WHAT KIND OF RELATIONSHIP DO YOU HAVE WITH YOUR TOLLERS?

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This paper describes a chemical process that had been operated in the laboratory and on pilot plant without incident. At this point the process was outsourced to a toller to operate on the large scale and an unforeseen incident occurred which resulted in an uncontrolled exothermic reaction. Fortunately, there were no serious consequences, but the incident raised the possibility that something had been missed in the original hazard/risk assessment.

The paper describes the procedure of hazard and risk assessment that was carried out prior to handing over the data package to the toller and discusses where the process may have failed. It gives details of the incident and how Syngenta safety specialists then worked with the toller to determine the likely causes of the temperature excursion, with a discussion around the actual chemistry of the process. It shows how a slight increase in concentration, dramatically affected the reaction kinetics.

The paper focuses on the relationship that manufacturers have with their tollers and questions whether concerns over future litigation issues can adversely affect the data transfer process, sometimes resulting in incomplete safety data packages being handed over, and increasing the risk of unsafe toll operations.

1. INTRODUCTION

Manufacturing once accounted for almost 40% of the UK's output. It now represents less than half that. It has declined steadily over the past 30 years, giving way to competition from abroad, particularly the Far East where labour is much cheaper. The minimum wage in this country is now around £6 an hour, whereas in China decent labour can be as little as 40p an hour. This has led some economists to argue that manufacturing in the UK is no longer a viable proposition. Manufacturing has also borne the brunt of the slowdown in world trade and is believed to be shedding about 10,000 jobs a month. Even die-hard manufacturing experts believe that British industry needs to adapt to the new conditions with many of the opinion that companies need to "change or die".

One way to do this is for the business to re-focus on what they do best and leave the rest to others. Contract manufacturing seems to fit neatly into this practice. In addition to allowing companies to focus on core competencies, contract manufacturers offer numerous other advantages over in-house manufacturing, including lower costs, flexibility, access to external expertise and reduced capital[1]. Recent research has shown that manufacturers are beginning to see the value of choosing to work with strategic outsourcing companies rather than those who can merely beat the competition on price. This is a reflection of the increasing closeness of outsourcing relationships, with more and more parties entering into longer-term partnerships rather than simply closing narrowly defined supply deals.

The dynamics of such relationships are changing accordingly, with factors such as the development of trust and close management contact becoming increasingly important[2].

This paper describes how such a relationship between the business and a contract (toll) manufacturer was essential in ensuring that a potentially hazardous chemical process was safely scaled up from the laboratory scale to full scale production.

2. PROCESS DETAILS

The initial process solution is material **A** in dimethyl sulphoxide (DMSO) with potassium hydroxide, potassium carbonate and a phase transfer catalyst. This is heated to 80–85°C under vacuum (10–20 mbar). The reactor is set to distil via a short column and still head condenser, routed to a binary separator. Dichloroethylether (DCEE) is charged over 2 hours at 80–85°C. Distillates contain water which is separated at the binary separator and the DMSO/DCEE lower phase returned to the reactor. On completion of the addition, the reaction is held for 4 hours to complete. The reaction mass is screened to remove inorganics and distilled at ca 140–150°C under reduced pressure to remove DMSO.

3. INITIAL SAFETY DATA

The process was examined in the safety laboratory, looking at the heat of reaction by heat flow calorimetry and adiabatic Dewar calorimetry and investigating the thermal stability of the raw materials, reaction mass and distillation products. The process assessed was quite dilute, involving the use of ca 12 mol:mol DMSO:**A**. The main concern at this stage was the fact that the solvent being used was DMSO.

