



Process Safety and Hazard Assessment

Avoiding Incidents in the Lab and in the Plant

METTLER TOLEDO

Process Safety and Hazard Assessment From Early Development to Manufacturing

The importance of process safety in the chemical and pharmaceutical industries cannot be overstated. Even from relatively minor incidents, financial losses mount up due to lost production and reduced throughput, repair and replacement of damaged equipment, exposure of personnel to hazardous and highly potent materials, as well as regulatory filing of accident reports. For serious accidents, these financial losses amount to millions of dollars, and in the case of the most tragic accidents, the deaths and injuries of employees and neighbors add an additional element of loss in company morale and reputation that goes far beyond the financials.



Chemical Synthesis System EasyMax™

METTLER TOLEDO is dedicated to reducing incidents and accidents through early identification and thorough analysis of thermal hazard risks in chemical processes. Fundamental understanding of the energy release of both desired reactions and possible side reactions is needed for the assurance of safe scale-up and operation of chemical reactions.

Early Identification of Thermal Risks

Early identification of thermal risk is the key to ensuring that the reaction will never be operated on a scale that can cause an incident. Some highly exothermic synthesis reactions, such as nitrations, polymerizations or those involving organometallic reagents, are obvious targets for thermal hazard analysis.

Other reactions may have risks that are more process related – but just as real. Especially when dealing with unfamiliar early phase chemistries or processes it's crucial to detect potential thermal risks as early as possible.

Automated lab reactor systems, such as the EasyMax™, LabMax® or the RC1e® provide detailed and precise information helping to identify potential hazards in chemical development at an early stage.

Reaction analysis, using *in-situ* ReactIR™ technology, provides characterization of reaction pathways and unstable intermediates that may present significant decomposition threats in the case of undesired thermal accumulation. An early understanding of these process limitations enables better decision making

Significant exotherm Reactor	Heat 30 W/L Tr-Tj (°C)
100-250 mL round-bottom flask	2
1 Liter jacketed vessel	5
250 Liter	16
1000 Liter	26
6300 Liter	44

and a faster route to an optimized, safe and scalable process.

Ensure a Safe Process Design

Detailed process safety investigations are necessary to assess the thermal risks of critical exothermic processes. Thus, key questions need to be addressed such as:

- Is your plant or lab reactor able to control the process under normal operating conditions?
- What are the ramifications related to abnormal operating conditions?
- Are there any unstable intermediates that may accumulate?
- How do you optimize the balance between the inherent risks and the economic performance of the process?

METTLER TOLEDO RC1e® technology has been the “Gold Standard” of Reaction Calorimetry for over 20 years, providing accurate measurement of heat profiles and the enthalpy of the desired reaction under plant-like process conditions. Reaction monitoring, with probe-based ReactIR™ mid-infrared technology, provides further safeguards through the real-time identification of reaction progress, including measurement of reaction initiation and completion, formation of undesirable or hazardous byproducts, and accumulation of reagents and intermediates that may raise the risk of thermal runaway.

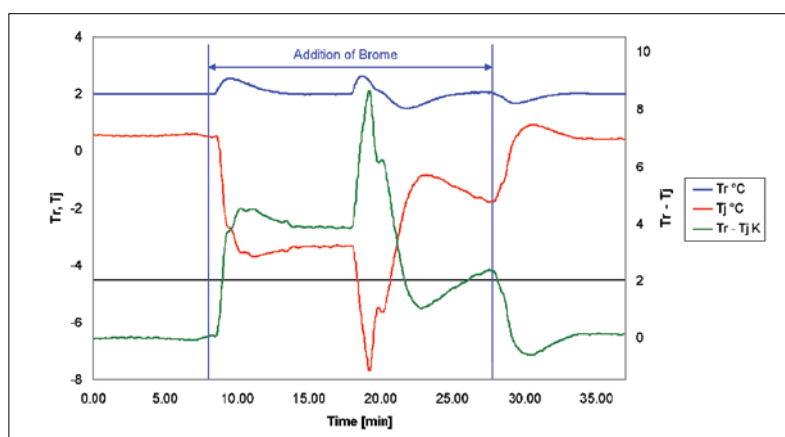


Figure 1
An exothermic reaction may not be dangerous at the laboratory level and pass the cooling capability test of a plant vessel in simple laboratory equipment undetected. However, by the time the thermal hazard is detected eventually, and the process may ultimately be unsuitable for operation in the plant a significant amount of time has been spent on process optimization already.

