Revisiting Thermal Safety

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Although the current trend in Fine and Specialty Chemistry is to gradually replace traditional semi-batch processes with Flow Chemistry processes, which are safer, cleaner, and faster, most production continues to be semi-batch. This paper is devoted to recovering the basic concepts of thermal safety of such semi-batch processes. Experimental techniques such as reaction calorimetry, differential scanning calorimetry and accelerating rate calorimetry are the key to safety studies. The data obtained allow the criticity of a process to be classified into the five Stoessel's classes, from less to most dangerous. The safety improvement strategy of a reaction process always consists of trying to lower its criticality class.

KEYWORDS: Fine Chemicals, Safety, Runaway prevention, Criticality classes.

Aunque la tendencia actual en química fina y de especialidades es reemplazar gradualmente los procesos semi-continuos tradicionales con procesos de química de flujo, que son más seguros, limpios y rápidos, la mayor parte de la producción continúa siendo semi-continua. Este trabajo está dedicado a recuperar los conceptos básicos de seguridad térmica de este tipo de procesos semi-continuos. Las técnicas experimentales, como la calorimetría de reacción, la calorimetría diferencial de barrido y la calorimetría autoacelerada, son la clave para los estudios de seguridad. Los datos obtenidos permiten clasificar la criticidad de un proceso en las cinco clases de Stoessel, de menor a mayor peligrosidad. La estrategia de mejora de la seguridad de un proceso de reacción consiste siempre en intentar bajar su clase de criticidad.

PALABRAS CLAVE: Química fina, Seguridad, Prevención de runaway, Clases de criticidad.

INTRODUCTION

These days, we authors are sorting and scanning many documents at our offices. They are the testimony of a long and extremely rich history. We want to focus our attention on just two of them.

The first is all the documentation for a course that we organized in 1989 within the framework of UNTEC, the Universitat Tècnica d'Estiu de Catalunya and organized by the Fundació Narcís Monturiol. The setting was the extraordinary Palau de Mar i Cel in Sitges. The course was focused on Fine Chemistry in general and concentrated on its three key factors: Safety - Quality - Environment. One of the most repeated drawings was that of Figure 1. We think it is still very alive!

Great professionals and extraordinary personalities participated. We can highlight Miquel Gassiot, at that time managing director of IQS and who shortly after would be the rector of the Universitat Ramon Llull; Ferran Relea, Director of the Junta de Residus; Iñaki Borrell, IQS professor; Alberto Benuzzi of the JRC of the European Commission; Alfredo Noman, General Director of Industrial Safety of the Generalitat de Catalunya, or Artur Blabé, General Secretary of CIRIT, among others. The contributions of Dow Chemical, IFP, Basf and some local consultants were crucial.

The second document corresponds to a course of lesser format, but not of lesser quality, organized at IQS on 1990. The title of the course was "Friendly Batch-Chemical Plants". In this case, the chosen image (Figure 2) was somewhat cryptic, a nod to the cabalas of Ramon Llull, who lends his name to our university. The best safety experts in Europe, if not the world, participated in it. Even at the risk of forgetting someone we try to list them. Besides the authors [1-4], the professors were C. von Carsten (Boehringer Ingelheim), S. Contini (JRC, Ispra), J. Steinbach [5] (Schering AG), J.A. Barton [6] (Health and Safety Executive, UK), F. Stoessel [9]

(Ciba-Geigy AG), R. Riesen [10,11] (Mettler-Toledo AG), P. F. Nolan [6, 7, 12] (South Bank Polytechnic, London), J.M. Zaldívar [13–15] (JRC, Ispra), P. Cardillo [16–18] (Stazione Sperimentale per i Combustibili), A. Benuzzi [19] (JRC, Ispra), D. Al-Khudhairy (JRC, Ispra), J. Signh [20–22] (HEL), A. Cilleruelo and P. Kramer (Siemens, SA) and H. Hernández [14, 23, 24] (JRC, Ispra). Spectacular, right?

Those were also times in which the authors actively participated in the now defunct European Contact Group on Ruanaway Reactions of the European Commission, in the Funktionale Sicherheit - Anlagensicherheit und Prozessleittechnik group of the German society Dechema or in the, still in force, European Process Safety Group, linked to IChemE.