3.1 DMSO

Dimethyl sulphoxide (DMSO) is a very good solvent that solubilizes many inorganic compounds and many other difficult-to-dissolve-materials. It is widely used in the chemical industry. It is a polar solvent that is high-boiling and thus is easy to dewater. DMSO is known to slowly decompose at temperatures at or above its boiling point (189°C). However, these properties lead to some of the specific hazards of this material:

- DMSO is not inert; the reactivity of solvents that play only a physical role in reactions is easily forgotten. DMSO decomposes with a significant release of heat and gas.
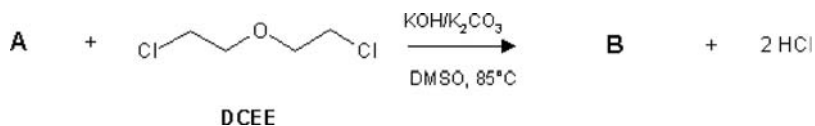

Figure 1. Reaction scheme

The decomposition reaction is already evident at the boiling point; DMSO cannot be distilled at ambient pressure without decomposition. This decomposition is self-accelerating and is accelerated by both acid and base, particularly with even trace amounts of organic or inorganic halogens. In some cases, the reaction is virtually instantaneous whilst others are characterized by the steady accumulation of heat and pressure with eventual runaway.

- The high boiling point hinders the dissipation of heat through vaporisation.
- Like many other solvents, DMSO reacts with many other reactive compounds, such as acid chlorides. However, in contrast to other solvents, the reactions with DMSO involve a large release of heat that cannot be dissipated through vaporization.

Many serious incidents involving the handling of DMSO have been reported.[1]

3.1.1 Thermal Stability Data for DMSO

Initial Differential Scanning Calorimetry (DSC) tests of pure DMSO (Fig. 2) indicated that it was stable up to its boiling point. DMSO recycled from the distilled reaction mass is likely to contain residual DCEE which could be expected to hydrolyse and reduce the pH of the DSMO, thereby having a detrimental effect on the thermal stability. Therefore recycled DMSO was generated in the lab and tested by DSC to determine the effect of the recycle. The dynamic DSC test (Fig. 3) indicated that the onset and peak temperatures of the decomposition were shifted to lower temperature and the decomposition itself was much sharper which indicated possible autocatalysis. This means that if held at any given temperature the DMSO would eventually decompose rapidly after an induction time, which would be dependent on the hold temperature. Isothermal DSC testing was therefore carried out to determine the likely induction times around the process temperature (Table 1).
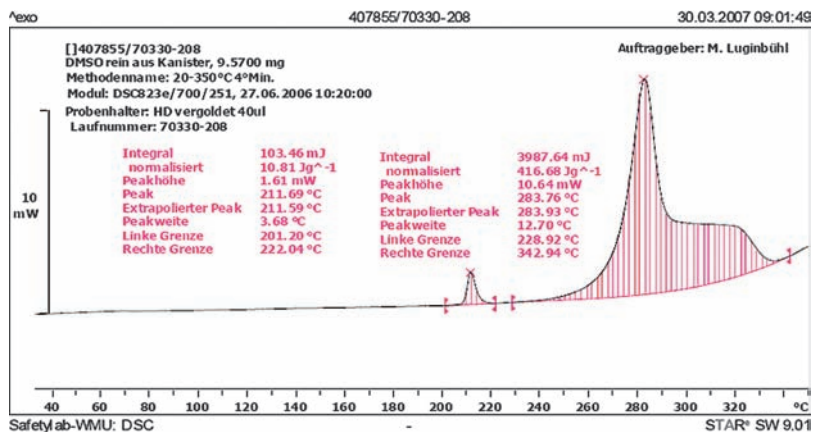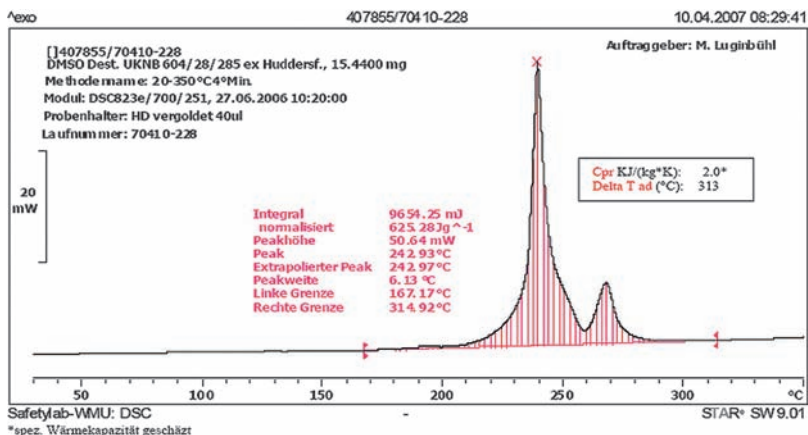

