objective than the Tonset, since the later may depend on the precision of the apparatus.
- It is necessary to compare this value with the MTSR. If $|MTSR-(T_{peak}-70)|>50$, then the approximation of $MAXTSAFE=T_{peak}-70$ can be considered correct. If this is not so, it is also required to perform an isothermal[3] DSC at MTSR followed by a dynamic register.
- If $MTSR>T_{peak}-70$, the isothermal register does not reveal any significant change of the mass reaction, and the dynamic register is equivalent to the first DSC performed, then it can be concluded that $MAXTSAFE>T_{peak}-70$ and therefore MAXTSAFE>MTSR.
- If $MTSR>T_{peak}-70$, the isothermal register does reveal significant change of the mass reaction (low velocity of the exothermal phenomena at the process temperature can be a problem for detection), and the dynamic register is not equivalent to the first DSC performed, then the approximation $MAXTSAFE=T_{peak}-70$ can be considered.
- If $MTSR<T_{peak}-70$, the isothermal register does not reveal any significant change of the mass reaction, and the dynamic register is equivalent to the first DSC performed, then the approximation $MAXTSAFE=T_{peak}-70$ can be considered.
- If $MTSR<T_{peak}-70$, the isothermal register does reveal significant change of the mass reaction, and the dynamic register is not equivalent to the first DSC performed, then it can be concluded that $MAXTSAFE<T_{peak}-70$ and therefore MAXTSAFE<MTSR.

At this point of the evaluation, it might be interesting to address to the on-line tool of ***HarsMeth***, which is available at the ***HarsNet*** web site. This is an Internet based program, which calculates the main parameters needed to perform the Gygax and Stoessel evaluations from experimental values. It is also very interesting the tutorial

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[2] Adiabatic induction time: induction period or time to an event under adiabatic conditions starting from specified operating conditions.

[3] When performing an isothermal DSC, it must be considered that a 12 hour experiment should be long enough. Besides, low velocity of the exothermal phenomena at the process temperature can be a problem for detection.

included in this interactive part of the methodology, which guides the user through the whole process, offering detailed and graphic explanations on the terms used.

Another interesting source of information is ***HarsBase***, a database developed by the ***HarsNet*** group which includes a list of commercially available calorimeters, indicating all the possible operation modes, parameters to determine, and other characteristics. ***HarsBook*** is also a reference guide for details on calorimetry techniques.

As it has been stated, the main (but not only) target of ***HarsMeth NP*** is SMEs, which usually have little resources to perform an accurate risk assessment. However, it should be a standard that at least one reaction calorimetry experiment on the desired reaction should be performed. Moreover, if it is found that the process could be considered potentially hazardous (Stoessel category 4 or 5), even adiabatic calorimetry tests should be carried out if the process is to be carried out in an industrial scale

4.3. Other Hazards Related to Chemical Reactions

While analysing the chemical reaction in the laboratory, it is important to be able to identify any necessary evolution in the final product after it comes out of the chemical reactor, in order to adapt it to its final use. This evolution may require changes in the physical conditions of the chemical substances involved in the process, which may also lead to hazardous situations.

Flammable, toxic or explosive situations should be identified. These hazards have already been introduced in the preliminary reaction analysis section, but it is possible that the analysis in the laboratory brings some new ideas on the operations that must follow the chemical reaction that were not identified before. If such situations are encountered, the principles of inherent safety and experimental tests described previously should be applied.

It is not the aim of ***HarsMeth NP*** to assess hazards other than those strictly related to the chemical reaction itself. However the user is encouraged to seek for further advice whenever any of these hazards are encountered. The S2S web site (S2S, 2007) offers interesting assessment tools on fires and explosion hazards

Next, a list of tables for process data and possible failure scenarios are presented, along with a set of questions to identify critical process parameters to identify hazards leading to runaway reactions.

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III. BENCH SCALE ANALYSIS CHECKLIST

Process conditions data

Step	Step description(1)	Quantity of heat released	Heat release rate	Quantity of gas generated(2)	Gas generation rate	Reaction kinetics(3)

1. Specify reactive step description, including substances involved, operations required (addition, heating, etc.) and process conditions, like temperature, pressure, etc.
2. If there is gas generation during the process, include data for quantity and rate of gas generation in order to identify pressure increase associated to normal process operation.
3. Include data to determine the speed of reaction. If possible, specify if the reaction follows an Arrhenius pattern.

Data of possible failure scenarios

Step	Process T (Tp)	Heat of reaction (ΔHr)	Specific heat (c_p)	Adiabatic T rise$^{(1)}$ (AdT)	MTSR$^{(2)}$	Boiling T (Tb)	MaxTsafe$^{(3)}$	Stoessel classification$^{(4)}$	TMR$^{(5)}$

1. $AdT=\Delta Hr / c_p$
2. $MTSR=Tp+AdT$
3. If adiabatic calorimetry data is available use the value for ADT24, otherwise see MaxTsafe description in this chapter.
4. Class 1): Tp < MTSR < Tb < MaxTsafe

   Class 2): Tp < MTSR < MaxTsafe < Tb

   Class 3) Tp < Tb < MTSR < MaxTsafe

   Class 4) Tp < Tb < MaxTsafe < MTSR

   Class 5) Tp < MaxTsafe < MTSR < Tb
5. As a general rule, the following classification can be considered according to the TMR value

   Class 1): if TMR > 24 hours, the process can be operated safely

   Class 2): if 8 hours < TMR < 24 hours, the process requires observation and control

   Class 3) if 4 hours < TMR < 8 hours, the process requires special control systems

   Class 4) if TMR < 4 hours, the process should be modified, or additional safety measures should be implemented

	Can variations in the following parameters affect the normal evolution of the process		
III.1	**Operation mode (batch/semi-batch?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.2	**Process temperature / cooling failure?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.3	**Catalyst concentration?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.4	**Solvent concentration?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.5	**Reactants concentration?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.6	**pH?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.7	**% conversion?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.8	**Reaction time / delayed reaction start?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.9	**Dosing rate / dosing failure (including wrong order of addition)?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.10	**Agitation speed / agitation failure?**		
	YES	*REVIEW SAFETY*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.11	**Flow rate of reactants?**		
	YES	*REVIEW SAFETY*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
	In case of a runaway scenario		
III.12	**Is the nature (vapour, gassy, hybrid) and rate of gas generation known to be hazardous?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.13	**Is the nature of substances formed (flammable, toxic, corrosive…) known to be hazardous**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

Use the following table to indicate the reactive steps identified as hazardous, the parameter the failure of which may generate a hazard, and the specific hazard associated to them.

Hazards

1. Unexpected reactions
2. Decomposition of reaction mass
3. Accumulation
4. Segregated phases
5. Hot spots

Possible consequences

1. Pressure increase due to gas generation
2. Formation of dangerous substances

Step	Critical parameter	Hazard identified	Possible consequences

5. PILOT PLANT ANALYSIS

Before a process can be carried out in a process plant, some design requirements must be taken into consideration to assure that the process studied in the laboratory can be performed under the same safety parameters at an industrial scale. A procedure to use can be to progressively perform the reaction in larger vessels.

The pilot plant analysis is an intermediate step between bench scale analysis and the industrial production. It involves the change of scale of the process, which is a procedure to transform the laboratory operations into an industrial process that generates the quantity of the desired product required for its commercialisation. In this stage, other processes different from the chemical reactions can be studied, generally involving physical transformations of the product. These processes are intended to adapt the desired product for its final use by consumers.

5.1 Change of scale

The bench scale analysis of the chemical reaction should have allowed the identification of some elements that can be critical for the safety of the reaction. Effects in the change of agitation, dosing, cooling, or the possibility of inhibition of the reaction must be known by now. However, some of these parameters may have a different behaviour when the reaction is tested at a larger scale. Some of the elements to consider in the change of scale are:

a) Momentum transfer

It must be assured that the chemical mixture will always keep its homogeneity at the same level it was experienced in the bench scale analysis. Particularly important is to assure the thermal uniformity of the mixture, avoiding formation of hot spots or the accumulation of non reacted chemicals. Appropriate reactor design and selection of an appropriate agitation system is essential. It often happens that the agitation systems used in the laboratory do not provide a real mixing of the reaction mass. The objective should be to use the same power number and geometry of the system rather than agitation speed.

b) Heat transfer

In order to maintain the reaction temperature at the value determined in the laboratory experiments, it is essential to assure a correct heat transfer between the reactor and the surroundings. The main problem related to heat transfer is that the increase in the reactor volume generates a difference in the surface-volume ratio between the coolant and the reaction vessel. Heat released increases with the volume, but heat removed depends on the surface area, which is a cubic to square ratio, so cooling may become inadequate. This is important for example to determine the time it will take a reaction mixture to cool from 1°C in different reaction scales. Given the same reaction and surroundings temperatures, this time can increase at an exponential rate as the reactor volume increases (Chilworth, 2001).

There are many possibilities for the design of heat exchange systems, ranging from jacket cooling, condensers, inner circuits (not appropriate for reactions involving solids) or external heat exchangers. Detailed guidance can be found in the literature (Wilson, 1915; Kern, 1950; Perry, 1998). Also construction materials must be taken into consideration, since steel reactors used for industrial process provide different heat conductivity and mechanical properties, compared to the typical glass equipment used in the laboratory. The influence of the vessel on the measure of the heat lost to the container is represented by the phi factor, which is the ratio between the sum of the specific heat of the reaction mixture and that of the vessel divided by the specific heat of the reaction mass.

For plant scale vessels the phi factor is usually low, ranging between 1.0 and 1.2 (Chilworth, 2001). These low factors should be reproduced at pilot plant scale, otherwise underestimation of decomposition temperatures and periods of runaway induction could occur, as well as wrong dimensioning of control and relief systems.

c) Kinetics

If the heat removal from an exothermic reaction fails, the evolution of the process may vary greatly. Here it is interesting to visualize the Semenov diagram (Figure 6) for the thermal explosion of a continuous process (Barton and Rogers, 1997).

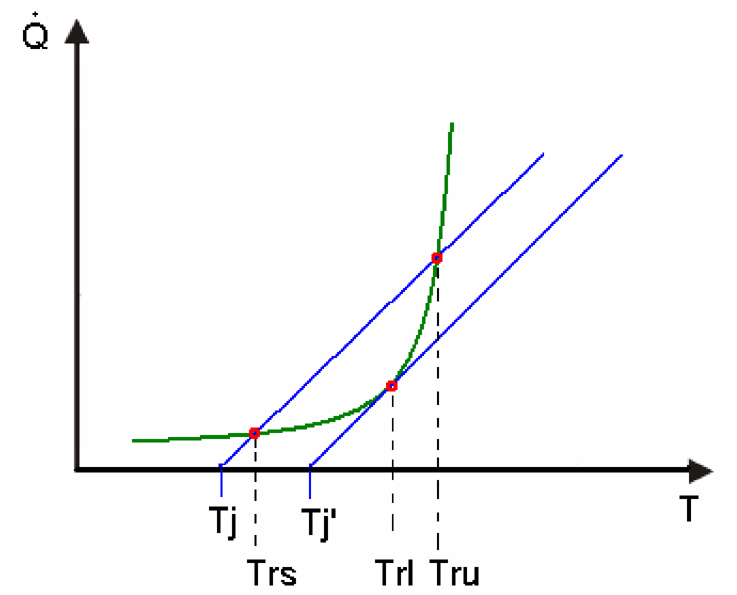

Figure 6. Semenov’s heat balance diagram

This diagram represents the evolution of heat versus temperature, reflecting the exponential increase of heat with reaction temperature, and the linear dependence of the heat exchanged with the cooling temperature. If a deviation occurs in reaction temperature working at the stable point (Trs), the system will eventually return to that position, since the cooling power will be greater than the heat generated by the reaction. However, at the unstable point, any oscillation above reaction temperature will lead to a runaway. The limit point (Trl) defines the maximum temperature for coolant that allows the process to be run under safety conditions.

One way to keep the reaction temperature under control is to turn from batch to semi-batch processes, in which the dosing speed of one of the reactants can be a way to control the heat generation of the reaction. Dosage must have the same duration in plant as in the laboratory, since it is the concentration relations and not the volume that is important from a chemical point of view. For this reason, it must be assured that the system can always eliminate all the heat generated by the reaction, otherwise dosing will be slower and this may lead to a different process from that studied in the laboratory.

As a conclusion, increasing the dosing time can be a way to keep control of the heat generated during the reaction, as long as it can be assured that the process remains unchanged.

d) Mass transfer

The key issue in mass transfer is to determine the homogeneity of the reaction mixture. Homogeneous systems with low viscosity are can be controlled by the kinetics of the reaction, while for heterogeneous systems the reaction time is defined by mass transfer coefficients.

The objective should be to have a kinetic control on the reaction, this can be achieved by enlarging specific surfaces of catalyzers or by increasing agitation speed. As in the case of dosing, any modification should be assessed for unwanted effects, since a too high increase in agitation speed may lead to the emulsification of the reaction mixture or an excessive vortex.

One particularly interesting consideration can be the scale-up of inhibition of a runaway reaction. It must be assured that the dispersion of inhibitor on a large scale will be enough to guarantee the efficiency of the inhibition (Snee, 2004).

5.2. Unit operations

The main source of chemical hazards in an industrial process is the reactor, due to the fact that it is in this equipment where substances are intended to interact generating new products. However, it must be considered that other operations in chemical plants are likely to generate reactive hazards due to possible unexpected conditions of the process. These operations involve mainly physical changes in the product in order to adapt it for its final transport to end users. In case of deviations in the expected conditions of the process, these changes may also lead to runaway situations. Unit operations are generally associated to normal process hazards involving many issues that fall out of the objective of ***HarsMeth NP***. This section of the methodology aims to identify possible unexpected chemical reactions triggered by upset evolution of a process.

The assessment procedure for unexpected reactions outside chemical reactors has been developed under the S2S project and can be found at the network web site (S2S, 2007). The method purposed (Weve et al., 2007) is based on a set of simple questions regarding reactivity, such as:

- Why is the reaction not taking place at process equipment other than the reactor?
- What is needed to make such equipment behave as a reactor?
- How can that happen in the process under study?

The questions to apply will depend on the equipment used for the process. Besides, possible hazardous properties of the substances should be taken into consideration, as well as the phase systems involved (V/L, L/L, S/L or V/S). For this reason, the answers given in section 2 regarding stability and compatibility of mixtures should be available and taken into consideration when analyzing unit operation hazards.

For a reaction to occur a combination of 3 factors needs to be fulfilled:

- Temperature of Reactants
- Concentration of Reactants
- Time for reaction

This can be described in a triangle like the fire triangle.

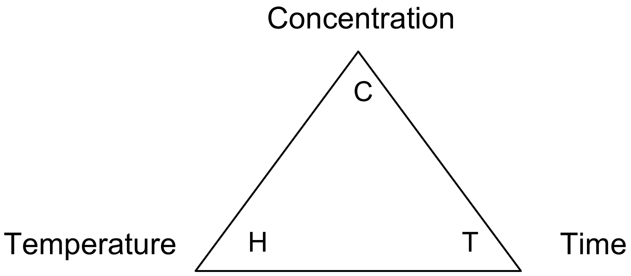

Figure 7. The reaction triangle

These three factors represent the most important free factors in process design and operation. As with the fire triangle, a reaction requires an appropriate combination of the three factors mentioned previously to take place; reducing the contribution of concentration, temperature or residence time in the triangle will reduce the possibility of a reaction to take place. There are some special reactions that need a catalyst or high interfacial area between phases. These factors could be added to the Time-corner as well, in a sense they 'help' time. Mixing of unexpected substances should be considered in the concentration corner.

A reactor would be precisely equipment somewhere near the middle of the triangle. A feed pre-heater, for instance, can be considered as equipment on the temperature-time side of the triangle. This means that it is supposed to heat a substance to reaction conditions, and it cannot avoid substantial time (2-5% of the reactor time), so it should have a low concentration of one of two reactants to prevent unintended reactions. In order to turn this equipment into an unintended reactor, it is necessary to increase the missing component, which is concentration. This situation would be generated by an unexpected event, maybe backflow from the reactor, maybe product remnants from another process step in a multipurpose plant. Like the feed pre-heater, all unit operations can be conceptualized with a specific task, and they can all be positioned on the sides of the reaction triangle. They will not pose hazards unless they move towards the middle. There are several ways in which equipment can vary their position in the reaction triangle. Some examples, related to each of the specified factors, could be:

- Temperature factor
    - Weather effects.
    - Friction or vibration due to rotary equipment.
    - Loss of temperature control or equipment failure (e.g. cooling failure).
- Concentration factor
    - Unexpected mixing of incompatible substances (e.g. backflow, corrosion, leakage, multiple feeds and so on).
    - Equipment failure generating accumulation of reactants.
    - Excessive evaporation leading to concentration of unstable products.
- Time factor
    - Incomplete or inefficient separation processes generating excessive time of contact between unstable phases.
    - Dead zones generating irregular flow distributions.

As a general rule, all the possible hazardous situations that have been studied in the previous sections should be considered here. For instance, if a substance is known to be pyrophoric or shock sensitive, measures should be put in place in order to avoid the hazards associated to these substances at any stage of the process. Again, inherently safer design should be applied when designing the process. If any operation is considered to be potentially hazardous, a better alternative from the safety point of view should be used where possible. For example, decanters or static filters could be used to replace centrifuge operations; thin film evaporation processes have been identified as a good option instead of batch distillation where unstable residues may be generated, by reducing temperature, hold-up and thermal exposure of the mixture (Suter and Glor, 2001).

It is also important to notice that a hazardous situation might be generated at the reactor step, but only materialised downstream at other process equipment, as could easily happen with the accumulation hazard. It must be reminded that a global vision of the process hazards must be kept along the safety analysis, even if it is performed step by step. Review of hazards related to unit operations can be found in the literature (CCPS, 1999).

In the following pages, a checklist for pilot plant analysis can be found.

IV. PILOT PLANT ANALYSIS CHECKLIST

	Are the hazards of scale up for the reaction been evaluated in front of the following parameters:		
IV.1	**Cooling / Heat transfer?**		
	YES	*Justify your answer:*	
	NO	*REVIEW SAFETY MEASURES*	
	UNKNOWN	CHECK IT!	
IV.2	**Dosing / reaction kinetics?**		
	YES	*Justify your answer:*	
	NO	*REVIEW SAFETY MEASURES*	
	UNKNOWN	CHECK IT!	
IV.3	**Agitation system?**		
	YES	*Justify your answer:*	
	NO	*REVIEW SAFETY MEASURES*	
	UNKNOWN	CHECK IT!	
IV.4	**Mass transfer?**		
	YES	*Justify your answer:*	
	NO	*REVIEW SAFETY MEASURES*	
	UNKNOWN	CHECK IT!	

Following is a list of typical operations or equipment in chemical plants. Next, a list of questions to identify reactive hazards in process equipment is included. Select those operations that are used in the process, and answer the questions that apply in each case. Use one copy of the checklist for each of the necessary operations. If there is more than one operation or equipment corresponding to the same group, consider the possibility of using different checklists if necessary. Identify each checklist with the name of the operation and a brief description (substances, purpose of the operation, etc.).

Operation / Equipment	Number	Answer question number
Vessels		
Pipes		
Valves		
Pumps		
Shared systems		
Heat exchangers		
Distillation		
Absorber		
Adsorber		
Centrifuges		
Filters		
Extractor		
Dryers		
Mills		
Drumming		
Flash drum		
Storage		

Operation / Equipment Name: **Description:**

IV.5	**Is the equipment exposed to severe weather conditions or nearby heat sources?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.6	**Does the equipment need external heating or cooling to prevent an unintended reaction?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.7	**Does the equipment have a stirrer or agitator (either mechanical or flow based)?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.8	**Does the equipment have seals, bearings, gearbox or shafts connected?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.9	**Can the feed enter at too high temperature?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.10	**Is vacuum needed to evaporate a product, reactant or solvent?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.11	**Is a low boiling solvent or reactant excess used to reduce the reaction hazard?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.12	**Are there a large pressure differences in the process?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.13	**Are there two or more non miscible streams involved in the process at the same time?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.14	**Are there high surface area solid materials (like glasswool piping insulation, filter aids or adsorption materials in driers) used?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.15	**Is there a vapour / liquid separation involving a catalyst, unreacted product or thermally unstable phases used?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.16	**Can unexpected mixing of substances take place during the process?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.17	**Can dead zones be generated during the process?**		
	YES	*REVIEW SAFETY MEASURES*	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

IV.5	Sunlight can result in unexpectedly high temperatures. Also other heat sources can radiate heat if they are close by and not insulated. This may remain unnoticed while liquid is flowing, but it becomes important in absence of flow, e.g. a blocked pipe section. On the other hand, at too low temperatures certain substances can start crystallization processes leading to a polymerization reaction that could block the system.
IV.6	The heating medium for plant equipment usually has a higher temperature than the onset temperature of a reaction. Too high temperatures can enhance reactions or trigger decomposition processes. Appropriate agitation (mixing or flow) is needed to prevent local high temperatures. On the other hand, a cooling failure may result in a runaway reaction for exothermic reactions. Too low temperature due to control failure can result in accumulation of reactants. The hazard is a delayed reaction later, generally at too high rates, at a different batch step or downstream equipment.
IV.7	Agitation is needed to prevent local high temperatures. Stirrers can fail by their power, engine, gear box, shaft, loosing impellers. Loss of agitation can result in local high temperatures, leading to accumulation of reactive materials. The hazard is a delayed reaction when the agitator is restarted, generally at too high rates, at a different batch step or downstream equipment. Generation of hot spots is another possible hazard arising from agitation failure. Besides, emulsification due to inadequate heat transfer areas leading to unexpected phase transitions can also be generated.
IV.8	Bearings, seals, gearboxes, etc. can generate heat due to wear. Besides, friction or vibration due to rotary equipment can generate a decomposition hazard when using unstable or shock sensitive materials.
IV.9	Cooling capacity may be designed for cold feeds, so insufficient cooling could result in a runaway.
IV.10	If vacuum is lost for a (partially) boiling system, there may be a dangerous temperature increase.
IV.11	Excessive evaporation due to external heating may result in both concentrating reactants and increasing the temperature. Both effects may accelerate possible unexpected reactions. An accidental loss of pressure for a reaction occurring at high pressure will also result in higher reactant concentration and may become dangerous if there is external heating to compensate for the evaporative cooling.
IV.12	If a switch in pressure differences occurs, there may be a vapour phase generation that would result in concentration changes, increasing the hazard of an unexpected reaction. Besides, backflow of materials through equipment could be generated. Incompatible materials may come in touch generating an undesired reaction.
IV.13	At normal operation, the surplus reactant will be separated. In finely dispersed systems, there is no separation and reactions can occur later or downstream in other process steps. An example is using a water or caustic wash to neutralise acid components in a organic product. Drumming the emulsion may result in a runaway during storage. If a substance is soluble in both phases, the concentration can change with the effectiveness of the process step.
IV.14	Absorptive material may concentrate reactive components, and act as catalysers for unexpected reactions.
IV.15	Foaming, liquid carry-over or leaking filters are some example of possible incomplete separation scenarios. These may result in unreacted product starting a runaway later, or a catalyst initiating a reaction at an unprotected process step. Overheating of products by removal of liquid from a thermally unstable phase is a common hazard in distillation processes.
IV.16	There are many possibilities for unexpected mixing of chemicals; some of them, like mistaken chemicals for charging or not checking of equipment contents prior to charging have already been mentioned. If multiple feeds are possible at the same time, compatibility of substances must be evaluated. This should also be done in case of shared vent systems. For multipurpose plants, cleaning is essential in order to assure that all remains of previous processes are eliminated before starting a new one, in order to avoid unintended reactions due to incompatibilities. Rust generated by corrosion could act as catalyzer for unexpected reactions. Besides, if different construction materials are used in plant equipment, rust generated in metallic sections can be transported to other containers where it could catalyze unexpected reactions. Decomposition of peroxides in plastic containers is known to have happened due to rust generated otherwise in plant. In case of a leakage, released material may react unexpectedly with construction materials.
IV.17	Presence of dead zones in equipment may lead to accumulation of reactive materials and also to partial decomposition. Irregular flow distribution can easily result in differences in residence time and hence introduce runaways.

Use the following table to indicate the process operations identified as hazardous and the specific hazard associated to them, according to the following classification:

For reactive steps, indicate what operation could generate a hazard from the change of scale point of view:

1. Cooling / Heat transfer
2. Dosing
3. Agitation
4. Mass transfer (including possible inhibition)

For process operations:

5. Temperature variations
6. Concentration of reactive materials, including unexpected mixing
7. Excessive residence time

Operation / Equipment / Reactive step	Identified hazard	Substances involved

6. INDUSTRIAL SCALE ANALYSIS

Once a reaction has been carried out successfully on a pilot plant scale, process conditions and equipment design should have been determined. The process can now be performed at full plant scale in safety, provided exactly the same conditions are applied each time. The challenge is therefore to assure the same conditions each time a reaction is carried out. But it is almost impossible to run a process repeatedly in time without error, change, failure or any external event that may alter the normal conditions of the process. For this reason, a system must be employed to ensure that whenever any kind of failure occurs there will be a back up system which will make the system safe.

6.1. Basis of Safety

Considering that sometimes a process will be carried out involving possible hazards, additional measures must be put in place to assure that no incident arising from the identified hazards will generate an accident. The relation of preventive measures taken in order to turn the process to be inherently safe and the additional safety measures will constitute the basis of safety of the process.

Those additional measures will include the last barrier of defence for people and installations against the consequences of a possible accident, for this reason it is agreed that a basis of safety should be definitive and proven to be reliable for the worst case maloperation that can occur for a given process (Rogers, 1991). When defining a basis of safety, two types of measures can be put forward.

6.1.1. Process Control

Safety can be ensured by the use of the appropriate process control measures to guarantee that the system remains within a defined operating window. Critical parameters for the safety of the process must have been identified completing the previous sections of ***HarsMeth NP***, as well as the safety margins for each one of those parameters. As seen before, the most common parameters to be determined are temperature margins, dosing rates, agitation speed, cooling capacity, gas generation, etc. However, any other specific property that may have been identified previously, the variation of which might be critical for the safety of the reaction should be considered in the design of the control system.

Whenever any parameter is identified as critical, a safety interlock should link the sensor related to the measurement of that parameter to the control system and to any possible device in order to try to regain control of the situation. For instance, an interlock should be included between the temperature probe (or any other measurement system that may give indication of a possible runaway) and the cooling system to increase cooling power in case of an increase in temperature. Also, a shut off to the dosing valve should be linked to high and low temperature values to stop adding reactants when the hazardous situation arises. Likewise, the dosing valve should be linked to the stirring system in order to stop the addition of reactants in case of failure of the agitation system. At the same time, the control system should link any of the sensors that may give indication of a runaway with actuation systems, like inhibitor or quenching vessels.

Finally, it should be policy to fit redundant control systems (both human and software) for measurements of temperature or any other parameter critical for safety whenever necessary.

6.1.2. Protective Measures

Protective measures to ensure safe operation have to either deal with or mitigate the consequences of the runaway reaction. Since the initial conditions markedly affect the course of a runaway reaction, the critical aspect for all protective systems is the interrelationship between their design and the definitions of the worst case i.e. the conditions leading to the runaway. In addition to suitable detection methods and the availability of process compatible systems, protective measures need time to act, which must be considered during the design phase. Time plays a primary role in the efficiency of all measures. The following steps must be realised from the instant a failure occurs up to recovery of the control of the process.

- Detection time. When a failure or a malfunction occurs, it must be first detected. The detection time can be influenced by the choice of appropriate alarm settings. But the most important is the choice of the adequate parameter that must be monitored to detect a malfunction. The design of alarms, interlocks and control strategies is an important part of process design.

- Action time. Once the alarm is switched on, there is some time required for the measure to be applied. Quenching or dumping require some time to complete the mass transfer, an emergency cooling must be switched on, the cooling medium must flow at the required temperature with the required flow rate, an so on.

- Time for effect. Time is required for the applied measure to become effective and influence the course of the runaway. This time factor must be estimated for an effective design of safety measures and compared with the dynamics of the runaway of the desired reaction and of decomposition reactions as shown in Figure 7.

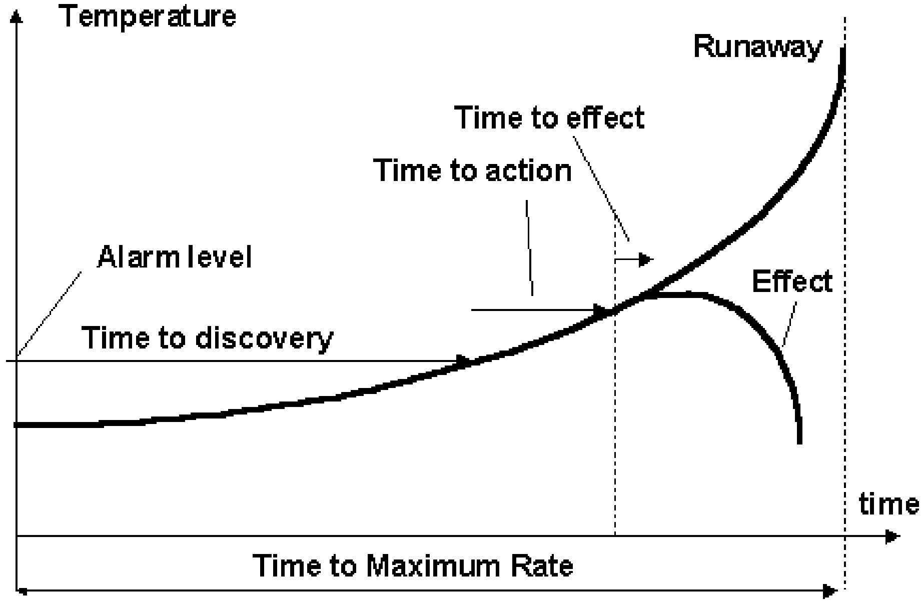

Figure 7. Time factors involved in preventing a runaway

The most common safety measures to cope with a runaway situation are listed below.

a) Emergency Cooling (Crash Cooling)

In this system, forced cooling is applied when the reaction deviates from set limits or if the cooling system fails. It is important that the magnitude and rate of heat release is quantified in order that reaction control can be maintained with the applied cooling. With such a system, it is critical that the temperature does not fall below the solidification point of the reaction mass, otherwise a crust would form, resulting in a reduced heat transfer, which again may favour the runaway situation. The agitation of the reaction mass is also critical. Without stirring large reaction masses behave adiabatically even if cooled on the outside. Here the injection of nitrogen or other inert gas into the bottom of the reaction mass has proved to be helpful for emergency mixing. These measures must be tested under practical conditions.

b) Quenching / Inhibition

Quenching and inhibition involve the rapid addition of a diluent or inhibitor to the reactor contents to stop the reaction. This is sometimes possible for catalytic reactions and polymerisation reactions where a “catalyst killer” can be added in small amounts. For other reactions a dilution by an inert and cold material may lower the temperature and slow down the reaction. The choice of diluent or inhibitor, the amount and rate of addition, the temperature of the quenching material and the efficiency of mixing require careful investigation. The required empty volume must also be available in the reactor. Calorimetric methods are of great help in the design of such measures as they allow the measurement of the heat of mixing which often is important. More information on quench design can be found in the literature (Hermann, 1995).

c) Dumping (Drown out)

This measure is similar to the quenching, with the difference that the reaction mass is not kept within the reactor, but rapidly emptied into a dump tank containing the inhibitor or the diluting compound. This dump vessel must be prepared to receive the reaction mass at any instant during the process. The transfer line is critical for the success of this measure. It must be designed to allow an emergency transfer even in case of breakdown of services. This measure is particularly suitable in cases where the reaction mass must be transferred for workup after a normal operation.

d) Containment

Containment is becoming more common as environmental pressures on the release of chemicals increase. Both the reactor and all auxiliary equipment have to be designed for the peak pressures/temperatures that may be reached. The main limitations, as well as cost, are problems associated with design and operation.

e) Controlled depressurisation

If a runaway is detected in an early stage where the temperature and the pressure increases are slow, a controlled depressurisation of the reactor may provide a method to reduce the temperature and prevent the runaway. Heat is removed from the reaction mass by evaporation. Naturally the temperature must be above the boiling point and there must be sufficient solvent available for evaporation. In addition facilities such as a suitable scrubber and condenser must be available and designed to work during the emergency.

f) Pressure relief (Venting)

Emergency reactor venting involves the provision of either a relief valve or bursting disc, which opens at a set pressure. The venting of material from the reactor by either single or two phase flow tempers the runaway reaction by removing heat and therefore maintaining the temperature and also the pressure in the case of a vapour phase system. The gas generation system (gassy, vapour-pressure or hybrid) must be studied, and also the possibility of self-tempered systems; i.e. in vapour pressure and some hybrid systems, vaporization removes enough heat to keep the temperature constant (Barton and Rogers, 1997). For purely gassy and hybrid systems that do not temper, the vent is sized to be able to cope with the peak gas generation rate and thus preventing any pressure increase. The design of an adequate venting system is particularly complex in multipurpose equipment, where the choice of the appropriate runaway scenario, which changes depending on the reaction involved, is difficult.

It is important to recognise that relief vents sized to cope with gas pressure and/or fire engulfment are rarely if ever adequate to provide protection against uncontrolled chemical runaway. The following steps are involved to ensure the design of an adequate emergency relief system:

- Identification of worst credible case scenario (upset conditions).
- Determination of flow characteristics (single, two, multiphase).
- Classification of reaction system type (gassy/vapour-pressure/hybrid).
- Characterisation of runaway reaction at relief conditions.
- Choice of relief device set pressure.
- Calculation of required vent area.
- Correction of vent area considering effect of piping, multiple choking, downstream equipment etc.
- Application of safety factor.
- Design of suitable disposal system.