The Fine and Specialty Chemicals Industry has evolved a great deal since then. Technological advances are immense. It is enough to mention the already unstoppable irruption of Flow Chemistry [25-27] or Process Analytical Technologies with all the

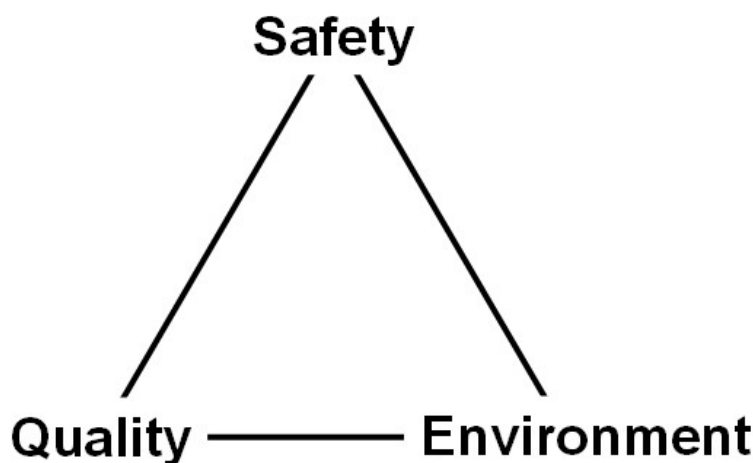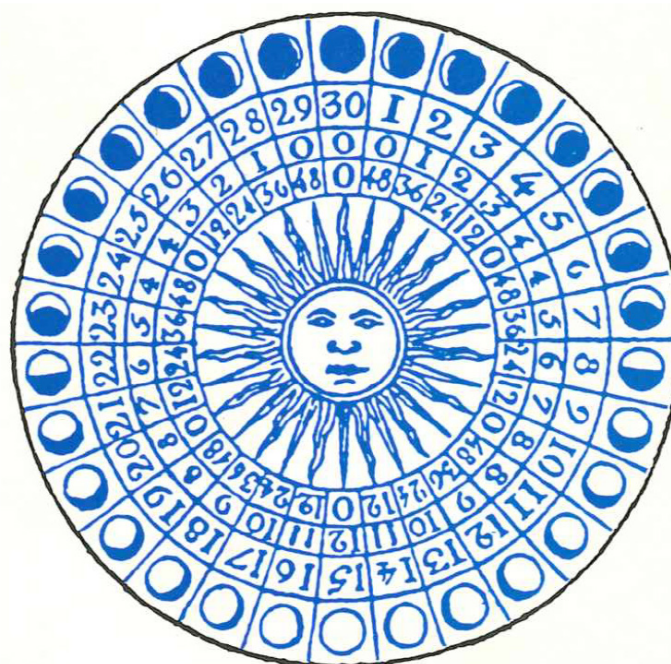FIGURE 1. Motto of the UNTEC'89 course on Fine Chemistry

FIGURE 2. Friendly Batch Chemical Plants course cover

advantages they offer. However, most of the production remains the same as it was seventy years ago. In the words of J. Woodcock, FDA area director, at the AAPS Annual Meeting, October 2011: "Right now, manufacturing experts from the 1950s would easily recognize the pharmaceutical manufacturing processes of today. It is predicted that manufacturing will change in the next 25 years as current manufacturing practices are abandoned in favour of cleaner, flexible, more efficient continuous manufacturing".

Given this scenario, we believe that it is necessary to remember the basic safety concepts of semi-batch processes, to try to contribute to guaranteeing the safety of the industry. We also want to remember in this article the teachings of the great masters of that time. They are teachings that, far from going out of fashion, continue to be very necessary. For all that, we dedicate this article to put them back on paper.

DISCUSSION

The most feared phenomenon of a semi-batch process is the so-called runaway. It is a difficult term to translate into any Romance language. The authors believe that it comes from the expression that any person in a chemical plant would shout when seeing that the thermometer and the pressure gauge of a reactor rise uncontrollably: run away!

But what is a runaway? Figure 3 shows the expected temperature profile of a standard semi-batch process. Initially, the reactor, empty and at room temperature (Tamb), is filled with the solvents and a part of the reagents or catalysts (Initial loading). Once the charge is finished, it is heated up to the process temperature (Tp) (Heating-up) and the necessary reagents or catalysts are dosed to complete the reaction (Dosing). After the time necessary for the reaction to complete (Maturation), it is cooled again to room temperature

(Cooling-down) and the final product is separated and purified (Work-up).

When things go wrong, the scenario changes drastically. Let us imagine that the failure occurs at the instant in which there is in the reactor the maximum accumulation of unreacted materials (Figure 4). The failure consists in losing the ability to refrigerate the reactor. Due to its small surface/volume ratio, the reactor now

behaves as an adiabatic vessel. Like a perfectly insulated Dewar flask. The heat released by the synthesis reaction raises the temperature to a value known as MTSR (maximum temperature due to the synthesis reaction). These temperature increases of temperature ($\Delta_{ad}T$) are usually moderate and, in many cases, would not cause more than a scare.