Figure 2. Fresh DMSO

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Figure 3. Recycled DMSO

Table 1. Recycled DMSO – induction time with temperature (from DSC)

Isothermal hold temperature (°C)	Induction time (mins)
170	25
160	50
150	116

The isothermal tests showed that the induction time at 150°C was only 116 min, to the start of decomposition, with the peak rate of the decomposition occurring after ca 290 mins. Whilst it is unlikely that DMSO alone would be subjected to such high temperatures, the reaction batch and crude product solution may be. During the normal reaction, the temperature of the batch should not exceed ca 85°C (unless cooling was lost and the reaction allowed to runaway, see 3.3.1). The main concern would be the DMSO recovery distillation stage which, if carried out in a batch distillation, could result in DMSO being heated to ca 150°C for prolonged periods. The maloperation scenario of agitator loss would also be a problem as the batch would be subjected to the service temperature (probably steam at ca 180°C).

The DSC tests were indicative of the effect in a sealed situation (as they were carried out in sealed, high pressure cells), whereas under normal circumstances the process vessels would be at ambient pressure. Hence the thermal stability of the reaction mass was investigated under ambient pressure conditions using Dewar calorimetry. The results of that experiment are discussed in section 3.3.2.

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3.2 MEASUREMENT OF THE HEAT OF REACTION

The reaction was investigated by both isothermal heat flow calorimetry and adiabatic Dewar calorimetry to determine the heat of reaction and the expected adiabatic temperature rise.

3.2.1 Isothermal Heat Flow Calorimetry

The reaction was carried out by controlled addition of DCEE over 2 hours to the batch whilst maintaining the reaction temperature at 85°C. The reaction was allowed to work-off for 3 hours after completing the addition.

Addition of DCEE resulted in an exothermic activity with a fairly even power output (see Fig. 4). After addition was stopped, there was a slow work off of accumulated reactant.

Heat of reaction (total), $\Delta H = -238.65$ kJ/mol (-57 kcal/mol) **A**
Accumulated heat $= -66.22$ kJ/mol (-15.6 kcal/mol) (ca 28%))
Heat capacity, Cp batch $= 89.47$ cal/K (2.14 J/K.g)
Adiabatic temp rise, $\Delta T = 82.8$ K
ΔT (accumulation only) $= 22.7$ K
No significant gas evolution was detected.

For the reaction conditions described above, with a batch heat capacity of 2.14 J/K.g, an adiabatic temperature rise of ca 83 K would be anticipated for a reaction without cooling. Hence, from a starting temperature of 85°C, the worst case possible is that the batch temperature would reach 168°C if cooling were lost at the start of the reaction.
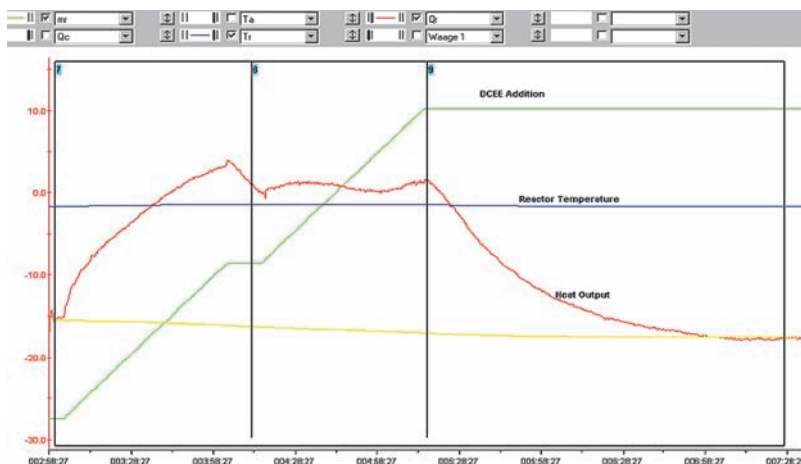
Figure 4. Dilute process (2hr DCEE addition) in RC1

3.3   ADIABATIC DEWAR CALORIMETRY
3.3.1   Reaction
The reagents were charged to a 250 ml narrow neck Dewar. The Dewar was then placed into a shield oven set on adiabatic control. The reagents were heated to 82°C with agitation and DCEE charged over 2 hours. The batch was then held adiabatically with agitation for 2 days (see Fig. 5).