The required vent size can be calculated using the DIERS methodology (Fisher *et al*., 1992), which requires thermal data, flow regime and viscosity characterisation to be measured under runaway conditions. The use of venting as a basis of safety requires the provision of a safe discharge area. This will often involve a dump or containment tank, particularly where the reactants or products of decomposition are flammable or toxic. Further information on the design of emergency relief systems can be found in the literature (Etchells and Wilday, 1998; CCPS, 1998).

6.2. Process and Plant Design

Along with hazard identification and definition of safety measures regarding the chemical reaction studied, process and plant design standards must be followed in order to assure a high degree of reliability of the chemical plant. Clearly it is not the aim of ***HarsMeth NP*** to be used as a guide to assess general issues of plant and process design. However, standard procedures for mass and heat balances, as well as mechanical design for vessels should always be taken into consideration, because otherwise flow rates or pressure relief design will be erroneous.

Some basic guidance for process and plant design can be found in the literature (McCabe *et. al*., 1993; Treybal, 1980; Kern, 1950; Perry and Green, 1998).

In the following pages, a relation of possible measures (including prevention, control and protection) are put forward, related to the possible hazards encountered in the previous sections of ***HarsMeth NP***. These have been divided into four areas, in order to facilitate implementation of measures. General recommendations included in the following checklist should always be taken into consideration regardless the hazard identified.

- Stability and compatibility. This will include measures for every hazard identified for the substances and mixtures considered at the preliminary study of the reaction, plus any other substance that is going to be stored at the facility.

- Chemical reaction. Measures described deal with the hazards encountered in the laboratory research performed on the synthesis reaction. It deals specifically with the reaction vessel and related equipment.

- Unit Operations. This part will deal with specific hazards for unit operations, giving general possibilities to avoid unexpected reactions in plant equipment.

- Process and Plant Design. This includes general recommendations for process design and control systems.

IV. INDUSTRIAL SCALE ANALYSIS CHECKLIST

Stability and compatibility

	General Recommendations	**OK**
V.1	Make sure that chemicals are stored and handled under compatibility criteria	
V.2	Make sure to establish effective and easy to follow storing and labelling rules	
V.3	Include verification process for charge and discharge from suppliers (be aware of possible change of specifications)	
V.4	Introduce measures to monitor and control the conditions of any parameter identified as critical (T, P, pH, concentration, physical characteristics of product and so on)	

	Decomposition hazards		**OK**
V.5	Introduce measures to detect long periods of storage (periodic sample analysis)		
	Autocatalytic hazards		**OK**
V.6	Identify inhibitors for substances or mixtures involved		
V.7	Introduce control systems for inhibitors activity (temperature, concentration, handling and so on)		
V.8	Keep inhibitors accessible to vessels containing autocatalytic substances		
	Fire and Flammability hazards		**OK**
V.9	Avoid ignition sources such as:		
	V.9.a	Static electricity	
	V.9.b	Welding or cutting	
	V.9.c	Hot surfaces	
	V.9.d	Light metals or alloys	
V.10	Avoid possible oxidant atmospheres (use of inert gases)		
V.11	Introduce fire detection systems		
V.12	Introduce fire protective systems such as:		
	V.12.a	Fire extinguishers	
	V.12.b	Water sprinklers (study water compatibility)	
	V.12.c	Anti-fire doors and walls	
	V.12.d	Personnel protection systems (showers, blankets, fire suits and so on)	
	Toxic hazards		**OK**
V.13	Introduce toxicity protective systems such as:		
	V.13.a	Toxic dilution systems	
	V.13.b	Ventilation	
	V.13.c	Personnel protection systems (masks, eye wash and so on)	
	Explosion hazards		**OK**
V.14	Provide pressure relief systems for vessels		
V.15	Consider the possibility of two-phase flow when designing relief systems		
	Reactivity hazards		**OK**
V.16	Introduce measures to avoid reactivity conditions, such as:		
	V.16.a	Oxidizer hazard: avoid presence of chemicals likely to be oxidized	
	V.16.b	Reducer hazard: avoid presence of chemicals likely to be reduced	
	V.16.c	Water reactivity hazard: avoid presence of water and humidity	
	V.16.d	Pyrophoric hazard: avoid exposure to ambient and presence of air	
	V.16.e	Shock sensitivity hazard: avoid exposure to friction, vibrations or shocks	

Chemical reaction

	General Recommendations	**OK**
V.17	Make sure that cooling system is started before starting addition of reactants	
V.18	Make sure that stirring system is started before starting addition of reactants	
V.19	Consider the possibility of using cooling capacity below its maximum capacity, in order to be able to use extra cooling in case of any possible failure scenario	
V.20	Introduce measures to assure correct charging operations (appropriate chemicals, quantities, order)	
V.21	Introduce measures to monitor and control the conditions of any parameter identified as critical (T, P, pH, concentration, physical characteristics of product and so on)[1]	
	Unexpected reactions / Decomposition hazards	**OK**
V.22	Include multiple temperature measurements	
V.23	Always keep temperature control while reactor is full even if operation is ended	
V.24	Prepare a dumping system in order to stop the reaction	
V.25	Prepare inhibitor solution or solvent for quenching (consider volume requirements for reactor)	
V.26	Include interlock between temperature measurement and inhibitor/solvent vessel valve	
V.27	Include interlock between dosing valve and cooling system to stop dosing in case of cooling failure	
V.28	Include interlock between temperature measurement and dosing valve in order to stop dosing in case of temperature value increases unexpectedly	
V.29	Include interlock between temperature measurement and cooling system in order to increase cooling power if temperature value increases unexpectedly (example break of dosing valve).	
	Accumulation hazards	**OK**
V.30	If possible, increase the addition time	
V.31	Include interlock between stirring failure and dosing valve in order to stop dosing in case of loss of agitation	
V.32	Improve agitation systems to avoid possible dead zones in vessels where reactants can accumulate	
	Segregated phases hazards	**OK**
V.33	Include multiple temperature measurements in order to detect non homogeneous distributions of temperature	
V.34	Include interlock between stirring failure and dosing valve in order to stop dosing in case of loss of agitation	
V.35	Include systems to restart agitation safely (speed control) in case of loss of agitation	
V.36	Improve agitation systems to avoid possible dead zones in vessels where reactants can accumulate	
	Hot spots hazards	**OK**
V.37	Include multiple temperature measurements in order to detect non homogeneous distributions of temperature	
V.38	Improve agitation systems to avoid possible dead zones in vessels where reactants can accumulate	
	Explosion / gas generation hazards	**OK**
V.39	Include a pressure relief system (bursting disk, relief valve, depressurisation, containment and so on)	
V.40	Consider the nature of gas generation (vapour, gassy, hybrid) when designing relief systems	
V.41	Consider the possibility of two-phase flow when designing relief systems	

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[1] Temperature is the most common physical property to monitor when preventing a runaway. All interlocks suggested in this checklist are related to temperature measurement. However, if there is another specific physical characteristic that is known to be indicative of triggering a runaway (such as pH variations, formation of foam…), interlocks between sensors for those parameters and possible actuation devices should be included.

Unit Operations

	General recommendations		**OK**
V.42	Introduce pressure relief systems if there is the possibility of overpressure in process equipment		
V.43	Control formation of unexpected reactive substances during unit operations		
V.44	Consider the possibility of using alternative unit operations in case hazards are detected, such as:		
	V.44.a	Distillation: vacuum or azeotropic distillation to lower boiling point of solvents	
	V.44.b	Centrifuge: decanters or static filters	
	V.44.c	Dryer: vacuum drying instead of atmospheric; cryogenic drying instead of vacuum rotary dryer	

	Temperature variations	**OK**
V.45	Introduce temperature control in process equipment	
V.46	Include multiple temperature measurements to detect non homogeneous distributions of temperature	
V.47	Improve agitation systems to avoid generation of hot spots or segregated phases	
V.48	Provide systems to keep appropriate conditions of substances in equipment (heating, cooling)	
V.49	Introduce measures to avoid effects of friction or vibration in equipment	
V.50	Control efficiency of vacuum operations	
	Concentration of reactive materials	**OK**
V.51	Prevent process backflow in feed lines, auxiliary services and shared systems (shared vents, drains)	
V.52	Improve agitation systems to avoid possible dead zones in vessels where reactants can accumulate	
V.53	Control agitation in order to avoid excessive mixing leading to emulsification and segregated phases	
V.54	Control evaporation rates to avoid concentration of unstable material	
V.55	Avoid concentration of reactive materials generated by absorptive materials	
V.56	Improve ventilation systems in order to avoid build-up of unstable materials	
V.57	Introduce measures to avoid corrosion in equipment that could catalyze unexpected reactions	
V.58	Control the possibility of wrong mixtures coming from multiple feeds	
V.59	Assure appropriate cleaning of multipurpose plants between different batches	
V.60	Assure joints in process equipment are properly designed to avoid leakage	
	Time variations	**OK**
V.61	Control efficiency of separation processes to avoid excessive time contact of unreacted products	
V.62	Include sensors to detect blockage of equipment	
V.63	Control flow rates in order to avoid dead zones in equipment	

Process and plant design

	General recommendations	OK
V.64	Assure that mass and heat balances for processes are reliable	
V.65	Assure that mechanical design for vessels and all plant equipment is reliable (including possible runaway scenarios)	
V.66	Assure that change of scale operations are reliable	
V.67	Arrange plant set-up according to ergonomic criteria to facilitate working procedures (separation distances)	
V.68	Provide confinement or shields for equipment to contain possible loss of containments (dikes, walls)	
V.69	Provide mitigation systems against releases (Foams, fans, water curtains)	
V.70	Calculate water supply for use simultaneously of sprinklers and hoses in various areas and maintenance of cooling in reactors and vessels	
	Control system	**OK**
V.71	Identify all instruments critical for safety (temperature probes, valves and so on)	
V.72	Use redundant control systems for any instrument critical for safety	
V.73	Identify possible critical liquid levels for measurements (probes, stirrers and so on)	
V.74	Assure that control system is connected to mitigation systems to provide actuation against releases	
V.75	Introduce measures to minimize time between detection and response in case of any emergency	

Maybe by the use of ***HarsMeth NP*** you are able to identify other measure that are critical for the safety of your process and should be taken into consideration. Please include them in the table below:

	Other recommendations	OK

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7. GLOSSARY.

- **Accumulation.** A build-up of unreacted materials.
- **Adiabatic.** A system condition in which no heat is exchanged between the chemical system and its environment, i.e. no heat transfer occurs to or from the environment surrounding the sample, including the sample container.
- **Adiabatic induction time.** Induction period or time to an event (spontaneous ignition, explosion, etc.) under adiabatic conditions starting at operating conditions.
- **Adiabatic calorimeter.** A calorimeter in which reactions proceed with little exchange of heat between the sample container and its surroundings. Common types of adiabatic calorimeter include the ARCTM, PHI-TECTM and VSPTM. The RSSTTM calorimeter may be considered as pseudo-adiabatic under some circumstances.
- **Adiabatic temperature rise.** The increase in temperature of a reacting mixture as a result of exothermic chemical reaction, when there is no heat transfer to or from the environment.

$$\Delta T = \Delta H/Cp$$

ΔT Adiabatic temperature rise (K)
Cp mean heat capacity (J/kg/K)
ΔH Heat release (J/kg)

- **Arrhenius rate equation.** The rate of a chemical reaction (k) increases exponentially with increasing temperature (T). This relationship is represented by the Arrhenius equation

$$k = A \,.\, \exp(-Ea/RT).$$

- **Autocatalysis.** The increase of the rate of reaction due to the catalysing effect of the reaction products.
- **Basis of safety.** The combination of measures relied upon to ensure safety. The basis of safety for a reactor highlights those aspects of the design and operation (hardware, protective systems and procedures) that are safety critical. The basis of safety can only be selected once all the significant hazards have been identified and evaluated.
- **Batch process.** An operation in which all the reactants including any solvent are added to a reactor at the start of a reaction.
- **Calorimeter.** See reaction calorimeter.

- **Containment.** A condition in which under no condition reactants or products are exchanged between the chemical system and its environment.

- **Continuous process.** A process that is characterised by a continuous flow of reactants into and out of the reaction system. Common examples of continuous reactors are the Plug Flow Reactor (PFR), the loop reactor and the Continuous Stirred Tank Reactor (CSTR).

- **Decomposition.** The breaking up of a chemical compound into by products. The temperature at which decomposition is observed depends on scale and is markedly dependent on the sensitivity of the measuring equipment.

- **Decomposition energy.** The decomposition energy is the maximum amount of energy, which can be released upon decomposition. The product of decomposition energy and total mass is an important parameter for determining the effects of a sudden energy release, e.g. in an explosion. The decomposition energy can occasionally be obtained from literature or calculated theoretically, however it is mostly determined experimentally, often by DSC.

- **Decomposition temperature.** Temperature at which spontaneous decomposition occurs. In practice, it is impossible to indicate the exact value of this temperature, because the reaction rate is only zero at absolute zero temperature (0 K) conforming to the equation of Arrhenius. Therefore, in measuring the decomposition temperature both sample quantity and sensitivity of the measuring device are very important. (See also onset temperature).

- **DIERS**. Design Institute for Emergency Relief Systems; Institute under auspices of the American Institute of Chemical Engineers founded to investigate design requirements for vent lines in case of two-phase venting.

- **Dewar.** A jacketed vacuum flask that can be used in calorimetry. The low rate of heat loss means that it can be used to simulate the behaviour of large reactors. See also adiabatic.

- **Differential scanning calorimetry (DSC).** A technique in which the change of the difference in the heat flow rate to the sample and to a reference sample is measured while they are subjected to a temperature regime. Note that in many process safety laboratories DSC and DTA are used interchangeably.

- **Differential thermal analysis (DTA).** A technique in which the change of the difference in the temperature between the sample and the reference sample is measured while they are subjected to a temperature regime. Note that in many process safety laboratories DSC and DTA are used interchangeably.

- **Endothermic.** A reaction is called endothermic if energy (heat) is absorbed during the reaction.

- **Exothermic.** A reaction is called exothermic if energy (heat) is released during the reaction.

- **Explosion.** A release of energy sufficient to cause a pressure wave.

- **Hazard.** A chemical or physical condition that has the potential for causing damage to people, property, or environment.

- **Hazard assessment.** The process of identifying the hazards present in any undertaking (whether arising from work activities or other factors) and those likely to be affected by them.

- **Hazardous chemical reactivity.** Any chemical reaction with the potential to exhibit rates of increase in temperature and/or pressure too high to be absorbed by the environment surrounding the system. Included are reactive materials and unstable materials.

- **Heat of reaction.** The total quantity of thermal energy liberated or absorbed during a chemical reaction.

- **Induction period/time.** Time interval (starting at operating conditions) after which a runaway shows its maximum effects.

- **Inherently safer.** A system is described as inherently safer if it remains in a non-hazardous situation after the occurrence of unintended deviations from normal operating conditions. Inherently safer is used, rather than inherently safe, because it is not possible to eliminate all hazards.

- **Inhibition.** A protective measure where the reaction can be stopped chemically by addition of another material.

- **Kinetic data.** Data associated with the conversion rate of a reaction, such as the activation energy, pre-exponential factor and order of reaction. (See Arrhenius rate constant).

- **Maximum pressure after decomposition.** The maximum pressure, which is obtained in a closed vessel. This pressure depends on the adiabatic temperature rise and the specific gas production.

- **Mitigating measures.** Measures to reduce the consequences of a runaway to an acceptable level.

- **MTSR Maximum Temperature of the Synthesis Reaction.** The maximum temperature reached following the occurrence of the desired (synthesis) chemical reaction under adiabatic conditions starting at the designed process temperature. For a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the synthesis reaction for those reactants that have accumulated during dosing.

- **Preventive measures.** Measures taken at the initial stages of a runaway to avoid further development of the runaway or to reduce its final effects.

- **Products.** Chemicals produced during a reaction process.

- **Quenching.** Rapid cooling of the reaction system in a short time (almost instantaneously). This condition 'freezes' the status of a process and prevents further reaction or decomposition.

- **Rate of reaction.** The rate at which the conversion of reactants takes place. The rate of reaction (r) is a function of concentrations (F(c)) and the reaction rate constant (k).

  $$r = k.F(cA, cB, \ldots, CX)$$

  The heat (q) produced by a reaction is a linear function of the rate of reaction, which makes the rate of reaction a basic parameter in determining the required cooling capacity during all stages of the reaction process.

- **Reactants.** Chemicals that are converted into (the required) products during the reaction process.

- **Reaction.** The process in which chemicals (reactants) are converted into other chemicals (products).

- **Reaction calorimeter.** A laboratory test apparatus for measuring thermal effects of chemical reactions or processes. For the purpose of this guidance, types of reaction calorimeters include isothermal, isoperibolic and adiabatic systems.

- **Reaction kinetics.** The complex of data that determine a reaction rate.

- **Reflux.** An operation, in which vapour is produced, condensed and subsequently returned to the originating vessel.

- **Runaway.** A reaction that is out of control because the rate of heat generation by an exothermic chemical reaction exceeds the rate of cooling available.

- **Semi-batch.** An operation in which some materials are added to the reactor at the start, with one or more other reactants added in a controlled manner during the reaction. See also semi-batch reactor.

- **Thermally unstable.** Chemicals and materials are thermally unstable if they decompose, degrade or react as a function of temperature and time at or about the temperature of use.

- **Thermodynamic data.** Data associated with the aspects of a reaction that are based on the thermodynamic laws of energy, such as the enthalpy (heat) of reaction.

- **TMR Time to maximum rate.** The time taken for a material to self-heat to the maximum rate of decomposition from a specific temperature, usually under adiabatic conditions.

- **TMRad.** Time to maximum rate from a specified temperature under adiabatic conditions.

- **Thermal runaway.** see runaway.

- **Unstable substance/material.** Substance or material that decomposes either in the pure state or in the state as normally produced.

- **Venting.** Emergency flow of vessel contents out of the vessel. The pressure is reduced by venting, thus, avoiding a vessel rupture due to over-pressurisation. The vent flow can be single or (a) multi-phase (one) with consequent differences in flow and depressurisation characteristics.

8. ANNEX I.

8.1. Chemical Compatibility Chart.

The following chart should be considered as overview guidance to detect possible hazards due to incompatibilities between different substances. Substances must be classified according to the functional group that is considered more reactive. It is important to notice that only those substances that are likely to be in contact during the process should be considered, but possible mixing of substances due to wrong labelling could also take place, so this possibility should not be ignored.

Because of the differing activities of the thousands of compounds that may be encountered, it is not possible to make any chart definitive and all-inclusive. It cannot be assumed to ensure compatibility of wastes because wastes are not classified as hazardous on the chart, nor do any blanks necessarily mean that the mixture cannot result in a hazard occurring. Detailed instructions as to hazards involved in handling and disposing of any given waste should be obtained from the originator of the waste.

27	**27**															
28		**28**														
29			**29**													
30		H, P		**30**												
31				H	**31**											
32				U		**32**										
33				H, GT			**33**									
34				H, P	H, P	U	H, P	**34**								
101				H, F, GT					**101**							
102				H, E	H, E		H, E	H, E	H, E	**102**						
103				P, H	P, H		P, H			H, E	**103**					
104	H, E	H, F	H, F	H, G	H, F	H, F, GT	H, F, GT	H, F, G	H, F, G	H, E	H, F, GT	**104**				
105	H, E			H, E	H, GF	H, GT, GF		H	H, GF	H, E	H, P, GF	H, F, E	**105**			
106							GT, GF						GF, GT	**106**		
107	<-EXTREMELY REACTIVE!!!! DO NOT MIX WITH ANY CHEMICAL OR WASTE MATERIAl->															**107**
	27	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**101**	**102**	**103**	**104**	**105**	**106**	**107**	

1	**1**																									
2		**2**																								
3		G, H	**3**																							
4	H	H, F	H, P	**4**																						
5	H, P	H, F	H, P		**5**																					
6	H	H, GT				**6**																				
7	H	H, GT	H		H		**7**																			
8	H, G	H, GT	H, G	H, G	H			**8**																		
9	H, G	H, GT						H, G	**9**																	
10	H	H	H		H				H, G	**10**																
11	GT, GF	GT, GF	GT, GF					G			**11**															
12	H, F, GF	H, F, GF	H, GT, GF		GT, GF		U	H, G				**12**														
13	H	H, F						H, G		H			**13**													
14	H	H, F												**14**												
15	GT	GT	GT												**15**											
16		H, F														**16**										
17	H, GT	H, F, GT					H, GT	H, G		H, GF	H						**17**									
18	H, G	H, F, GT	H, G	H, P			H, P	H, G		H, P, G	H, G	U						**18**								
19	H	H, F						H, G		H	H								**19**							
20	GT, GF	H, F, GT						H, G									H	H	H	**20**						
21	H, F, GF	H, F, GF	H, F, GF	H, F, GF	H, F, GF	GF, H	GF, H	GF, H	GF, H	GF, H	GF, H	GF, H, GT	GF, H				H, E	GF, H	GF, H	GF, H	**21**					
22	H, F, GF	H, F, GF	G, F					H, F, GT	U	GF, H							H, E	GF, H		H, F, GF		**22**				
23	H, F, GF	H, F, GF						H, F, G									H, F						**23**			
24	S	S	S			S	S			S														**24**		
25	GF, HF	H, F, E	H, GF	H, E, GF	GF, H			U	H, G	U	GF, H	GF, H	GF, H				GF, H	U	GF, H	GF, H	E				**25**	
26	H, GT, GF	H, F, GT	H							U											H, P			S	GF, H	**26**
27		H, F, GT			H					H, E											H, E, GF				H, E, GF	
28	H	H, F			H																	H, E				
29		H, F																								
30	H, G	H, E		H, F	H, G		H, GT	H, F, E	H, F, GT		H, E, GT	H, F, GT					H, E	H	E	H, F, GT	H, E	H, G		H, G	H, E, GF	H, P, GT
31	H	H, F						H, G										H, P			GF, H				GF, H	
32	H, GT	H, GT						U		H, E											H					
33	GT,GF	HF, GF	GT		H			E										H								
34	H, P	H, P	H, P	H, P	U		H, P	H, P		H, P	H, P	U								H, P	H, P	H, P		H, P	H, P	
101	H, G	H, F, GT																			H, F, GT				H, F, GF	
102	H, E	H, E	H, E					H, E		H, E			H, E								H, E	H, E	H, E	E	E	
103	P, H	P, H	P, H					P, H	P, H	P, H	P, H	U									P, H	P, H	P, H	P, H	P, H	
104	H, GT		H, GT	H, F	H, F	H, F, GT	H, F, GT	H, E	H, F, GT		H, E, GT	H, F, GT	H, F	H, F		H, F	H, GT	H, F, GT	H, F	H, F, GT	H, F, E	H, F, E	H, F		H, F, E	H, F, GT
105	H, GF	H, F, GT	H, GF	H, F, GF	H, F, GF	H, GF	H, G				H, GT	H, F				H, F, E	H, E	H, GF	H, GF	H, GF						H, GF
106	H	H						G										H, G			H, GF	H, GF		S	H, GF	
107	<---------EXTREMELY REACTIVE!!!! DO NOT MIX WITH ANY CHEMICAL OR WASTE MATERIAL------------->																									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**

LEGEND

Code	Consequences
H	Heat Generation
F	Fire
G	Innocuous and non-flammable gas generation
GT	Toxic Gas formation
GF	Flammable Gas formation
E	Explosion
P	Violent Polymerization
S	Solubilization of toxic substance
U	May be hazardous, but Unknown

No.	Reactivity Group Name
1	Acids, Mineral, Non-oxidizing
2	Acids, Mineral, Oxidizing
3	Acids, Organic
4	Alcohols and Glycols
5	Aldehydes
6	Amides
7	Amines, Aliphatic and Aromatic
8	Azo Compounds, Diazo Compounds and Hydrazines
9	Carbamates
10	Caustics
11	Cyanides
12	Dithiocarbamates
13	Esters
14	Ethers

No.	Reactivity Group Name
15	Fluorides, Inorganic
16	Hydrocarbons, Aromatic
17	Halogenated Organics
18	Isocyanates
19	Ketones
20	Mercaptans and Other Organic Sulfides
21	Metals, Alkali and Alkaline Earth, Elemental
22	Metals, Other Elemental & Alloys as Powders, Vapors, or Sponges
23	Metals, Other Elemental & Alloys as Sheets, Rods, Drops, etc.
24	Metals and Metal Compounds, Toxic
25	Nitrides
26	Nitriles
27	Nitro Compounds, Organic
28	Hydrocarbons, Aliphatic, Unsaturated
29	Hydrocarbons, Aliphatic, Saturated
30	Peroxides and Hydroperoxides, Organic
31	Phenols and Cresols
32	Organophosphates, Phosphothioates, Phosphodithioates
33	Sulfides, Inorganic
34	Epoxides
101	Combustible and Flammable Materials, Miscellaneous
102	Explosives
103	Polymerizable Compounds
104	Oxidizing Agents, Strong
105	Reducing Agents, Strong
106	Water and Mixtures Containing Water
107	Water Reactive Substances

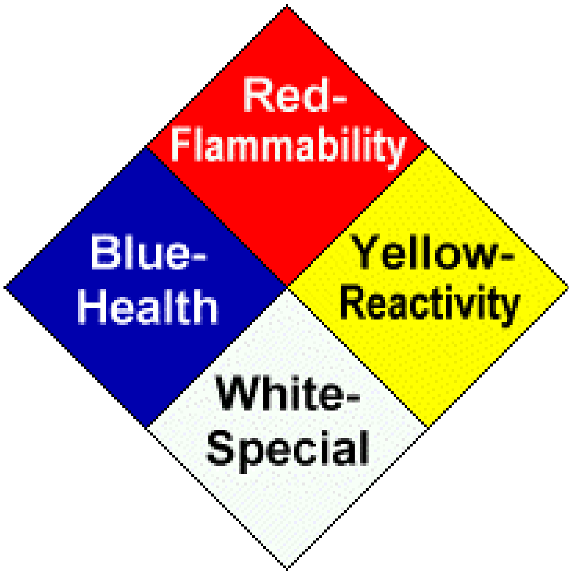
No.	Substances																				
1		1																			
2			2																		
3				3																	
4					4																
5						5															
6							6														
7								7													
8									8												
9										9											
10											10										
11												11									
12													12								
13														13							
14															14						
15																15					
16																	16				
17																		17			
18																			18		
19																				19	
20																					20
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
🟥																					
🟦																					
🟨																					
⬜																					

NOTES

1.- Interaction with water and iron must be considered for all processes.

2.- Construction materials and wastes have to be included in the substances considered

The colours at the bottom of the table are referred to the NFPA index. This is an identification process that can facilitate the comprehension of the chemical behaviours of different substances. The summary of the NFPA codes is shown next.



Rating Summary		
Health (Blue)		
4	Danger	May be fatal on short exposure. Specialized protective equipment required
3	Warning	Corrosive or toxic. Avoid skin contact or inhalation
2	Warning	May be harmful if inhaled or absorbed
1	Caution	May be irritating
0		No unusual hazard
Flammability (Red)		
4	Danger	Flammable gas or extremely flammable liquid
3	Warning	Flammable liquid flash point below 37 °C
2	Caution	Combustible liquid flash point of 37 °C to 93 °C
1		Combustible if heated
0		Not combustible
Reactivity (Yellow)		
4	Danger	Explosive material at room temperature
3	Danger	May be explosive if shocked, heated under confinement or mixed with water
2	Warning	Unstable or may react violently if mixed with water
1	Caution	May react if heated or mixed with water but not violently
0	Stable	Not reactive when mixed with water
Special Notice Key (White)		
W		Water Reactive
Oxy		Oxidizing Agent

Table 1. Summary of the NFPA identification codes.

APPENDIX 2.1

List of MARS accidents analysed

Accident	chemical description	Main features of accident
A-001	acid-base reaction; NaClO + acid waste	tanks connected erroneously; blocked valve due to crystals formation
A-002	ethylene oxide reacted with ancillary equipment	leakage; possible hot spot in column
A-003	ethylene oxide reacted with moisture to form non-volatile polyethylene glycols in the insulation material which auto oxidized	leakage in weld due to fatigue
A-004	phenol crystallization	lack of pipe heating led to blockage
A-005	$TiCl_4$ reacted with water	control system not disconnected during maintenance led to tank overflow; external operators did not know way out
A-006	ethylene mixed with air, oxygen started decomposition of ethylene	incorrect purging of installation
A-007	decomposition of nitro compounds due to temperature rise	climatic conditions lead to freezing of waste condensate
A-008	unexpected formation of methylnitrate in tank containing chlorine residuals	introduction of hydrogen chloride contaminated with methanol
A-009	decomposition of 1-nitro-anthraquinone	unknown catalytic effect of impurities (inorganic salts)
A-010	$TiCl_4$ reacted with water from cooling circuit	leakage in cooling circuit made water mix with $TiCl_4$; leakage due to corrosion for incorrect cleaning procedures
A-011	self-ignition of substances in storage area	unexpected unstable behaviour of substance
A-012	mixture formaldehyde/air exploded due to a temperature increase	welding operation in a tank containing flammable mixture generated an explosion
A-013	mixture of zinc powder and air	explosion due to hitting equipment with a hammer generating a hot nucleus of zinc powder
A-014	NaClO + HClO releasing chlorine	labels of tanks had been interchanged
A-015	decomposition of crystallized hypophosphorous acid; formation of explosive air/phosphine mixture	formation of crystalline incrustation in tank; failure in steam supply line
A-016	flammable vapours ignited	excessive heating from worn bearing of the agitator
A-017	mixture of methanol, methylacetate and air ignited	incorrect maintenance procedures
A-018	crystalline SO_3 formed due to contact between oleum and ammonium sulphate	introduction of air increased pressure in blocked pipe
A-019	acid mixture in contact with water generated release of nitrous gases	storage tank not properly emptied, cleaning water reached tank
A-020	NaClO + acid releasing chlorine	label mismatch, tank used for NaClO was exceptionally loaded with acid, then forgotten
A-021	self-ignition of substances in storage area for wastes	unexpected unstable behavior of substance
A-022	ferric chloride sulphate + sodium chloride released chlorine	no verification of vessel contents
A-023	decomposition of H_2O_2 due to presence of impurities	ventilation pipe used for safe drainage of H_2 blocked, possibility of product backflow
A-024	aqueous caustic soda solution + alkyl residues generating flammable gases	the container had been sealed infringing operating instructions
A-025	uncontrolled formation of phenylphosphine	unexpected unstable behaviour of substance
A-026	flammable vapours ignited	ignition due to use of halogen lamp in highly flammable tank
A-027	ignition of polyvinylpyrrolidine	oxidation and ignition due to atmospheric air feed instead of nitrogen
A-028	release of polychloroacetone	faulty pipe connection
A-029	release of phenol-water solution	operator erroneously opened valve
A-030	mixture of air/styrene vapours ignited	mixture ignited due to static electricity
A-031	release of acetylene and decomposition products	leakage of pipe
A-032	release of SO_2 due to different exothermic reactions	incorrect storage procedures; no toxic detectors
A-033	decomposition of fertilizers producing NOx vapours due to wrong mixture of products containing Cu and Cl	incorrect process analysis

List of MARS accidents analysed

Accident	chemical description	Main features of accident
A-034	ignition of air/ethyl alcohol mixture	mixture ignited due to static electricity
A-035	ignition of flammable materials due to overheating	incorrect storage procedures
A-036	explosion of mixture of volatile elements and fuel-oil	unexpected unstable behaviour of substance
A-037	NaClO + HCl releasing chlorine	tank rupture; pipe containing incompatible materials broke as well
A-038	fire of sodium dichloroisocyanurate associated with the release of chlorine	rupture of bag, product reached drainage, ignited in touch with wastes and oils
A-039	decomposition of fertilizers	incorrect storage procedures
A-040	decomposition of H_2O_2 due to presence of impurities	control failure + human error; valves opened that should have been closed
A-041	release of hydrochloric acid and sulphur dioxide due to mixture of sulphur chloride and water	operator cleaned tank with water
A-042	spontaneous ignition of pyrophoric iron sulphides deposit	no verification of vessel contents
A-043	NaClO + HCl releasing chlorine	chemicals picked from wrong container
A-044	trichloromethylsilane + water releasing chlorine	operator mixed wrong chemicals
A-045	isocyanuric acid + water	label mismatch
A-046	ignition of sodium chlorate + combustible substances in storage area	incorrect storage procedures
A-047	explosion of sodium hydroborate	unexpected unstable behaviour of substance
A-048	sulphuric acid + sodium bisulphite released SOx	no verification of vessel contents, wrong chemical used
A-049	release of SO_2	wrong handling of chemical drum
A-050	spontaneous combustion of sodium dichloroisocyanurate polluted with organic compounds	incorrect storage procedures; hazard was foreseen but no measures put in place
A-051	ethoxyalkylphenol + water	operator mixed wrong chemicals
A-052	water + benzoyl chloride	leakage due to failure of joint in condenser
A-053	tosyl isocyanate + metal container released H_2S, HCl, sawdust added as inhibitor but did not work	incorrect operation procedures; addition of sawdust to inhibit reaction did not work
A-054	sodium chloride + ferric chloride	NaClO introduced erroneously in tank containing $FeCl_3$
A-055	dust cloud ignition	chemical reacted with container material; blockage of aerosol outlet
A-056	decomposition of 2-azo-bis-methylbutyronitrile	one plate of the dryer was broken; excessive heating over safe temperature
A-057	release of HCN	incorrect process analysis
A-058	reaction of water + toluene diisocyanate	leakage
A-059	$KMNO_4$ + ethanol solution	no verification of compatibility of mixture
A-060	benzoyl chloride + methanol released HCl	verification of compatibility of mixture inadequate
A-061	release of SO_2	accumulation of product in equipment; improvement of agitation systems required
A-062	trichloromethylbenzol reacted with humidity releasing HCl	wrong connections
A-063	formation of polymer of ethylene oxide	valve blockage
A-064	self-ignition of white phosphorus	air admission in drum during loading
A-065	release of vapours and ignition due to welding	incorrect procedures for maintenance
A-066	ignition of vapours	wrong application of foam; compatibility of auxiliary services
A-067	decomposition of azodibutyronitrile	unexpected unstable behaviour of substance
A-068	mixture of H_2, light hydrocarbon gases and CO ignited by pyrophoric carbon deposits	incorrect maintenance procedures
A-069	ignition of different materials accumulated	long overheating of materials; incorrect tests to determine thermal stability
A-070	ignition of unstable residues containing nitrotoluenes and nitrocresols	incorrect management and maintenance; failure of tests for stability