Thorough and accurate thermal hazard assessment provides an understanding of the energy involved in the desired reaction, and enables an effective redesign of the process conditions to eliminate the inherent risks of experiencing an uncontrolled runaway reaction.

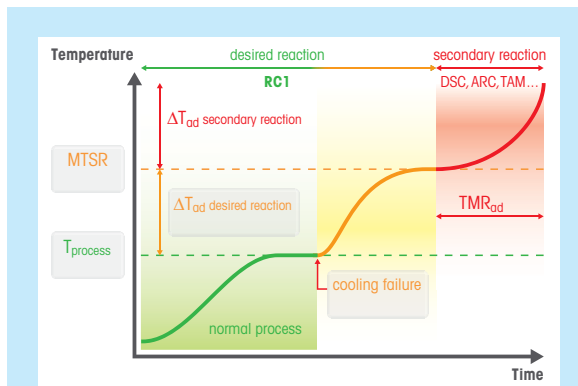
Assurance of Safe Working Conditions

Understanding the complexity of an entire process requires employing the right combination of tools. Making the correct interpretation of the data is crucial in order to assess the thermal risks associated with it. Ensuring the correct interpretation iC Safety™ is a tool for evaluating the thermal risks of a chemical reaction at industrial scale for use by novice, as well as advanced users in only one click. It's designed to help to quickly understand the risks of process hazards and to get the process right the first time, and in less time.

iC Safety™ summarizes key safety information in an easy-to-understand graphical format resulting in an automatically-generated report.

The importance of safety is not restricted to the manufacturing plant. Accidents and exposure to hazardous chemicals also occur on a laboratory scale, putting equipment and people at unnecessary risk. Safe working conditions from the laboratory through to manufacturing are enhanced by the use of fully automated reactors that have been designed to ensure safe operations. In addition, the use of process analytical tools (PAT) provides critical information *in-situ* and in real time eliminating the risks associated with sampling during hazardous reactions.

METTLER TOLEDO's Automated Laboratory Reactor (ALR) systems operate using unique and powerful high-performance thermostats providing unparalleled cooling capacity and temperature measurement to maintain control of highly exothermic and potential runaway reactions. Automated reactor control, including automated dosing of reagents, minimizes exposure to hazardous chemicals and thus assure safe working conditions.



Process Safety Saves Lives and Money

Early Identification of Thermal Risks

We cannot predict accidents or their outcome, but we can reduce their likelihood:

- The full process must be understood in its entire complexity

Ensure a Safe Process Design

Balance between risk, hazard and operational performance is a skill:

- Skill and knowledge transfer is critical for safe operations

Assurance of Safe Working Conditions

High profile accidents may attract the attention and actions at government levels:

- Process safety is critical to business sustainability



Example Case Study

Development of a Highly Hazardous Reaction

Goal of the Study

Development of a viable, economic and scalable synthetic route for the synthesis of 2,4-Diformylmesitylene (DFM). The key step in this synthesis is the presence of potassium 2-nitropropane which is known as an extremely unstable and dangerous reactant. Accidents and fires were reported repeatedly.

Key Results

- Thorough and rapid investigation of the reaction and its heat release based on various procedures
- Identification of the large hazardous potential of the reaction and its individual components by reaction calorimetry and associated techniques such as DSC and RADEX
- Use of the key results from RC1^e® and iC Safety™ to verify thermal conversion and large scale simulation



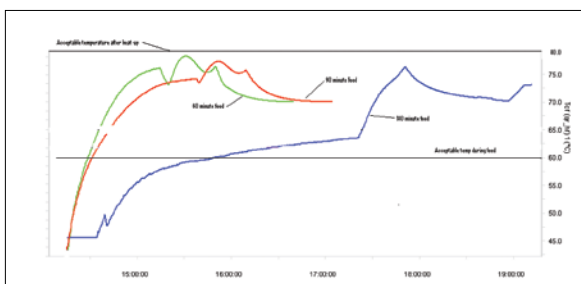
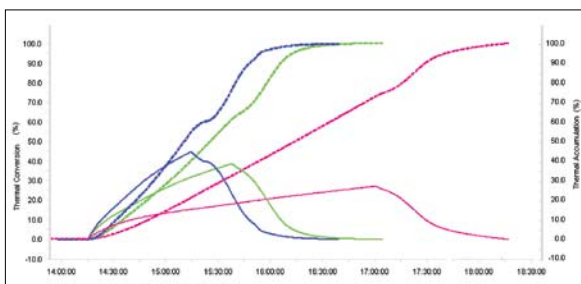
Value / Return on Investment