The DCEE addition resulted in an immediate exothermic reaction and the batch temperature reaching a maximum of 162.3°C.

Adiabatic temp rise, $\Delta T = 80.3$ K.
Cp batch = 89.47 cal/K (2.14 J/K.g)
Heat of reaction, $\Delta H = -30.07$ kJ (-7.18 kcal)
$\quad\quad\quad\quad\quad\quad\quad = -233$ KJ/mol (-55.3 kcal/mol) A

The reaction was accompanied by gas evolution at a maximum rate equivalent to 0.04 l/min/kg batch, which slowed down to a rate of ca 0.003 l/min/kg batch as the reaction completed. This gassing continued at a similar rate as the batch temperature dropped slowly to ca 152°C over the next 48 hours.

3.3.2   Reaction Mass Thermal Stability
3.3.2.1   Product B Solution in DMSO   The product **B** solution (in DMSO) was charged to a narrow necked squat Dewar flask. The Dewar was then placed in a shield oven. The sample was agitated and heated to 180°C over ca 60 min before switching the heater off. The sample was held adiabatically with slow stirring for over 20 hours (see Fig. 6).
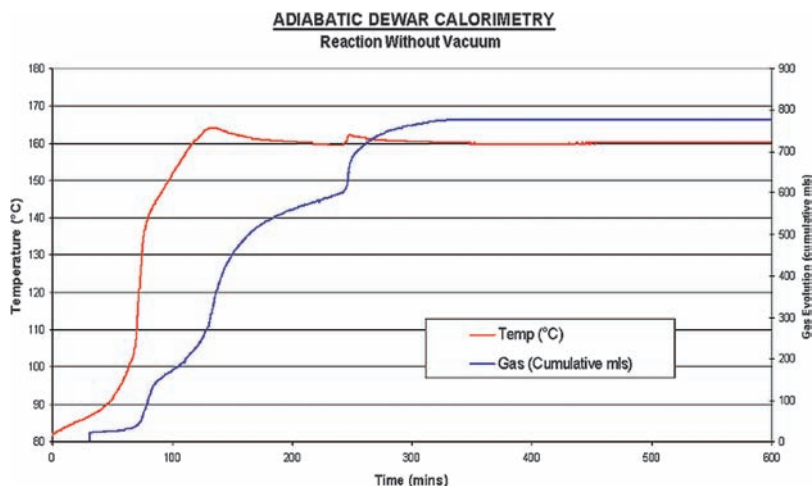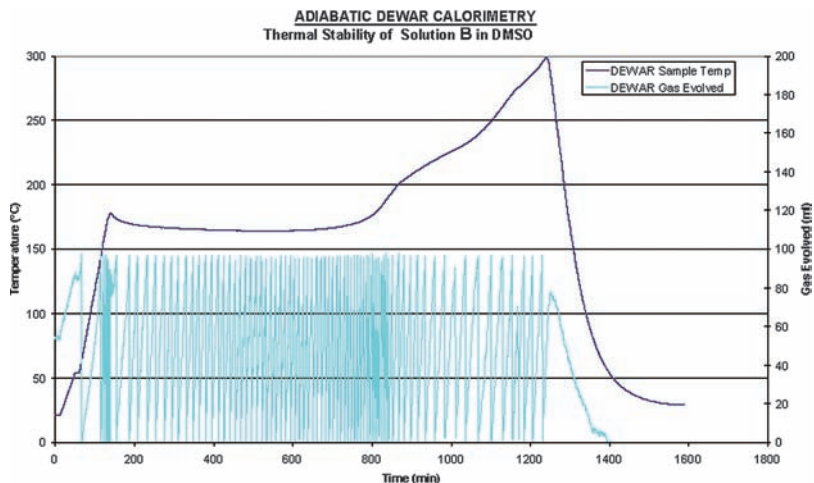