List of MARS accidents analysed

Accident	chemical description	Main features of accident
A-071	mixture of water with SO_3 releasing H_2SO_4	erroneous introduction of water, no verification of vessel contents
A-072	sodium chloride + epichlorohydrin generated an exothermic reaction	no verification of vessel content
A-073	SCl_2 + water releasing SO_2	monochlorobenzene provided by supplier contaminated with water
A-074	release of hydrogen sulphide gas, formed when waste chemicals were mixed	incorrect process analysis
A-075	ignition of methoate	operator forgot to switch off heater, lead to overheating
A-076	ignition of solvent vapours, acetone, methanol	static electricity from polyethylene bags
A-077	powdered pharmaceutical product ignited	static electricity, incorrect process analysis
A-078	explosion of highly flammable liquids	teflon coating worn out, metal-to-metal contact generated the explosion
A-079	explosion of methanol vapours/air mixture	no inertization, monitoring of flammables, explosive or smoke detectors
A-080	nitric acid + formic acid	wrong connections; mistaken tank
A-081	explosion of different solvents	unknown catalytic effect of impurities (inorganic salts)
A-082	release of flammable hydrocarbons + NaOH solution	human error during diluting mixture; flammable reached zone of welding work; stop of electricity supply induced explosions in other zones
A-083	ignition of acrylonitrile, vinyl acetate polymers	accumulation of product in equipment; ignition due to friction generating sparks
A-084	explosion involving thioridazine hydrochloride	residues from previous process, incomplete cleaning of vessel; ignition due to static electricity; no investigation of previous incidents
A-085	release of PCl_3 in contact with water generates HCl and phosphines which self-ignited	wrong connections; reaction with rain water; extinguishing with water increased HCl cloud
A-086	decomposition of organic peroxides	overheating; incorrect procedures for heating; control and management failures
A-087	flammable vapours ignited due to self-heating	incorrect process analysis; no flame arrestors installed
A-088	$TiCl_4$ and $AlCl_3$ + water pressure increase and HCl release	deposit of $AlCl_3$ and $TiCl_4$ formed in tube
A-089	decomposition of NO_2 due to overheating	overheating due to pump bearing; pumps inadequately cooled
A-090	polymer waste explosion	operators not aware of possible flammables inside vessel
A-091	ignition of flammable materials	leakage + ignition due to welding operations
A-092	phenol-formaldehyde polymerization	mischarging; operator error, lack of training
A-093	polyvinylchloride polymerization	supplies failure
A-094	epichlorohydrin polymerization	cooling failure
A-095	copper phthalocyanine + chlorosulphonic acid	dosing failure; no interlock between sensors
A-096	azo compounds for paints	agitation failure; operation error restarting agitation
A-097	nickel-metal + nitric acid	cooling failure
A-098	ketone-colors manufacture, Dimethylaniline Chloroform, Phosgene and Dyphenilketone	dosing failure; erroneous use of water
A-099	unknown, dymethilsulphate involved	dosing failure; operator error
A-100	azo compounds for paints	impurities / contamination
A-101	azo compounds for paints	impurities / contamination
A-102	resin synthesis (maleic anhydride, lithium hydroxide…)	mischarging; control system erroneously programmed
A-103	production of dimethyl-phosphorochloridothioate and diethyl-phosphorochloridothioate	dosing failure; insufficient cooling
A-104	polyvinylchloride polymerization	pressure increase due to unknown reasons; safety valve did not work
A-105	unknown, involved SO_2	impurities / contamination; presence of water unnoticed

List of MARS accidents analysed

Accident	chemical description	Main features of accident
A-106	polyvinylchloride polymerization	supplies failure; inhibition did not work
A-107	polyvinylchloride polymerization	dosing failure; rupture disk broken releasing gas in the atmosphere
A-108	fine chemical production (sodium borohydride)	pressure increase due to unknown temperature rise, breaking down process intermediate; reactor was on stand by
A-109	synthesis of 3-methylthioaniline	dosing failure; inversion of order in reactants
A-110	styrene polymerization	supplies failure; false indication in control room
A-111	various chemicals for production of textile and plastic industries; emulsion oil and water	mischarging; incorrect pH control
A-112	production of zirconium sponges (involving Mg)	impurities / contamination
A-113	synthesized active ingredients for the pharmaceutical industry,	dosing failure; incorrect working procedures; inexperienced worker
A-114	production of pectines	dosing failure
A-115	phenol-formaldehyde polymerization	supplies failure; incorrect working procedures
A-116	phenol-formaldehyde polymerization	dosing failure; incorrect working procedures
A-117	pharmaceutical synthesis (p-chlorobenzaldehyde instead of o-chloronitrobenzene)	mischarging; labelling mismatch from supplier
A-118	H_2O_2 + alcohol vapours	impurities / contamination; bursting disks did not work; no investigation of previous similar incidents
A-119	fertilizers production	impurities / contamination
A-120	o-nitrobenzylnitrate was produced instead of o-nitrobenzaldehyde	impurities / contamination; dumping system did not operate
A-121	difluoronitrobenzene contaminated with water	impurities / contamination; decomposition T of intermediates were known, but unexpected that the presence of water could generate such T raise
A-122	ethylene production	unknown causes for the runaway; isolation and dump valves did not work; hot carbon particles generated during the fire ignited vapours
A-123	unknown (involved ethanol and Ni Raney)	cooling failure; control failure; pyrophoric nickel as source of ignition
A-124	dosing failure involving H_2O_2	dosing failure; operator error; failure of quenching system
A-125	hydrogen explosion	leakage; ignition due to static electricity; agitator failure; no study of previous incidents; failure of bursting disk
A-126	manufacture of bulk fine chemicals (1-methyl-2-fromyl-1 nitroimidazole)	unknown; incorrect laboratory analysis procedures; accident during change of scale trials
A-127	isopropyl alcohol recovery	unknown; potential for runaway not detected previous to production
A-128	phthalocyamines process unit	dosing failure; operator error; no monitoring of pH; pressure relief system inadequate
A-129	production of chemicals to reduce grease	mischarging; wrong chemicals; inexperienced operator; no emergency measures available
A-130	polyvinylchloride polymerization	mischarging; operator error; extra cooling didn't work; formation of corrosive substance attacked reactor wall; sprinkler system worked
A-131	polymerization of dicyclopentadiene	mischarging; incorrect working procedures; inadequate training
A-132	production of ferric chloride	dosing failure; no pH monitoring; incorrect working procedures

APPENDIX 2.2

HarsMeth version 2

A short cut chemical process safety assessment procedure for SMEs

TABLE OF CONTENTS

I. PREFACE

THE BASICS

In order to carry out chemical reactions on a plant scale over a long period of years in safety, it is necessary to control many different factors over the life of the process. However at the very basis of process safety, its fundamentals, are four principles:

1) Good Basic Data (about the materials used and the process).
2) Good Process Engineering.
3) Good Process Design.
4) Good Process Practice (State Evaluation)

1) GOOD BASIC DATA

It is imperative that the fundamental thermokinetics of the desired process and any side reactions and decompositions are determined and understood. In addition much physical data on raw materials, intermediates and final products is required.

Tables of the data required and their methods of procurement are detailed (Section II).

2) GOOD PROCESS ENGINEERING

Clearly, unless good basic chemical engineering standards are met no amount of additional data or analysis will redeem the situation. For example, if the electricity supply is subject to frequent (more than once a month) and prolonged (more than one hour) interruption then **THIS** is the problem and it must be fixed first. A similar argument applies to all other utilities, water, steam, air, nitrogen, communications and computer functions. At a lower level each safety element (e.g. a thermometer or pressure gauge) must have normal industrial reliability and good standards applied to purchase and maintenance are essential.

In order to assist companies assess their chemical engineering systems a checklist is provided (Section III).

3) GOOD PROCESS DESIGN

Good robust process design is also essential. If a process cannot meet the requirements of quality, yield and throughput it will be constantly changed and updated to meet demand. Eventually this updating process will lead to unsafe conditions unless strict control of the process changes is maintained.

In order to assist in the production of a good basic process a checklist is provided (Section IV).

4) GOOD PROCESS PRACTICE

After design and engineering have been completed, it is necessary to have a tool to follow up the evolution of the process. This tool must be clear and efficient so that workers and engineers can easily identify possible risk arising from the way they carry out their processes.
A number of questions structured as a “yes/no tree” are proposed. Each step of the process has to be referred to one process area and then the proper list of questions has to be followed. The what if/checklist questions are structured in the way that at the end of each “tree” of questions only tree possibilities can be achieved: justification of the answer given, a review of existing safety measures, or a check request if unknown.

In order to assist in the evaluation of the process, tree-structured checklists for each step are provided.

5) RISK ANALYSIS

These elements must be brought together in an interactive and systematic manner by means of a Risk Analysis. The Risk Analysis will identify hazards arising from 1, 2, 3 and 4 and the interaction between them. These will be classified in two kind of hazards: **knowledge** or **process** hazard. Knowledge hazard will come from unknown chemical or physical values of substances or mixtures or from unknown parameters or safety measures adopted in the process. If a risk of this kind is determined, this means that the unknown ones have to be determined before going on with the risk analysis. Process hazards are a consequence of the industrial activity itself. The number of this kind of hazards encountered will give an idea of the safety of the process.

Once the Risk has been assessed, measures can be put in place to control the Risk to an acceptable level or better still eliminate the Risk completely. Even though some general ideas or guidelines can be given, this measures must come from the workers and engineers of the SME carrying the analysis. It must be taken into account that the enterprises are the best expert of the process: the experience of the persons that are working on it can be used to define which measures can better be applied to each single case.

An intent of the previous checklists is to make thinking the persons that are performing the safety analysis in order to generate a discussion in which the knowledge of the process can be improved and all necessary measures to manage all possible risks arisen form the analysis can be defined.

Once these 5 elements are in place:

1) Good Basic Data
2) Good Engineering Design
3) Good Process Design
4) Good Process Practice
5) Risk Analysis and Measures

MANAGEMENT

Then all five elements can be Planned, Organised, Controlled, Monitored, Audited, Reviewed and Spot-checked (POCMARS) by a formal (written) according to ISO 14000, for example, or informal Management System. The system is shown schematically in the appended Process Safety Overview (Figure 3) and a checklist for a basic management system is appended.

Clearly few companies will run formal management systems which cover every aspect referred to in the overview, except possibly for high hazard operations.

However the basic elements of 1, 2, 3, 4, 5 and 6 must be in place to ensure a minimum level of safety.

PROCESS SAFETY OVERVIEW

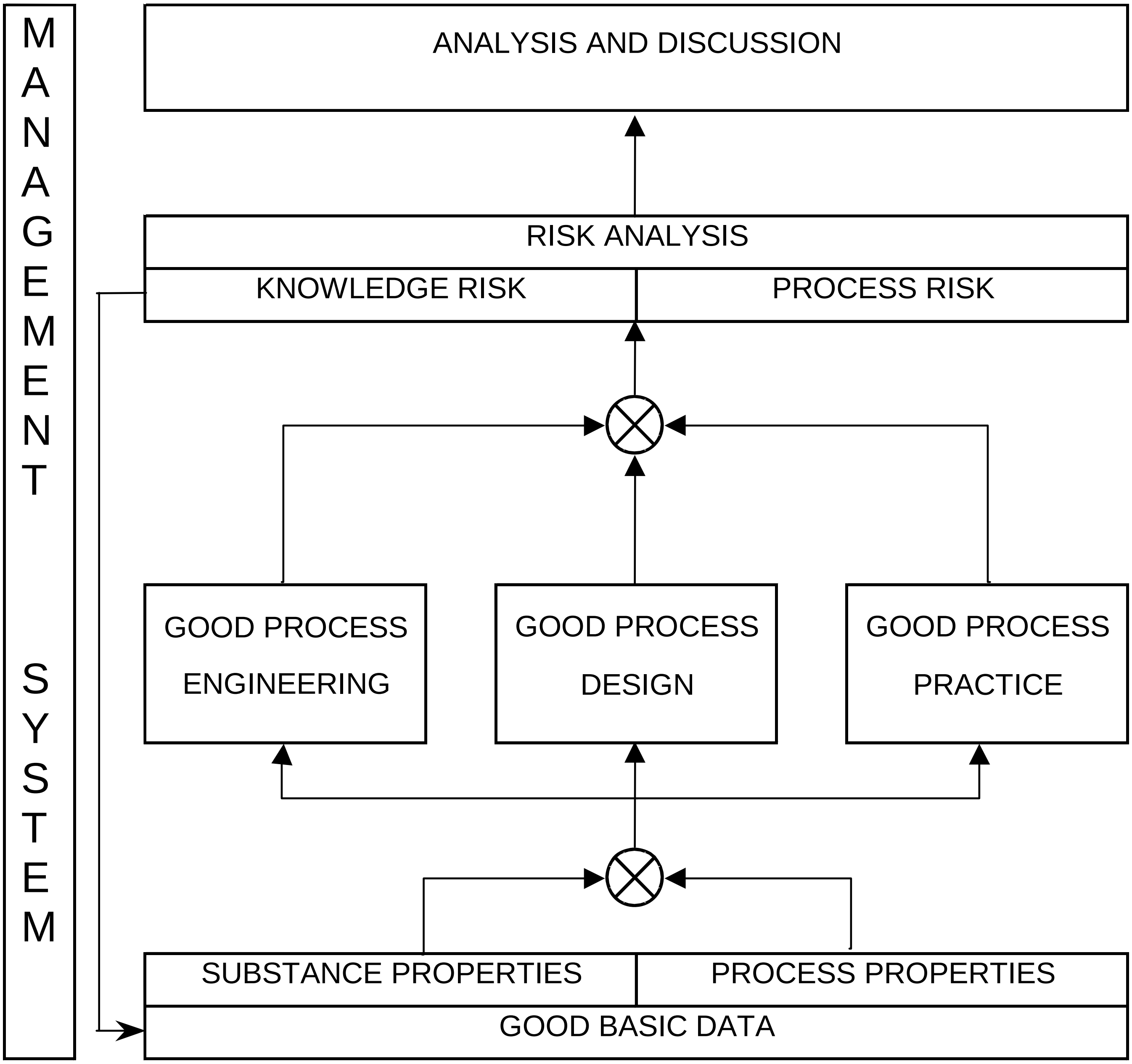


Fig.3

II. GOOD BASIC DATA

SUBSTANCES[(1)] AND MIXTURES	Chemical composition and CAS number	homologation or identification number[(2)]	Purity[(3)]	Phase			Report of handling conditions[(4)]	Specific heat[(7)]	Thermal activity at $T_{STORAGE}$[(8)]	Detonation and deflagration sensitivity[(9)]
				G	L	S				

NOTES:

1.-.Considered in the all possible phases on which the substances are used in the process (storage steps, reaction steps, etc).

2.-.Enterprise's internal identification of the substances.

3.-.Degree of purity as specified in each process.

4.-.Inhibitors, triggering agents, chemical substances able to influence the rate of reaction, etc.

5.-.Temperature to leave of which a different phase from the one expected under normal conditions appears.

6.-.Pression to leave of which a different phase from the one expected under normal conditions appears.

7.-.In case of lack of data for mixtures, make one medium of the values of the single substances.

8.-.Stable or unstable, considering the maximum storage period.

9.-.High, medium, low.

CALCULATE ALL THE VALUES USING INTERNATIONAL SYSTEM UNITS.

REACTION and PROCESS CONDITIONS

STEP(1)	**T**	**P**	**Substances(2)**	**Specific heat of the mixture(3)**	**Heat of reaction(4)**	**MTSR(5)**	**Kinetic behaviour(6)**	**Total adiabatic temperature rise(7)**	**Thermal activity at the end of the step**	**MAXTSAFE(8)**	**Influence of hot spots**

NOTES:

1-Subdivide the process in steps and define if the step refers to process (P) or reaction (R).

2-Consider all the substances present in each step.

3-Use the experimental value if known, otherwise consider one medium of the values of the single substances.

4-It can be known from: experimental calculations, literature or internet source (see DATA SOURCE)or simulations programs (as CHETAH).

5-The maximum temperature reached following the occurrence of the desired (synthesis) chemical reaction under adiabatic conditions starting at the designed process temperature. For a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the accumulated reactants of the desired reaction.

6-Specify if the reaction is an Arrhenius, catalytic (homogeneous or heterogeneous) or autocatalytic type.

7-Increase of temperature of the reaction mass under adiabatic conditions due to accumulation of the heat released, coming from both the synthesis reaction and all the possible secondary reactions involved.

8-If known, use ADT24; if not, MAXTSAFE can be calculated as the critical T at which in a short time decomposition or other thermal evolution of the final reaction mass takes place. It can be evaluated with a DSC, considering the T of the first exothermal peak less 70º (if beta=5K/min) or less 100º (if beta=10K/min).

CALCULATE ALL THE VALUES USING INTERNATIONAL SYSTEM UNITS

COMPATIBILITY CHART

No.	Substances													
1		1												
2			2											
3				3										
4					4									
5						5								
6							6							
7								7						
8									8					
9										9				
10											10			
11												11		
12													12	
13														13
		1	2	3	4	5	6	7	8	9	10	11	12	13
🟦														
🟥														
🟨														
⬜														

NOTES 1-Interaction with water and iron must be considered for all processes.

2-Construction materials and wastes have to be included in the substances considered.

3-The colors at the bottom of the table are referred to the NFPA index. Include this identification in order to better comprehend the substance's chemical behaviour.

Legend

Code	Consequences
H	Heat Generation
F	Fire
G	Innocuous and non-flammable gas generation
GT	Toxic Gas formation
GF	Flammable Gas formation
E	Explosion
P	Violent Polymerization
S	Solubilization of toxic substance
U	May be hazardous, but Unknown

General Chemical Compatibility Chart

EPA-600/2-80-076 April 1980

A METHOD FOR DETERMINING THE COMPATIBILITY OF CHEMICAL MIXTURES

Legend

Code	Consequences
H	Heat Generation
F	Fire
G	Innocuous and non-flammable gas generation
GT	Toxic Gas formation
GF	Flammable Gas formation
E	Explosion
P	Violent Polymerization
S	Solubilization of toxic substance
U	May be hazardous, but Unknown

***Caution*: This Chart is intended as an indication of some of the hazards that can be expected on mixing chemical wastes. Because of the differing activities of the thousands of compounds that may be encountered, it is not possible to make any chart definitive and all inclusive. It cannot be assumed to ensure compatibiltiy of wastes because wastes are not sclassified as hazardous on the chart, nor do any blanks necessarily mean that the mixture cannot result in a hazard occuring. Detailed instructions as to hazards involved in handling and disposing of any given waste should be obtained from the originator of the waste.**

No.	Reactivity Group Name																																									
1	Acids, Mineral, Non-oxidizing	1																																								
2	Acids, Mineral, Oxidizing		2																																							
3	Acids, Organic		G H	3																																						
4	Alcohols and Glycols	H	H F	H P	4																																					
5	Aldehydes	H P	H F	H P		5																																				
6	Amides	H	H GT				6																																			
7	Amines, Aliphatic and Aromatic	H	H GT	H		H		7																																		
8	Azo Compounds, Diazo Compounds and Hydrazines	H G	H GT	H G	H G	H			8																																	
9	Carbamates	H G	H GT						G H	9																																
10	Caustics	H	H	H		H				H G	10																															
11	Cyanides	GT GF	GT GF	GT GF					G			11																														
12	Dithiocarbamates	H,F GF	H,F GF	H,GT GF		GF GT		U	H G				12																													
13	Esters	H	H F						H G		H			13																												
14	Ethers	H	H F												14																											
15	Fluorides, Inorganic	GT	GT	GT												15																										
16	Hydrocarbons, Aromatic		H F														16																									
17	Halogenated Organics	H GT	H,F GT					H GT	H G		H GF	H						17																								
18	Isocyanates	H G	H,F GT	H G	H P			H P	H G		H,P G	H G	U						18																							
19	Ketones	H	H F						H G		H	H								19																						
20	Mercaptans and Other Organic Sulfides	GT GF	H,F GT						H G									H	H	H	20																					
21	Metals, Alkali and Alkaline Earth, Elemental	H,F GF	H,F GF	H,F GF	H,F GF	H,F GF	GF H	GF H	GF H	GF H	GF H	GF H	GF,H GT	GF H				H E	GF H	GF H	GF H	21																				
22	Metals, Other Elemental & Alloys as Powders, Vapors, or Sponges	H,F GF	H,F GF	G F					H,F GT	U	GF H							H E	GF H		H,F GF		22																			
23	Metals, Other Elemental & Alloys as Sheets, Rods, Drops, etc.	H,F GF	H,F GF						H,F G									H F						23																		
24	Metals and Metal Compounds, Toxic	S	S	S			S	S			S														24																	
25	Nitrides	GF HF	H,F E	H GF	H,E GF	GF H			U	H G	U	GF H	GF H	GF H				GF H	U	GF H	GF H	E				25																
26	Nitriles	H,GT GF	H,F GT	H							U											H P			S	GF H	26															
27	Nitro Compounds, Organic		H,F GT			H					H E											H,E GF				H,E GF		27														
28	Hydrocarbons, Aliphatic, Unsaturated	H	H F			H																	H E						28													
29	Hydrocarbons, Aliphatic, Saturated		H F																											29												
30	Peroxides and Hydroperoxides, Organic	H G	H E		H F	H G		H GT	H,F E	H,F GT		H,E GT	H,F GT					H E	H	E	H,F GT	H E	H G		H G	H,E GF	H,P GT		H P		30											
31	Phenols and Cresols	H	H F						H G										H P			GF H				GF H					H	31										
32	Organophosphates, Phosphothioates, Phosphodithioates	H GT	H GT						U		H E											H									U		32									
33	Sulfides, Inorganic	GT GF	HF GF	GT		H			E										H												H GT			33								
34	Epoxides	H P	H P	H P	H P	U		H P	H P		H P	H P	U								H P	H P	H P		H P	H P					H P	H P	U	H P	34							
101	Combustible and Flammable Materials, Miscellaneous	H G	H,F GT																			H,F G				H,F GF					H,F GT					101						
102	Explosives	H E	H E	H E					H E		H E			H E								H E	H E	H E	E	E					H E	H E		H E	H E	H E	102					
103	Polymerizable Compounds	P H	P H	P H					P H		P H	P H	U									P H	P H	P H	P H	P H					P H	P H		P H			H E	103				
104	Oxidizing Agents, Strong	H GT		H GT	H F	H F	H,F GT	H,F GT	H E	H,F GT		H,E GT	H,F GT	H F	H F		H F	H GT	H,F GT	H F	H,F GT	H,F E	H,F E	H F		H,F E	H,F GT	H E	H F	H F	H G	H F	H,F GT	H,F GT	H,F G	H,F G	H E	H,F GT	104			
105	Reducing Agents, Strong	H GF	H,F GT	H GF	H,F GF	H,F GF	H GF	H G				H GT	H F				H,F E	H E	H GF	H GF	H GF						H GF	H E			H E	H GF	H,GT GF		H	H GF	H E	H,P GF	H,F E	105		
106	Water and Mixtures Containing Water	H	H						G										H G			H GF	H GF		S	H GF								GT GF						GF GT	106	
107	Water Reactive Substances	<--------EXTREMELY REACTIVE!!!! DO NOT MIX WITH ANY CHEMICAL OR WASTE MATERIAL!!!!-------->																			<---------EXTREMELY REACTIVE!!!! DO NOT MIX WITH ANY CHEMICAL OR WASTE MATERIAL!!!! EXTREMELY REACTIVE!!!!------------->																					107
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	101	102	103	104	105	106	107

Table 6
Overview on the information obtainable from thermodynamic and kinetic test methods.

	Thermal Data	**Methods**	***Kinetic Data***	**Methods**	***Physical Data***	**Methods**
Desired Reaction	*Heat of reaction* *Heat capacity* *MTSR* *Pmax*	Reaction calorimetry Isoperibolic Adiabatic	*Degree of Accumulation* *Temp=f(time)* *P=f(time)*	Reaction calorimetry	*B.Pts* *M.Pts* *Gas evolution as f(temp)* *Venting runaway*	Standard methods Gas analysis Vent sizing apparatus
Undesired Reaction/ Decomposition	*Heat of reaction* *Tmax* *Pmax*	DSC Adiabatic calorimetry	*Time to maximum rate* *dP/dt*	Adiabatic calorimetry Kinetic study	*Gas evolution* *Venting decomposition*	Gas analysis Vent sizing apparatus
Secondary or Side reactions	*Relative proportions*	Analytical methods	*Competing reactions*	Analytical methods	*Effect on physical properties*	Standard methods

III. GOOD PROCESS ENGINEERING

Note: This checklist is not exhaustive but represents minimum standards of good.
All the answers must be given from the safety point of view.

CHK.1	**CHECKLIST**			
1.1	***Are there critical instruments in the process?***			
	YES	*Have you identified those critical for safety (see list 1 on next page)?*		
		YES	*Has calibration and maintenance schedule been set for safety critical instruments?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
1.2	***Are the reagents in use compatible with the material of construction (see compatibility chart in Good Basic Data)?***			
	YES	*Justify your answer:*		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
1.3	***Is computer control used?***			
	YES	*Do safety critical instruments have a control system that can be used in case of computer failure?*		
		YES	*Which?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

1.4	***Can cooling (condenser or jacket) remove the heat generated during the reaction under normal operating conditions?***				
	YES	*How is it assured?*			
	NO	REVIEW YOUR SAFETY MEASURES			
	UNKNOWN	CHECK IT!			
1.5	***Are there critical liquid levels for:***				
1.5.a	***Agitation?***	YES	*Are they controlled?*		
			YES	*How?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	*Justify your answer:*		
		UNKNOWN	CHECK IT!		
1.5.b	***Temperature measurement?***	YES	*Are they controlled?*		
			YES	*How?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	*Justify your answer:*		
		UNKNOWN	CHECK IT!		
1.5.c	***Maximum allowed volume?***	YES	*Are they controlled?*		
			YES	*How?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	*Justify your answer:*		
		UNKNOWN	CHECK IT!		

1.5.d	***Sampling points?***	YES	*Are they controlled?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
1.5.e	***Heels?***	YES	*Are they controlled?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
1.5.f	***Dip pipes?***	YES	*Are they controlled?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
1.5.g	***Others:*_______________**	YES	*Are they controlled?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	

1.6	***Is it known which is the correct valve position before starting the process?***		
	YES	*How is it checked?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
1.7	***Is overpressure relieve needed?***		
	YES	*Is it periodically revised?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

List for 1.1

- ✓ Temperature probes
- ✓ Pressure probes
- ✓ Humidity probe
- ✓ pH probe
- ✓ Agitator axis rotation
- ✓ Flow indicators
- ✓ Security valves
- ✓ Rupture disk
- ✓ Addition valves and pumps
- ✓ Blow up
- ✓ Others (specify):

IV. GOOD PROCESS DESIGN

CHK.2	**CHECKLIST**		
2.1	***Has the repeatability of the process been checked?***		
	YES	*How?*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
2.2	***Are quality and yield consistent under the proposed plant conditions?***		
	YES	*Justify your answer:*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
2.3	***Do small temperature variations (at most ± 5ºC) produce small changes in quality or yield?***		
	YES	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

2.4	***Has the reproducibility of the process been checked?***		
	YES	*How?*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
2.5	***Have less toxic materials been considered?***		
	YES	*Justify your answer:*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
2.6	***Have non-flammable or less flammable materials been considered?***		
	YES	*Justify your answer:*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	

V. GOOD PROCESS PRACTICE

STORAGE

CHK.3	**CHECKLIST**		
3.1	***Is there the possibility of dangerous mix formation due to:***		
31.a	***Wrong labelling?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
3.1.b	***Cleaning operations or reparation works?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

3.1.c	***Adding new chemicals in vessels already in use?***			
	YES	*Are operators sufficiently trained to avoid it?*		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
3.1.d	***Possibility of contact between substances?***			
	YES	*Are operators sufficiently trained to avoid it and safety interlocks used?*		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
3.2	***Is showing any of the substances stored an autocatalytic or radical chain reactive behaviour (as polymerisation)?***			
	YES	*Is it controlled with inhibitors?*		
		YES	*Is their concentration controlled?*	
			YES	*How is it controlled?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

3.3	***Is there the possibility of formation of a segregated phase (due also to weather effects)?***			
	YES	*Are the formed phases thermally stable?*		
		YES	*Justify your answer:*	
		NO	*Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?*	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
3.4	***Is there the possibility of decomposition of any of the stored substances at ambient temperature?***			
	YES	*Is a cooling device installed and T controlled in the storage site of each unstable substance?*		
		YES	*Can T control detect inhomogeneous distribution?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

GENERAL RECOMMENDATIONS

- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Some basic safety scenarios (as loss of stirring, loss of cooling, longer storage period, missing of inhibitors, etc) have to be studied for each step.

PROCESS

CHK.4	**CHECKLIST**		
4.1	***Is there the possibility of dangerous mix formation due to:***		
4.1.a	***Wrong labelling or picking up from storage?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
4.1.b	***Cleaning operations or reparation works?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

4.1.c	***Unavailability of chemicals?***			
	YES	*Are operators sufficiently trained to avoid it?*		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
4.1.d	***Possibility of contact between substances?***			
	YES	*Are operators sufficiently trained to avoid it and safety interlocks used?*		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
4.2	***Is showing any of the substances stored an autocatalytic or radical chain reactive behaviour (as polymerisation)?***			
	YES	*Is it controlled with inhibitors?*		
		YES	*Is their concentration controlled?*	
			YES	*How is it controlled?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

4.3	***Is there the possibility of crystallisation or formation of a segregated phase (especially on cool down operations)?***			
	YES	*Are the formed phases thermally stable?*		
		YES	*Justify your answer:*	
		NO	*Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?*	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
4.4	***Is there the possibility of hot spot?***			
	YES	*Can T control detect inhomogeneous distribution?*		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
4.5	***Is there the possibility of decomposition of any substances at process temperature?***			
	YES	*Is T controlled?*		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

GENERAL RECOMMENDATIONS

- Hot spots may be avoided by heating up not too quick and under turbulent flow conditions.
- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Some basic safety scenarios (as loss of stirring, missing of inhibitors, etc) have to be studied for each step.

REACTION

If the reaction is a full batch, is there a justification for not being semi-batch?

CHK.5	**CHECKLIST**		
5.1	***Is there the possibility of dangerous mix formation (involving both reagents and products) due to:***		
5.1.a	***Wrong order of adding?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
5.1.b	***Wrong chemicals used?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

5.1.c	***Wrong rate of addition?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
5.1.d	***Wrong quantities of chemicals used?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
5.2	***Is a solvent used?***		
	YES	*Is its amount controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

5.3	***Are catalysts or inhibitors used?***			
	YES	*Is their concentration controlled?*		
		YES	*How is it controlled?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
5.4	***Is showing any of the substances involved (or a mixture of them) an autocatalytic or radical chain reactive behaviour?***			
	YES	*Is it controlled?*		
		YES	*How is it controlled?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
5.5	***Is there the possibility of crystallisation or formation of a segregated phase in the reaction mixture (especially on cool down operations and at minimum jacket temperature)?***			
	YES	*Can it affect thermal behaviour of the reaction mass or T control, or is the phase thermally unstable?*		
		YES	*Are there measures to manage or prevent it (mixing, separation, re-homogenisation, etc)?*	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

5.6	***Is the maximum dosing rate known?***		
	YES	*Does it exceed the maximum safe dosing rate?*	
		YES	REVIEW REACTOR SETUP
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	NO	CHECK IT!	
5.7	***Is dosing interlocked in any way with mixing to always assure turbulent conditions?***		
	YES	*How?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
5.8	***Will accumulation increase dramatically if the reaction temperature is low by 10K?***		
	YES	*Is T control interlocked in any way with dosing rate?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
5.9	***In case of automatic dosing, is it interlocked with cooling system?***		
	YES	*Can dosing be totally stopped (dosing set inherently safe)?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

5.10	***Does cooling system work always below 80% of its maximum capacity?***		
	YES	*How is it guaranteed?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
5.11	***Is T controlled when the reaction is ended but the reactor is still full?***		
	YES	*How?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
5.12	***Is there the possibility of hot spot?***		
	YES	*Can T control detect inhomogeneous distribution?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
5.13	***Is any kind of interlock between cooling system failure and dosage stop present?***		
	YES	*How is it realised?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

GENERAL RECOMMENDATIONS

- As a general rule, exothermic reactions need always T, dosing and stirring control.
- Report on known quick ways to stop the desired reaction (extra cooling, chemical inhibition, venting, quenching, etc).
- Hot spots may be avoided by heating up not too quick and under turbulent flow conditions.
- Report on chemical substances able to influence the rate of reaction and substances that can poison catalysts and inhibitors or that can act as unexpected catalysts for the reaction (impurities, etc).
- The maximum temperature that can be reached in case of cooling failure (MTSR) depends on the type of reactor. For example in case of a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the “worst-case” accumulated reactants of the desired reaction.
- Some basic safety scenarios (as loss of stirring, loss of cooling, dosing control, etc) have to be studied for each step.