However, MTSR can initiate side

FIGURE 3. Expected (normal) temperature profile of a common semi-batch process
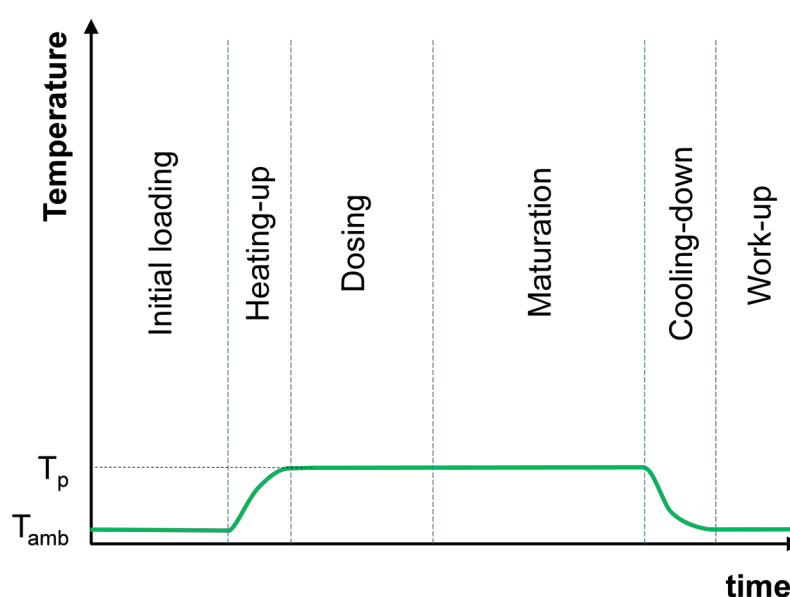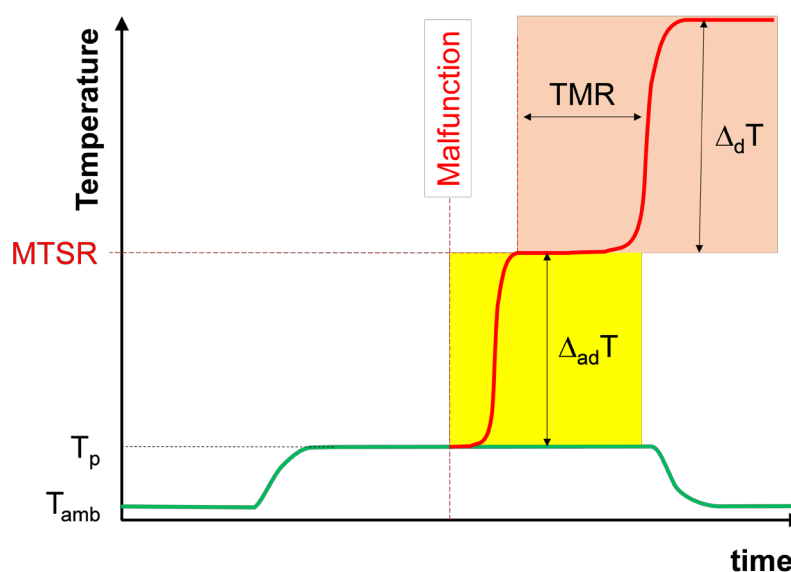

FIGURE 4. Temperature profile of a runaway

reactions, usually decomposition reactions. These generate energies that can be ten times that of the synthesis reaction. They can have more or less long latency periods or time to maximum rate (TMR), but they are very fast and very often self-accelerate. They generate gases and, therefore, very rapid pressure increases. The result can be the (thermal) explosion of the reactor.

If we go back to our 80's classics [6, 7], we will see how 34 % of the runaways are due to not knowing what happens in the reactor. Another study (Cardillo) places this factor at 31 % [18]. In any case, the fact that approximately one-third of the cases are due to ignorance of the chemistry that has led to an accident is extremely high and alarming. Indeed, it must be recognized that synthetic chemists rarely concern themselves with the thermodynamics of the processes they perform.

Determining the basic parameters of the safety of a chemical reaction is not difficult. It is enough to select the appropriate means. The heat of reaction and the specific heat of the reaction mixture, which allow the adiabatic temperature increase to be

» The safety improvement strategy of a reaction process always consists of trying to lower its criticality class

calculated, is obtained with great precision by reaction calorimetry. It is not a very widespread technique, but it is key. At IQS we have a service that offers it. Reaction calorimetry makes it possible to reproduce the conditions of the industrial process and obtain the heat balance of the reactor. In addition, reaction calorimetry gives information very useful for scaling up the process, such as the heat transfer coefficient or the accumulation of unreacted materials.

The determination of the TMR is key to evaluate the safety of a process. In fact, it is the time available to apply measures to prevent the explosion of the reactor. There are various criteria for this subject. Formerly, it was accepted that if the TMR was greater than 8 hours, it was already possible to prepare and apply all the

necessary measures to avoid the final explosion. Currently, the TMR must be greater than 24 hours. It is usual to define maximum safety temperature (MAXST) as that temperature at which the TMR is 24 hours.