Figure 5. Reaction profile in adiabatic Dewar

Figure 6. Reaction mass thermal stability

Heat-up to 180°C was accompanied by gas evolution which became rapid from ca 150°C. After the heater was switched off, the sample temperature fell to ca 164°C over the next 7 hours. The gas evolution rate initially dropped then slowly increased with time. The temperature and gas rate then started to increase again; the temperature rose to 300°C over the next 11 hours, at a maximum rate of 23 K/hr at ca 175°C which occurred about 4 hours into the exotherm. The gas rate reached a maximum at 175°C then tailed off. At this point the test was terminated by the automatic maximum temperature trip. During the experiment ca 71% of the batch was distilled out and the total amount of gas evolved was ca 36 l/kg.

This test showed that if the reaction mass is heated to ca 180°C (i.e. to the service temperature) it could go into thermal runaway after ca 8 hours. However, the decomposition may be tempered somewhat by distillation of the DMSO, and consequently a significant amount of distillate was collected during the experiment.

3.4 CONCLUSIONS FROM THE SAFETY DATA

The main safety concern in terms of chemical reaction hazards of the process was considered to be the thermal stability of the reaction mass, the bulk of which is DSMO solvent. The thermal hazards of DMSO are well documented, and the tests carried out in the safety lab also suggested that there were potential problems both in the reaction stage and the DMSO recovery distillation stage.

It was shown in the sealed tests (DSC) that recycled DMSO can decompose autocatalytically with quite a short induction time at the recovery distillation process temperature. Also, if a maloperation were to occur in the reaction stage, with loss of cooling, the batch

temperature could possibly reach the DMSO decomposition temperature. Adiabatic Dewar calorimetry indicated that the decomposition under ambient pressure conditions is tempered somewhat by the distillation of DMSO and is therefore not considered a significant problem in an open vessel, but a blocked vent leading to a pressurised situation could result in a catastrophic event. Further tests (not detailed here) carried out on relief vent sizing for this scenario suggested that the decomposition was not relievable (i.e. the vent size would be prohibitively large). These findings suggest that a short-path, low residence time vacuum distillation would be preferable to a batch process for this recovery stage. The reaction stage was considered safe to operate with appropriate control measures to avoid loss of cooling.

4.   PILOT PLANT CAMPAIGN – FIRST SCALE UP

While the safety testing was being carried out, the process was being further developed in the lab. The reaction had initially been developed at fairly low concentration (ca 12 mol: mol DMSO:**A**) which gave the optimum product yield. However, as the product became a viable option for scale-up, economic considerations came to the fore and a more concentrated process (ca 8.5 mol:mol DMSO:**A**) was developed to save processing costs associated with DMSO recovery.

It was decided to use the concentrated process for the first scale-up in the pilot plant, which was used to produce ca 500 kg of material for toxicity screening. A Process Risk Assessment (PRA) team (including safety specialists) evaluated the process and determined the basis of safety for the pilot plant campaign after consideration of the safety data generated for the dilute process. The team decided that this data could be used and applied to the concentrated process (by calculation) and did not consider that any further safety testing was necessary.

The pilot facility consisted of a general purpose reaction vessel, fitted with an all purpose distillation column. The campaign was carried out and monitored by specialist technical operators, as was standard practice for pilot plant operations. The process ran to plan, with reaction profiles similar to the laboratory experiments, product quality and cycle times were as predicted, and no safety concerns were noted.

5.   CONTACT WITH TOLLERS

At this stage, the business decision for the product was to send out the process to contact manufacture. A number of (Swiss and European) tollers were approached, all of whom had been involved with the company on previous occasions with positive results. A series of face to face meetings took place at which the process was discussed in detail and a data package was handed over. The data package contained details of the process that had been investigated thus far, with protocols, batch data and engineering details from the pilot plant campaign. All the safety data that had been produced to date was shared, but no interpretation, conclusions or recommendations were included. This is common practice and is done to make sure the toller does not (unintentionally) misinterpret any conclusions made by the Syngenta safety specialist and requires the toller to use the raw data,

apply it to the situation in their plant, and to determine the basis of safety for themselves. This is to try to avoid future litigation issues should there subsequently be an incident with the process.