VI. “STOESSEL THERMAL EVALUATION”

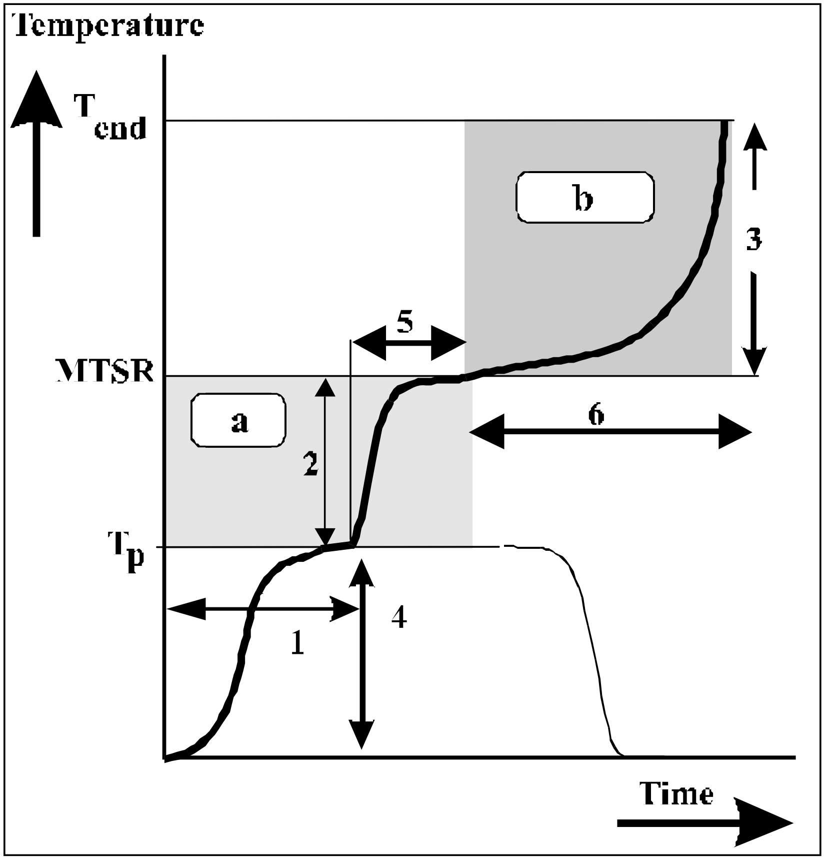


Fig. 5
Schematic presentation of a cooling failure scenario according to Gygax.

Consequences: a = desired reaction b = secondary effects

1: time to cooling failure

2: temperature increase due to loss of cooling

3: temperature increase due to secondary reactions

4: temperature increase under normal operating conditions

5: time to reach the maximum temperature due to synthetic reaction (accumulation)

6: adiabatic induction time of the secondary process

It is helpful for the evaluation of the cooling failure scenario to discuss four temperature levels and their interactions, as was first developed by Stoessel:

- the process temperature, which corresponds to the initial temperature in a maloperation scenario (**T_P**).
- the temperature to be reached under upset conditions, e.g. the **MTSR**.
  NOTE: MTSR should be calculated in the worst case scenario of the considered process, e.g. for semi-batch should be considered three scenarios: *batch* (all reactants are mixed at the beginning of the process, adiabatic conditions are assumed); *stop* (dosing is stopped after a cooling failure. Only the actual accumulation is considered at each time); *non-stop* (dosing is not stopped when adiabatic conditions are established. Actual accumulation and remaining heat of reaction should be considered), and the worst one have to be considered.

- A safety maximum temperature value considered, **MAXTSAFE**. It can be determined by adiabatic calorimetry as the temperature at which the adiabatic induction time of a possible decomposition reaction falls below a specific limit value, **ADT24**. If adiabatic calorimetry data is not available, MAXTSAFE can be obtained by means of a dynamic DSC register of the reaction mass, with a heating rate of 5 K/min, following the detailed procedure:
    - the value of MAXTSAFE can be determined, at a first step, as the temperature at the first exothermal peak less 70 K. This safety reference is more objective than the Tonset, since the later may depend on the precision of the apparatus.
    - it is necessary to compare this value with the MTSR. If $|\mathrm{MTSR}-(T_{peak}-70)|>50$, then the approximation of MAXTSAFE=T_{peak}-70 can be considered correct. If this is not so, it is also required to perform an isothermal DSC at MTSR followed by a dynamic register.
    - if MTSR>T_{peak}-70, the isothermal register does not reveal any significant change of the mass reaction, and the dynamic register is equivalent to the first DSC performed, then it can be concluded that MAXTSAFE>T_{peak}-70 and therefore MAXTSAFE>MTSR.
    - if MTSR>T_{peak}-70, the isothermal register does reveal significant change of the mass reaction (low velocity of the exothermal phenomena at the process temperature can be a problem for detection), and the dynamic register is not equivalent to the first DSC performed, then the approximation MAXTSAFE=T_{peak}-70 can be considered.
    - if MTSR<T_{peak}-70, the isothermal register does not reveal any significant change of the mass reaction, and the dynamic register is equivalent to the first DSC performed, then the approximation MAXTSAFE=T_{peak}-70 can be considered.
    - if MTSR<T_{peak}-70, the isothermal register does reveal significant change of the mass reaction, and the dynamic register is not equivalent to the first DSC performed, then it can be concluded that MAXTSAFE<T_{peak}-70 and therefore MAXTSAFE<MTSR.

  When performing an isothermal DSC, it must be considered that a 12 hour experiment should be long enough. Besides, low velocity of the exothermal phenomena at the process temperature can be a problem for detection.

- the boiling point of the reaction mass (**T_b**).

The possible different positions of the temperature levels relative to each other are presented in Figure 6, sorted by increasing degree of hazard (criticality).

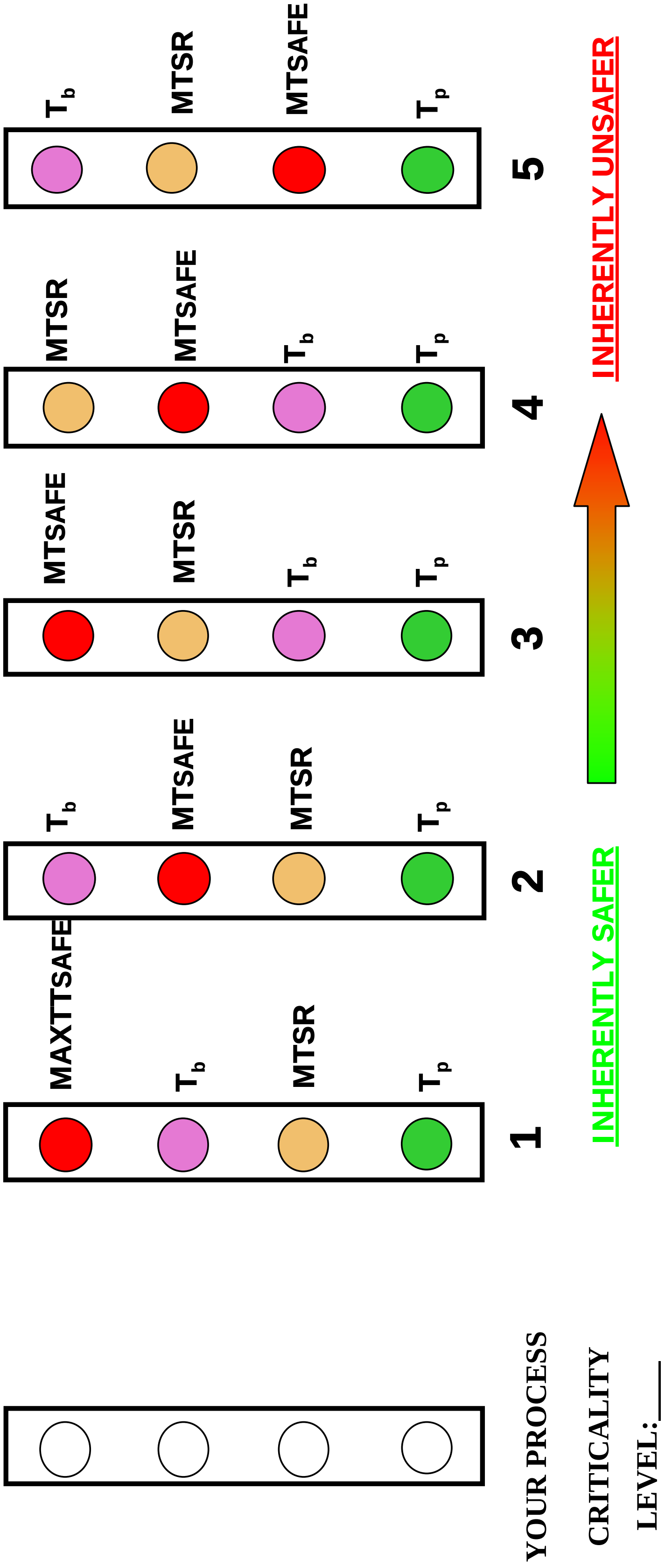


Fig. 6. Scenarios with increasing criticality according to Stoessel.

EVALUATION

CASE 1: in a case one scenario, neither the boiling point of the mixture nor the dangerous region in which the decomposition reaction becomes effective within a critical time is ever reached. Such processes may be regarded as inherently safe with respect to the process deviation evaluated.

CASE 2: also in the second case, which differs from the first by the absence of the boiling point barrier between MTSR and MAXTTSAFE, the process may be regarded as safe.

CASE 3: in the third case, the boiling point with its latent heat of evaporation may be looked upon as a safety barrier, provided the condenser is adequately designed. If the process is performed in a closed system, the apparatus must be designed for the maximum expectable overpressure or be equipped with a pressure relief device.

CASE 4: scenarios with case four characteristics must be evaluated as to whether or not the evaporation capacity provides sufficient safety. If this is not the case, additional organisational or technical measures have to be implemented. Should the operation be performed in a closed system, then the temperature corresponding to the relief valve's set pressure may not be much higher than the level of T_b.

CASE 5: the fifth case must in any case be rated problematic. Plant and/or process modifications usually cannot be avoided in such situations.

VII. RISK ANALYSIS

Once a reaction has been carried out successfully on a plant scale it can be repeated in safety provided exactly the same conditions are applied each time.
The challenge is therefore to provide exactly the same conditions each time a reaction is carried out. This can only be done if no errors occur, no failures occur and no external events take part.
Over the life of a process this also means that no deliberate or accidental changes to the process or process conditions (temperature, time, addition rate, order of changing, quantities etc.) can be allowed without risk.

It is in fact impossible to run a process even a small number of times without error, change, failure or external event. So that a system must be employed to ensure that where change, failure external event or error occur there will be a back-up which will make the systems safe.

The search for critical errors, failures etc. and the provision of back-up is called Risk Analysis and the back-up are called Measures.

As a general rule for addition controlled exothermic reactions temperature control and agitation are essential. A shut-off to the feed should be hard wired to agitator stopped and temperature high and temperature low. This should be in addition to process control by operators or software.

As a general rule temperature measurement is critical for process control. It should be policy to fit (or retrofit on a planned basis) dual cross checking thermometry probes (duplex thermometry).

Overall where thermally critical conditions have been identified there are two general approaches:
1. Fit an engineering solution, or
2. Change the process to reduce the criticality.

In general option 2 is to be preferred as it offers permanent solutions and reduces capital costs and levels of risk.

1. Engineering Solutions

The following list is provided to provoke thinking along the correct lines. The exact solutions for a determined hazard varies widely from case to case and expert advice should be sought where doubt exists.
General
- Avoid common mode failure. Whatever safety engineering solution is imposed it must work when the initial cause of the loss of control is still active e.g. loss of electricity, water etc.
- Fit high reliability safety equipment. The safety system will be rarely activated but it must work with ultra high reliability if called upon.

Test and Maintain
- Essential safety equipment must be tested and maintained on a predetermined routine basis.

Detailed Engineering Solutions
- Drown out / Dump. In critical conditions send the batch to a drown-out vessel to cool, dilute and quench. Thinner, volume, mixing and transfer time need careful consideration under fault conditions.
- Quench. In critical situations add a diluent to prevent runaway. Again all the consideration in the case above apply. Also an inhibitor can be added in some cases.
- Vent and Contain. It may be possible to allow the reaction to runaway and safely discharge via a vent pipe and relief system to a safe place. Exact thermal data is required to size the vent and expert input is essential.
- Back-up utilities. Back up supplies which avoid common mode failure are possible for electricity (diesel engines), water (header tanks), agitation (N_2 purge), UPS for computer control, Instrument Air (local reserve cylinders), etc.

- Occasionally if jacket control is lost and reflux occurs, control can be re-established by an independent water supply to the condenser (also the reverse is occasionally possible if reflux control is lost).

2. Change the Process

- Reduce the amount of accumulation. High levels of accumulation can always be reduced. Typical methods to achieve this include:
    - Increase the addition time
    - Increase the reaction temperature
    - Change the catalyst
    - Reverse the additions
    - Dose wait, Dose wait
    - Vary the dose over the addition time
    - Dilute the reaction
    - Ultimately one can use a different synthetic route
- Increase the TMRad
    - Dilute the reaction
    - Reduce the accumulation (lower MTSR)
    - Operate at a lower temperature
    - Use a different solvent or synthetic route
    - Consider continuous rather than semi-batch to reduce volumes

VIII. MANAGEMENT SYSTEM

NOTE: A checklist like the following one should be filled up for each plant considered.

CHK.6		**CHECKLIST**	**DONE?**
6.6	PLANNING	There should be a written policy of how chemical synthesis will be carried out in safety.	
6.2		The policy should be issued to all graduates, operators and managers allied to production.	
6.3		Senior managers should demonstrate their commitment to the policy.	
6.4		A plan to conform to the policy organisation should be drawn up.	
6.5		The person(s) responsible for obtaining the basic safety data must be nominated.	
6.6		The persons responsible for carrying out the risk analysis must be nominated.	
6.7		The person responsible for implementing the measures must be named.	
6.8	CONTROL	The senior production manager must sign off the Risk analysis as acceptable and complete.	
6.9		The person responsible for supervising measures should authorise the start-up on the basis of a complete report of deficiencies at the start of production and expected completion date.	
6.10		A procedure of management of change to Monitor, Audit, Recover process plant and system must be in place.	
6.11		Production must ensure that all required measures are in place and operational on a routine basis.	
6.12		Senior management should promote an annual internal audit of all process to ensure they conform to policy.	
6.13		There should be an annual review of the process safety situation across all production areas and places shown up to comply with policy.	
6.14		All processes Risk Analysis must be reviewed every 5 years or when a significant change occurs to the plant or the process.	
6.15	CHANGE	Is there a Permit-to-Work[1] scheme in operation?	
6.16		Does the Management of Change include a written safety procedure for:	
		• Plant modifications?	
		• Process modifications?	
		• Software modification?	
		• Documentation modification?	
		• Personnel training modification?	
		• Changes in raw materials?	

[1] A Permit to Work is a written document system which assesses the hazard of any non-routine job to be carried out in a chemical area and defines safety precautions to be applied.

X. GLOSSARY

- **Accumulation:** A build-up of unreacted materials.
- **Activation energy**: Constant Ea in the exponential part of the Arrhenius rate equation associated with the minimum energy difference between the reactants and an activated complex (transition state which has a structure intermediate to those of the reactants and the products), or with the minimum collision energy between molecules that is required to enable a reaction.
- **Adiabatic:** A system condition in which no heat is exchanged between the chemical system and its environment, i.e. no heat transfer occurs to or from the environment surrounding the sample, including the sample container.
- **Adiabatic induction time**: Induction period or time to an event (spontaneous ignition, explosion, etc.) under adiabatic conditions starting at operating conditions.
- **Adiabatic calorimeter:** A calorimeter in which reactions proceed with little exchange of heat between the sample container and its surroundings. Common types of adiabatic calorimeter include the ARC™, PHI-TEC™ and VSP™. The RSST™ calorimeter may be considered as pseudo-adiabatic under some circumstances.
- **Adiabatic temperature rise:** The increase in temperature of a reacting mixture as a result of exothermic chemical reaction, when there is no heat transfer to or from the environment.

$$\Delta T = \Delta H/Cp$$

  ΔT Adiabatic temperature rise (K)
  Cp mean heat capacity (J/kg/K)
  ΔH Heat release (J/kg)

- **Apparent activation energy:** In practice, reaction rates are often determined by physical processes (e.g. mass flow, diffusion, mass transfer area) as well as by chemical processes. The activation energy observed in these cases is called the apparent activation energy.
- **Arrhenius rate equation:** The rate of a chemical reaction (k) increases exponentially with increasing temperature (T). This relationship is represented by the Arrhenius equation $k = A \,.\, \exp(-Ea/RT)$. See also pre-exponential factor.
- **Arrhenius plot:** Graph that shows the logarithmic rate of heat production ln(q) versus the inverse temperature (1/T) in Kelvin. This results in a straight line with a gradient -Ea/R. In practice, the rate of reaction is often affected by physical processes (e.g. diffusion), which results in the occurrence of an apparent activation energy.
- **Autocatalysis:** The increase of the rate of reaction due to the catalysing effect of the reaction products.
- **Basis of safety:** The combination of measures relied upon to ensure safety. The basis of safety for a reactor highlights those aspects of the design and operation (hardware, protective systems and procedures) that are safety critical. The basis of safety can only be selected once all the significant hazards have been identified and evaluated.
- **Batch process:** An operation in which all the reactants including any solvent are added to a reactor at the start of a reaction.
- **Blowdown:** Rapid discharge of a vessel.
- **Calorimeter:** See reaction calorimeter.
- **Condensed phase explosion**: An explosion that occurs when the fuel is present in the form of a liquid or solid.
- **Confined explosion**: An explosion of a fuel-oxidant mixture (usually in the gas phase) inside a closed system (e.g. vessel or building).
- **Consequences**: A description of what would occur in the event of a hazard occurring.
- **Containment:** A condition in which under no condition reactants or products are exchanged between the chemical system and its environment.
- **Continuous reactors:** A reactor that is characterised by a continuous flow of reactants into and out of the reaction system. Common examples are the Plug Flow Reactor (PFR), the loop reactor and the Continuous Stirred Tank Reactor (CSTR) but these are not considered in the HarsNet project.
- **Critical mass:** Minimum mass that is required to enable the occurrence of an explosion.
- **Critical temperature:** Maximum temperature of coolant at which all heat that is generated by a chemical reaction can still be transferred to the coolant (either gas or liquid).

- **Decomposition:** The breaking up of a chemical compound into by products. The temperature at which decomposition is observed depends on scale and is markedly dependent on the sensitivity of the measuring equipment.
- **Decomposition energy:** The decomposition energy is the maximum amount of energy, which can be released upon decomposition. The product of decomposition energy and total mass is an important parameter for determining the effects of a sudden energy release, e.g. in an explosion. The decomposition energy can occasionally be obtained from literature or calculated theoretically, however it is mostly determined experimentally, often by DSC.
- **Decomposition temperature:** Temperature at which spontaneous decomposition occurs. In practice, it is impossible to indicate the exact value of this temperature, because the reaction rate is only zero at absolute zero temperature (0 K) conforming to the equation of Arrhenius. Therefore, in measuring the decomposition temperature both sample quantity and sensitivity of the measuring device are very important. (See also onset temperature).
- **DIERS**: Design Institute for Emergency Relief Systems; Institute under auspices of the American Institute of Chemical Engineers founded to investigate design requirements for vent lines in case of two-phase venting.
- **Dewar:** A jacketed vacuum flask that can be used in calorimetry. The low rate of heat loss means that it can be used to simulate the behaviour of large reactors. See also adiabatic.
- **Differential scanning calorimetry (DSC):** A technique in which the change of the difference in the heat flow rate to the sample and to a reference sample is measured while they are subjected to a temperature regime. Note that in many process safety laboratories DSC and DTA are used interchangeably.
- **Differential thermal analysis (DTA):** A technique in which the change of the difference in the temperature between the sample and the reference sample is measured while they are subjected to a temperature regime. Note that in many process safety laboratories DSC and DTA are used interchangeably.
- **Endothermic:** A reaction is called endothermic if energy (heat) is absorbed during the reaction.
- **Event tree (analysis):** A graphical logical model that identifies possible outcomes following an initiating event. With suitable data it can be used to quantify the occurrence of an event.
- **Exothermic:** A reaction is called exothermic if energy (heat) is released during the reaction.
- **Explosion:** A release of energy sufficient to cause a pressure wave.
- **Fault tree (analysis):** A method for representing the logical combinations of various system states which lead to a particular outcome (Top event). With suitable data it can be used to quantify the probability or frequency of an event.
- **Frequency:** The number of specified events occurring in unit time.
- **HAZOP or Hazard and Operability Study:** A systematic method for identifying possible hazards and potential operating problems in a plant or process by the application of so called ‘guidewords’ (e.g. more, less, other etc.) to the plant or process flow sheet to study process deviations.
- **Hazard:** A chemical or physical condition that has the potential for causing damage to people, property, or environment.
- **Hazardous chemical reactivity:** Any chemical reaction with the potential to exhibit rates of increase in temperature and/or pressure too high to be absorbed by the environment surrounding the system. Included are reactive materials and unstable materials.
- **Heat of reaction:** The total quantity of thermal energy liberated or absorbed during a chemical reaction.
- **Heat Wait Search (HWS):** An experimental technique in which a substance is heated in stages until very slow decomposition is detected. The experimental apparatus then becomes adiabatic and the course of the decomposition is monitored.
- **Induction period/time:** Time interval (starting at operating conditions) after which a runaway shows its maximum effects.
- **Inherently safer:** A system is described as inherently safer if it remains in a non-hazardous situation after the occurrence of unintended deviations from normal operating conditions. Inherently safer is used, rather than inherently safe, because it is not possible to eliminate all hazards.

- **Inhibition:** A protective measure where the reaction can be stopped chemically by addition of another material.
- **Isoperibolic:** A system in which the controlling jacket temperature is kept constant.
- **Isothermal:** A system condition in which the temperature remains constant. This implies that potential temperature increases and decreases are compensated by sufficient heat exchange with the environment of the system.
- **Isothermal calorimeter:** A calorimeter in which the energy exchange with its surroundings is measured whilst the temperature of its contents remains essentially constant. Common types of calorimeter that can be operated in the isothermal mode include the autoMATETM, ChemisensTM, RC1TM and SIMULARTM.
- **Jacket temperature:** The temperature of the fluid contained in the reactor jacket used to indirectly heat or cool the reactor contents.
- **Kinetic data:** Data associated with the conversion rate of a reaction, such as the activation energy, pre-exponential factor and order of reaction. (See Arrhenius rate constant).
- **Maximum pressure after decomposition:** The maximum pressure, which is obtained in a closed vessel. This pressure depends on the adiabatic temperature rise and the specific gas production.
- **Microcalorimetry:** Isothermal techniques of high sensitivity in which heat fluxes from the converting sample material are measured very accurately. Differential Microcalorimetry is performed if the heat fluxes from the sample are compared with those of a reference material.
- **Mitigating measures:** Measures to reduce the consequences of a runaway to an acceptable level.
- **MTSR Maximum Temperature of the Synthesis Reaction:** The maximum temperature reached following the occurrence of the desired (synthesis) chemical reaction under adiabatic conditions starting at the designed process temperature. For a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the synthesis reaction for those reactants that have accumulated during dosing.
- **Onset temperature**: Defined as the temperature at which the heat released by a reaction can no longer be completely removed from the reaction vessel, and consequently, results in a detectable temperature increase. The onset temperature depends on detection sensitivity, reaction kinetics, vessel size and on cooling, flow and agitation characteristics. Scaling of onset temperatures and application of 'rules of thumb' concerning onset temperatures should be used with extreme care.
- **Permanent gas:** A gas that cannot be condensed (or solidified) under the range of conditions of interest (eg temperature or pressure).
- **Phi-factor:** A correction factor which is based on the ratio of the total heat capacity of a vessel (mass of vessel * Cp of vessel) and the total heat capacity of the vessel contents (mass of contents * Cp of contents).

  Phi = 1 + (mass of vessel * Cp of vessel) /(mass of contents * Cp of contents).

  The phi-factor is used to correct the measured heat release, and heat release rate, for the heat that is absorbed by the test cell.
- **Pre-exponential factor (also known as the frequency factor):** Constant A (also denoted as Z, k*, k_o or k_∞ in the Arrhenius equation (also called frequency factor). The pre-exponential factor is associated with the frequency of collisions between molecules (entropy) and with the probability that these collisions result in a reaction. See also Arrhenius rate equation.
- **Preventive measures:** Measures taken at the initial stages of a runaway to avoid further development of the runaway or to reduce its final effects.
- **Probability:** The expression for the likelihood of occurrence of an event or event sequence during an interval of time or the likelihood of a success or failure of an event on test or demand. By definition, probability is expressed as a number ranging from 0 to 1.
- **Products:** Chemicals produced during a reaction process.
- **Quenching:** Rapid cooling of the reaction system in a short time (almost instantaneously). This condition 'freezes' the status of a process and prevents further reaction or decomposition.

- **Rate of reaction:** The rate at which the conversion of reactants takes place. The rate of reaction (r) is a function of concentrations (F(c)) and the reaction rate constant (k):

  $$r = k.F(cA, cB,....,CX)$$

  The heat (q) produced by a reaction is a linear function of the rate of reaction, which makes the rate of reaction a basic parameter in determining the required cooling capacity during all stages of the reaction process.
- **Rate equation:** See Arrhenius rate equation.
- **Reactants:** Chemicals that are converted into (the required) products during the reaction process.
- **Reaction:** The process in which chemicals (reactants) are converted into other chemicals (products).
- **Reaction calorimeter:** A laboratory test apparatus for measuring thermal effects of chemical reactions or processes. For the purpose of this guidance, types of reaction calorimeters include isothermal, isoperibolic and adiabatic systems.
- **Reaction kinetics:** The complex of data (thermodynamic and kinetic) that determine a reaction rate.
- **Reaction rate constant:** The constant k in the rate of reaction. The reaction rate constant is a strong function of temperature as represented by the Arrhenius equation.
- **Reasonably practicable:** The degree of risk in a particular job or workplace needs to be balanced against the sacrifice in time, trouble, cost and physical difficulty of taking measures to avoid or reduce the risk. Measures must be taken to eliminate or control the risks unless it is clear that the sacrifice incurred in doing so is grossly disproportionate to the level of the risk. However, the ability' to pay for additional control measures is not a deciding factor as to whether they are necessary.
- **Reflux:** An operation in which vapour is produced, condensed and subsequently returned to the originating vessel.
- **Risk:** The chance of something adverse happening where 'something' refers to a particular consequence of the manifestation of a hazard. Risk reflects both the likelihood that harm will occur and its severity in relation to the number of people who might be affected, and the consequences to them.
- **Risk assessment:** The process of identifying the hazards present in any undertaking (whether arising from work activities or other factors) and those likely to be affected by them. Also evaluating the extent of the risks involved, bearing in mind whatever precautions are already being taken.
- **Runaway:** A reaction that is out of control because the rate of heat generation by an exothermic chemical reaction exceeds the rate of cooling available.
- **SADT (Self-Accelerating Decomposition Temperature):** The lowest ambient temperature at which auto-accelerated decomposition of an unstable substance is observed (minimum self-heating rate of 5 °C/week), when the substance is packaged in its commercial container and is subjected to that temperature during one week in the testing facility (see also CSST).
- **Semi-batch:** An operation in which some materials are added to the reactor at the start, with one or more other reactants added in a controlled manner during the reaction. See also semi-batch reactor.
- **Temperature of no return:** The temperature under conditions of thermal decomposition at which the rate of heat generation is equal to the maximum rate of cooling available.
- **Thermally unstable:** Chemicals and materials are thermally unstable if they decompose, degrade or react as a function of temperature and time at or about the temperature of use.
- **Thermodynamic data:** Data associated with the aspects of a reaction that are based on the thermodynamic laws of energy, such as Gibbs' free energy, and the enthalpy (heat) of reaction.
- **TMR Time to maximum rate:** The time taken for a material to self-heat to the maximum rate of decomposition from a specific temperature, usually under adiabatic conditions.
- **TMRad:** Time to maximum rate from a specified temperature under adiabatic conditions.
- **Thermal runaway:** see runaway.
- **Unstable substance/material:** Substance or material that decomposes either in the pure state or in the state as normally produced.

- **Venting:** Emergency flow of vessel contents out of the vessel. The pressure is reduced by venting, thus, avoiding a vessel rupture due to over-pressurisation. The vent flow can be single or (a) multi-phase (one) with consequent differences in flow and depressurisation characteristics.

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APPENDIX 2.3

HarsMeth version 2

A short cut chemical process safety assessment procedure for SMEs

REVISION PROPOSAL

GOOD BASIC DATA

Note: This checklist is not exhaustive but represents minimum standards of good.
All the answers must be given from the safety point of view. This checklist must be answered for each project.

I	CHECKLIST	
I.1	***Have test data on reactive chemicals been gathered and evaluated versus worst case scenarios for the following:***	
I.1.a	***Process materials (substances), mixtures and wastes that are normal to the operation?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
I.1.b	***Mixtures that may result from abnormal conditions?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
I.1.c	***Materials of construction throughout the process (steel, iron, dust…)?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT! (may cause a catalytic effect to accelerate the reaction)
I.1.d	***Auxiliary materials (cooling tower, steam, chemicals that are normal to the operation…)?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
I.1.e	***Materials of Instruments and maintenance (lubricants, thread compound, instrument filling fluids, seal fluids…)?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!

I.2	***Are materials and conditions that can cause accelerated corrosion or auto ignition in the system well known and are unacceptable conditions monitored for?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
I.3	***Is the compatibility chart posted where all unit employees can use it?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
I.4	***Are there predefined responses to the inadvertent mixing of the high hazard potential chemicals indicated on the compatibility chart?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES (establish key lines of defence)
	UNKNOWN	CHECK IT!
I.5	***Have side reactions in the process been researched and identified?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES (establish key lines of defence)
	UNKNOWN	CHECK IT!
I.6	***Have conditions for unwanted reactions been identified such as pH, water, contaminants, Temperature excursions…?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES (establish key lines of defence)
	UNKNOWN	CHECK IT!
I.7	***Do reaction data include total potential energy available in case a runaway reaction occurs?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES (establish key lines of defence)
	UNKNOWN	CHECK IT!

<table>
<tr><td>I.8</td><td colspan="3"><i>Is any part of the process or storage subject to formation of shock sensitive materials? (peroxide, acetylide, azide or other)</i></td></tr>
<tr><td rowspan="7"></td><td rowspan="5">YES</td><td><i>Substances:</i></td><td></td></tr>
<tr><td colspan="2"><i>Is it controlled?</i></td></tr>
<tr><td>YES</td><td><i>How it is controlled?</i></td></tr>
<tr><td>NO</td><td>REVIEW YOUR SAFETY MEASURES</td></tr>
<tr><td>UNKNOWN</td><td>CHECK IT!</td></tr>
<tr><td>NO</td><td colspan="2"><i>Justify your answer:</i></td></tr>
<tr><td>UNKNOWN</td><td colspan="2">CHECK IT!</td></tr>
</table>

GOOD PROCESS ENGINEERING

Note: This checklist is not exhaustive but represents minimum standards of good.
All the answers must be given from the safety point of view.

II	**CHECKLIST**				
II.1.	***Are there critical instruments in the process?***				
	YES	*Have those critical for safety been identified (see list 1 on next page)?*			
		YES	*Has calibration and maintenance schedule been set for safety critical instruments?*		
			YES	*Instruments:*	
				How?	
			NO	*Instruments:*	
				REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			
II.2	***Is computer control used?***				
	YES	*Do safety critical instruments have a control system that can be used in case of computer failure?*			
		YES	*Which?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			

II.3	***Can cooling (condenser or jacket) remove the heat generated in a worst-case scenario?***			
	YES	*How is it assured?*		
	NO	*Step[1]:*		
		REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
II.4	***Are there critical liquid levels for:***			
II.4.a	***Agitation?***	YES	*Are they controlled and easily available by the operator?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
II.4.b	***Temperature measurement?***	YES	*Are they controlled and easily available by the operator?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
II.4.c	***Maximum allowed volume?***	YES	*Are they controlled and easily available by the operator?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
II.4.d	***Sampling points?***	YES	*Are they controlled and easily available by the operator?*	

---

(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
II.4.e	***Dip pipes?***	YES	*Are they controlled and easily available by the operator?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
II.4.f	**pH measurement?**	YES	*Are they controlled and easily available by the operator?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
II.4.g	***Others:*__________________	YES	*Are they controlled and easily available by the operator?*	
			YES	*How?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	

II.5	***Has the system fitted a duplex thermometry (dual cross checking thermometry probes)?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
II.6	***Have relief devices been calculated for reactive chemicals runaway?***		
	YES	*Are they periodically revised?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
II.7	***Have relief devices been calculated for two-phase flow?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
II.8	***Are relief device vent systems common to more than one system?***		
	YES	*Has the system been sized for backpressure when one or more systems relieve at the same time?*	
		YES	*Justify your answer:*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
II.9	***Have discharge velocity reaction forces been calculated and included in designs for PSV(1) and vent lines?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

---

(1) Pressure Security Valves

II.10	***Has water supply been calculated for use simultaneously of sprinklers and hoses in various areas and maintenance of cooling in reactors / storage site?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
II.11	***Is the containment of residual water from the extinction of a fire properly designed for the worst-case scenario?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES (Containment in vats, sewers,)
	UNKNOWN	CHECK IT!
II.12	***Has process backflow been effectively prevented in feed lines, nitrogen connections, air, steam, condensed steam, gas cylinders and from the scrubber?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!

List for II.1

- ✓ Temperature probes
- ✓ Pressure probes
- ✓ Humidity probe
- ✓ pH probe
- ✓ Agitator axis rotation
- ✓ Flow indicators
- ✓ Security valves
- ✓ Rupture disk
- ✓ Addition valves and pumps
- ✓ Addition vessels
- ✓ Blow up
- ✓ Others (specify):____
  ____

GOOD PROCESS DESIGN

Note: This checklist must be answered for each project.

