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The interpretation of thermal analytical data in the determination of a safe operating envelope for the pilot plant scale-up of chemical processes

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Abstract

The use of various thermal analytical techniques as screening tools to identify process hazards during early process development has been well documented. This paper will discuss the interpretation of this thermal screening data, with respect to processing conditions, to determine the safe operating parameters/safe operating envelope for pilot plant operations.

The early identification of thermal hazards associated with a process, such as large/rapid heats of reaction, exothermic decompositions and the potential for thermal runaways, facilitates process modifications before any large scale operations are undertaken. Merck has developed a three-tier safety assessment program which identifies thermal hazards and evaluates them for potential initiation during processing.

The correct interpretation of this thermal data is critical in determining the risk for thermal runaway. The factors which must be evaluated are: (1) the size and rate of the heat release; (2) the size and rate of pressure generation; (3) whether gases generated during decomposition are condensable; and (4) the heat of reaction and its potential impact upon exothermic decompositions present in the reaction. Once these potential hazards are identified and evaluated, it can be determined whether a safe operating envelope exists or if the process must be modified to eliminate the potential thermal hazard. Examples will be presented where these principles have been applied.

Keywords: Thermal analysis; Process safety; Thermal hazards; Safe operating envelope

1. Three-tier testing program

A critical aspect in the development of a chemical process is the identification of energetic materials and the evaluation of the resulting potential risk of a thermal runaway. A three-tier assessment program used at Merck identifies both thermal and chemical hazards and evaluates the potential risk of thermal runaway. This program determines if a safe operating envelope can be developed using the tested chemistry or if new chemistry must be developed. In tiers I and II, various thermal analytical techniques are used to identify hazards which can lead to thermal runaways. Using differential thermal analysis (DTA), differential scanning calorimetry (DSC), Mettler's RC1 calorimeter and FAI's reactive system screening tool (RSST), a process safety screen can be performed rapidly, providing information on heats of reaction and exothermic oxidation/decomposition reactions including initiation temperatures and the accompanying rates of temperature and pressure increases. Tier III

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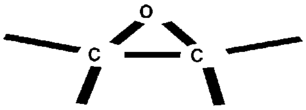
provides for a review of the identified chemical and thermal hazards and heat of reaction data in the context of the process description and in conjunction with a hazards analysis review. The hazards analysis review, provided by the process development team, identifies chemical hazards and potential processing hazards and is used to help define an intrinsically safe process. A minimum of tiers I and III is required for all processes before any pilot plant operations are undertaken and when any changes are made to existing pilot plant processes.

Tier I testing identifies potential chemical and thermal hazards which could lead to thermal runaway. The evaluation begins with a specially designed operational hazards safety data sheet, filled out jointly by the chemist and chemical engineer, which is used to identify chemical and potential processing hazards. This data sheet provides information on the known chemistry, potential toxicity, heats of reactions, balanced equations, identification of reaction by-products, interactions with service fluids and interactions between chemicals in the process. The structure of starting chemicals, intermediates and final products are also evaluated to identify potentially hazardous compounds (as shown in Table 1). This data sheet also includes a hazardous situation checklist which includes a checklist to identify undesirable scenarios and an expected and deviation reaction tables. Once this data sheet is evaluated the second part of the tier I evaluation, the identification and quantification of exothermic activity for both process samples and heats of reaction, is started. DSC and DTA are used to identify and quantify exothermic activity in process samples. These two techniques provide information on the size, rate of heat release and initiation temperatures of exothermic decompositions or oxidations. Various calorimetric test methods to evaluate heats of reactions and a sealed RSST [1] are used to quantify the heat release/gas generations associated with the intrusion of water/jacket services into the reaction mixtures.

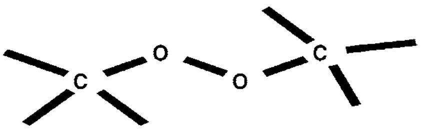
Tier II evaluates the risk of potential thermal runaway which could arise from the exothermic decompositions,

Table 1
Potentially hazardous structures

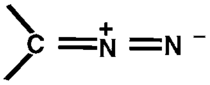
ACETYLENE



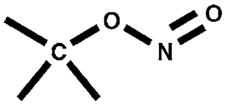
EPOXIDE



DIALKYL PEROXIDE



DIAZO COMPOUND



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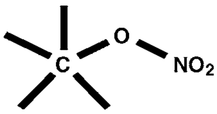
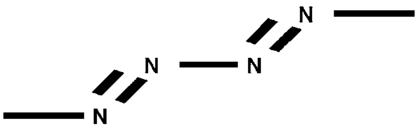
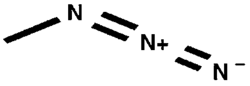