PRA data for the pilot plant campaign was not part of the package but information on all known safety hazards was discussed. The tollers took the information away for consideration, some carrying out preliminary laboratory work to determine the feasibility of operation of the proposed process.

5.1   DECISION ON TOLL MANUFACTURER

After a number of weeks, the tollers were invited to discuss their proposals for operating the process. They had brought laboratory data for discussion and one toller also invited their own (contracted) safety consultants to discuss some queries they had around the safety data. The discussion on the safety data was mainly around clarifying the interpretation of the raw data available. No further safety advice was given on our part but the discussion raised a number of additional queries which one toller felt required further safety testing before they could make a final decision on the process operation. This testing was carried out by the toller's safety consultants but the results were not shared with us.

After a further few weeks, the tollers returned with their final proposals. At this point some of the tollers dropped out on the grounds that they felt they would be either not able or not willing to manufacture the product. The reasons given were either economic grounds or inadequate kit or through safety concerns. The toller that was awarded the contract gave reassurance that they had adequate kit and an economically viable process. They had no concerns over the safety of the operation.

Whilst open discussions had been carried out throughout the decision process to this point, it is always possible that a toller may have given an overly positive impression of their situation in order to win the contract. Whilst every effort is always made to ensure that all the relevant information is passed on by the toller, at this stage there also has to be a good degree of trust. The chosen toller was a relatively small operation, with a small technical team, able to and capable of making personal decisions on the ground, with a relaxed attitude to the process hazards and a feeling that they understood them and were able to manage them. They also had synergies with our company as they were already manufacturing some other products for us under contract (including DCEE). Therefore, the technical team were quite well known to us and some good working relationships had been developed.

5.2   FOLLOW-UP CONTACT WITH TOLLER

The toller carried out their own PRA (with their safety consultants) then went ahead to manufacture product **B** on a 5000 kg scale. After they had carried out a number of batches, they contacted us to say they had been observing unusual and unforeseen temperature excursions during the reaction stage. They had been seeing large sudden exotherms part-way through the reaction, with the batch temperature reaching up to 150°C on occasions.

No reason could be seen for this occurrence as this effect had never been seen in any of our laboratory tests. However, the information raised serious concerns about the safety of the process as the temperature excursions that were being reported were taking the batch close to the temperature at which DSMO may be expected to decompose autocatalytically. Due to the safety concerns, a Syngenta team visited the toller's site to see if there was any obvious reason for the temperature excursion. They were looking for particular engineering problems with the kit being used or significant process changes.

The team found that the process was being operated as expected with no obvious changes to the original process that had been handed over. In terms of the engineering, a check on temperatures and pressures around the distillation column during the reaction suggested that it was not functioning as it should. The column function was to condense the distillate, collect and separate the water and return the DMSO/DCEE phase to the vessel. The temperatures and pressures in the column indicated that the column was being flooded and was not removing water as desired. Engineering calculations quickly determined that the column was undersized for the required duty. However, this could still not immediately explain the temperature excursions that had been noted.

Further discussions were carried out to try to determine the source of the problem. From the information received from the site visit, it was suggested that the problem of the temperature excursions was probably linked to the column inadequacies. It was postulated that if the column was under-sized then water would not be removed properly, which may have an effect on the reaction rate. No such effect had been seen in the original safety tests, which had been carried out without vacuum (i.e. no water was actually removed during the calorimetry experiments) or in the pilot plant campaign. However, it was quickly realised that the original safety testing had been carried out in a dilute system, and the more concentrated process had not been re-assessed in the laboratory. The pilot plant campaign had been with the concentrated process, however the column present on the pilot plant reactor was adequately sized and therefore it was likely that all the water had been removed very efficiently from the reaction in this case.

At this stage it was agreed that as the safety concerns were so serious that further safety testing would be carried out by Syngenta to investigate the problem.

6. FURTHER SAFETY DATA

The safety testing carried out was on the reaction stage for the concentrated process, again this involved using both isothermal heat flow calorimetry and adiabatic Dewar calorimetry. The isothermal heat flow calorimetry would show the extent of the power output due to the expected and/or unexpected exothermic reaction and the adiabatic Dewar calorimetry would show the expected consequences of a loss of cooling scenario.

