RSC | Advancing the Chemical Sciences

Environment, Health and Safety Committee
Note on:
SAFETY ISSUES IN THE SCALE UP OF CHEMICAL REACTIONS

This Note provides some basic guidance on safety issues raised by the scale up of chemical reactions from laboratory scale to full sized commercial plant. The RSC believes that chemists should be fully aware of the safety problems associated with the scale up of chemical processes and should contribute to the scale up procedure in order to ensure the health and safety of all persons involved. Guidance is, therefore, provided, for members who either manage laboratories or are employed in laboratories where the scale up of chemical reactions is undertaken.

The Note assumes familiarity with basic terms such as 'risk' and 'hazard'. The Note is intended to be an introduction rather than a full or definitive guide. Readers are urged to obtain more detailed information and/or expert advice if this is required.

1. INTRODUCTION

Amongst the chemical incidents that are reported to the Health and Safety Executive each year, as dangerous occurrences under Reporting of Injuries, Diseases and Dangerous Occurrences Regulations, there are some 20 to 30 exothermic runaways. There may be other chemical incidents that are either not reported or which do not fit the legal definition of a 'dangerous occurrence'. It is likely that many of these are attributable to inadequate scale up procedures.

Chemical processes usually originate on a small scale in the laboratory and their development is normally carried out by conducting the reactions on successively larger scale, through pilot plant stages, before transferring to full size production plant. In the early stages of process development limited quantities of chemicals are used and full information about the reaction or side reactions is not usually available. Risk assessment studies and the scale up procedure enable further information to be obtained which is relevant to the final process plant design.

Failure to scale up properly and to take appropriate precautions may lead to the loss of process control which in turn may result in a runaway exothermic reaction and /or the generation or release of toxic materials. The hazards of a runaway reaction and over pressurisation are the two greatest concerns during the scale up process. In the past, there have been a number of failures to take these issues fully into account which have led to multiple fatalities, severe damage to property, environmental damage and business loss.

Other problems that have arisen from inadequate scale up procedures include for example:

- dust and vapour explosions inside vessels due to the mishandling of reactants and solvents;
- fires due to overfilling of vessels;

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- failure to correctly assess electrical equipment for use in hazardous areas identifying all possible sources of ignition;

- auto-ignition of flammable vapours, usually resulting in a flash fire but sometimes an explosion; and

- inadequate mixing of reactants and solvents.

It is important to remember that most reactions are exothermic. Such reactions move to a heat balance within the reactor where removal balances production and this balance is at a temperature above that of the reactor; scale up alters both rates of heat removal and production.

The main factors affecting the removal of heat are the size of the reactor, stirring and cooling. The main factors affecting heat production are concentration of reactants and catalysts, size and starting temperature. These factors can be subject to change in order to achieve more production in a shorter time. However, because of the Arrhenius dependence of rate on temperature, small changes increase heat production more than they increase heat removal, which hardly changes with increased starting temperature. Therefore, an attractive production change can move the system from stable balance to one where stability can never be achieved. Finally, a maximum stable temperature rise within a system is usually 10 to 20° C, above that is runaway.

The first and most critical step in the scale up procedure is to undertake a risk assessment of the proposed chemical process at the concept stage. Where appropriate, this should include a study of the thermochemistry of the proposed reaction.

2. ASSESSMENT OF REACTION HAZARDS

The risk assessment undertaken on all new or modified reactions should be recorded and should involve the consideration, where appropriate, of the following:

- the physical and chemical properties of the reactants, intermediates, products and wastes;

- the thermochemistry of both of the desired and potential undesired reactions, in particular the rate of heat output;

- the rate of gas generation and the potential for vessel over-pressurisation;

- the fire and explosion hazards;

- the possibility of hazardous reactions if there are deviations from set parameters;

- the potential for the substances in use to corrode plant;

- the health hazards and associated COSHH and Personal Protective Equipment (PPE) assessments;

- scale-up problems (see below);

- plant design characteristics, including control systems, service needs (eg cooling water, inert gas) and the adequacy and reliability of safety devices such as pressure relief valves, bursting discs, vents, etc.;

- the application of hazard identification methods, such as ‘What If’ studies, Hazard and Operability Studies (HAZOPS) and quantified risk assessment techniques;

- environmental effects;

- new or modified process instructions; and

- the training needs of operators.

The first stage in the risk assessment is data collection. This will enable desktop screening of the hazards of the proposed reaction to be undertaken and, if possible, thermochemical calculations to be carried out. In this exercise consideration should be given to the reactive group(s) of the reactants and comparisons should be made with analogous substances or reactions. A number of publications are cited in the Bibliography which may be useful in this desktop screening exercise.

It is current best practice to subject all new processes to thermochemical investigations in order to identify the potential for exothermic reactions, particularly runaway reactions. Various calorimetric techniques are available which can be used in such a study. For example, differential scanning calorimetry or Carius tube studies can be used for basic thermal stability screening tests. Isothermal calorimetry can be used mainly to measure reaction kinetics and heats of reaction. Adiabatic calorimetry can be used to examine the potential for runaways. Relief vent sizing tests can also be carried out.

As a result of the risk assessment the principles of elimination, reduction and control should be applied. If the risks associated with the proposed reaction are unacceptable then an alternative route to the product should be considered, if possible using inherently safer methods. If, however, the reaction is to proceed the risk assessment should specify the control measures and safety procedures which should be adopted to ensure the safe operation at all stages of the scale-up process.