III	CHECKLIST		
III.1	***Has the repeatability of the process been checked?***		
	YES	*How?*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
III.2	***Are quality and yield consistent under the proposed plant conditions to the results obtained in Laboratory?***		
	YES	*Justify your answer:*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
III.3	***Has the reliably of the extrapolation of the results obtained in Laboratory or Pilot plant to Production been checked?***		
	YES	*How?*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	

III.4	***Do small temperature variations (at most ± 5ºC or ±10%) produce small changes in quality or yield?***		
	YES	*Step(1):*	
		Could it be a problem from the safety point of view?	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
III.5	***Has the reproducibility of the process been checked?***		
	YES	*How?*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
III.6	***Have less toxic materials been considered?***		
	YES	*Justify your answer:*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	

---

(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

III.7	***Have non-flammable or less flammable materials been considered?***		
	YES	*Justify your answer:*	
	NO	*Could it be a problem from the safety point of view?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
III.8	***Can extended time during agitation cause a hazardous temperature rise?***		
	YES	*Step[1]:*	
		REVIEW YOUR SAFETY MEASURES	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

---

[1] A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

6. GOOD PROCESS PRACTICE

This chapter covers the evaluation of how the chemical process takes place. Whereas the previous chapters focused on general aspects of the chemical plant and process studied before it is actually performed, here the analysis is based on the different steps necessary to develop the desired product in the plant, starting from the study of the storage of all the substances in the plant, the reaction phase (which should be the part where most thermal hazards might appear) and other operations complementary of the chemical reaction, but which might also generate a loss of control of the thermal evolution of the process.

The Good Process Practice checklists are structured as is shown in Figure 5.

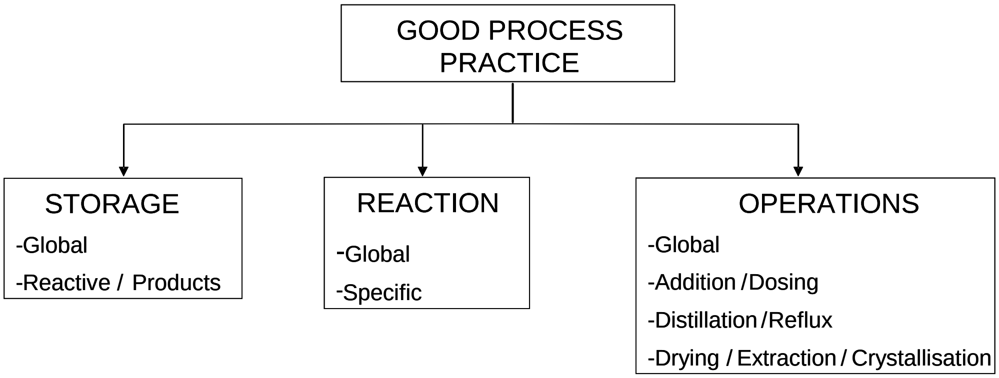

Figure 5. Good Process Practice Scheme.

The Good Process Practice questionnaires must be used as follows:

- ***Global Storage***: it must be applied for the warehouse where substances are stored for long periods of time. It should be revised every time this facility of the chemical plant suffers a relevant modification.
- ***Reactive / Products Storage***: it must be applied once for all reactants used and once for all products generated in the considered process. This warehouse corresponds to the place where reactants and products are placed for a brief period of time before or after they are used or generated, depending on the case.
- ***Global Reaction***: it must be applied once for the whole process considering all the steps that include a chemical reaction.
- ***Specific Reaction***: it must be applied once for each chemical reaction clearly differentiated from another one.
- ***Global Operations***: it must be applied once for the whole process, considering those operations where no chemical reactions take place.
- ***Specific Operation***: the specified questionnaire must be applied every time that such operation is performed during the process.

Once all the situations have been studied, the ***Process Safety Situations*** checklist can be used. This is a questionnaire that deals with existing intervention measures available in case of detecting a risk, and enumerates all the possible maloperation scenarios that may be encountered during the performance of the process.

GLOBAL STORAGE

Note: This checklist has to be applied to the warehouse, where all the substances are storage for a period of time (the answers shall include the possible different places for storage of flammable, unstable… substances). This checklist must be responded periodically or when changes have been done to the storage site.

IV	**CHECKLIST**		
IV.1	***Is there the possibility of dangerous mix formation due to:***		
IV.1.a	***Wrong labelling?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.1.b	***Cleaning operations or reparation works?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

IV.1.c	***Adding new chemicals in vessels already in use?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.1.d	***Contact between substances?***		
	YES	*Are operators sufficiently trained to avoid it and adequate safety interlocks used (vats and/or sewers of capacity to contain all the substances)?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES (review state of substance container for any crack or fissure)
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.1.e	***Transport or wrong manipulation (fall, leave the container mistakenly closed…)?***		
	YES	*Are operators sufficiently trained to avoid it and crosschecking of the state of container used?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

IV.1.f	***Look-alike chemicals (name or packing) that can be put together in a mislabelled container or wrongly used?***				
	YES	*Substances:*			
		Are operators sufficiently trained to avoid it and crosschecking used?			
		YES	*How?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			
IV.2	***Is showing any of the substances stored an auto catalytic or radical chain reactive behaviour (as polymerisation)?***				
	YES	*Substance:*		*Substance presence in Process(1):*	
		Is it controlled with inhibitors?			
		YES	*Is their concentration and temperature controlled periodically?*		
			YES	*How is it controlled?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	*In case of small quantities of substance (< 5L) is the ambient temperature controlled and are the inhibitors nearly?*		
			YES	*Justify your answer:*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
			Other cases	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			

---

(1) Name of the production project where this substance is used.

IV.3	***Is there the possibility of formation of a segregated phase (due also to weather effects)?***				
	YES	*Substance:*		*Substance presence in Process*	
		Are there measures to detect the formation of a segregated phase?			
		YES	*Which?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
		Are the formed phases thermally stable?			
		YES	*Justify your answer:*		
		NO	*Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?*		
			YES	*Which?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		UNKNOWN	CHECK IT! (Make a dynamic DSC of the mixture)		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			
IV.4	***Is there the possibility of decomposition of any of the stored substances at ambient temperature?***				
	YES	*Substance:*		*Substance presence in Process*	
		Is a cooling device installed and T controlled in the storage site of this unstable substance?			
		YES	*Can T control detect inhomogeneous distribution?*		
			YES	*How?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			

IV.5	***Are there measures to detect:***		
IV.5.a	***A longer period of storage and control the status of the product?***		
	YES	*Which?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
IV.5.b	***A loss of cooling and control the status of the product?***		
	YES	*Which?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
IV.5.c	***An ignition of a reactive or product and activate automatic methods of suffocation?***		
	YES	*Which?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
IV.6	***Is there any substance in sufficient amount subject to the application of the regulations (RAPQ and ITC)?***		
	YES	*Substance:*	
		Are the regulations properly implemented?	
		YES	*Justify your answer:*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IV.7	***Are your chemicals stored according to compatibility criteria?***		
	YES	*Have they been identified and separated in the following groups (see list 1 on this section)?*	
		YES	*Justify your answer:*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

List for IV.7

- Flammable substances compatible with water
- Flammable substances incompatible with water
- No Flammable substances compatible with water
- No Flammable substances incompatible with water
- Unstable substances at greater Temperatures than the storage
- Unstable substances or highly volatile at storage Temperature
- Pyrophoric substances
- Compressed, liquefied gas or solutions of it contained in bottle…

GENERAL RECOMMENDATIONS

- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Report on inhibitors effectiveness. This property can be temperature dependant, for example, a too low temperature can cause separation of the inhibitor from the product.

REACTANTS / PRODUCTS STORAGE

Note: This checklist has to be applied to the place where the products obtained and the reactants in excess are placed for a small period of time after or during the process. This checklist must be answered for each project.

V	**CHECKLIST**		
V.1	***Is there the possibility of dangerous mix formation due to:***		
V.1.a	***Wrong labelling?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
V.1.b	***Cleaning operations or reparation works?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

V.1.c	***Adding new chemicals in vessels already in use or not cleaned?***				
	YES	*Are operators sufficiently trained to avoid it?*			
		YES	*How?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			
V.1.d	***Contact between substances?***				
	YES	*Are operators sufficiently trained to avoid it adequate safety interlocks used (vats, sewers…)?*			
		YES	*How?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			
V.1.e	***Look-alike chemicals (name or packing) that can be mixed by error?***				
	YES	*Substances:*		*Presence in steps(1):*	
		Are operators sufficiently trained to avoid it and crosschecking used?			
		YES	*How?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			

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(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

V.1.f	***Mixing of waste streams?***				
	YES	*Are operators sufficiently trained to avoid it?*			
		YES	*How?*		
		NO	REVIEW YOUR SAFETY MEASURES		
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			
V.2	***Is showing any of the substances stored an auto catalytic or radical chain reactive behaviour (as polymerisation)?***				
	YES	*Substance:*		*Substance presence in Steps:*	
		Is it controlled with inhibitors?			
		YES	*Is their concentration and temperature controlled?*		
			YES	*How is it controlled?*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		NO	*Is the ambient temperature controlled and are the inhibitors nearly?*		
			YES	*Justify your answer:*	
			NO	REVIEW YOUR SAFETY MEASURES	
			UNKNOWN	CHECK IT!	
		UNKNOWN	CHECK IT!		
	NO	*Justify your answer:*			
	UNKNOWN	CHECK IT!			

V.3	***Is there the possibility of formation of a segregated phase (due also to weather effects)?***					
	YES	*Substance:*			*Substance presence in Steps:*	
		Are there measures to detect the formation of a segregated phase?				
		YES	*Which?*			
		NO	REVIEW YOUR SAFETY MEASURES			
		UNKNOWN	CHECK IT!			
		Are the formed phases thermally stable?				
		YES	*Justify your answer:*			
		NO	*Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?*			
			YES	*Which?*		
			NO	REVIEW YOUR SAFETY MEASURES		
			UNKNOWN			
		UNKNOWN	CHECK IT! (Make a dynamic DSC of the mixture)			
	NO	*Justify your answer:*				
	UNKNOWN	CHECK IT!				
V.4	***Is there the possibility of decomposition of any of the stored substances at ambient temperature?***					
	YES	*Substance:*			*Substance presence in Steps:*	
		Is the temperature controlled in the storage site of this unstable substance?				
		YES	*Can T control detect inhomogeneous distribution?*			
			YES	*How?*		
			NO	REVIEW YOUR SAFETY MEASURES		
			UNKNOWN	CHECK IT!		
		NO	REVIEW YOUR SAFETY MEASURES			
		UNKNOWN	CHECK IT!			
	NO	*Justify your answer:*				
	UNKNOWN	CHECK IT!				

V.5	***Is there a system to prevent incompatible chemicals from being placed side by side?***	
	YES	*Justify your answer:*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
V.6	***Are there measures to detect:***	
V.6.a	***A longer period of storage and control the status of the product or waste?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
V.6.b	***An ignition of a substance or a mixture of substances?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!

GENERAL RECOMMENDATIONS

- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Report on inhibitors effectiveness. This property can be temperature dependant, for example, a too low temperature can cause separation of the inhibitor from the product.

GLOBAL REACTION

Note: This checklist must be answered once for the whole project, considering all the steps where a chemical reaction takes place.

VI	**CHECKLIST**		
VI.1	***Is there the possibility of dangerous mix formation (involving both reagents and products) due to:***		
VI.1.a	***Wrong order of adding***?		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VI.1.b	***Wrong chemicals used?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VI.1.c	***Wrong rate of addition?***		
	YES	*Is it controlled? (The intermediate measures and safety margins of time of addition are available by the operators)*	
		YES	*How is it controlled*?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	

	UNKNOWN	CHECK IT!	
VI.1.d	***Wrong quantities of chemicals used?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VI.1.e	***Heels?***		
	YES	*Is it controlled?*	
		YES	*How is it controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VI.2	***Is dosing interlocked in any way with mixing to always assure turbulent conditions?***		
	YES	*How is it assured?*	
	NO	REVIEW YOUR SAFETY MEASURES (Introduce an electric resistance in the reactor with several temperature probes, select an initial rate of agitation and increase the rate of agitation until the reaction mass is thermally homogenous. This is the rate of agitation that assures turbulent conditions that may be manually selected)	
	UNKNOWN	CHECK IT!	
VI.3	***In case of automatic dosing, is it interlocked with cooling system?***		
	YES	*Can dosing be totally stopped (dosing set inherently safe)?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

SPECIFIC REACTION

Note: This checklist must be answered for each reaction included in one project.

VII	CHECKLIST			
VII.1	***Is the reaction a full batch?***			
	YES	*Is there a justification for not being semi-batch?*		
		YES	*Justify your answer:*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
VII.2	***Is a solvent used?***			
	YES	*Is there the possibility of evaporate or eliminate it from the mass of reaction (solvent can be reactive, discomposes, reflux...)?*		
		YES	*Is its amount controlled during the reaction?*	
			YES	*How it is controlled?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

VII.3	***Are catalysts or inhibitors used?***			
	YES	***Is their quantity initially added controlled?***		
		YES	*Is the mass of reaction sufficiently agitated to assure the dissolution of the substance added?*	
			YES	*How it is assured?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
VII.4	***Is showing any mixture of substances an autocatalytic or radical chain reactive behaviour at MTSR?***			
	YES	*Mixture of Substances:*		
		Is it controlled?		
		YES	*How is it controlled?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT! (Perform an isothermal DSC of 12h at MTSR of the mixture and consequentially a Dynamic DSC segment (30-400 K; 5 K/min) and compare it with another dynamic DSC of the same mixture performed without an isothermal segment		

VII.5	***Is there the possibility of crystallisation or formation of a segregated phase in the reaction mixture (especially on cool down operations and at minimum jacket temperature)?***			
	YES	*Can it affect thermal behaviour of the reaction mass, reaction rate or T control, or is the phase thermally unstable?*		
		YES	*Are there measures to manage or prevent it (mixing, separation, re-homogenisation, etc)?*	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
VII.6	***Is the maximum dosing rate known?***			
	YES	*Which*?		
		Does it exceed the maximum safe dosing rate?		
		YES	REVIEW REACTOR SETUP (Introduce a second valve (in case of rupture) or orifice plate with flow control)	
		NO	*Justify your answer:*	
		UNKNOWN	CHECK IT! (Perform a reaction calorimetry study and evaluate the maximum possible flow of cooling fluid)	
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		

VII.7	***Will accumulation increase dramatically (+10%) if the reaction temperature is low by 10K?***			
	YES	*In case of full batch, are there measures to prevent the modification of temperature?*		
		YES	*Which?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
		In case of semi-batch, is the T control interlocked in any way with dosing rate? (even manually)		
		YES	*How?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
VII.8	***Does cooling system work always below 80% of its maximum capacity?***			
	YES	*How is it guaranteed?*		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
VII.9	***Is T controlled frequently when the reaction is ended but the reactor is still full?***			
	YES	*How?*		
	NO	*Is the maximum safe temperature known of the mass reaction (MAXTSAFE)?*		
		YES	*Does the actual temperature (when no operations are in course) plus 100ºC exceed the maximum safe temperature or suspect that the mass reaction can be thermally unstable?*	
			YES	REVIEW YOUR SAFETY MEASURES
			NO	*Justify your answer:*
			UNKNOWN	CHECK IT!
		NO	REVIEW YOUR SAFETY MEASURES (make a DSC 30-400ºC at 5 K/min and estimate it)	
		UNKNOWN	CHECK IT!	
	UNKNOWN	CHECK IT!		

VII.10	***Is there the possibility of hot spot?***			
	YES	*Can temperature control detect inhomogeneous distribution?*		
		YES	*How?*	
		NO	*Is the mass of reaction sufficiently agitated to assure turbulent flow conditions?*	
			YES	*How it is assured?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

GENERAL RECOMMENDATIONS

- As a general rule, exothermic reactions need always temperature, dosing and stirring control.
- Report on known quick ways to stop the desired reaction (extra cooling, chemical inhibition, venting, quenching, etc).
- Hot spots may be avoided by heating up not too quickly and under turbulent flow conditions.
- Report on chemical substances able to influence the rate of reaction and substances that can poison catalysts and inhibitors or that can act as unexpected catalysts for the reaction (impurities, etc).
- The maximum temperature that can be reached in case of cooling failure (MTSR) depends on the type of reactor. For example in case of a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the “worst-case” accumulated reactants of the desired reaction [15].
- Some basic safety scenarios (as loss of stirring, loss of cooling, dosing control, etc) have to be studied for each step.

GLOBAL OPERATION

Note: This checklist must be answered for each project.

VIII	**CHECKLIST**		
VIII.1	***Is there the possibility of dangerous mix formation due to:***		
VIII.1.a	***Wrong labelling or picking up from storage?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VIII.1.b	***Cleaning operations or reparation works?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

VIII.1.c	***Unavailability of chemicals?***		
	YES	*Are operators sufficiently trained to avoid it?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VIII.1.d	***Badly connections or bad conditions of the system / pipe?***		
	YES	*Are operators sufficiently trained to avoid it and lists of checking used?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VIII.1.e	***Mixing of waste streams?***		
	YES	*Are operators sufficiently trained to avoid it and reactivity charts easily available by operators?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES (monitor the mixing for reactivity)
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

VIII.1.f	***Possibility of contact between substances?***		
	YES	*Are operators sufficiently trained to avoid it and adequate safety interlocks used (vats, sewers…)?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT! (pipe's elbow, pipe's used in separation…)
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
VIII.2	***Is it known which is the correct valve position before starting one step(1) of the process?***		
	YES	*How is assured the correct valve position?*	
	NO	REVIEW YOUR SAFETY MEASURES (Make a checklist of correct valve position)	
	UNKNOWN	CHECK IT!	
VIII.3	***Is it known which is the maximum safe Pressure and Temperature reachable by the equipment in current conditions?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

GENERAL RECOMMENDATIONS

- Hot spots may be avoided by heating up not too quick and under turbulent flow conditions.
- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Some basic safety scenarios (as loss of stirring, missing of inhibitors, etc) have to be studied for each operation.

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(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

OPERATION-Addition / Dosing

Note: This checklist must be answered for each project, taking into account all the steps where this operation is performed in the process.

IX	CHECKLIST		
IX.1	***Is any reaction activated or provoked by the addition or dosing of the new substance to the mass of reaction?***		
	YES	*Substance Added:*	
		Which type of reaction is it? (endothermic or exothermic)	
		Answer:	
		UNKNOWN	CHECK IT!
		MUST RESPOND THE CHECKLIST FOR REACTION (X.X)	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IX.2	***Is the maximum dosing rate known?***		
	YES	*Does it exceed the maximum safe dosing rate?*	
		YES	REVIEW REACTOR SETUP (Dosing of Solids: Introduce a screw or train the operators / / Dosing of Liquids: Introduce a second valve (in case of rupture) or orifice plate with flow control)
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT! (Perform a reaction calorimetry study and evaluate the maximum possible flow of cooling fluid)
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IX.3	***Is the mass of reaction sufficiently agitated to assure the dissolution of the substance added / dosed?***		
	YES	*How is it assured?*	
	NO	REVIEW YOUR SAFETY MEASURES (Introduce an electric resistance in the reactor with several temperature probes, select an initial rate of agitation and increase the rate of agitation until the mass reaction is thermally homogenous. This is the rate of agitation that assures Turbulent Conditions that may be manually selected)	
	UNKNOWN	CHECK IT!	

IX.4	***Is the cooling system online before the start of addition / dosing on for precaution?***		
	YES	*Can dosing or addition be totally stopped (dosing set inherently safe)?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
IX.5	***Is there the possibility of formation of a segregated phase in the reactant (due also to weather, time effects)?***		
	YES	*Substance:*	
		Are there measures to detect the formation of a segregated phase before the start of the addition / dosing?	
		YES	*Which?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IX.6	***Is there the possibility of decomposition of any substances at process temperature?***		
	YES	*Substance:*	
		Is temperature controlled?	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
IX.7	***In case of addition of solids, is there a justification for not preparing previously a solution of the solid and dosing the dissolution?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

OPERATION-Distillation / Reflux

Note: This checklist must be answered for each project, taking into account all the steps where it is done this operation in the process.

X	**CHECKLIST**			
X.1	***Is there the possibility of formation of hot spots?***			
	YES	*Can temperature control detect inhomogeneous distribution?*		
		YES	*How?*	
		NO	*Is the mass of reaction sufficiently agitated to assure turbulent flow conditions?*	
			YES	*How it is assured?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
X.2	***Can material be concentrated or built up on certain trays to the point of instability**?*			
	YES	*Is it controlled?*		
		YES	*How it is controlled?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
X.3	***Is the amount of solvent controlled during the operation?***			
	YES	*How it is controlled?*		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		

X.4	***Is it known which is the maximum safe temperature (MAXTSAFE) of the mass reaction and it is available by operators?***		
	YES	MAXTSAFE:	
	NO	REVIEW YOUR SAFETY MEASURES (see chapter 2)	
	UNKNOWN	CHECK IT!	
X.5	***Is temperature controlled frequently when the operation is ended but the reactor is still full?***		
	YES	*How?*	
	NO	*Does the actual temperature (when no operations are in course) plus 100ºC exceed the maximum safe temperature or suspect that the mass reaction can be thermally unstable?*	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	*Justify your answer:*
		UNKNOWN	CHECK IT!
	UNKNOWN	CHECK IT!	
X.6	***Have the effects of low and high flow rates on process stability around the distillation operation been evaluated? (reflux, overhead and bottoms…)?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
X.7	***It is known which are the characteristics of the auxiliary fluid of condenser or jacket? (MAXTSAFE, Temp boiling, Temp ignition…)***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

X.8	***Is there the possibility of formation of a segregated phase (especially on distillation operations)?***			
	YES	*Step(1):*		
		Are the formed phases thermally stable?		
		YES	*Justify your answer:*	
		NO	*Step(1):*	
			Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

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(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

OPERATION-Drying / Extraction / Crystallisation

Note: This checklist must be answered for each project, taking into account all the steps where it is done this operation in the process.

XI	**CHECKLIST**			
XI.1	***Is there the possibility of formation of hot spots?***			
	YES	*Can T control detect inhomogeneous distribution?*		
		YES	*How?*	
		NO	*Is the mass of reaction sufficiently agitated to decrease the probability of formation of hot spot?*	
			YES	*How it is assured?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
XI.2	***Can unstable components build up on mass reaction create a hazard?***			
	YES	*Is it controlled?*		
		YES	*How it is controlled?*	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		
XI.3	***Is the amount of solvent controlled during the operation?***			
	YES	*How it is controlled?*		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		

XI.4	***Is there the possibility of crystallisation or formation of a segregated phase (especially on cool down operations)?***			
	YES	*Step(1):*		
		Are the formed phases thermally stable?		
		YES	*Justify your answer:*	
		NO	*Step(1):*	
			Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?	
			YES	*Which?*
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	*Justify your answer:*		
	UNKNOWN	CHECK IT!		

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(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

PROCESS SAFETY SITUATIONS

Note: This checklist is not exhaustive but represents minimum standards of good. All the answers must be given from the safety point of view. This Checklist must be answered for each project.

XII	**CHECKLIST**	
XII.1	***Are there measures to detect and control the reaction if:***	
XII.1.a	***There is a loss of stirring?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
XII.1.b	***There is a loss of electricity?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
XII.1.c	***There is a loss of general cooling service?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
XII.1.d	***There is a loss of dosing control?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
XII.1.e	***There is a loss of recycle?***	
	YES	*Which?*
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!

XII.1.f	***There is a loss of supply of compressed air?***		
	YES	*Which?*	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
XII.2	***Has agitator failure (power failure) been evaluated during all steps to determine if a runaway can occur?***		
	YES	*Justify your answer:*	
	NO	*Step(1):*	
		REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
XII.3	***Are the hazards of restarting an agitator during a batch identified and understood (potential for an accelerated reaction)?***		
	YES	*Justify your answer:*	
	NO	REVIEW YOUR SAFETY MEASURES (training)	
	UNKNOWN	CHECK IT!	
XII.4	***Are there measures to regain control of an uncontrolled reaction?***		
	YES	*Which?*	
	NO	REVIEW YOUR SAFETY MEASURES (Extra Cooling, Quenching, adequate Venting, Chemical Inhibition…)	
	UNKNOWN	CHECK IT!	
XII.5	***Are there measures to control the leakage if one of the pipes of addition vessels breaks?***		
	YES	*Which?*	
	NO	REVIEW YOUR SAFETY MEASURES (vats, sewers…)	
	UNKNOWN	CHECK IT!	
XII.6	***Does the failure of any heat transfer system (pump, pipe, heat exchanger…) result in an uncontrollable condition?***		
	YES	*Has TNR and TMR been defined for the equipment?*	
		YES	*How?*
		NO	REVIEW YOUR SAFETY MEASURES (duplicate pump, duplicate pipe,…)
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

XII.7	***Can tube wall temperature in exchangers cause degradation or runaway over time?***		
	YES	REVIEW YOUR SAFETY MEASURES (reduce the temperature of the heating fluid)	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
XII.8	***Would a fire in trenches, ditches, sewers, etc., expose the plant or loading area?***		
	YES	REVIEW YOUR SAFETY MEASURES	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
XII.9	***Can chemicals residues accumulate on high surface area (packing or tower components) to create a hazard during maintenance or at other times?***		
	YES	*Is it controlled?*	
		YES	*How it is controlled?*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	

HISTORICAL ANALYSIS

Note: This checklist is not exhaustive but represents minimum standards of good.
All the answers must be given from the safety point of view. This Checklist must be answered **after** the process has been done in production in order to evaluate the errors occurred or the possible improvements that can be applied.

XIII	**CHECKLIST**		
XIII.1	***Have Process Safety / Reactive Chemicals incidents / accidents or human errors occurred during the process?***		
	YES	*Situation:*	
		Have any changes been done to prevent recurrence?	
		YES	*Justify your answer:*
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
XIII.2	***Has any risk situation arisen from (general storage, storage of reactants and products):***		
XIII.2.a	***Cleaning operations or reparation works? (sparks, explosive atmosphere…)***		
	YES	*Justify your answer:*	
	NO	PROCEED TO THE NEXT QUESTION	
	UNKNOWN	CHECK IT!	
XIII.2.b	***Look-alike chemicals (name or packing) that can be put together in a mislabelled container or wrongly used?***		
	YES	*Justify your answer:*	
	NO	PROCEED TO THE NEXT QUESTION	
	UNKNOWN	CHECK IT!	

XIII.2.c	***Mixing of waste streams?***	
	YES	*Justify your answer:*
	NO	PROCEED TO THE NEXT QUESTION
	UNKNOWN	CHECK IT!
XIII.2.d	***Transport or wrong manipulation (fall, leave the container mistakenly closed)?***	
	YES	*Justify your answer:*
	NO	PROCEED TO THE NEXT QUESTION
	UNKNOWN	CHECK IT!
XIII.3	***Has any risk situation arisen from (reaction, operations):***	
XIII.3.a	***Wrong chemicals used?***	
	YES	*Justify your answer:*
	NO	PROCEED TO THE NEXT QUESTION
	UNKNOWN	CHECK IT!
XIII.3.b	***Wrong rate of addition?***	
	YES	*Justify your answer:*
	NO	PROCEED TO THE NEXT QUESTION
	UNKNOWN	CHECK IT!
XIII.3.c	***Wrong quantities of chemicals used?***	
	YES	*Justify your answer:*
	NO	PROCEED TO THE NEXT QUESTION
	UNKNOWN	CHECK IT!
XIII.3.d	***Contact between substances?***	
	YES	*Justify your answer:*
	NO	PROCEED TO THE NEXT QUESTION
	UNKNOWN	CHECK IT!

XIII.4	***Has the mass of reaction been agitated sufficiently to assure the dissolution of all the substances added?***		
	YES	PROCEED TO THE NEXT QUESTION	
	NO	*Justify your answer:*	
	UNKNOWN	CHECK IT!	
XIII.5	***Has cooling (condenser or jacket) removed the heat generated during all the steps in the process without reaching its maximum capacity?***		
	YES	*Justify your answer:*	
	NO	*Step(1):*	
		REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
XIII.6	***Has temperature been controlled frequently during all the steps of the process?***		
	YES	*Justify your answer:*	
	NO	*Step(1):*	
		Maximum process temperature possible at this step:	
		MaxTsafe (see chapter 2):	
	UNKNOWN	CHECK IT!	
XIII.7	***Has any of the safety situations occurred or being about to take place?***		
	YES	*Justify your answer:*	
	NO	PROCEED TO THE NEXT QUESTION	
	UNKNOWN	CHECK IT!	

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(1) A Step is any operation that has to be done in order to complete the process (addition, heating, agitation...)

8. MANAGEMENT SYSTEM

NOTE: A checklist like the following one should be filled up for each plant considered.

XIV		CHECKLIST	DONE?
XIV.1	PLANNING	There should be a written policy of how chemical synthesis will be carried out in safety.	
XIV.2		The policy should be issued to all graduates, operators and managers allied to production.	
XIV.3		Senior managers should demonstrate their commitment to the policy.	
XIV.4		A plan to conform to the policy organisation should be drawn up.	
XIV.5		The person(s) responsible for obtaining the basic safety data must be nominated.	
XIV.6		The persons responsible for carrying out the risk analysis must be nominated.	
XIV.7		The person responsible for implementing the measures must be named.	
XIV.8	CONTROL	The senior production manager must sign off the Risk analysis as acceptable and complete.	
XIV.9		The person responsible for supervising measures should authorise the start-up on the basis of a complete report of deficiencies at the start of production and expected completion date.	
XIV10		A procedure of management of change to Monitor, Audit, Recover process plant and system must be in place.	
XIV.11		Production must ensure that all required measures are in place and operational on a routine basis.	
XIV.12		Senior management should promote an annual internal audit of all process to ensure they conform to policy.	
XIV.13		There should be an annual review of the process safety situation across all production areas and places shown up to comply with policy.	
XIV.14		All processes Risk Analysis must be reviewed every 5 years or when a significant change occurs to the plant or the process.	
XIV.15	CHANGE	Is there a Permit-to-Work[1] scheme in operation?	
XIV.16		Does the Management of Change include a written safety procedure for:	
		• Plant modifications (material construction, Venting…)?	
		• Process modifications?	
		• Software modification?	
		• Documentation modification?	
		• Personnel training modification?	
		• Changes in raw materials?	

[1] A Permit to Work is a written document system, which assesses the hazard of any non-routine job to be carried out in a chemical area, and defines safety precautions to be applied.

XIV		**CHECKLIST**	**DONE?**
XIV.17	RISK	Have the scenarios and potential consequences for chemical spills and gas releases been reviewed with:	
		• Supervision?	
		• Plant Operators / Technicians?	
		• Other Affected Employees (Maintenance, Constructors, Distribution, Contractors)?	
XIV.18		Does the plant have written procedures detailing how to mitigate releases of chemicals in the plant (pump to another vessel, apply foam, temporally plug hole…)?	
XIV.19		There should be a formal emergency valve-testing program to ensure that all equipment is protected from excessive pressure.	
XIV.20		The design data and basis for all equipment and pressure/vacuum relief systems should be documented (Max P, Max T, Max flow or capacity…).	
XIV.21		Is a special training on reactivity conducted/tested/documented for each individual working in the unit? Is the compatibility chart included?	
XIV.22		Are all employees who regularly work around the chemicals (maintenance, distribution, contractors, constructors, visitors…) included in general training?	
XIV.23		Are case histories of past incidents in your unit and in the chemical industry included in the training program?	
XIV.24		Have potentially wrong mixtures or procedures been addressed?	
XIV.25	EMERGENCY PLAN	There should be a written policy of how the personnel must proceed in case of an emergency has been declared.	
XIV.26		The policy should be issued to all graduates, operators and managers allied to production and to all the people who work/enter frequently in the plant.	
XIV.27		The person(s) responsible for co-ordinating the actions that must be done in case of emergency must be nominated (Chief of emergency).	
XIV.28		The persons responsible for co-ordinating the actions that must be done in each department in case of emergency must be nominated (Co-ordinators of emergency).	
XIV.29		Are there different alarms according to different degrees / localisation of hazard?	
XIV.30		Are all the alarms properly identified by:	
		• Plant Operators / Technicians / Co-ordinators of emergency?	
		• Other Affected Employees (Maintenance, Constructors, Distribution, Contractors, Visitors)?	
XIV.31		The co-ordinators of emergency must ensure that all the alarms and speakers are in good status and that they can be listened from any place of the department in normal conditions.	
XIV.32		Does the plant conduct routine, periodic emergency drills on the release of toxic chemicals, ignition of substances…?	
XIV.33		Does the emergency drill include the activation of key lines of defence and its performance is evaluated afterwards?	
XIV.34		Do all the personnel know which is their meeting point with their co-ordinator of emergency? Do they know that they must rest in their place of work until new command?	

VIII.3		**CHECKLIST**	**DONE?**
XIII.35		There should be a way of communication between the chief of emergency and the co-ordinators of emergency when no electricity / telephone is available.	
XIII.36		The safe way of stopping any activity in case of evacuation should be documented and transmitted to all the personnel (Operators, Technicians, Maintenance, Distribution, Constructors…).	
XIII.37		The different possible routes of evacuation for each department must be selected, analysed, documented and transmitted to the co-ordinators of emergency of each department.	
XIII.38		The person(s) responsible for improving and implementing the measures decided to be applied after the evaluation of the performance of the emergency drill / plan must be named.	