6.1 ISOTHERMAL HEAT FLOW CALORIMETRY

The reaction was carried out as previously described (3.2.1) with a 2 hour addition of DCEE, this time using the more concentrated process (see Fig. 7).
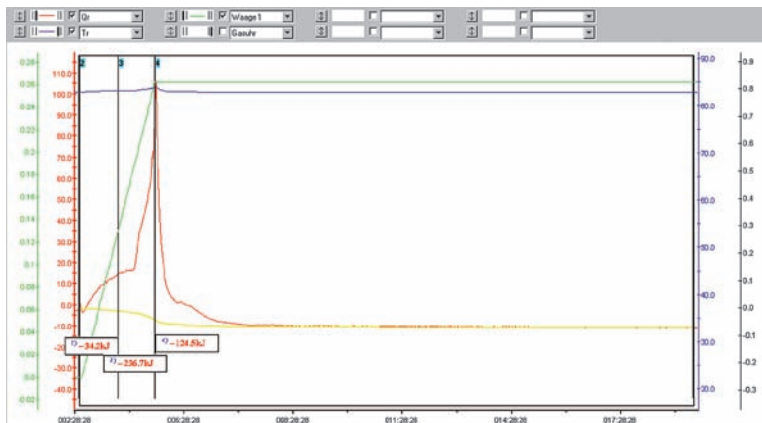
Figure 7. Concentrated process (2hr DCEE addition) in Rc1

The rate of heat output during DCEE addition was similar to that previously seen with the dilute process up to ca 1.5 hours into the addition. At this point a rapid increase in heat output was observed, indicative of a very rapid exothermic reaction, which then subsided just as rapidly. The total heat for the reaction was similar to that previously measured for the dilute process.

A further test was carried out using a 4 hour addition of DCEE (Fig. 8) which again showed a rapid exotherm, but this occurred later and had a lower instantaneous power output.
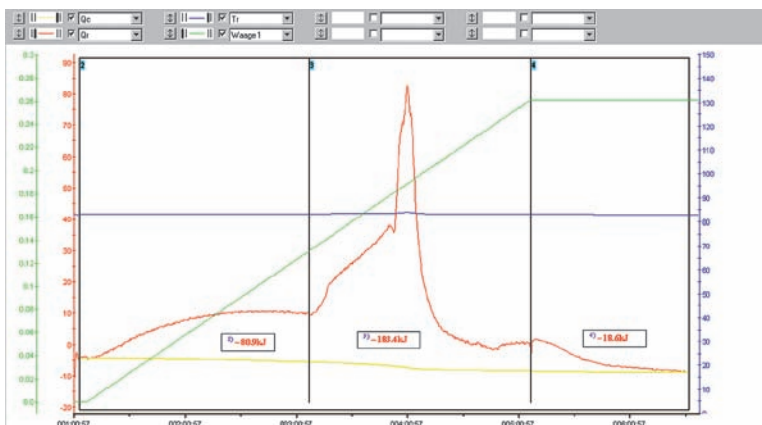

Figure 8. Concentrated process (2hr DCEE Addition) in RC1

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6.2   ADIABATIC DEWAR CALORIMETRY

The same reaction was carried out in a Dewar to simulate the worst case, zero cooling, scenario, with the DCEE added over 2 hours.

Very little reaction was observed over the first hour and then a rapid exotherm occurred. The rates of temperature rise and gas evolution were so great that the batch primed and ca 60% of the batch was lost from the Dewar vessel. The experiment was repeated with 4 and 6 hour DCEE additions and the rate of temperature rise/gas evolution compared (see Fig. 9 & 10).