There are several ways to safely determine the TMR. The simplest is through a kinetic adjustment of DSC measurements [28–30]. DSC measurements in high-pressure crucible also allow for the detection of unknown reactions, which can contribute to reactor explosion [31].

However, the DSC measurements do not provide a very important datum: the pressure evolution along the runaway. To determine the maximum pressure that is going to be reached and the maximum speed of pressure increase, it is necessary to go to the Accelerating Rate Calorimetry

FIGURE 5. Stoessel's classes of criticality
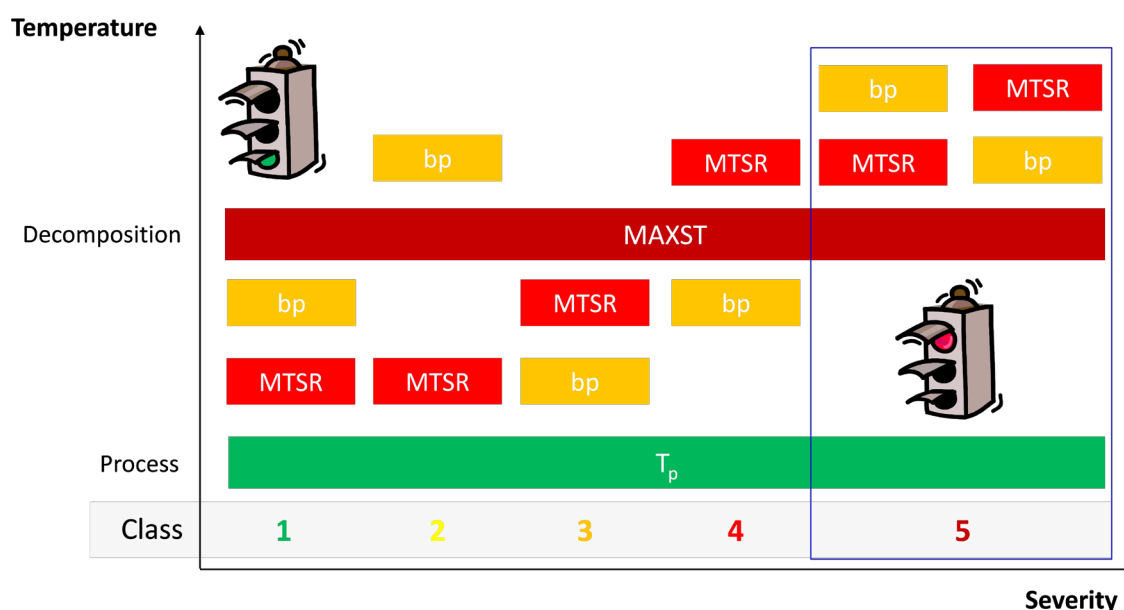
(ARC). The pressure data will be useful in designing pressure relief systems such as safety valves or bursting discs [32].

Finally, a very convenient and visual way of classifying a synthesis process is the one proposed by F. Stoessel [9, 33] taking into account the relative position of four temperatures: Tp, MTSR, the boiling point (bp) and MAXST (Figure 5). This allows defining five classes of criticality of the processes. For example, the loss of thermal control in a reactor where a class 1 process is carried out would not have any consequence from the point of view of safety. MTSR would not even cause the reaction mixture to boil. In contrast, in a class 5 process, the MAXST would be reached and a serious emergency would occur. The safety improvement strategy of a reaction process always consists of trying to lower its criticality class.

CONCLUSIONS

Although the current trend in Fine and Specialty Chemistry is to gradually replace traditional semi-batch processes with Flow Chemistry processes, which are safer, cleaner, and faster, most production continues to be semi-batch.

Thermal safety analysis of semi-batch processes requires the application of experimental techniques such as reaction calorimetry, differential scanning calorimetry and accelerating rate calorimetry.

The data obtained allow the criticity of a process to be classified into five classes, from less to most dangerous. The safety improvement strategy of a reaction process always consists of trying to lower its criticality class.

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AAPS: American Association of Pharmaceutical Scientists.
CIRIT: Comissió Interdepartamental de. Recerca i Innovació Tecnològica
DSC: Differential Scanning Calorimetry
JRC: Joint Research Center
MAXST   Maximum temperature of safety
MPEG: Methyl Polyethylene Glycol
MTSR: Maximum Temperature due to the Synthesis Reaction
Tamb: Ambient Temperature
TMR: Time to Maximum Rate
Tp: Process Temperature
Δ_ad T: Adiabatic Temperature Increase (Synthesis Reaction)

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