ACYL & ALKYL NITRATES

AZO COMPOUNDS



TETRAZOLES



AZIDES

Table 2
Determination of the need for tier II level testing

Exothermic initiation temperature versus operating temperature (°C)			Size of exotherm (cal/g)			Estimated rate of exothermic heat release			Size of heat input and size and ease of control of exothermic heats of reaction				
0 < 50	≥50 < 100	≥100	<10	≥10 < 25	≥25	Slow	Moderate	Rapid/det.	3[a]	4[b]	5[c]	6[d]	7[e]
X					X			X	A/B[f]	A/B	A/B	A/B	A/B
X				X				X	A/B	A/B	A/B	A/B	A/B
	X				X			X	B	A/B	A/B	A/B	A/B
		X			X			X	B	A/B	A/B	A/B	A/B
X					X		X		B	A/B	A/B	A/B	A/B
X				X			X		B	A/B	A/B	A/B	A/B
	X				X		X		B	A/B	A/B	A/B	A/B
	X			X				X	B	A/B	A/B	A/B	A/B
	X			X			X		B	A/B	A/B	A/B	A/B
		X			X		X		B	A/B	A/B	A/B	A/B
		X		X				X	B	A/B	A/B	A/B	A/B
X					X	X			B	A/B	A/B	A/B	A/B
		X		X			X		B	B	A/B	A/B	A/B
X				X		X			B	B	B	A/B	A/B
	X				X	X			B	B	B	A/B	A/B
	X			X		X			B	B	B	B	A/B
X			X					X	NT[g]	B	B	B	B
	X		X					X	NT	B	B	B	B
		X			X	X			NT	B	B	B	B
X			X				X		NT	NT	B	B	B
	X		X				X		NT	NT	NT	B	B
		X		X		X			NT	NT	NT	NT	B
		X	X					X	NT	NT	NT	NT	NT
	X		X			X			NT	NT	NT	NT	NT
X			X			X			NT	NT	NT	NT	NT
		X	X				X		NT	NT	NT	NT	NT
		X	X			X			NT	NT	NT	NT	NT

These guidelines should be used as guidelines in determining required tier II testing. Every sample should be individually assessed and not simply assigned to a specific category as presented in this table.

[a] No heat input to sample re-batch temperature ambient or less and no exothermic heat of reaction.

[b] Either low heat input or a small easily controllable heat of reaction, one or the other not both.

[c] Low heat input and a small easily controllable heat of reaction, both are allowed.

[d] Low heat input and a moderate easily controllable heat of reaction, both are allowed.

[e] Any high heat input or a moderate/high difficult to control heat of reaction regardless of any other low heat input or small/moderate easily controllable heat of reaction.

[f] A: rates of temperature and pressure increases (RSST/VSP/Radex testing) associated with the exothermic decomposition must be determined; B: SSIA or SSAD testing must be done to determine the initiation temperature of the exothermic decomposition.

[g] No tier II testing required.

heats of reactions and the heat releases associated with water/jacket service intrusions which were identified in tier I testing. Various test methods are used to identify exothermic onset temperatures, determine rates of temperature and pressure releases associated with the decomposition and identify potential shock sensitivity. Initiation temperatures are determined using isothermal age techniques such as the Merck small scale isothermal age technique [2] or dewar ages. The rate of temperature increase and pressure generation and rates are determined using the RSST. These tests determine the potential for and results of initiation of the exothermic decomposition during the processing. Samples with heat releases >100 cal/g are also subjected to drop weight testing to determine the potential for shock sensitivity.

The information, generated in the tiers I and II evaluations, is used in tier III to determine if a safe operating envelope can be developed in which the material can be safely handled or if changes in chemistry and/or operating procedures are required to control the potential for thermal runaway and allow for safe scale-up operations. The basic criteria looked at in the determination for the need for tier II testing are exothermic initiation temperature versus operating temperature, the size of the exotherm, the estimated rate of exothermic heat release, the size of the heat input and the ease of control of exothermic heats of reaction. The basic guidelines for the determination for the need for tier II testing are presented in Table 2 [3].