APPENDIX 2.4

HarsMeth version 2

A short cut chemical process safety assessment procedure for SMEs

Proposed questions for plant operations

Name of operation: IV.1 CHARGING / REACTION

1	**Is there a possibility of dangerous mixtures formation due to:**		
	Wrong order of addition?		
	YES	Is it controlled?	
		YES	How is it controlled?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
	Wrong quantities of reactants?		
	YES	Is it controlled?	
		YES	How is it controlled?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
2	**If a solvent is used, is its nature known?**		
	YES	Are the necessary measures for its use taken?	
		YES	Justify your answer (describe protective equipment used)
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
3	**Is it necessary to prepare solutions prior to the reaction?**		
	YES	How and where are they prepared?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
4	**Can water be added to the inicial phase or during development of the reaction?**		
	YES	When is it added?	
		What is the aceptable proportion?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
5	**Is the proportion and quantity of solven controlled?**		
	YES	How is it controlled?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
6	**Has the compatibility of the solvent with the construction materials been taken into consideration?**		
	YES	How?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
7	**Is the charging and handling of catalyzers and inhibitors controlled?**		
	YES	How?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
8	**Do any of the substances (or their mixtures) used show autocatalytic or polymerizing behaviour?**		
	YES	Is it controlled?	
		YES	How is it controlled?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	

9	**Is there the possibility of precipitation or formation of segregated phases in the reaction mass?**			
	YES	Can the thermal behaviour of the reaction or the unstable phase be affected?		
		YES	Are there measures to handle the segregation?	
			SÍ	Justify your answer (describe protective equipment used, such as agitation control, cooling control)
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	Justify your answer:	
		UNKNOWN	CHECK IT!	
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
10	**Is dosing connected to the agitation system in order to always ensure turbulent conditions?**			
	YES	How is it guaranteed?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
11	**Is the temperature of the reaction mass controlled when the reaction is finished but the reactor is still full?**			
	YES	How is it controlled?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
12	**Is there the possibility of formation of hot spots?**			
	YES	Can the temperature control detect a non homogeneous distribution of temperature?		
		YES	How?	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
13	**Is there a temperature control system to detect a failure in the cooling system?**			
	YES	Justify your answer:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
14	**Is it strictly necessary to take samples during the development of the reaction?**			
	YES	How is the sampling done?		
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
15	**Is it necessary to keep a control of the reaction?**			
	YES	How is it performed?		
		Is there a possibility to eliminate such control in future batches?		
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
16	**Is it necessary to control / desactivate the reactant excess before performing the following operation?**			
	YES	How is it performed?		
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		

Name of operation: IV.2 ADDITION / DOSING

1	**Is any reaction activated by the addition or dosing of new substances to the reaction mass?**		
	YES	Substance:	
		What kind of reaction?	(Endothermic o exothermic)
		UNKNOWN	CHECK IT!
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
2	**Is the maximum safety dosing speed known?**		
	YES	Is it ever exceeded?	
		YES	REVIEW YOUR SAFETY MEASURES
		NO	Justify your answer:
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
3	**Is the mass of reaction sufficiently to ensure the integration of the substances added / dosed?**		
	YES	How is it assured?	
	NO	REVIEW YOUR SAFETY MEASURES (Choose another reactor, concentrate the reaction mass, scale-up)	
	UNKNOWN	CHECK IT!	
4	**Is the cooling system operative before starting the addition / dosing in case the thermal conditions of the process require so?**		
	YES	Can the process be stopped completely in case of failure of the cooling system?	
		YES	How?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
5	**Is there the possibility of decomposition of any substance at the process temperature?**		
	YES	Substance:	
		Is the temperature controlled?	
		SÍ	How is it controlled?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
6	**In case of addition of solids, is there a justification to not prepare a solution earlier and dosing the solution?**		
	YES	Justify your answer:	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
7	**In case of automatic addition / dosing, is it connected to the cooling system?**		
	YES	Can the dosing be stopped completely?	
		YES	How?
		NO	REVIEW YOUR SAFETY MEASURES
		UNKNOWN	CHECK IT!
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

<u>Name of operation</u>: IV.3 DESTILLATION / REFLUX

1	**Is there the possibility of formation of hot spots?**			
	YES	Can the temperature control detect a non homogeneous distribution of temperature?		
		YES	How?	
		NO	Is the reaction mass sufficiently agitated in order to ensure turbulent flux conditions?	
			SÍ	How is it assured?
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
2	**Can the reaction mixture be concentrated to a point of becoming thermally unstable during the operation?**			
	YES	Is it controlled?		
		YES	How is it controlled?	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
3	**Is the solvent quantity controlled during the operation?**			
	YES	How is it controlled?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
4	**Is the maximum safety temperature (MAXTSAFE) for the reaction mass known and is this value available to the operators?**			
	YES	MAXTSAFE:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
5	**Is the temperature controlled after the operation is ended but the reactor is still full?**			
	YES	How is it controlled?		
	NO	Does the temperature under these conditions (no other operation in course) plus 100ºC exceed MaxTsafe or is it suspected that the reaction mass may be thermally unstable?		
		YES	REVIEW YOUR SAFETY MEASURES	
		NO	Justify your answer:	
		UNKNOWN	CHECK IT!	
	UNKNOWN	CHECK IT!		
6	**Once the liquid level reaches a point at which it is not in touch with the temperature probe anymore, is the temperature still controlled?**			
	YES	How is it controlled?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
7	**Have thee effects of low and high flow speed on the stability of the process been evaluated?**			
	YES	Which effects have been identified?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		

8	**Are the conditions of the auxiliary fluids of condenser or jacket known? (MAXTSAFE, Tboiling, Tignition…)**			
	YES	What are those conditions?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
9	**Is there the possibility of formation of segregated phases?**			
	YES	Step:		
		Can the formation of segregated phases be a problem from the safety point of view?		
		YES	Are there measures to control segregation?	
			YES	Justify your answer:
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	Justify your answer:	
		UNKNOWN	CHECK IT!	
		Are the phases formed thermally stable?		
		YES	Justify your answer:	
		NO	Step:	
			Are there measures to control segregation?	
			YES	Which?
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		UNKNOWN	CHECK IT!	
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
10	**Is it necessary to control the presence of water in the installation?**			
	YES	How is it controlled?		
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
11	**In order to collect the distilled products, is it taken into consideration:**			
	Whether the appropriate containers for their storage are available?			
	YES	Which is the procedure to select the container? (depending on compatibility, further use of product…)		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT		
	Whether the appropriate measures for handling them have been taken?			
	YES	Justify your answer (describe protective equipment used, like grounding to earth, use of gloves, masks, protective clothing)		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
12	**Is it necessary to collect the solute or the waste mixture from the reactor?**			
	YES	Are there appropriate containers for their storage?		
		YES	Which is the procedure to select the container? (depending on compatibility, further use of product…)	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
		Are the appropriate measures for their handling taken into consideration?		
		YES	Which is the procedure to select the container? (depending on compatibility, further use of product…)	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		

Name of Operation IV. 4 PRECIPITATION

1	**Are the conditions for precitpitation and the characteristics of the precipitated mass known?**		
	YES	Which are the conditions?	
		Which are the characteristics?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
2	**Is the quantity of solven enough / appropriate to perform the operation?**		
	YES	How is it controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
		In case of obtaining a too thick mass, or in case of deficient agitation, how is the emptying to centrifuge performed?	
	UNKNOWN	CHECK IT!	
3	**Is a solvent added to avoid precipitation?**		
	YES	Solvent:	
		What is the chemical compatibility with the rest of substances?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
4	**Is a seeding process necessary for the precipitation?**		
	YES	How is the seeding process performed?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
5	**Is the volume agitation ratio controlled during precipitation?**		
	YES	Are stirring conditions appropriate for the volume of precipitation?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
6	**Is there an appropriate heat exchange between the reactor and the cooling jacket?**		
	YES	How is it controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
7	**Once the liquid level reaches a point at which it is not in touch with the temperature probe anymore, is the temperature still controlled?**		
	YES	How is it controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

Name of Operation: IV. 5 CENTRIFUGE

1	**Is the inertization system connected before starting the operation?**			
	YES	How is it controlled?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
2	**Is the appropriate quantity of N_2 controlled in order to perform the operation?**			
	YES	How is it controlled?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
3	**Is the solvent flammable?**			
	YES	Solvent/s:		
		Is the material to use prepared against static electricity		
		YES	Material type:	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
4	**Is the quantity of solvent in the mass to be centrifuged appropriate?**			
	YES	How is it controlled?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
5	**In order to collect filtration waters, is it taken into account:**			
	The nature of the solvents?			
	YES	What is the chemical compatibility with the rest of substances?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
	Whether there is a container available for the storage?			
	YES	Container:		
		Is inertization provided for the container?		
		YES	How is it controlled?	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT		
	Whether the necessary measures for their handling are provided?			
	YES	Justify your answer (describe protective equipment used, like grounding to earth, use of gloves, masks, protective clothing)		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
6	**Is the nature of the washing solvent used?**			
	YES	Washing solvent:		
		Necessary amount:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
7	**Is inertization provided during washing?**			
	YES	How is it assured?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
8	**In case of failure of the O_2, analyser, which is the minimum time necessary to use N_2 for inertization and ensure minimum concentration of O_2?**			
	YES	Time:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		

Nombre Operación: IV. 6 FILTRACIÓN / TRANSFER

1	**Is the temperature at which the filtration has to be performed known?**			
	YES	Filtration temperature:		
		Crystallization Temperature:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
2	**Is it necessary to pass solvent through the filter before starting the operation?**			
	YES	How is it performed? (Temperature, hoses need pre-heating?)		
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		
3	**In case of filtering a catalyzer:**			
	Is the nature of the catalyzer known?			
	YES	Catalyzer:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
	Is it necessary to humidify the filtration mixture (pyrophoric catalyzer)?			
	YES	Substance:		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
	Are the necessary measures known?			
	YES	Justify your answer (describe protective equipment used, like grounding to earth, use of gloves, masks, protective clothing)		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
4	**In case of collecting a catalyzer:**			
	Are there appropriate containers available?			
	YES	How is it collected?		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
	Are the necessary measures known?			
	SÍ	Justify your answer (describe protective equipment used)		
	NO	REVIEW YOUR SAFETY MEASURES		
	UNKNOWN	CHECK IT!		
5	**Once the operation is finished, is there a washing of the filtering system?**			
	YES	How is it performed?		
		Is the nature of the washing solvent known?		
		YES	Solvent:	
		NO	REVIEW YOUR SAFETY MEASURES	
		UNKNOWN	CHECK IT!	
		Is the filter finally dismantled?		
		YES	Is the nature of the filtration medium known?	
			YES	Justify your answer (describe protective equipment used)
			NO	REVIEW YOUR SAFETY MEASURES
			UNKNOWN	CHECK IT!
		NO	Justify your answer:	
		UNKNOWN	CHECK IT!	
	NO	Justify your answer:		
	UNKNOWN	CHECK IT!		

6	**In order to collect the filtered mixture, is it taken into consideration:**	
	In what vessel is it collected?	
	YES	How is it collected (appropriate volume)
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT
	Are the necessary measures known	
	YES	Justify your answer (describe protective equipment used, like grounding to earth, use of gloves, masks, protective clothing)
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
7	**In order to collect the filtration medium is it taken into consideration:**	
	Whether there are appropriate containers available?	
	YES	How is it performed? What is the destination?
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT
	Are the necessary measures for its handling taken?	
	YES	Justify your answer (describe protective equipment used, like grounding to earth, use of gloves, masks, protective clothing)
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!
8	**Is there a procedure to act against possible solvent leaks?**	
	YES	Justify your answer:
	NO	REVIEW YOUR SAFETY MEASURES
	UNKNOWN	CHECK IT!

Name of Operation: IV. 7 EXTRACTION / DECANTING / pH FIXING

1	**Is the nature of the different solvents known?**		
	YES	Solvent:	
		What are their characteristics?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
2	**Is it necessary to change the pH to enable the extraction?**		
	YES	Is it necessary to add an acid or a base?	
		Is the thermal behaviour known?	
	NO	Justify your answer:	
	UNKNOWN	CHECK IT!	
3	**In case of more than one pH adjustment, are the necessary measures known?**		
	YES	Justify your answer (describe protective equipment used: container to be used, remove excess of acid/base, washing equioment)	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
4	**Is the phase of the product known at all times?**		
	YES	Phase:	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
5	**Is the interface treatment known**		
	YES	How is it performed?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
6	**Is there the possibility of formation of emulsions?**		
	YES	How are they treated?	
	NO	Justify your answer	
	UNKNOWN	CHECK IT!	
7	**Is the necessary time to separate the phases (before considering an emulsion known?**		
	YES	Time:	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
8	**Is there a control of phases during decanting?**		
	YES	How is it performed?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
9	**Is there a control at the end of decanting?**		
	YES	How is it performed?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
10	**Is the final destination of the different phases known?**		
	YES	How are they handled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
11	**Do the decanted phases require filtering?**		
	YES	How is it performed?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

Name of Operation: IV. 8 DRYING

1	**Are the drying time and temperature necessary to avoid degradation of the product known?**		
	YES	Temperature:	
		Time:	
		How are they controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
2	**In order to charge the humid product, is it taken into consideration:**		
	Whether the appropriate trays are available?		
	YES	Are they clean?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT	
	Whether the appropriate measures for their handling are taken?		
	YES	Justify your answer (describe protective equipment used, like use of gloves, masks, protective clothing)	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
	Whether the exposure to solvents during charging is controlled		
	YES	Is the nature of the solvents known?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
3	**In order to discharge the dry product, is it taken into consideration:**		
	Whether the product has been cooled in order to handle for a better handling?		
	YES	How is it controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
	Whether the necessary measures are taken in order to avoid dust accumulation?		
	YES	How is it controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
	Whether the appropriate measures for their handling are taken?		
	YES	Justify your answer (describe protective equipment used, like use of gloves, masks, protective clothing)	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

Name of Operation: IV.9 MICRONIZATION / GRINDING

1	**Is it known whether the substance in dust form can generate explosive atmospheres?**		
	YES	Necessary parameters:	
		Minimum Flammable Energy (mJ):	
		Minimum Flammable Temperature (ºC):	
		Maximum Flammable Temperature (ºC):	
		Minimum Explosive Concentration (g/m^3):	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
2	**Are the parameters and conditions of the operation known?**		
	YES	Describe: (feeding velocity, compressed gas pressure in micronizer, micronizer pressure, hammer or blades position, sieve used, water connection, etc.)	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
3	**During ensambling, disambling and cleiaining, is it verified whteher the equipment is disconnected from electricity supply?**		
	YES	Justify your answer:	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT	
4	**Is it checked whether the equipment is clean before charging the product?**		
	YES	Justify your answer:	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT	
5	**Are the necessary measures taken for charging / discharging according to the nature of the product?**		
	YES	Justify your answer (describe protective equipment used, like use of gloves, masks, protective clothing)	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
6	**Is the inertization of the equipment before charging controlled?**		
	YES	How is it controlled?	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
7	**Are the necessary measures taken in order to avoid dust accumulation?**		
	YES	Justify your answer:	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	
8	**Are the necessary measures taken during the operation?**		
	YES	Justify your answer (describe protective equipment used, like grounding to earth, use of containers protected against static electricity)	
	NO	REVIEW YOUR SAFETY MEASURES	
	UNKNOWN	CHECK IT!	

APPENDIX 3.1

HarsMeth version 1

TABLE OF CONTENTS

I. PREFACE

THE BASICS

In order to carry out chemical reactions on a plant scale, over a long period of years, in safety it is necessary to control many different factors over the life of the process. However at the very basis of process safety, its fundamentals, are three principles:

1) Good Engineering Design and Practice.
2) Good Process Design.
3) Good Basic Data about the materials used and about the process.

1) GOOD ENGINEERING

Clearly, unless good basic chemical engineering standards are met no amount of additional data or analysis will redeem the situation. For example, if the electricity supply is subject to frequent (more than once a month) and prolonged (more than one hour) interruption then **THIS** is the problem and it must be fixed first. A similar argument applies to all other utilities, water, steam, air, nitrogen, communications and computer functions. At a lower level each safety element (e.g. a thermometer or pressure gauge) must have normal industrial reliability and good standards applied to purchase and maintenance are essential.

In order to assist companies assess their chemical engineering systems a checklist is provided (Section III).

2) GOOD PROCESS DESIGN

Good robust process design is also essential. If a process cannot meet the requirements of quality, yield and throughput it will be constantly changed and updated to meet demand. Eventually this updating process will lead to unsafe conditions unless strict control of the process changes is maintained.

In order to assist in the production of a good basic process a checklist is provided (Section IV).

3) GOOD BASIC DATA

Once the plant and the process are established on a sound basis, then it is imperative that the fundamental thermokinetics of the desired process and any side reactions and decompositions are determined and understood. In addition much physical data on raw materials, intermediates and final products is required.

Tables of the data required and their methods of procurement are detailed (Section IX).

THE RISK

These elements must be brought together in an interactive and systematic manner by means of a Risk Analysis. The Risk Analysis will identify hazards arising from 1, 2 and 3 and the interaction between them. These hazards can be assessed for the probability of occurrence and the severity of the consequences or more simply the Risk.
Once the Risk has been assessed, measures can be put in place to control the Risk to an acceptable level or better still eliminate the Risk completely.

II. GENERAL METHODOLOGY

STEP 1	**Look for the hazards**
STEP 2	**Decide who may be harmed and how**
STEP 3	**Evaluate the risk arising from the hazards and decide whether existing precautions are adequate or if you need to do more**
STEP 4	**Record your significant findings**
STEP 5	**Review your assessment from time to time and revise it if necessary**

This generic methodology can be performed at different levels of detail. One step further in detail is given in one of the most recommended procedures: PHASE

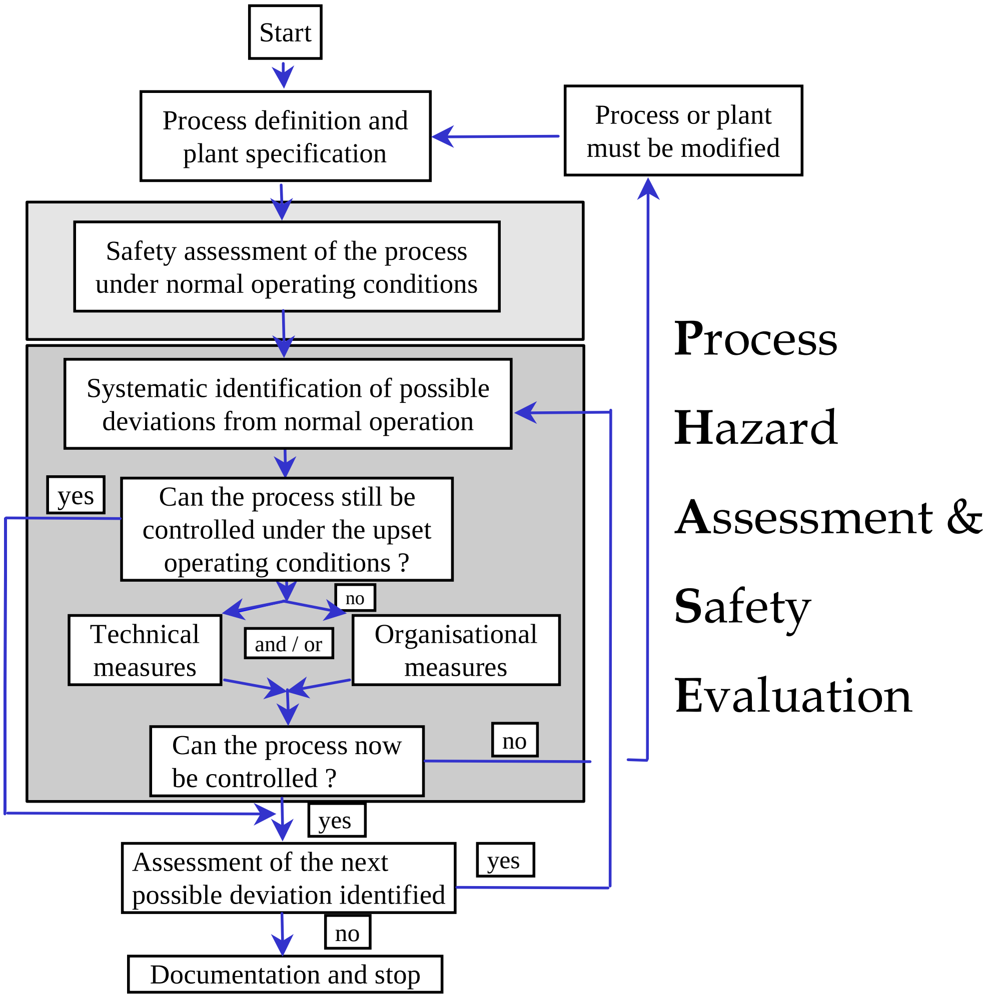


Fig.1

As outlined in this flow chart normal as well as upset operating conditions have to be assessed individually. One example on how to perform such an assessment for normal operating conditions is given in the next figure.

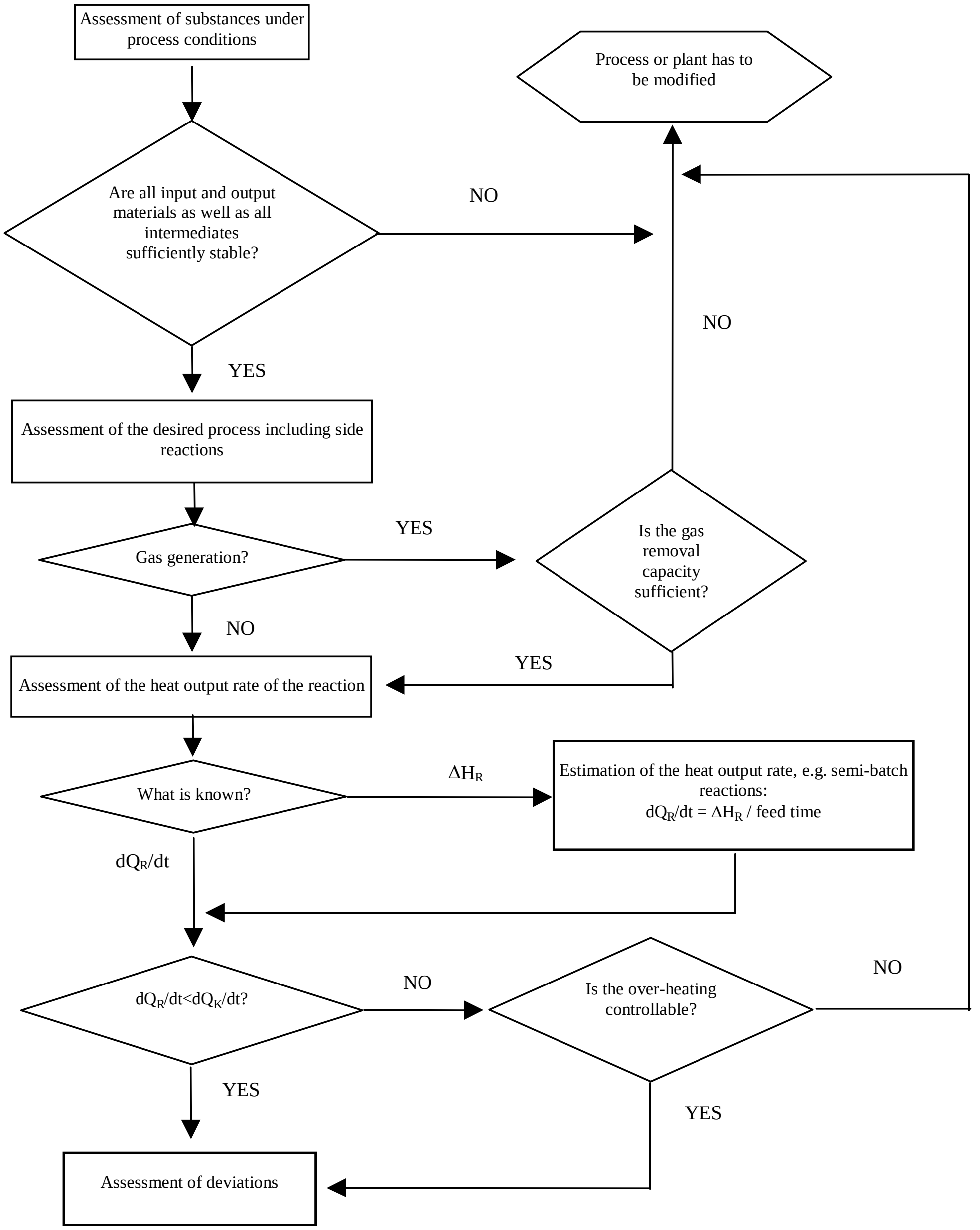


Fig. 2

The conduction of the complete hazard analysis requires experts and sophisticated equipment.

The following principles should be followed:

SUBSTITUTE	replace a material with a less hazardous substance or a hazardous reaction with a less hazardous reaction;
MINIMISE	use smaller quantities of hazardous substances in the process at any one time (also known as process intensification);
MODERATE	use less hazardous conditions, a less hazardous form of a material or facilities which minimise the impact of a release of hazardous material or energy (also known as attenuation);
SIMPLIFY	design facilities that eliminate unnecessary complexity and make operating errors less likely and which are forgiving of errors (also known as error tolerance).

Once these 5 elements are in place:

1) Good Engineering Design
2) Good Process Design
3) Good Basic Data
4) Risk Analysis
5) Measures

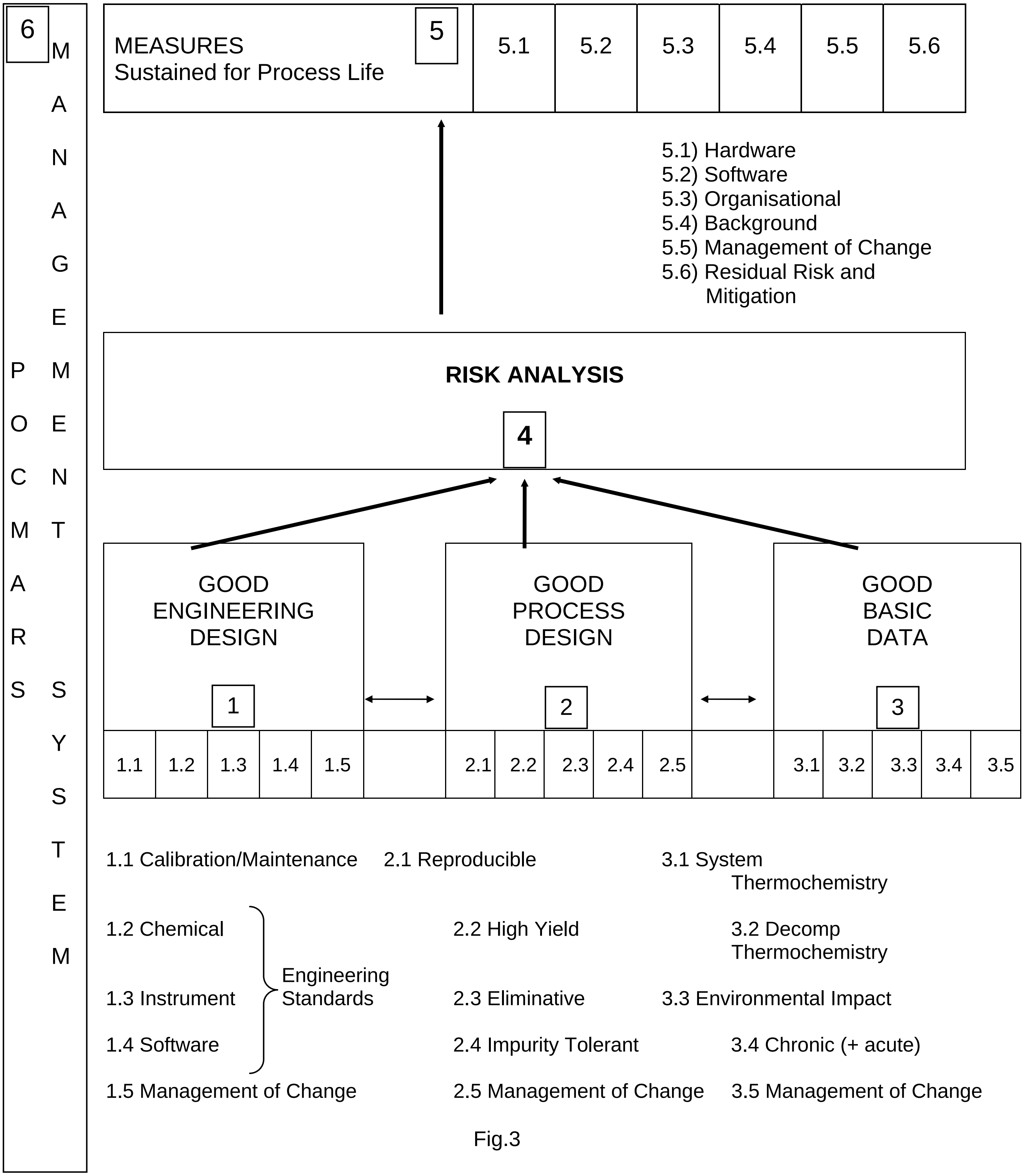
MANAGEMENT

Then all five elements can be Planned, Organised, Controlled, Monitored, Audited, Reviewed and Spot-checked (POCMARS) by a formal (written) according to ISO 14000, for example, or informal Management System. The system is shown schematically in the appended Process Safety Overview (Figure 3) and a checklist for a basic management system is appended.

Clearly few companies will run formal management systems which cover every aspect referred to in the overview, except possibly for high hazard operations.

However the basic elements of 1, 2, 3, 4, 5 and 6 must be in place to ensure a minimum level of safety.

PROCESS SAFETY OVERVIEW



5.1) Hardware
5.2) Software
5.3) Organisational
5.4) Background
5.5) Management of Change
5.6) Residual Risk and
Mitigation

1.1 Calibration/Maintenance
1.2 Chemical
1.3 Instrument
1.4 Software
(1.2–1.4: Engineering Standards)
1.5 Management of Change

2.1 Reproducible
2.2 High Yield
2.3 Eliminative
2.4 Impurity Tolerant
2.5 Management of Change

3.1 System Thermochemistry
3.2 Decomp Thermochemistry
3.3 Environmental Impact
3.4 Chronic (+ acute)
3.5 Management of Change

Fig.3

III. GOOD ENGINEERING DESIGN

All Answers should be Yes

	CHECKLIST	YES/NO
1.1	Have safety critical instrument been identified?	
1.2	Has calibration and maintenance schedule been set for safety critical instruments?	
1.3	Is there a separate maintenance and calibration schedule for non-safety related instruments?	
1.4	For addition controlled operations (semi-batch) is there a shut-off valve in the supply linked to agitator stopped?	
1.5	For addition controlled operations (semi-batch) is there a shut-off valve in the supply linked to reaction mass temperature high?	
1.6	For addition controlled operations (semi-batch) is there a shut-off valve in the supply linked to reaction mass temperature low?	
1.7	Are the reagents in use compatible with the material of construction?	
1.8	If computer control is used do safety critical instruments have hard wire back up (a control system that can be used in case of computer failure), e.g. 1.5, 1.6?	
1.9	For new processes can cooling (condenser or jacket) remove heat of reaction?	
1.10	Is there a Permit-to-Work scheme in operation (a written document system which assesses the hazard of any non routine job to be carried out in a chemical area and defines safety precautions to be applied)?	
1.11	Is there a Management of Change procedure for plant modifications?	
1.12	Is there a Management of Change procedure for software modification?	
1.13	Have all critical liquid levels in vessels been identified for:	
	Agitation?	
	Temperature measurement?	
	Maximum allowed volume?	
	Sampling points?	
	Heels?	
	Dip pipes?	
	Other measurement (e.g. pH, P, etc.)?	
	Is this data available to the Operations Team?	
1.14	Has a pre-campaign checklist for valve positions, etc. been made available?	
1.15	Are maximum working pressure and temperature known?	
1.16	Is overpressure relieve provided?	

Note: This checklist is not exhaustive but represents minimum standards of good.

IV. GOOD PROCESS DESIGN

Ideally a full Quality Risk Analysis should be carried out (which will include yield). This will look at the effect of the following on the Quality and Yield:

- Materials quality as supplied.
- Materials quantities as charged.
- Process variations (time, common impurities, temperature, pressure, pH, rate of heating, catalysts and rate of addition etc.).
- Storage and handling.
- Safety Stops will be identified where Quality and Yield will be least affected (this is also done for thermal safety see section 3).

However the following minimum requirements should be met.

All Answers should be Yes

	CHECKLIST	**YES/NO**
2.1	Does the reaction proceed normally and similarly on repeated laboratory experiments?	
2.2	Are quality and yield consistent under the proposed plant conditions?	
2.3	Do small (± 10ºC) temperature variations produce small changes in quality or yield?	
2.4	Is the average yield better than 90%?	
2.5	Is the reaction mass unaffected by:	
	• Water?	
	• Air?	
	• Rust?	
	• Excess of any adduct?	
2.6	Has the process been carried out with identical results by two different people?	
2.7	If the reaction is full batch (all-in) is there a written justification for it not being semi-batch (addition controlled)?	
2.8	Have less toxic materials been considered?	
2.9	Have non-flammable (less flammable) solvents been considered?	
2.10	In semi-batch is the accumulation (or work-out, the time after the stop of the addition during which is necessary to hold the reaction mass at temperature to allow the reaction to go to completion) low?	
2.11	Is there a written safety procedure to follow to introduce a process modification to the plant?	

V. THE KEVIN DIXON-JACKSON SHORT CUT

Clearly obtaining all the basic data and carrying out a rigorous Risk Analysis for every process would be very consuming of time, money and human resource. In order to achieve acceptable results in a short time the following truncated methodology may be followed. It is stressed at this stage that this is simply an “90/10” approach whereby 90% of the problems will be dealt with for 10% of the effort. In critical situations where the energies involved are high and where highly toxic (to man or the environment) materials or by-products are used then a detailed methodology must be followed. Where there is doubt about criticality expert advice must be obtained.

For batch and semi-batch reactions the following flow chart can be used. This flow chart leads to a selection of checklists, which should be completed prior to carrying out the abbreviated risk analysis in Section VII.

