The Design of Safe Chemical Processes

By Dr Jasbir Singh
at HEL Ltd

A systematic approach is required for the design of safe chemical processes; this not only ensures a safe plant but can also speed up process development, especially in the pilot stages.

A typical process in the pharmaceutical and related industries consists of a number of sequential steps where a range of carefully selected compounds are allowed to react in order to produce the required product or intermediate. In many cases, the reactions involved are exothermic, and therefore require cooling and careful process control in order to ensure safe operation. In addition, some of the raw materials or products may be unstable and have a tendency to thermally explode under certain operating conditions.

Experienced chemists will often be aware of some potential problems based purely on a knowledge of the chemical species involved, but this is frequently insufficient to ensure safe operation. It is now widely accepted that the chemist's experience must be supplemented by bench scale testing using suitable test procedures. The objective of this article is to make process chemists aware of the presently accepted techniques for hazard evaluation, and how these can affect both development and scale-up of chemical reactions.

A STEP-WISE APPROACH

In order to ensure that all potential hazards are properly understood, the following step-wise approach is suggested:

(i) Screen potential hazards

This will involve suitable consideration of all feeds, products and intermediates, as well as the main reactions using up to a few grams of sample. The methods used for screening must by necessity be inexpensive and fast, but the key is also the reliability of the data as a false negative reading is potentially disastrous.

Figure 1: Thermal screening unit (TSU) for screening thermally unstable chemicals

(ii) Evaluate main reactions

If the screening work permits, the evaluation can be increased to, say, the one litre scale and can concentrate on the main reactions, looking both at the safety and operability aspects. Here reaction calorimetry is the main method of study.

(iii) Evaluate `what if' scenarios

When the intended process has been suitably demonstrated, it is necessary also to consider deviations from the desired conditions. A typical example would be:

- Failure of cooling water
- Agitation failure
- Operator error (for example, too much catalyst)

Ideally, these questions need to be asked at the same time as the process is being developed, but this is not always possible.

THERMAL SCREENING

This is a vital step in getting a safe process, and the test is historically performed in standard differential scanning calorimetry (DSC) equipment using only a few milligrams of sample. However, this is widely recognised as being inadequate and sometimes even unsafe, and it is far better to use a larger sample size and – importantly – to measure pressure generation.

An example of a system suited to screening in this way is the thermal screening unit (TSU) shown in Figure 1, and sample data is shown in Figure 2. This shows the pressure generated by the sample as the temperature is raised by heating an 'oven.' Even a cursory look at the data in Figure 2 shows that the test sample begins to seriously decompose at below 140ºC, and will generate around 50 bar pressure rather quickly. A more detailed review of the data can give a more precise figure for the 'onset' of the runaway; the energy release and kinetics can also be quantified.

Figure 2: Typical thermal screening data

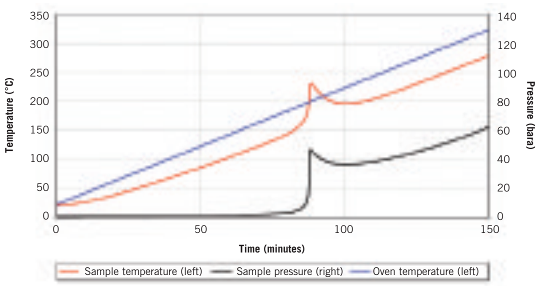


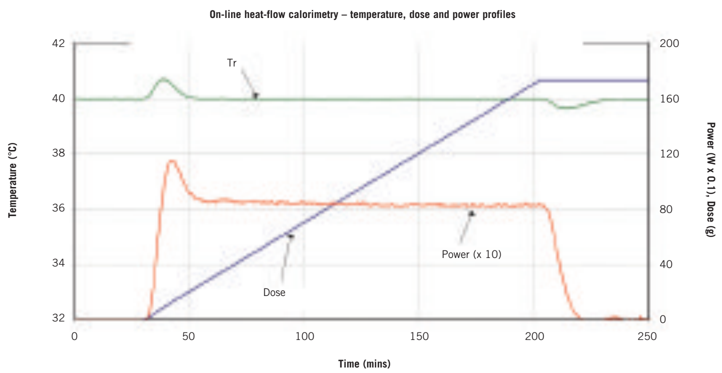
Figure 3: Example of reaction calorimeter (SIMULAR)

The test can be performed in a couple of hours, requires a sample of only around one gram and generates data that is easy to interpret.

DETAILED EVALUATION

If the materials being handled, including the product, have been screened in terms of stability, attention can next shift to an understanding of the chemistry, ensuring that it does not deviate from the prescribed route after scale up to the plant. In order to do this, the key objective is to evaluate the instantaneous heat output rate as the chemistry proceeds. For example, if the feed rate is too high, it may become impossible to remove the heat generated and hence keep the reaction under control, leading to the possibility of an uncontrolled explosion.

Figure 4: Typical heat flow data from reaction calorimeter



Dr Jasbir Singh is founder and Managing Director of HEL Ltd, an international company that specialises in research and pilot-scale chemical reactors and related tools for process R&D in the pharmaceutical, fine chemical and petrochemical industries. A chemical engineering graduate of Imperial College (London), he undertook a PhD at Imperial conducting research into combustion and explosions. Jasbir then spent many years in process design for the chemical and petrochemical industries. Email: jsingh@helgroup.com

Therefore, this is a very important step for successful scale up. The best method for evaluating a semi-batch reaction is reaction calorimetry.

Reaction calorimeters in principle are designed to allow the normal process chemistry to be exactly replicated at the laboratory scale, while measuring the heat release rate. The heat data can be used to understand the broad kinetics, which then helps to develop the process; also, in the context of a safe plant, this information is invaluable. An example of a reaction calorimeter (the SIMULAR) is shown in Figure 3.

The results of an evaluation in the SIMULAR reaction calorimeter are shown in Figure 4. This shows the heat output rate (in watts) and reagent dosed into a reactor containing typically one other reactant in solution. The numerical value of the heat output and even the shape of the curve provide useful insight into the chemistry.

The heat output rate can be scaled directly to a large-scale plant; this will specify the cooling duty needed. The total heat that can potentially be released can be translated into an equivalent temperature rise if, for some reason, cooling is lost. Since the data in Figure 4 is generated by performing the reaction in the same way as a full-scale process would be run, it will provide valuable insight into any potential control problems. It may also point to any by-product gas that may be generated.

ESTABLISH 'WORST CREDIBLE CASE'

The next stage of the evaluation is to consider what happens if things go wrong and, in particular, the worst possible but still credible scenario. In order to do this, a hazard and operability study (HAZOP) is frequently carried out. This involves consideration of each operating step and each process line individually, and postulating deviations from the normal. Where the deviations (for example, loss of cooling) are credible (for example, cooling pump failure) then the consequences are considered in more detail. An assessment of this type may be carried out at several stages during the development of a process and would involve chemists, chemical engineers, instrument engineers and possibly other specialists.

CONCLUSION

The design of safe processes requires a systematic approach during development, and this includes using certain types of calorimetry tools. It is widely recognised that this not only produces a safe plant, but also speeds up the development, especially in the pilot stages. Thus, the payback is considerable and is often understated.