Tier III identifies an intrinsically safe process through several steps. In the first step, potential chemical and thermal hazards are identified and reviewed in conjunction with the factors involved in thermal runaways and the causes of thermal runaways. Next the implications of these hazards on pilot plant scale-up are determined by reviewing them in context to the process description and the data provided in the safety data sheet. It is then determined if operating restrictions can provide for a safe operating envelope or if alternate chemistry must be developed to provide for an intrinsically safe process. Table 3 provides a review of chemical hazards, thermal hazards and factors involved in thermal runaways and Table 4 for operating procedures which can be controlled and the types of process chemistry changes which have been used at Merck.

There are five main classifications of processes which contain exothermic decompositions: (1) those which are shock sensitive, where the shock sensitivity cannot be eliminated by dilution/solubilization or inplace destruction, and for which new chemistry must be developed; (2) those for which vent sizing is not possible, where alternate chemistry can not be developed which require the design of a continuous reaction system or emergency quench system; (3) those for which existing pilot plant venting is satisfactory and for which a high level of technical coverage is required; (4) those for which there is a low rate of pressure increase and little or no residual pressure for which the problem is loss of yield and not thermal

Table 3
Factors used in identifying an intrinsically safe chemical process

Chemical hazards	Toxicity Water reactive Chemical interactions Vapor phase reactions Toxic gas by-product Incompatibility of process streams and materials of construction
Thermal hazards	Size and rate of temperature increase Size and rate of pressure generation Residual pressure Initiation temperature versus operating temperature Thermally unstable process intermediates
Factors in thermal runaways	Size, rate and initiation temperature of heat release (decomposition/heat of reaction) Pressure generation (condensable/non-condensable) Vapor phase reaction Loss of process control Loss of solvent barrier Water/jacket service intrusion

Table 4
Control of operating procedures and types of process changes used to control potential thermal hazards

Controllable operating procedures	Limit reaction temperature Limit concentrations Dilution Limiting rates of addition Design of a continuous reaction system Extraction of highly exothermic streams Emergency quench Equipment venting[a] Equipment locks[a] Facility construction[a]
Changes to process chemistry	Revised isolations Non-isolation of intermediates Replacement of starting materials to prevent formation of hazardous intermediates or to eliminate hazardous starting materials Solubilization of shock sensitive products Replacement of a solvent system to provide a large heat sink Inplace destruction of a hazardous by-product Development of new chemistry to avoid formation of a shock sensitive chemical

[a] Not commonly used in pilot plants and are replaced with "highly trained technical coverage".

runaway; (5) those for which the thermal hazard is related to the heat of reaction. The basic guidelines and examples for these scenarios are presented below.

2. Determination of a safe operating envelope for pilot plant processes

2.1. Potentially shock sensitive compounds which require new or revised chemistry

Examples: The potential shock sensitivity of the following compounds was eliminated through the following actions: dodecylbenezesulfonyl azide–limiting concentration; peracetic acid—solubilized by the addition of acetic acid; an oxime by-product—destroyed in the reaction before it precipitated; an oxime-tosylate—brought forward as a solution to the next step to eliminate its isolation; R-dioxybenzene concentration replaced with an extraction; and a nitrosulfonylchloride replaced with a nitrosulfonamide.

2.2. Continuous reaction system

Highly energetic compound/reaction mixture for which vent sizing is not possible, initiation temperature is at or below the operating temperature and alternative chemistry cannot be used or found.

Example: A continuous reactor system was developed for a process in which there was a large heat release accompanied by extremely rapid and violent rates of temperature and pressure increases which made the reaction unventable. The majority of this heat release was associated with a polymerization, with the remaining heat being attributable to the heat of reaction. An adiabatic dewar age indicated that there was a slow and continuous heat release which initiated at ∼50 °C which was capable of raising the batch ∼2 °C and upon approaching ∼80 °C the rate of heat release was sufficient to initiate the polymerization of the batch with a heat release >200 cal/g. The key to the successful scale-up of this process, which is run at the exothermic decomposition onset temperature, was the development of a continuous reactor system in which the use of a cold feed and the removal of the warm product provided for heat removal. An emergency quench procedure was also in place to stop any potential thermal runaway. In addition, the reactor was ventable due to the small amount of product present at any time.