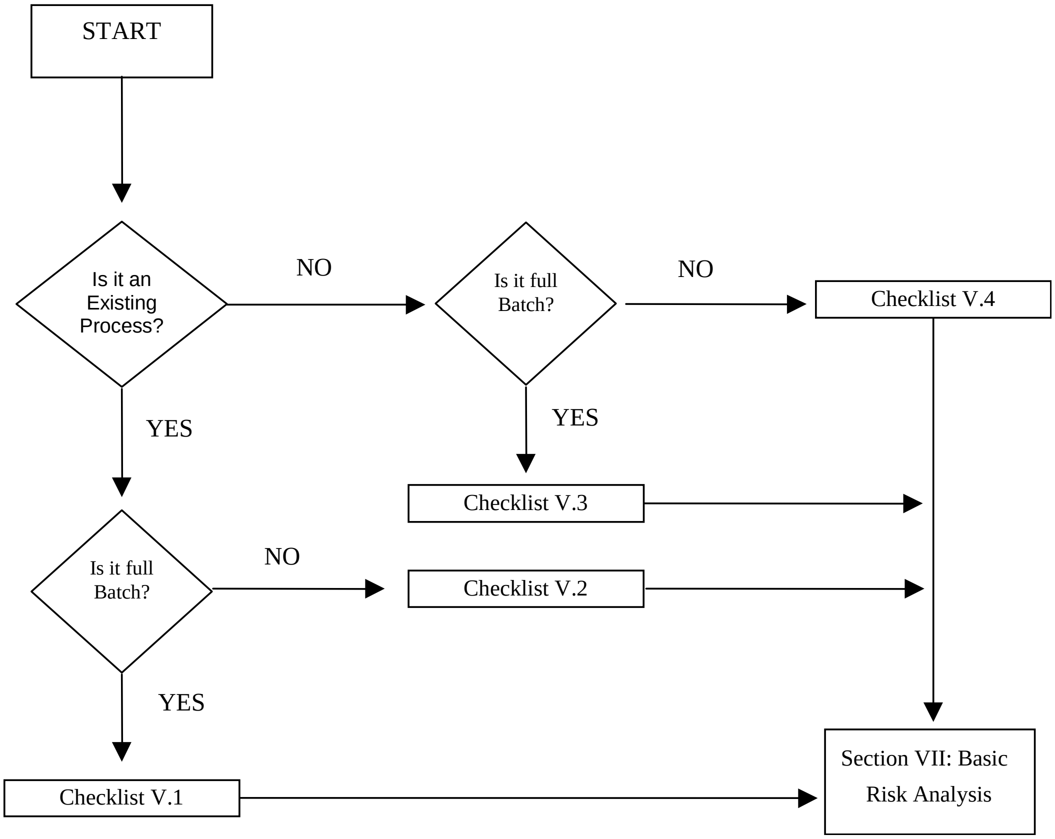


Fig. 4

CHECKLIST FOR AN EXISTING FULL BATCH PROCESS

V.1	CHECKLIST
1.1	What is the maximum safe starting temperature (T_{SAFE})?
1.2	What is the thermal stability (TMRad) at the final mass temperature?
1.3	What is the boiling point of the mass?
1.4	Which components (catalysts/reagents/solvents) are critical at the charging stage?
1.5	What is the temperature rise without cooling (MTSR)?
1.6	Is cooling (jacket/condenser) needed?
1.7	What happens if cooling fails?
1.8	If the process conditions are changed (temperature, concentration, solvent, catalyst etc.) is there a procedure to review 1.1 to 1.7?

NOTES: 1) T_{SAFE} can be calculated from experimental tests, simulations or a value known to be safe for the specific plant can be considered (e.g. the maximum T reached by the process without the appearance of safety problems).

2) TMR_{ad} can be calculated from experimental tests or a safety value known for the specific plant can be considered (see note 1).

3) MTSR can be known from experimental tests or simulations. To define which process failure conditions have to be considered, see following Evaluation chapter (pg.14).

CHECKLIST FOR AN EXISTING SEMI-BATCH PROCESS

V.2	CHECKLIST
2.1	Is cooling required during the addition (if yes estimate heat of reaction)?
2.2	Is a work-out required (if yes, estimate % of accumulation on work-out)?
2.3	What is TMRad of final reaction mass at normal operating temperature?
2.4	What is TMRad of reaction mass if cooling fails and accumulation causes the temperature to rise?
2.5	Will accumulation increase dramatically if the reaction temperature is lowered by 10ºC?
2.6	Does speeding the addition increase accumulation?
2.7	If the process conditions are changed (temperature, concentration, solvent, catalyst etc.) is there a procedure to review 2.1 to 2.6?

CHECKLIST FOR A NEW FULL BATCH PROCESS

Write up a justification for full batch as opposed to the safer semi-batch operation.

V.3	**CHECKLIST**
3.1	What is the final mass temperature?
3.2	What variation (expressed as a %) from the expected process value of the following parameters should be considered as critical to avoid that the final mass temperature increases:
	• Start temperature ±?
	• Catalyst concentration?
	• Solvent concentration?
	• Reagent concentration?
	• Substrate concentration?
3.3	What is TMRad at final mass temperature?
3.4	What is the TMRad at the worst case (3.2) mass temperature?

CHECKLIST FOR A NEW SEMI-BATCH PROCESS

V.4	**CHECKLIST**
4.1	What is rate of heat production under normal conditions?
4.2	What is TMRad of final mass at normal process temperature?
4.3	What is % accumulation?
4.4	What is ΔTad due to accumulation?
4.5	What is TMRad at temperature rise due to accumulation under fault conditions? [4.4 + T in 4.2]
4.6	How does temperature change ± 10ºC affect 4.1 and 4.3?
4.7	If the process conditions are changed (temperature, concentration, solvent, catalyst etc.) is there a procedure to review 4.1 to 4.6?

VI. EVALUATION OF THE CHECKLISTS' ANSWERS

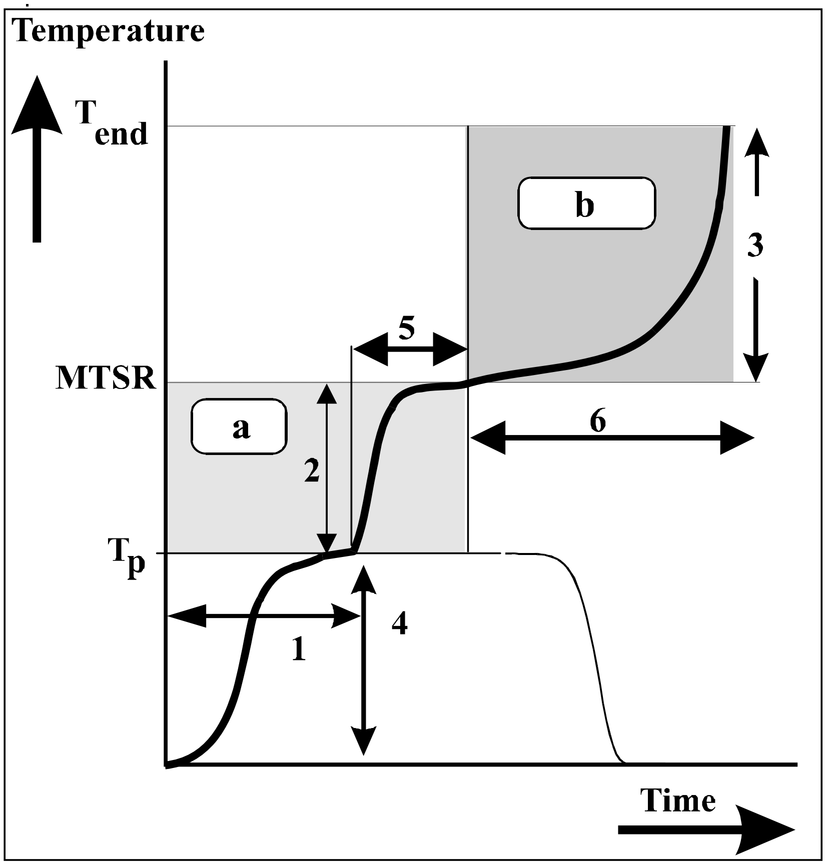


Fig. 5 Schematic presentation of a cooling failure scenario according to Gygax.

Consequences:	a = desired reaction	b = secondary effects

1: time to cooling failure

2: temperature increase due to loss of cooling

3: temperature increase due to secondary reactions

4: temperature increase under normal operating conditions

5: time to reach the maximum temperature due to synthetic reaction (accumulation)

6: adiabatic induction time of the secondary process

Applying the worst case principle, it must be assumed that the cooling failure occurs at the point in time where the maximum accumulation potential is present. This could be due to agitation failure, cooling pump failure, electricity failure, or thermometer failure.

It is helpful for the evaluation of the cooling failure scenario to discuss four temperature levels and their interactions, as was first developed by Stoessel:

- the process temperature, which corresponds to the initial temperature in a maloperation scenario (**T_P**).
- the temperature to be reached under upset conditions, e.g. the **MTSR**.
  NOTE: MTSR should be calculated in the worst case scenario of the considered process, e.g. for semi-batch should be considered three scenarios: *batch* (all reactants are mixed at the beginning of the process, adiabatic conditions are assumed); *stop* (dosing is stopped after a cooling failure. Only the actual accumulation is considered at each time); *non-stop* (dosing is not stopped when adiabatic conditions are established. Actual accumulation and remaining heat of reaction should be considered), and the worst one have to be considered.
- the temperature at which the adiabatic induction time of a possible decomposition reaction falls below a company specific limit value, **ADT24** or equivalent limit value.
- the boiling point of the reaction mass (**T_b**).

The possible different positions of the temperature levels relative to each other are presented in Figure 6, sorted by increasing degree of hazard (criticality).

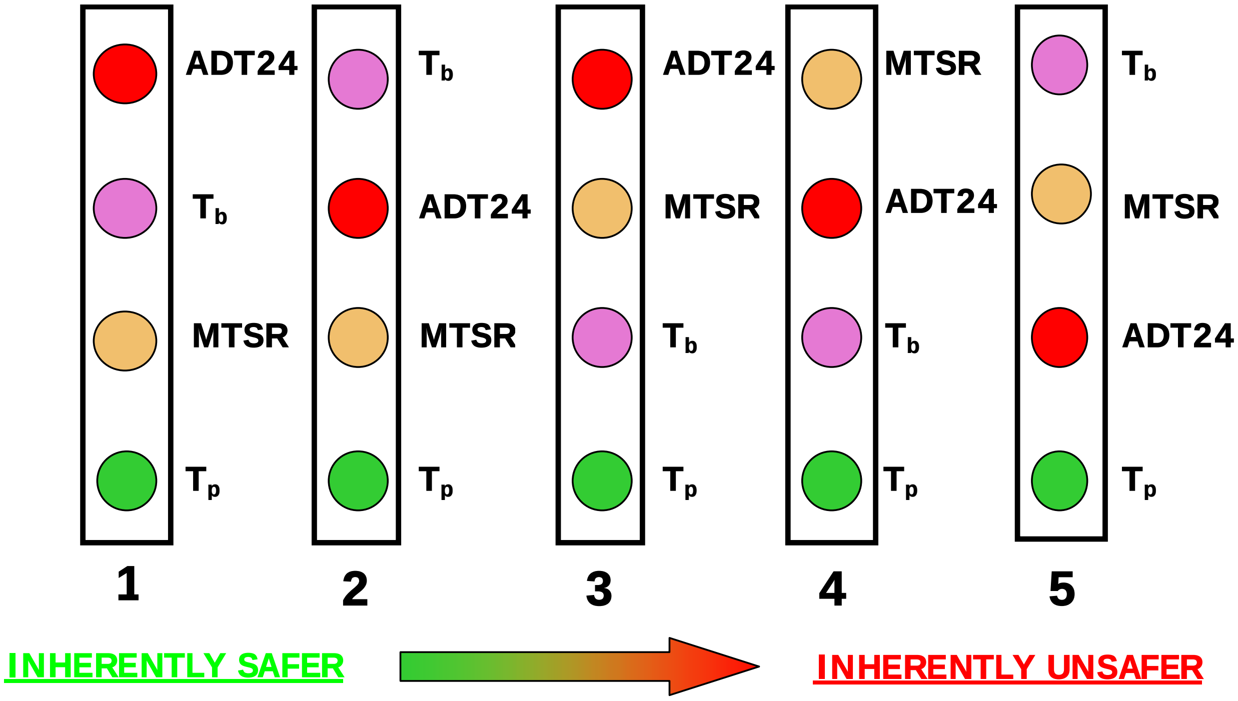


Fig. 6. Scenarios with increasing criticality according to Stoessel.

EVALUATION

CASE 1: in a case one scenario, neither the boiling point of the mixture nor the dangerous region in which the decomposition reaction becomes effective within a critical time is ever reached. Such processes may be regarded as inherently safe with respect to the process deviation evaluated.

CASE 2: also in the second case, which differs from the first by the absence of the boiling point barrier between MTSR and ADT24, the process may be regarded as safe.

CASE 3: in the third case, the boiling point with its latent heat of evaporation may be looked upon as a safety barrier, provided the condenser is adequately designed. If the process is performed in a closed system, the apparatus must be designed for the maximum expectable overpressure or be equipped with a pressure relief device.

CASE 4: scenarios with case four characteristics must be evaluated as to whether or not the evaporation capacity provides sufficient safety. If this is not the case, additional organisational or technical measures have to be implemented. Should the operation be performed in a closed system, then the temperature corresponding to the relief valve's set pressure may not be much higher than the level of T_b.

CASE 5: the fifth case must in any case be rated problematic. Plant and/or process modifications usually cannot be avoided in such situations.

VII. OPERATIONAL RISK ANALYSIS

Once a reaction has been carried out successfully on a plant scale it can be repeated in safety provided exactly the same conditions are applied each time.

The challenge is therefore to provide exactly the same conditions each time a reaction is carried out. This can only be done if no errors occur, no failures occur and no external events take part.

Over the life of a process this also means that no deliberate or accidental changes to the process or process conditions (temperature, time, addition rate, order of changing, quantities etc.) can be allowed without risk.

It is in fact impossible to run a process even a small number of times without error, change, failure or external event. So that a system must be employed to ensure that where change, failure external event or error occur there will be a back-up which will make the systems safe.

The search for critical errors, failures etc. and the provision of back-up is called Risk Analysis and the back-up are called Measures.

Ideally a formal written Risk Analysis should be employed. In the chemical industry Hazop (1) and Check-list (2) methods are the most popular. These are thorough and exhaustive methods and are highly recommended.

(1) Hazop I.Chem E, 165-189 Railway Terrace, Rugby CV21 3HQ - ISBN 0 852954271

(2) Ciba Risk Analysis - K Dixon-Jackson, Ciba Specialty Chemicals, Charter Way, Macclesfield, SK10 2NX

However, the following general checklist will give a good if incomplete Risk Analysis and if the measures suggested are implemented and maintained risks will be reduced significantly.

OPERATIONAL RISK ANALYSIS CHECKLIST

As a general rule for addition controlled exothermic reactions temperature control and agitation are essential. A shut-off to the feed should be hard wired to agitator stopped and temperature high and temperature low. This should be in addition to process control by operators or software.

As a general rule temperature measurement is critical for process control. It should be policy to fit (or retrofit on a planned basis) dual cross checking thermometry probes (duplex thermometry).

VII.1	**CHECKLIST**	**YES/NO**
1.1	Can chemicals with similar names or in similar packages be easily mixed up?	
	If yes, promote cross-checking and sign off on batch sheet.	
1.2	Are part bags or part drums used?	
	If yes, adjust charges to use only full bags or drums.	
1.3	Are there supply lines which contain chemicals but which will not be used?	
	If yes, disconnect and blank-off all redundant lines.	
1.4	Are any of the quantities charged critical?	
	If yes, promote cross-checking and sign off on batch sheet.	
1.5	Is the order of charging critical?	
	If yes, promote cross-checking and sign off on batch sheet.	
1.6	Is the rate of addition critical?	
	If yes, fit orifice plate for liquid and control flow. For solids provide training for operators.	
1.7	Are any other parameters critical (e.g. pH, pressure, moisture, etc.)?	
1.8	Is it safe to leave the reaction mass without temperature control?	

Overall where thermally critical conditions have been identified there are two general approaches:
1. Fit an engineering solution, or
2. Change the process to reduce the criticality.

In general option 2 is to be preferred as it offers permanent solutions and reduces capital costs and levels of risk.

1. Engineering Solutions

The following list is provided to provoke thinking along the correct lines. The exact solutions for a determined hazard varies widely from case to case and expert advice should be sought where doubt exists.

General

- Avoid common mode failure. Whatever safety engineering solution is imposed it must work when the initial cause of the loss of control is still active e.g. loss of electricity, water etc.
- Fit high reliability safety equipment. The safety system will be rarely activated but it must work with ultra high reliability if called upon.

Test and Maintain

- Essential safety equipment must be tested and maintained on a predetermined routine basis.

Detailed Engineering Solutions

- Drown out / Dump. In critical conditions send the batch to a drown-out vessel to cool, dilute and quench. Thinner, volume, mixing and transfer time need careful consideration under fault conditions.
- Quench. In critical situations add a diluent to prevent runaway. Again all the consideration in the case above apply. Also an inhibitor can be added in some cases.
- Vent and Contain. It may be possible to allow the reaction to runaway and safely discharge via a vent pipe and relief system to a safe place. Exact thermal data is required to size the vent and expert input is essential.
- Back-up utilities. Back up supplies which avoid common mode failure are possible for electricity (diesel engines), water (header tanks), agitation (N_2 purge), UPS for computer control, Instrument Air (local reserve cylinders), etc.
- Occasionally if jacket control is lost and reflux occurs, control can be re-established by an independent water supply to the condenser (also the reverse is occasionally possible if reflux control is lost).

2. Change the Process

- Reduce the amount of accumulation. High levels of accumulation can always be reduced. Typical methods to achieve this include:
    - Increase the addition time
    - Increase the reaction temperature
    - Change the catalyst
    - Reverse the additions
    - Dose wait, Dose wait
    - Vary the dose over the addition time
    - Dilute the reaction
    - Ultimately one can use a different synthetic route
- Increase the TMRad
    - Dilute the reaction
    - Reduce the accumulation (lower MTSR)
    - Operate at a lower temperature
    - Use a different solvent or synthetic route
    - Consider continuous rather than semi-batch to reduce volumes

VIII. MANAGEMENT SYSTEM

NOTE: A checklist like the following one should be filled up for each plant considered.

VIII.1		CHECKLIST	DONE?
1.1	PLANNING	There should be a written policy of how chemical synthesis will be carried out in safety.	
1.2		The policy should be issued to all graduates, operators and managers allied to production.	
1.3		Senior managers should demonstrate their commitment to the policy.	
1.4		A plan to conform to the policy organisation should be drawn up.	
1.5		The person(s) responsible for obtaining the basic safety data must be nominated.	
1.6		The persons responsible for carrying out the risk analysis must be nominated.	
1.7		The person responsible for implementing the safety measures must be named.	
1.8	CONTROL	The senior production manager must sign off the Risk analysis as acceptable and complete.	
1.9		The person responsible for the implementation of all the safety measures should report on completion and deficiencies at the expected start of production and expected completion date for all outstanding items.	
1.10		Procedures must be in place which insure that any significant change to the plant, the control system, the process, the operating instructions or the software are subject to a written Risk Assessment prior to the implementation of any change.	
1.11		Production must ensure that all required measures are in place and operational on a routine basis.	
1.12		Senior management should promote an annual internal audit of all process to ensure they conform to policy.	
1.13		There should be an annual review of the process safety situation across all production areas and places shown up to comply with policy.	
1.14		All processes Risk Analysis must be reviewed every 5 years or when a significant change occurs to the plant or the process.	

IX. GOOD BASIC DATA (and their Experimental Determination Methods)

Table 6: Overview on the information obtainable from thermodynamic and kinetic test methods.

	Thermal Data	**Methods**	***Kinetic Data***	**Methods**	***Physical Data***	**Methods**
Desired Reaction	*Heat of reaction* *Heat capacity* *MTSR* *Pmax*	Reaction calorimetry Isoperibolic Adiabatic	*Degree of Accumulation* *Temp=f(time)* *P=f(time)*	Reaction calorimetry	*B.Pts* *M.Pts* *Gas evolution as f(temp)* *Venting runaway*	Standard methods Gas analysis Vent sizing apparatus
Undesired Reaction/ Decomposition	*Heat of reaction* *Tmax* *Pmax*	DSC Adiabatic calorimetry	*Time to maximum rate* *dP/dt*	Adiabatic calorimetry Kinetic study	*Gas evolution* *Venting decomposition*	Gas analysis Vent sizing apparatus
Secondary or Side reactions	*Relative proportions*	Analytical methods	*Competing reactions*	Analytical methods	*Effect on physical properties*	Standard methods

X. GLOSSARY

- **Accumulation:** A build-up of unreacted materials.
- **Activation energy**: Constant Ea in the exponential part of the Arrhenius rate equation associated with the minimum energy difference between the reactants and an activated complex (transition state which has a structure intermediate to those of the reactants and the products), or with the minimum collision energy between molecules that is required to enable a reaction.
- **Adiabatic:** A system condition in which no heat is exchanged between the chemical system and its environment, i.e. no heat transfer occurs to or from the environment surrounding the sample, including the sample container.
- **Adiabatic induction time**: Induction period or time to an event (spontaneous ignition, explosion, etc.) under adiabatic conditions starting at operating conditions.
- **Adiabatic calorimeter:** A calorimeter in which reactions proceed with little exchange of heat between the sample container and its surroundings. Common types of adiabatic calorimeter include the ARCTM, PHI-TECTM and VSPTM. The RSSTTM calorimeter may be considered as pseudo-adiabatic under some circumstances.
- **Adiabatic temperature rise:** The increase in temperature of a reacting mixture as a result of exothermic chemical reaction, when there is no heat transfer to or from the environment.

$$\Delta T = \Delta H/Cp$$

ΔT	Adiabatic temperature rise (K)	Cp	mean heat capacity (J/kg/K)
ΔH	Heat release (J/kg)		

- **Apparent activation energy:** In practice, reaction rates are often determined by physical processes (e.g. mass flow, diffusion, mass transfer area) as well as by chemical processes. The activation energy observed in these cases is called the apparent activation energy.
- **Arrhenius rate equation:** The rate of a chemical reaction (k) increases exponentially with increasing temperature (T). This relationship is represented by the Arrhenius equation $k = A \cdot \exp(-Ea/RT)$. See also pre-exponential factor.
- **Arrhenius plot:** Graph that shows the logarithmic rate of heat production ln(q) versus the inverse temperature (1/T) in Kelvin. This results in a straight line with a gradient -Ea/R. In practice, the rate of reaction is often affected by physical processes (e.g. diffusion), which results in the occurrence of an apparent activation energy.
- **Autocatalysis:** The increase of the rate of reaction due to the catalysing effect of the reaction products.
- **Basis of safety:** The combination of measures relied upon to ensure safety. The basis of safety for a reactor highlights those aspects of the design and operation (hardware, protective systems and procedures) that are safety critical. The basis of safety can only be selected once all the significant hazards have been identified and evaluated.
- **Batch process:** An operation in which all the reactants including any solvent are added to a reactor at the start of a reaction.
- **Blowdown:** Rapid discharge of a vessel.
- **Calorimeter:** See reaction calorimeter.
- **Condensed phase explosion**: An explosion that occurs when the fuel is present in the form of a liquid or solid.
- **Confined explosion**: An explosion of a fuel-oxidant mixture (usually in the gas phase) inside a closed system (e.g. vessel or building).
- **Consequences**: A description of what would occur in the event of a hazard occurring.
- **Containment:** A condition in which under no condition reactants or products are exchanged between the chemical system and its environment.
- **Continuous reactors:** A reactor that is characterised by a continuous flow of reactants into and out of the reaction system. Common examples are the Plug Flow Reactor (PFR), the loop reactor and the Continuous Stirred Tank Reactor (CSTR) but these are not considered in the HarsNet project.
- **Critical mass:** Minimum mass that is required to enable the occurrence of an explosion.
- **Critical temperature:** Maximum temperature of coolant at which all heat that is generated by a chemical reaction can still be transferred to the coolant (either gas or liquid).

- **Decomposition:** The breaking up of a chemical compound into by products. The temperature at which decomposition is observed depends on scale and is markedly dependent on the sensitivity of the measuring equipment.
- **Decomposition energy:** The decomposition energy is the maximum amount of energy, which can be released upon decomposition. The product of decomposition energy and total mass is an important parameter for determining the effects of a sudden energy release, e.g. in an explosion. The decomposition energy can occasionally be obtained from literature or calculated theoretically, however it is mostly determined experimentally, often by DSC.
- **Decomposition temperature:** Temperature at which spontaneous decomposition occurs. In practice, it is impossible to indicate the exact value of this temperature, because the reaction rate is only zero at absolute zero temperature (0 K) conforming to the equation of Arrhenius. Therefore, in measuring the decomposition temperature both sample quantity and sensitivity of the measuring device are very important. (See also onset temperature).
- **DIERS**: Design Institute for Emergency Relief Systems; Institute under auspices of the American Institute of Chemical Engineers founded to investigate design requirements for vent lines in case of two-phase venting.
- **Dewar:** A jacketed vacuum flask that can be used in calorimetry. The low rate of heat loss means that it can be used to simulate the behaviour of large reactors. See also adiabatic.
- **Differential scanning calorimetry (DSC):** A technique in which the change of the difference in the heat flow rate to the sample and to a reference sample is measured while they are subjected to a temperature regime. Note that in many process safety laboratories DSC and DTA are used interchangeably.
- **Differential thermal analysis (DTA):** A technique in which the change of the difference in the temperature between the sample and the reference sample is measured while they are subjected to a temperature regime. Note that in many process safety laboratories DSC and DTA are used interchangeably.
- **Endothermic:** A reaction is called endothermic if energy (heat) is absorbed during the reaction.
- **Event tree (analysis):** A graphical logical model that identifies possible outcomes following an initiating event. With suitable data it can be used to quantify the occurrence of an event.
- **Exothermic:** A reaction is called exothermic if energy (heat) is released during the reaction.
- **Explosion:** A release of energy sufficient to cause a pressure wave.
- **Fault tree (analysis):** A method for representing the logical combinations of various system states which lead to a particular outcome (Top event). With suitable data it can be used to quantify the probability or frequency of an event.
- **Frequency:** The number of specified events occurring in unit time.
- **HAZOP or Hazard and Operability Study:** A systematic method for identifying possible hazards and potential operating problems in a plant or process by the application of so called ‘guidewords’ (e.g. more, less, other etc.) to the plant or process flow sheet to study process deviations.
- **Hazard:** A chemical or physical condition that has the potential for causing damage to people, property, or environment.
- **Hazardous chemical reactivity:** Any chemical reaction with the potential to exhibit rates of increase in temperature and/or pressure too high to be absorbed by the environment surrounding the system. Included are reactive materials and unstable materials.
- **Heat of reaction:** The total quantity of thermal energy liberated or absorbed during a chemical reaction.
- **Heat Wait Search (HWS):** An experimental technique in which a substance is heated in stages until very slow decomposition is detected. The experimental apparatus then becomes adiabatic and the course of the decomposition is monitored.
- **Induction period/time:** Time interval (starting at operating conditions) after which a runaway shows its maximum effects.
- **Inherently safer:** A system is described as inherently safer if it remains in a non-hazardous situation after the occurrence of unintended deviations from normal operating conditions. Inherently safer is used, rather than inherently safe, because it is not possible to eliminate all hazards.

- **Inhibition:** A protective measure where the reaction can be stopped chemically by addition of another material.
- **Isoperibolic:** A system in which the controlling jacket temperature is kept constant.
- **Isothermal:** A system condition in which the temperature remains constant. This implies that potential temperature increases and decreases are compensated by sufficient heat exchange with the environment of the system.
- **Isothermal calorimeter:** A calorimeter in which the energy exchange with its surroundings is measured whilst the temperature of its contents remains essentially constant. Common types of calorimeter that can be operated in the isothermal mode include the autoMATETM, ChemisensTM, RC1TM and SIMULARTM.
- **Jacket temperature:** The temperature of the fluid contained in the reactor jacket used to indirectly heat or cool the reactor contents.
- **Kinetic data:** Data associated with the conversion rate of a reaction, such as the activation energy, pre-exponential factor and order of reaction. (See Arrhenius rate constant).
- **Maximum pressure after decomposition:** The maximum pressure, which is obtained in a closed vessel. This pressure depends on the adiabatic temperature rise and the specific gas production.
- **Microcalorimetry:** Isothermal techniques of high sensitivity in which heat fluxes from the converting sample material are measured very accurately. Differential Microcalorimetry is performed if the heat fluxes from the sample are compared with those of a reference material.
- **Mitigating measures:** Measures to reduce the consequences of a runaway to an acceptable level.
- **MTSR Maximum Temperature of the Synthesis Reaction:** The maximum temperature reached following the occurrence of the desired (synthesis) chemical reaction under adiabatic conditions starting at the designed process temperature. For a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the synthesis reaction for those reactants that have accumulated during dosing.
- **Onset temperature**: Defined as the temperature at which the heat released by a reaction can no longer be completely removed from the reaction vessel, and consequently, results in a detectable temperature increase. The onset temperature depends on detection sensitivity, reaction kinetics, vessel size and on cooling, flow and agitation characteristics. Scaling of onset temperatures and application of 'rules of thumb' concerning onset temperatures should be used with extreme care.
- **Permanent gas:** A gas that cannot be condensed (or solidified) under the range of conditions of interest (eg temperature or pressure).
- **Phi-factor:** A correction factor which is based on the ratio of the total heat capacity of a vessel (mass of vessel * Cp of vessel) and the total heat capacity of the vessel contents (mass of contents * Cp of contents).

  Phi = 1 + (mass of vessel * Cp of vessel) /(mass of contents * Cp of contents).

  The phi-factor is used to correct the measured heat release, and heat release rate, for the heat that is absorbed by the test cell.
- **Pre-exponential factor (also known as the frequency factor):** Constant A (also denoted as Z, k*, k_o or k_∞ in the Arrhenius equation (also called frequency factor). The pre-exponential factor is associated with the frequency of collisions between molecules (entropy) and with the probability that these collisions result in a reaction. See also Arrhenius rate equation.
- **Preventive measures:** Measures taken at the initial stages of a runaway to avoid further development of the runaway or to reduce its final effects.
- **Probability:** The expression for the likelihood of occurrence of an event or event sequence during an interval of time or the likelihood of a success or failure of an event on test or demand. By definition, probability is expressed as a number ranging from 0 to 1.
- **Products:** Chemicals produced during a reaction process.
- **Quenching:** Rapid cooling of the reaction system in a short time (almost instantaneously). This condition 'freezes' the status of a process and prevents further reaction or decomposition.

- **Rate of reaction:** The rate at which the conversion of reactants takes place. The rate of reaction (r) is a function of concentrations (F(c)) and the reaction rate constant (k):

  $$r = k.F(cA, cB,....,CX)$$

  The heat (q) produced by a reaction is a linear function of the rate of reaction, which makes the rate of reaction a basic parameter in determining the required cooling capacity during all stages of the reaction process.
- **Rate equation:** See Arrhenius rate equation.
- **Reactants:** Chemicals that are converted into (the required) products during the reaction process.
- **Reaction:** The process in which chemicals (reactants) are converted into other chemicals (products).
- **Reaction calorimeter:** A laboratory test apparatus for measuring thermal effects of chemical reactions or processes. For the purpose of this guidance, types of reaction calorimeters include isothermal, isoperibolic and adiabatic systems.
- **Reaction kinetics:** The complex of data (thermodynamic and kinetic) that determine a reaction rate.
- **Reaction rate constant:** The constant k in the rate of reaction. The reaction rate constant is a strong function of temperature as represented by the Arrhenius equation.
- **Reasonably practicable:** The degree of risk in a particular job or workplace needs to be balanced against the sacrifice in time, trouble, cost and physical difficulty of taking measures to avoid or reduce the risk. Measures must be taken to eliminate or control the risks unless it is clear that the sacrifice incurred in doing so is grossly disproportionate to the level of the risk. However, the ability' to pay for additional control measures is not a deciding factor as to whether they are necessary.
- **Reflux:** An operation in which vapour is produced, condensed and subsequently returned to the originating vessel.
- **Risk:** The chance of something adverse happening where 'something' refers to a particular consequence of the manifestation of a hazard. Risk reflects both the likelihood that harm will occur and its severity in relation to the number of people who might be affected, and the consequences to them.
- **Risk assessment:** The process of identifying the hazards present in any undertaking (whether arising from work activities or other factors) and those likely to be affected by them. Also evaluating the extent of the risks involved, bearing in mind whatever precautions are already being taken.
- **Runaway:** A reaction that is out of control because the rate of heat generation by an exothermic chemical reaction exceeds the rate of cooling available.
- **SADT (Self-Accelerating Decomposition Temperature):** The lowest ambient temperature at which auto-accelerated decomposition of an unstable substance is observed (minimum self-heating rate of 5 °C/week), when the substance is packaged in its commercial container and is subjected to that temperature during one week in the testing facility (see also CSST).
- **Semi-batch:** An operation in which some materials are added to the reactor at the start, with one or more other reactants added in a controlled manner during the reaction. See also semi-batch reactor.
- **Temperature of no return:** The temperature under conditions of thermal decomposition at which the rate of heat generation is equal to the maximum rate of cooling available.
- **Thermally unstable:** Chemicals and materials are thermally unstable if they decompose, degrade or react as a function of temperature and time at or about the temperature of use.
- **Thermodynamic data:** Data associated with the aspects of a reaction that are based on the thermodynamic laws of energy, such as Gibbs' free energy, and the enthalpy (heat) of reaction.
- **TMR Time to maximum rate:** The time taken for a material to self-heat to the maximum rate of decomposition from a specific temperature, usually under adiabatic conditions.
- **TMRad:** Time to maximum rate from a specified temperature under adiabatic conditions.
- **Thermal runaway:** see runaway.
- **Unstable substance/material:** Substance or material that decomposes either in the pure state or in the state as normally produced.

- **Venting:** Emergency flow of vessel contents out of the vessel. The pressure is reduced by venting, thus, avoiding a vessel rupture due to over-pressurisation. The vent flow can be single or (a) multi-phase (one) with consequent differences in flow and depressurisation characteristics.