3. SCALE-UP PROCEDURE

The design of a commercial plant can be accomplished by scaling up from laboratory equipment using pilot plant. In some cases several pilot plants of increasing size may be used to effect the best design for the larger plant. During the scale up process it is useful to develop a “basis for safe operation” that spells out the key controls that avoid the development of unsafe conditions.

Risk assessment is an evolving process as scale-up progresses. At each stage of the scale up procedure the information generated should be used to review the risk assessment to enable a decision to be made as to whether or not to proceed to the next stage. If the process is to proceed, the risk assessment should specify the controls and operating conditions required.

The rate of a chemical reaction is fixed at any given temperature but temperature may be influenced by mass transfer and heat transfer, which are in turn affected by the size and design of the reactor. It is not always possible to theoretically assess these effects on a quantitative basis and in such cases it is usual to carry out trials with water or inert substances in the intended plant. If this is not feasible purpose built reactor calorimeters will be required.

Laboratory experiments, carried out in test tubes, small flasks etc., produce a required chemical or product but do not necessarily indicate side effects of the reaction, i.e. by-products, release of gases or vapours which may be toxic or flammable. Heat releases may be absorbed by the equipment or surroundings and not noticed. The chemicals used may be pure materials rather than bulk commercial chemicals, which may contain traces of impurities. In order to overcome these problems it is essential that the apparatus, materials and chemicals used at all stages of the scale up accurately reflect those that will be used in the final plant. In the laboratory reactions are usually carried out in glass vessels but the scaled up process may well be carried out in containers made of other materials. With some reactions such changes may be important and could result in unexpected reactions or problems including catalytic or inhibition effects.

As scale increases the time required to carry out each operation is also likely to increase and appropriate allowance should be made for this.

Pilot plant is used to assist in the scale up of the chemical process design rather than the mechanical design. It provides information for economic design, operating parameters, and safety considerations. In addition, pilot plants can be used in small scale production for evaluation and trial marketing. Information should be obtained from pilot plant studies to confirm the decisions made as a result of the risk assessment stage in relation to:

- operating conditions;
- design parameters;

- reactor problems, design, materials of construction;
- unit operations problems;
- materials handing and sampling problems;
- thermal instability and other decomposition;
- phase problems;
- impurities;
- corrosion;
- fouling;
- analytical problems;
- operating procedures;
- working and environment problems; and
- effluent and waste disposal problems.

Laboratory chemicals are often more pure than bulk chemicals. It is important that reactions are undertaken at an early stage with the bulk chemicals that it are intended to be used in the final reaction process.

Impurities in bulk chemicals used can cause many problems and these can be identified in pilot plant studies. Impurities can occur in the feedstock or arise from side reactions, decompositions, polymerisations, etc. which can cause unexpected effects. Leaks into the system may bring in unwanted materials such as pump lubricant, seal fluids or heat transfer media, including water. These may lead to blockages and other problems. Some impurities can catalyse undesirable explosive reactions or may be thermally unstable themselves.

Pilot plant studies can reveal corrosion problems. These can be associated with minor components such as gaskets and diaphragms or with impurities in the reactants.

Scaling up in various size plants can produce variations in reactions, and apparently identical reactors can give slightly different products with apparently the same feed materials and operating conditions. This is most marked in fermentation processes.

Pilot plants should be operated by trained and competent personnel. The extra unknown or unforeseen hazards associated with pilot plant should be compensated for by better instrumentation and technical control by the operators. If practical, remote handling systems should be used to minimise the effects of any unforeseen reactions. It must be remembered, however, that accidents on pilot plant, despite their size, can still have serious consequences.

It is important, therefore, that scale-up of chemical reactions is done correctly so that the eventual reactions can be carried out safely in full size production plant.

4. SAFE OPERATION

Information obtained from the risk assessment of the chemical process and the scale-up studies will enable decisions to be made on the most appropriate controls to ensure a safe operation. The main options that could be considered for a safe operation are:

- inherently safer methods which use less hazardous materials or alternative reaction routes to eliminate or reduce hazards;

- preventative measures such as process controls using sensors, trips, alarms (temperature, pressure, stirrer, cooling water failure) and other control systems which initiate automatic remedial action; and

- protective measures such as pressure relief valves, bursting discs, vents, reaction inhibition, crash cooling, drown out/quenching or secondary containment which will limit the consequences of a runaway reaction.

There is no single best option for controls and protective measures that can be applied in all cases. Whichever option is chosen, it must cater for the worst credible scenario and reduce the risk as far as is reasonably practicable.

The option chosen must also be supported by appropriate occupational health and safety management systems which cover operating procedures, the training and supervision of operators and maintenance personnel, the maintenance of plant and equipment, the control of plant modifications, software and emergency procedures. It is essential that there is good communication and co-operation between the risk assessment team, the process plant team and maintenance personnel so that everyone concerned is fully aware of the operating parameters and limitations of the process plant. It may be appropriate, particularly for complex activities, to appoint a Project Manager to oversee and co-ordinate the scale-up process.

Once the process is operational it is important to ensure that clear written operating procedures are prepared and agreed. These procedures must be followed by all personnel. There must be no deviation or change in raw materials unless further risk assessments are undertaken, including pilot plant studies if appropriate.

5. CONCLUSION

It is essential that suitable and sufficient risk assessments are undertaken of all new and modified reactions during the scale-up of laboratory processes to full sized commercial plant. Appropriate process controls and protective measures are needed to reduce the risk of a runaway exothermic reaction and/or the generation or release of toxic materials to a level that is as low as reasonably practicable. This not only ensures that legal requirements are complied with but also avoids the disruption, cost, potential damage and injuries that can be caused by the loss of control of chemical reactions.

6. FURTHER READING

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