Faster Development – Saving Time

- Only a small number of runs were required to obtain key information of the process
- The RC1^e® and iC Safety™ together with DSC data quickly provided an excellent insight into the process and its hazardous potential. As a result the development time of the process could be reduced substantially
- iC Safety™ significantly reduced the turnaround time from running the reaction to issuing the final data as the data is available immediately
- Due to highly precise and reproducible experiment control less repeated experiments were required

Safe Process Design – Safe Working Conditions – Business Sustainability

- The information obtained permitted fast development of runaway and cooling failure scenarios as well as the calculation of the correct cycle times
- High confidence made the process become safe and scaleable for pilot plant production
- More accurate data led to a more accurate costing of the desired molecule



For more application examples visit

► www.mt.com/ac-webinars

Know your Process – Measure Thermodynamics

Understanding the thermodynamics of a chemical process is one of the key objectives in every risk assessment. The hazard potential is directly linked to the energy of the reaction and the reagent accumulation.

The RC1_e[®] is the “Gold Standard” to measure heat profiles, enthalpies and chemical conversion of the desired process under process-like conditions. The information obtained establishes the basis for full understanding of the process, safety assessments and scale-up simulations.

Rapidly Explore your Chemistry

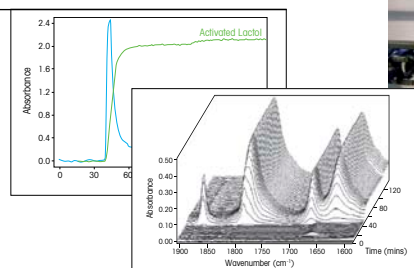
EasyMax™ is designed for chemical development and combines ease-of-use and flexibility with precision, reproducibility and acquisition of information. Fast heating and cooling without an additional cryostat, simple touchpad operation, flexibility, and workplace safety are some of the features of EasyMax™.





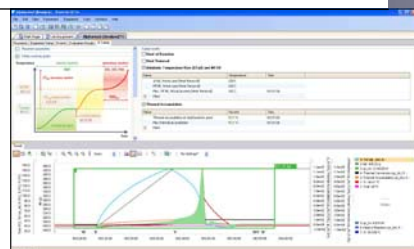
Monitor Chemical Reactions

The ReactIR™ based reaction analysis system provides composition information in real-time allowing the monitoring of key reaction species *in-situ* without sampling which leads to an increased process understanding faster.



Comprehensive Safety Information

Convert data into information, quickly understand the risks, and get your process right the first time with iC Safety™. It is a crucial tool for evaluating the thermal risks of a chemical reaction at industrial scale for use by novice, as well as advanced users.



Capturing, Understanding and Reporting of Information

iControl RC1e™ combines precise and accurate reactor control with flexibility, simple data integration with online analytics, and an effective report generator. The clearly arranged graphical interface of iControl RC1e™ improves efficiency while reducing training time to a minimum. The highly effective software interface assures that development goals can be accomplished better in less time.



METTLER TOLEDO

Global Services and Support

METTLER TOLEDO is the world leader in the field of reaction control, calorimetry, and process safety.

Our technologies have been used extensively in the pharmaceutical and chemical industries for the past twenty-five years. With over 1500 installations in laboratory, process research and process development worldwide, we have the experience and global support to assist you in understanding and optimization of your processes.

Our highly-specialized team of Technology and Application Consultants provide global training and support services to ensure our products perform optimally in the characterization, optimization, and control of your reaction processes.

Learn More with our Technical Webinar Program

Our live and on-demand webinars (web seminars) provide application and industry information relevant to you. These interactive presentations, provided by industry experts and our own applications team, give you an opportunity to learn more about your specific area of interest.

Topics include:

- Avoiding incidents during scale-up
- Reducing the risk of highly reactive chemistry
- Plus many other applications including topics in green chemistry, organic synthesis, fermentation, high pressure chemistry and more

The on-demand webinar library is available 24/7 enabling you to view the extensive list of webinars at your own convenience.

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For more information

Mettler-Toledo AutoChem Inc.

7075 Samuel Morse Drive
Columbia, MD 21046, USA
Phone +1-410 910 8500
Fax +1-410 910 8600

Internet www.mt.com/autochem
E-Mail autochem@mt.com

Subject to technical changes.

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