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APPENDIX 3.2

CHECK CARDS FOR RUNAWAY

CCR DEVELOPMENT

Table of Contents

1. Introduction

The main target of the CCRs project is to obtain a simple tool to quickly evaluate the safety level of a chemical plant liable to suffer a runaway reaction. In order to define a tool to assess chemical hazards, one of the most important points is to find a coherent and defined starting point from which analyse all the factors that may influence or cause an accident.

Investigating the hazard's anatomy, some basic components can be identified:

- CAUSE – it is an individual and certain event that will trigger the appearance of a hazard. Causes are defined depending on the process that is being assessed; they are not of general application, but the consequences that arise from them may be common to all processes. Preventive safety measures will depend on the causes defined.

- CRITICAL FACTORS - a critical factor is a generic hazard that is able to appear in a certain process as a consequence of an initial cause. Generic hazards or factors are defined on a theoretical basis. All factors defined must always be studied to find out which ones are important in the process. If the factor is likely to appear in the process causing a hazardous situation, then it is called CRITICAL FACTOR. Critical factors will define the parameters that must be tracked in the installation to control the process and to set up the alarm conditions and the safety measures.

- CHEMICAL BEHAVIOUR – is the behaviour that chemicals exhibit under process conditions or under credible special conditions. The most interesting chemical properties for a runaway assessment are those related with exothermic activity and reactions with other substances. Chemical behaviour together with critical factors is of importance to define which are the dangerous conditions for a chemical system.

A factor-based strategy was thought to be the best possible way to define a tool for a hazard assessment. It would focus on defining generic situations for hazard assessment.
It is important to notice that a generic factor will be classified as critical or not depending on the chemical behaviour of the substance involved and the process conditions considered. From the conjunction of chemical behaviour, process conditions and Critical Factor the Hazardous Process Deviation arises. This deviation may develop and constitute an accident or kept under control with the emergency safety measures and became a near miss.
Factors make easy to define which data are required for their evaluation, and from that data the tests can be specified. Moreover, once detected the critical ones, it will be clear which errors or failures will trigger them.

In the first version of CCRs, six factors were defined to assess a runaway event; it was believed that with these most of the runaway scenarios were taken into account. The factors were mainly derived from the 10 runaway courses described by Gustin ("Runaway Reactions, Their Courses, and the Methods to Establish Safe Process Conditions", ISSN 0272-4332, vol.12, issue 4, 1992).

The chemical process had been split in three areas, which are thought to be essentially different from each other. In this way it is possible to explain better the influence of a factor on a certain process zone. These areas are:

- Storage (not intended change on physical or chemical properties)
- Process (changes on physical properties but not on chemical structure or properties)
- Reaction (changes on both physical and chemical properties).

2. Changes brought to the new version of CCRs

2.1 *Revision on Critical Factors*

In the new version of the methodology the factors are reduced to five, considering the fact that the Critical Factor "Bulk Adiabatic Behaviour" can be included in the "Temperature Hazard" one, as the effect is essentially the same on the process.
Moreover, instead of "Non-Arrhenius Reactions", the definition "Autocatalytic Reactions" is preferred thinking that it is easier to comprehend.

The factors used now are:

- *Mistaken Chemicals* – this factor focuses on scenarios where a chemical mixture showing a violent and exothermic behaviour is achieved by error. As the system has not been designed to handle the reactive behaviour triggered, the heat released will surely exceed the normal cooling measures, thus leading the system to enter on runaway conditions. The "Incompatible Chemicals" scenario is enclosed by definition in this factor. A hazardous situation may also appear while handling the right chemicals: an error on proportions, concentration or mixing order may cause an undesired exothermal behaviour, even if the intended reaction is taking place.

- *Autocatalytic Reactions* – there are chemical reactions that do not follow the Arrhenius law. In this type of reactions, the rate of reactions may change at a constant temperature. Chemicals exhibit this behaviour must be handled with grate care. Even if the reaction mass or bulk in storage vessels is well below a safety temperature, the reaction may lead to a runaway if the handling time is too large at that temperature. Examples of this behaviour are autocatalytic and radical chain polymerisation reactions.

- *Segregation* – the segregation of a phase may be a hazard for different reasons. The most important one is that the segregated phase may show unstable exothermic behaviour. Besides, segregation may also affect the composition of the main phase from where the new phase separates, making it unstable. The third way in which segregation is dangerous is because it may jam measurement devises like level, temperature or pressure indication. Loss of stirring or too low temperature are typical causes of segregation. A grater problem occurs when the segregated phase is highly unstable and can have shock sensitive or detonating properties.

- *Accumulation* – the accumulation problem arises from a misbalance between reactant consumption and dosing rate. The concentration of the controlling reactant in the bulk will be higher or lower depending on dosing rate and temperature. If this concentration reaches a too high value, then the reaction is triggered too fast and high exothermal behaviour appears which may cause a runaway. As an accumulation scenario is directly related to the problem of dosing a reactant, this factor is only described for the Reaction zone, and not defined for Storage or Process zones.

- *Temperature Hazard* – this kind of hazard may arise from two different situations: a too high global temperature or a too high local temperature or hot spot. A too high global temperature situation may be reached because of an extra heat input to the system by error or a too low heat removal. On the hot spot scenario care must be taken with mixture showing a sensible behaviour to heat: a hot spot may initiate an exothermic reaction that can propagate through the whole reaction mass. Hot spots are especially critical on vessels containing substances with detonating, deflagrating or self-igniting properties.

2.2 Review on CCRs first version structure and application

While applying the first version of CCRs to test processes in collaboration with a few SMEs, some problems were encountered:

- The first one is to detect a critical factor considering all parts of the process related to each of the three areas at the same time. It is thought that the easiest way to settle this is to subdivide the process into steps and to refer each step to one of the three areas. The reason of this choice is that chemical industries commonly subdivide processes in steps and as a consequence this analysis criterion may be easier understood.
  Therefore, the factor detection follows a scheme that is peculiar to each area. In this way, the analysis should be more complete and easier to carry out, considering all the problems involved with each single step.

- Another problem found in the analysis of the first version is that during the identification of a critical factor there is no way to consider the safety measures utilised by the company to prevent hazards due to this factor. For this reason, it has been developed a “*what if/checklist*” in which a “*yes/no tree*” of questions permits to consider the criticality of the factor due to its chemical behaviour and process conditions, and to control if the safety measures implemented are sufficient.

- Data collection is another problem of the old cards’ version: a lot of data are asked in each factor’s card and most of them are related to different factors at the same time. Moreover, is not specified in which conditions they have to be calculated. For this reason, all necessary data have been moved in a separated part of the cards, structured in two tables: one regarding the chemical properties of each substance involved in the process (included construction materials and wastes); the other concerning with process and reaction conditions, where properties are referred to each single step. In this way all necessary data can be found in one site and be used in every moment during the safety analysis.

3. Structure of the new version of CCRs

The new version of the methodology is structured as follows: first of all, the cards are subdivided in *Data Collection Cards* and *Data Analysis Cards*.
In the *Data Collection Cards* are included:

- A Chemical properties table (that has to be filled with known data about the substances involved in the process)
- A Process and Reaction Conditions table (that has to be filled with data about each step of the process)
- A general Compatibility Chart
- A Compatibility Chart specific of the process considered
- A "Data Sources", in which a list of books and Internet sites where to find literature's data and estimations methods is presented.

This data collection is intended to make easier answering to the "what if/checklists" contained in the *Data Analysis Cards*, having all the necessary data in one site.

In the *Data Analysis Cards* a number of questions structured as a "yes/no tree" are proposed. Each step of the process has to be referred to one process area and then the proper list of questions has to be followed. For each step all the critical factors that can come up in each area are considered and for each factor a list of questions to investigate its criticality is presented. The what if/checklist questions are structured in the way that at the end of each "tree" of questions only two possibilities can be achieved:

- A justification of the non criticality of the factor considered, due to the chemical behaviour of the substances involved, the process conditions considered or the safety measures used. The intent is to make think the person that is doing the analysis, to be sure the question has been considered in all its points of view.
- Or "REVIEW YOUR SAFETY MEASURES" when the factor is found as critical and a review on process or safety measures is necessary.

Afterwards each list of questions for each area, a scheme to be used in answering is included.
As a general rule, literature's and estimated data can be used only to obtain a roughly safety analysis of the process and a pointer to the steps that need to be deeply investigated. For a complete analysis, only experimental data have to be considered.

DATA

COLLECTION

CARDS

CHEMICAL PROPERTIES

SUBSTANCES[1] AND MIXTURES	**Chemical composition and CAS number**	**homologation or identification number[2]**	**Purity[3]**	**Phase**			**Report of handling conditions[4]**	**Phase stability Vs T[5]**	**Phase stability Vs P[6]**	**Specific heat capacity[7]**	**T_{boil}**	**Thermal activity at $T_{STORAGE}$[8]**	**Deflagration or detonation sensitivity[9]**
				G	L	S							

NOTES:

1 - Considered in the all possible phases on which the substances are used in the process (storage, reaction, etc).
2 - Enterprise's internal identification of the substances.
3 - Degree of purity as specified in each process.
4 - Inhibitors, triggering agents, chemical substances able to influence the rate of reaction, etc.
5 - Temperature to leave of which a different phase from the one expected under normal conditions appears.
6 - Pressure to leave of which a different phase from the one expected under normal conditions appears.
7 - In case of lack of data for mixtures, make one medium of the values of the single substances.
8 - Stable or unstable, considering the maximum storage period.
9 - High, medium, low.
CALCULATE ALL THE VALUES USING INTERNATIONAL SYSTEM UNITS.

REACTION and PROCESS CONDITIONS

STEP(1)	**T**	**P**	**Substances(2)**	**Specific heat of the mixture(3)**	**Heat of reaction(4)**	**MTSR(5)**	**Kinetic behaviour(6)**	**Total adiabatic temperature rise(7)**	**Thermal activity at the end of the step**	**MAXTSAFE(8)**	**Influence of hot spots**

NOTES:

1 - Subdivide the process in steps and define if the step refers to process (P) or reaction (R).
2 - Consider all the substances present in each step.
3 - Use the experimental value if known, otherwise consider one medium of the values of the single substances.
4 - It can be known from: experimental calculations, literature or internet source (see DATA SOURCE)or simulations programs (as CHETAH).
5 - The maximum temperature reached following the occurrence of the desired (synthesis) chemical reaction under adiabatic conditions starting at the designed process temperature. For a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the accumulated reactants of the desired reaction.
6 - Specify if the reaction is an Arrhenius, catalytic (homogeneous or heterogeneous) or autocatalytic type.
7 - Increase of temperature of the reaction mass under adiabatic conditions due to accumulation of the heat released, coming from both the synthesis reaction and all the possible secondary reactions involved.
8 - If known, use ADT24; if not, MAXTSAFE can be calculated as the critical T at which in a short time decomposition or other thermal evolution of the final reaction mass takes place. It can be evaluated with a DSC, considering the T of the first exothermal peak less 70º (if beta=5K/min) or less 100º (if beta=10K/min).

CALCULATE ALL THE VALUES USING INTERNATIONAL SYSTEM UNITS

COMPATIBILITY CHART

No.	Substances													
1		1												
2			2											
3				3										
4					4									
5						5								
6							6							
7								7						
8									8					
9										9				
10											10			
11												11		
12													12	
13														13
		1	2	3	4	5	6	7	8	9	10	11	12	13
🟦														
🟥														
🟨														
⬜														

NOTES 1-Interaction with water and iron must be considered for all processes.

2-Construction materials and wastes have to be included in the substances considered.

3-The colors at the bottom of the table are referred to the NFPA index. Include this identification in order to better comprehend the substance's chemical behaviour.

Legend

Code	Consequences
H	Heat Generation
F	Fire
G	Innocuous and non-flammable gas generation
GT	Toxic Gas formation
GF	Flammable Gas formation
E	Explosion
P	Violent Polymerization
S	Solubilization of toxic substance
U	May be hazardous, but Unknown

General Chemical Compatibility Chart

EPA-600/2-80-076 April 1980

A METHOD FOR DETERMINING THE COMPATIBILITY OF CHEMICAL MIXTURES

Legend

Code	Consequences
H	Heat Generation
F	Fire
G	Innocuous and non-flammable gas generation
GT	Toxic Gas formation
GF	Flammable Gas formation
E	Explosion
P	Violent Polymerization
S	Solubilization of toxic substance
U	May be hazardous, but Unknown

***Caution*: This Chart is intended as an indication of some of the hazards that can be expected on mixing chemical wastes. Because of the differing activities of the thousands of compounds that may be encountered, it is not possible to make any chart definitive and all inclusive. It cannot be assumed to ensure compatibiltiy of wastes because wastes are not sclassified as hazardous on the chart, nor do any blanks necessarily mean that the mixture cannot result in a hazard occuring. Detailed instructions as to hazards involved in handling and disposing of any given waste should be obtained from the originator of the waste.**

No.	Reactivity Group Name																																									
1	Acids, Mineral, Non-oxidizing	1																																								
2	Acids, Mineral, Oxidizing		2																																							
3	Acids, Organic		G H	3																																						
4	Alcohols and Glycols	H	H F	H P	4																																					
5	Aldehydes	H P	H F	H P		5																																				
6	Amides	H	H GT				6																																			
7	Amines, Aliphatic and Aromatic	H	H GT	H		H		7																																		
8	Azo Compounds, Diazo Compounds and Hydrazines	H G	H GT	H G	H G	H			8																																	
9	Carbamates	H G	H GT						G H	9																																
10	Caustics	H	H	H		H				H G	10																															
11	Cyanides	GT GF	GT GF	GT GF					G			11																														
12	Dithiocarbamates	H,F GF	H,F GF	H,GT GF		GF GT		U	H G				12																													
13	Esters	H	H F						H G		H			13																												
14	Ethers	H	H F												14																											
15	Fluorides, Inorganic	GT	GT	GT												15																										
16	Hydrocarbons, Aromatic		H F														16																									
17	Halogenated Organics	H GT	H,F GT					H GT	H G		H GF	H						17																								
18	Isocyanates	H G	H,F GT	H G	H P			H P	H G		H,P G	H G	U						18																							
19	Ketones	H	H F						H G		H	H								19																						
20	Mercaptans and Other Organic Sulfides	GT GF	H,F GT						H G									H	H	H	20																					
21	Metals, Alkali and Alkaline Earth, Elemental	H,F GF	H,F GF	H,F GF	H,F GF	H,F GF	GF H	GF H	GF H	GF H	GF H	GF H	GF,H GT	GF H				H E	GF H	GF H	GF H	21																				
22	Metals, Other Elemental & Alloys as Powders, Vapors, or Sponges	H,F GF	H,F GF	G F					H,F GT	U	GF H							H E	GF H		H,F GF		22																			
23	Metals, Other Elemental & Alloys as Sheets, Rods, Drops, etc.	H,F GF	H,F GF						H,F G									H F						23																		
24	Metals and Metal Compounds, Toxic	S	S	S			S	S			S														24																	
25	Nitrides	GF HF	H,F E	H GF	H,E GF	GF H			U	H G	U	GF H	GF H	GF H				GF H	U	GF H	GF H	E				25																
26	Nitriles	H,GT GF	H,F GT	H							U											H P			S	GF H	26															
27	Nitro Compounds, Organic		H,F GT			H					H E											H,E GF				H,E GF		27														
28	Hydrocarbons, Aliphatic, Unsaturated	H	H F			H																	H E						28													
29	Hydrocarbons, Aliphatic, Saturated		H F																											29												
30	Peroxides and Hydroperoxides, Organic	H G	H E		H F	H G		H GT	H,F E	H,F GT		H,E GT	H,F GT					H E	H	E	H,F GT	H E	H G		H G	H,E GF	H,P GT		H P		30											
31	Phenols and Cresols	H	H F						H G										H P			GF H				GF H					H	31										
32	Organophosphates, Phosphothioates, Phosphodithioates	H GT	H GT						U		H E											H									U		32									
33	Sulfides, Inorganic	GT GF	HF GF	GT		H			E										H												H GT			33								
34	Epoxides	H P	H P	H P	H P	U		H P	H P		H P	H P	U								H P	H P	H P		H P	H P					H P	H P	U	H P	34							
101	Combustible and Flammable Materials, Miscellaneous	H G	H,F GT																			H,F G				H,F GF					H,F GT					101						
102	Explosives	H E	H E	H E					H E		H E			H E								H E	H E	H E	E	E					H E	H E		H E	H E	H E	102					
103	Polymerizable Compounds	P H	P H	P H					P H		P H	P H	U									P H	P H	P H	P H	P H					P H	P H		P H			H E	103				
104	Oxidizing Agents, Strong	H GT		H GT	H F	H F	H,F GT	H,F GT	H E	H,F GT		H,E GT	H,F GT	H F	H F		H F	H GT	H,F GT	H F	H,F GT	H,F E	H,F E	H F		H,F E	H,F GT	H E	H F	H F	H G	H F	H,F GT	H,F GT	H,F G	H,F G	H E	H,F GT	104			
105	Reducing Agents, Strong	H GF	H,F GT	H GF	H,F GF	H,F GF	H GF	H G				H GT	H F				H,F E	H E	H GF	H GF	H GF						H GF	H E			H E	H GF	H,GT GF		H	H GF	H E	H,P GF	H,F E	105		
106	Water and Mixtures Containing Water	H	H						G										H G			H GF	H GF		S	H GF								GT GF						GF GT	106	
107	Water Reactive Substances	<--------EXTREMELY REACTIVE!!!! DO NOT MIX WITH ANY CHEMICAL OR WASTE MATERIAL!!!!-------->																			<---------EXTREMELY REACTIVE!!!! DO NOT MIX WITH ANY CHEMICAL OR WASTE MATERIAL!!!! EXTREMELY REACTIVE!!!!------------->																				107
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	101	102	103	104	105	106	107

DATA SOURCES

Thermodynamic and chemical properties

From literature:

- J.B. Pedley, R.D. Naylor, and S.P. Kirby, "Thermochemical Data of Organic Compounds, Second Edition, Chapman and Hall, (1986).

- J.D. Cox, G. Pilcher, "Thermochemistry of Organic and Organometallic Compounds, Academic Press, London, UK, (1970).

- L. Bretherick, "Bretherick's Handbook of Reactive Chemical Hazards", Sixth Ed., Butterworths, 1999.

- CHETAH 7.2, The ASTM Computer Program for Chemical Thermodynamic and Energy Release Evaluation; Prepared by ASTM E27.07, also available as NIST Special Database 16, (1998).
  Also see: http://www.chetah.usouthal.edu/
  http://www.normas.com/ASTM/BOOKS/DS51C.html

- Harsbook's "Desktop Screening", that can be found at http://www.harsnet.de

Safety information

From Internet:

- http://ull.chemistry.uakron.edu/erd/
- http://www.ilo.org/public/english/protection/safework/cis/products/icsc/dtasht/index.html
- http://chemfinder.cambridgesoft.com/
- http://www.scirus.com/

MSDS

- From Internet:

- (general) http://www.ilpi.com/msds/#Internet
- http://www.cdc.gov/niosh/msds.html
- http://hazard.com/msds/index.php
- http://www.jtbaker.com/asp/Catalog.asp
- http://msds.pdc.cornell.edu/msdssrch.asp
- http://physchem.ox.ac.uk/MSDS/#MSDS

DATA
ANALYSIS
CARDS

If the reaction is a full batch, is there a justification for not being semi-batch?

STEP

CRITICAL FACTOR: Mistaken chemicals

CHECKLIST:

1. Is there the possibility of a dangerous mix formation (involving both reagents and products) due to: a) wrong order of adding?
   b) wrong chemicals used?
   c) wrong rate of addition?
   d) wrong quantities of chemicals used?

   If yes, go to 1.1); if no, go to 1.3); if unknown, CHECK IT!
   1.1) Is it controlled?
   If yes, go to 1.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   1.2) How is it controlled?
   1.3) Justify your answer.
2. Is a solvent used?
   If yes, go to 2.1); if no, go to 2.3); if unknown, CHECK IT!
   2.1) Is its amount controlled?
   If yes, go to 2.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   2.2) How is it controlled?
   2.3) Justify your answer.
3. Are catalysts or inhibitors used?
   If yes, go to 3.1); if no, go to 3.3); if unknown, CHECK IT!
   3.1) Is their concentration controlled?
   If yes, go to 3.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   3.2) How is it controlled?
   3.3) Justify your answer.

CRITICAL FACTOR: Autocatalytic reactions

CHECKLIST:

4. Is showing any of the substances involved (or a mixture of them) an autocatalytic or radical chain reactive behaviour?
   If yes, go to 4.1); if no, go to 4.3); if unknown, CHECK IT!
   4.1) Is it controlled?
   If yes, go to 4.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   4.2) How is it controlled?
   4.3) Justify your answer.

CRITICAL FACTOR: Segregation

CHECKLIST:

5. Is there the possibility of crystallisation or formation of a segregated phase in the reaction mixture (especially on cool down operations and at minimum jacket temperature)?
   If yes, go to 5.1) and then to 5.2); if no, go to 5.5); if unknown, CHECK IT!
   5.1) Can it affect thermal behaviour of the reaction mass or T control?
   If yes, go to 5.3); if no, go to 5.5); if unknown, CHECK IT!
   5.2) Is the phase thermally unstable?
   If yes, go to 5.3); if no, go to 5.5); if unknown, CHECK IT!
   5.3) Are there measures to manage or prevent it (mixing, separation, re-homogenisation, etc)?
   If yes, go to 5.4), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   5.4) Which?
   5.5) Justify your answer.

CRITICAL FACTOR: Accumulation

CHECKLIST:

6. Is the maximum dosing rate known?
   If yes, go to 6.1); if no, CHECK IT!
   6.1) Does it exceed the maximum safe dosing rate?
   If yes, REVIEW REACTOR SETUP; if no, go to 6.2); if unknown, CHECK IT!
   6.2) Justify your answer.
7. Is dosing interlocked in any way with mixing to always assure turbulent conditions?
   If yes, go to 7.1); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   7.1) How?
8. Will accumulation increase dramatically if the reaction temperature is low by 10K?
   If yes, go to 8.1); if no, go to 8.3); if unknown, CHECK IT!
   8.1) Is T control interlocked in any way with dosing rate?
   If yes, go to 8.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   8.2) How?
   8.3) Justify your answer.
9. In case of automatic dosing, is it interlocked with cooling system?
   If yes, go to 9.1); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   9.1) Can dosing be totally stopped (dosing set inherently safe)?
   If yes, go to 9.2); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!
   9.2) How?

CRITICAL FACTOR: Temperature Hazard

CHECKLIST:

10. Does cooling system work always below 80% of its maximum capacity?

    If yes, go to 10.1); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    10.1) How is it guaranteed?

11. Is T controlled when the reaction is ended but the reactor is still full?

    If yes, go to 11.1); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    11.1) How?

12. Is there the possibility of hot spots?

    If yes, go to 12.1); if no, go to 12.3); if unknown, CHECK IT!

    12.1) Can T control detect inhomogeneous distribution?

    If yes, go to 12.2); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    12.2) How?

    12.3) Justify your answer.

13. Is any kind of interlock between cooling system failure and dosage stop present?

    If yes, go to 13.1); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    13.1) How is it realised?

14. In which of the five criticality levels defined by the harsmeth methodology (according to Stoessel) is your process, using MAXTSAFE as safety limit value?

    NOTES: if |MAXTSAFE – MTSR| < 50º, a deeper analysis should be done to prevent possibly mistakes in the calculation of the limit value.

    If 1 or 2: the process is “thermally” SAFE, but the reaction mass should not be held for longer time under heat accumulation conditions.

    If 3: If the evaporative cooling is able to keep the reaction mass under control, check that the equipment is designed for that purpose; if not, a backup cooling system or quenching has to be previewed. If the process is performed in a close system, the apparatus must be designed for the maximum expectable overpressure or be equipped with a pressure relief device.

    If 4: as in 3, but the additional heat release due to the secondary reaction has to be taken into account. If the operation is performed in a close system, the T corresponding to the relief valve’s set pressure may not be much higher than the boiling point of the reaction mass.

    If 5: NEED OF PLANT and/or PROCESS MODIFICATIONS, in order to achieve a lower criticality level (reduce the concentration, change from batch to semi-batch, optimise semi-batch operating conditions in order to minimise the accumulation, change to continuous operation, etc).

GENERAL RECOMMENDATIONS

- As a general rule, exothermic reactions need always T, dosing and stirring control.
- Report on known quick ways to stop the desired reaction (extra cooling, chemical inhibition, venting, quenching, etc).
- Hot spots may be avoided by heating up not too quick and under turbulent flow conditions.
- Report on chemical substances able to influence the rate of reaction and substances that can poison catalysts and inhibitors or that can act as unexpected catalysts for the reaction (impurities, etc).
- The maximum temperature that can be reached in case of cooling failure (MTSR) depends on the type of reactor. For example in case of a batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the desired reaction. For a semi-batch reactor the MTSR is equivalent to the process temperature plus the adiabatic temperature rise of the "worst-case" accumulated reactants of the desired reaction.
- Some basic safety scenarios (as loss of stirring, loss of cooling, dosing control, etc) have to be studied for each step.

REACTION - Answers

Answers of the checklist

NOTE: mark the yes/no answers for each case and fill up, if necessary, the remaining answers.

STEP

CRITICAL FACTOR: Mistaken chemicals

1. a) If yes, 1.1) If yes, 1.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ______________________________

b) If yes, 1.1) If yes, 1.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ______________________________

c) If yes, 1.1) If yes, 1.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ______________________________

d) If yes, 1.1) If yes, 1.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ______________________________

2. If yes, 2.1) If yes, 2.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 2.3) ______________________________

3. If yes, 3.1) If yes, 3.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 3.3) ______________________________

CRITICAL FACTOR: Autocatalytic reactions

4. If yes, 4.1) If yes, 4.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 4.3) ______________________________

CRITICAL FACTOR: Segregation

5. If yes, 5.1) If yes, 5.3) If yes, 5.4) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 5.5) ____

5.2) If yes, 5.3) If yes, 5.4) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 5.5) ____

If no, 5.5) ____

CRITICAL FACTOR: Accumulation

6. If yes, 6.1) If yes, REVIEW REACTOR SETUP

If no, 6.2) ____

If no, CHECK IT!

7. If yes, 7.1) ____

If no, REVIEW YOUR SAFETY MEASURES

8. If yes, 8.1) If yes, 8.2) ____

If no, REVIEW YOUR SAFETY MEASURES

If no, 8.3) ____

9. If yes, 9.1) If yes, 9.2) ____

If no, REVIEW YOUR SAFETY MEASURES

If no, REVIEW YOUR SAFETY MEASURES

CRITICAL FACTOR: Temperature Hazard

10. If yes, 10.1) ____________________

If no, REVIEW YOUR SAFETY MEASURES

11. If yes, 11.1) ____________________

If no, REVIEW YOUR SAFETY MEASURES

12. If yes, 12.1) If yes, 12.2) ____________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 12.3) ____________________

13. If yes, 13.1) ____________________

If no, REVIEW YOUR SAFETY MEASURES

STORAGE - Checklists

STEP #

CRITICAL FACTOR: Mistaken chemicals

CHECKLIST:

1. Is there the possibility of a dangerous mix formation due to:
   a) wrong labelling?
   b) cleaning operations or reparation works?
   c) adding new chemicals in vessels already in use?
   d) possibility of contact between substances?

If yes, go to 1.1); if no, go to 1.3); if unknown, CHECK IT!

1.1) Are operators sufficiently trained to avoid it and, in d) case, safety interlocks used?

If yes, go to 1.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

1.2) How?

1.3) Justify your answer.

CRITICAL FACTOR: Autocatalytic reactions

CHECKLIST:

2. Is showing any of the substances stored an autocatalytic or radical chain reactive behaviour (as polymerisation)?

If yes, go to 2.1); if no, go to 2.4); if unknown, CHECK IT!

2.1) Is it controlled with inhibitors?

If yes, go to 2.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

2.2) Is their concentration controlled?

If yes, go to 2.3), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

2.3) How is it controlled?

2.4) Justify your answer.

CRITICAL FACTOR: Segregation

CHECKLIST:

3. Is there the possibility of formation of a segregated phase (due also to weather effects)?

    If yes, go to 3.1); if no, go to 3.4); if unknown, CHECK IT!

    3.1) Are the formed phases thermally stable?

    If yes, go to 3.4); if no, go to 3.2); if unknown, CHECK IT!

    3.2) Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?

    If yes, go to 3.3), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    3.3) Which?

    3.4) Justify your answer.

CRITICAL FACTOR: Temperature Hazard

CHECKLIST:

4. Is there the possibility of decomposition of any of the stored substances at ambient temperature?

    If yes, go to 4.1); if no, go to 4.4); if unknown, CHECK IT!

    4.1) Is a cooling device installed and T controlled in the storage site of each unstable substance?

    If yes, go to 4.2); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    4.2) Can T control detect inhomogeneous distribution?

    If yes, go to 4.3); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

    4.3) How?

    4.4) Justify your answer.

GENERAL RECOMMENDATIONS

- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Some basic safety scenarios (as loss of stirring, loss of cooling, longer storage period, missing of inhibitors, etc) have to be studied for each step.

STORAGE - Answers

Answers of the checklist

NOTE: mark the yes/no answers for each case and fill up, if necessary, the remaining answers.

STEP

CRITICAL FACTOR: Mistaken chemicals

1. a) If yes, 1.1) If yes, 1.2) ____________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____________________

b) If yes, 1.1) If yes, 1.2) ____________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____________________

c) If yes, 1.1) If yes, 1.2) ____________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____________________

d) If yes, 1.1) If yes, 1.2) ____________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____________________

CRITICAL FACTOR: Autocatalytic reactions

2. If yes, 2.1) If yes, 2.2) If yes, 2.3) ____________________

If no, REVIEW YOUR SAFETY MEASURES

If no, REVIEW YOUR SAFETY MEASURES

If no, 2.4) ____________________

CRITICAL FACTOR: Segregation

3. If yes, 3.1) If yes, 3.4) ____

If no, 3.2) If yes, 3.3) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 3.4) ____

CRITICAL FACTOR: Temperature Hazard

4. If yes, 4.1) If yes, 4.2) If yes, 4.3) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, REVIEW YOUR SAFETY MEASURES

If no, 4.4) ____

PROCESS - Checklists

STEP

CRITICAL FACTOR: Mistaken chemicals

CHECKLIST:

1. Is there the possibility of a dangerous mix formation due to:
    - a) wrong labelling or picking from storage?
    - b) cleaning operations or reparation works?
    - c) unavailability of chemicals?
    - d) possibility of contact between substances?

If yes, go to 1.1); if no, go to 1.3); if unknown, CHECK IT!

1.1) Are operators sufficiently trained to avoid it and, in d) case, safety interlocks used?

If yes, go to 1.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

1.2) How?

1.3) Justify your answer.

CRITICAL FACTOR: Autocatalytic reactions

CHECKLIST:

2. Is showing any of the substances involved an autocatalytic or radical chain reactive behaviour?

If yes, go to 2.1); if no, go to 2.4); if unknown, CHECK IT!

2.1) Is it controlled with inhibitors?

If yes, go to 2.2), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

2.2) Is their concentration controlled?

If yes, go to 2.3), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

2.3) How is it controlled?

2.4) Justify your answer.

CRITICAL FACTOR: Segregation

CHECKLIST:

3. Is there the possibility of crystallisation or of formation of a segregated phase (especially on cool down operations)?

If yes, go to 3.1); if no, go to 3.4); if unknown, CHECK IT!

3.1) Are the formed phases thermally stable?

If yes, go to 3.4); if no, go to 3.2); if unknown, CHECK IT!

3.2) Are there measures to manage or prevent the segregation (mixing, separation, re-homogenisation, etc)?

If yes, go to 3.3), if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

3.3) Which?

3.4) Justify your answer.

CRITICAL FACTOR: Temperature Hazard

CHECKLIST:

4. Is there the possibility of hot spots?

If yes, go to 4.1); if no, go to 4.3); if unknown, CHECK IT!

4.1) Can T control detect inhomogeneous distribution?

If yes, go to 4.2); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

4.2) How?

4.3) Justify your answer.

5. Is there the possibility of decomposition of any substance at process temperature?

If yes, go to 5.1); if no, go to 5.3); if unknown, CHECK IT!

5.1) Is T controlled?

If yes, go to 5.2); if no, REVIEW YOUR SAFETY MEASURES; if unknown, CHECK IT!

5.2) How?

5.3) Justify your answer.

GENERAL RECOMMENDATIONS

- Hot spots may be avoided by heating up not too quick and under turbulent flow conditions.
- Report on chemical substances that can act as unexpected catalysts for exothermic reactions (impurities, etc).
- Some basic safety scenarios (as loss of stirring, missing of inhibitors, etc) have to be studied for each step.

PROCESS - Answers

Answers of the checklist

NOTE: mark the yes/no answers for each case and fill up, if necessary, the remaining answers.

STEP

CRITICAL FACTOR: Mistaken chemicals

1. a) If yes, 1.1) If yes, 1.2) ____

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____

b) If yes, 1.1) If yes, 1.2) ____

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____

c) If yes, 1.1) If yes, 1.2) ____

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____

d) If yes, 1.1) If yes, 1.2) ____

If no, REVIEW YOUR SAFETY MEASURES

If no, 1.3) ____

CRITICAL FACTOR: Autocatalytic reactions

2. If yes, 2.1) If yes, 2.2) If yes, 2.3) ________________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, REVIEW YOUR SAFETY MEASURES

If no, 2.4) ____

CRITICAL FACTOR: Segregation

5. If yes, 3.1) If yes, 3.4) ______________________________

If no, 3.2) If yes, 3.3) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 3.4) ______________________________

CRITICAL FACTOR: Temperature Hazard

3. If yes, 4.1) If yes, 4.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 4.3) ______________________________

4. If yes, 5.1) If yes, 5.2) ______________________________

If no, REVIEW YOUR SAFETY MEASURES

If no, 5.3) ______________________________