2.3. Restrict operating conditions and provide a high level of technical coverage

Compound/reaction mixture in which the vent size in the pilot plant is satisfactory for rates of temperature and pressure increases associated with the exothermic decomposition. Run the chemistry as is, restrict the operating temperature and conditions while providing a high level of technical coverage.

Example: A fully vented reaction system and a maximum operating temperature of 40 °C were recommended for a reaction in which there was an exothermic decomposition which was accompanied by rapid rates of temperature increases along with moderate rates of pressure increases which were ventable with the existing vent size in the pilot plant equipment. Isothermal and adiabatic RSST ages indicated that there was no decomposition at 50 °C. A high temperature alarm set at 40 °C and supervisory coverage on the floor were required during the processing.

2.4. No operation restrictions

No operating restrictions are placed on compound/reaction mixtures with any rate of temperature increase which are accompanied by low rates of pressure increases and little or no residual pressure. There are warnings provided that there will be a loss of product if the exotherm is initiated during processing.

Example: A compound had a low temperature exothermic decomposition which was accompanied by low rates of temperature increase. The maximum rate of pressure increase was <1.0 psi/min and the residual pressure was <1.0 psi. A recommendation to carefully control the process temperature was made to avoid the loss of product.

2.5. Revision due to uncontrollable heat of reaction

Example: The original process called for a controlled addition of peroxide at 30 °C. An RC1 calorimetry run indicated that the heat generation was at a maximum after ∼40% addition of the peroxide and that the concentration of the unreacted peroxide continued to increase throughout the addition period.

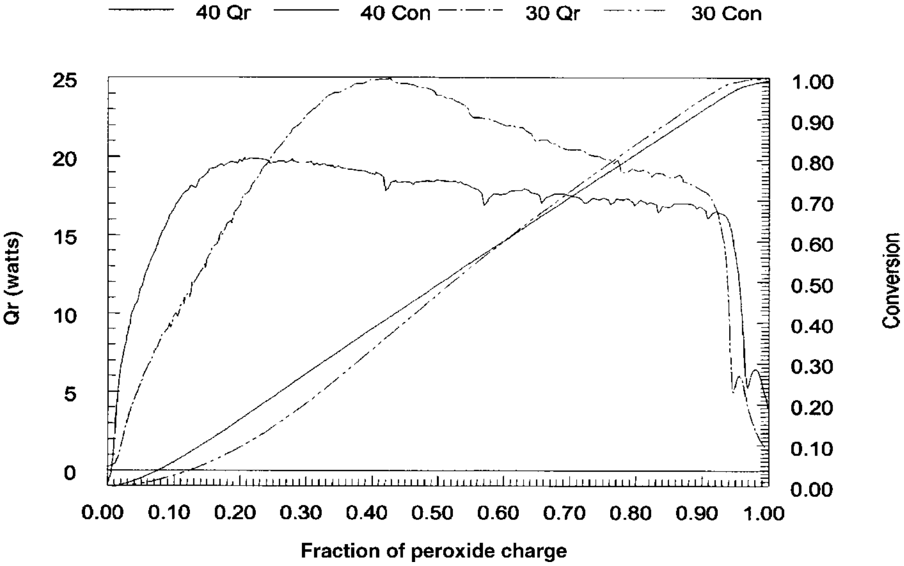


Fig. 1. Hydrogen peroxide addition.

This presented the possibilities of a sudden release of excess energy and/or a rapid release of oxygen from the decomposition of peroxide which could result in a flammable vapor phase. The revised procedure called for an increase in the reaction temperature to 40 °C, which resulted in a reduction in the maximum heat flow and results in a more uniform heat flow as shown in Fig. 1 [4].

2.6. Revision of existing chemistry

2.6.1. Determination that a starting material was unstable

Example: During two laboratory runs of a cyclization there were incidents of bumping with evidence of polymerization. Thermal testing indicated that the size of the polymerization exotherm was unpredictable and that air dramatically increased the size of the polymerization exotherm and lowered the onset temperature and time to thermal runaway. Additional testing indicated that the problem was the result of an unstable starting material which was used in a 3:1 ratio. Alternate chemistry was developed which eliminated the unstable starting material and resulted in the process having no significant thermal hazards.

3. Conclusion

Merck has successfully utilized this three-tier program to identify intrinsically safe processes for over 10 years. The testing scenarios presented in this paper should be used as guidelines and all processes should be evaluated on a case by case basis. A “safe operating envelope” should be individually determined for each process and not simply assigned to a specific example or category as presented in this paper.

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