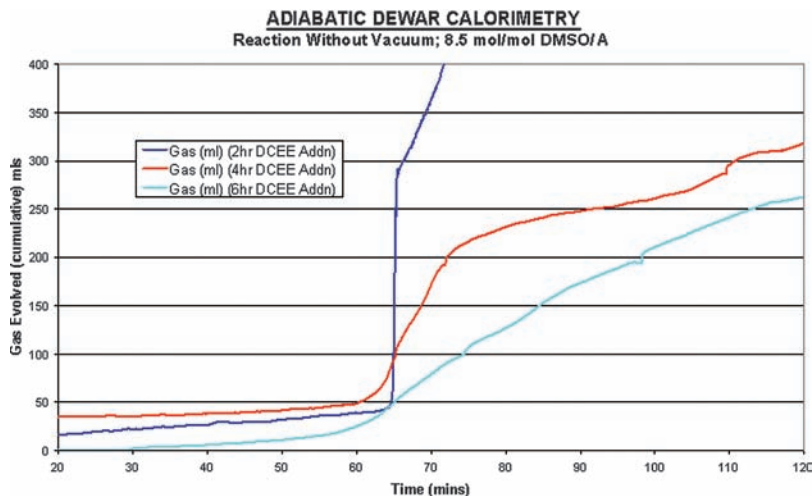The rates of temperature rise and gas evolution for the three experiments are summarised in the table below:

These additional tests suggested that a slower addition rate of DCEE would allow greater control of the temperature excursion should it occur.

6.3   CONCLUSIONS FROM ADDITIONAL DATA

This additional safety data strongly suggested that the concentration of water in the batch played a critical role with respect to the reaction rate. The rate of reaction was thought to be dependent on the rate of deprotonation of the molecule **A**. This is therefore dependent on the availability of base, in this case KOH. At the start of the reaction, as very little water is present, the deprotonation of **A** is dependent on the phase transfer catalyst, which is required to help solid KOH come into contact with **A** in DMSO solution. As water is produced, KOH dissolves, and at a critical water concentration becomes miscible with
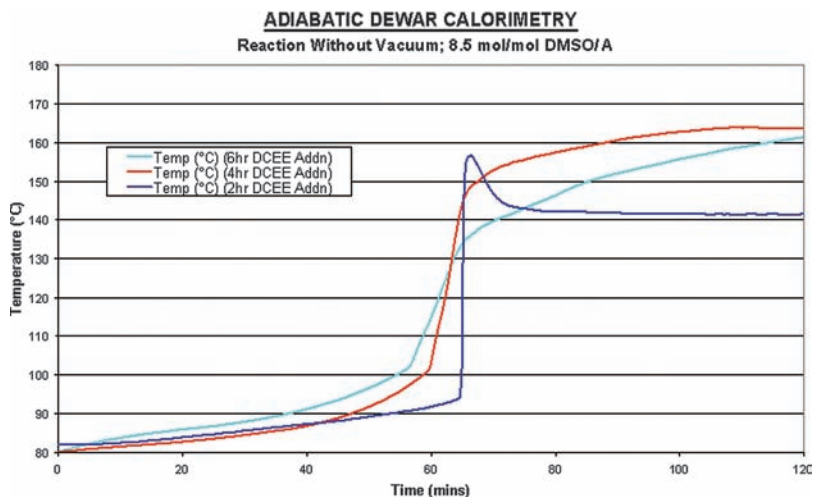
Figure 9. Concentrated process (Comparison 1 – temperature rise)

Figure 10. Concentrated process (Comparison 2 – gas evolution)

Table 2. DCEE addition rate – comparative data summary

DCEE addition time (hrs)	Maximum instantaneous rate of temperature rise (°C/min)	Maximum instantaneous rate of gas evolution (ml/min)
2	180	900
4	10	50
6	4	8

DMSO. This immediately makes significantly more KOH available for reaction with **A**. As the rate of reaction starts to increase, more water is produced, dissolving more KOH which increases the rate further. In addition, the exothermic reaction causes the batch temperature to rise, which also increases the rate, producing an overall rate of reaction that is much faster than the expected exponential reaction rate. The situation is also exacerbated by the relatively high accumulation of DCEE to this point.

6.3.1   Manufacturing Plant Observations

The rapid rate of reaction seen in the calorimetry work (6.1 & 6.2) was shown only to occur if water was not removed from the reaction mass, or if water entered the mass before significant reaction had occurred. On the production plant, it was found that the temperature excursions were occurring almost every other batch, even though the reaction was

being carried out under vacuum and with a distillation column in place. It had been noted that the temperatures and pressures across the column were not in line with expectations and indicated that the column was becoming flooded early in the distillation. When vacuum was broken, the batch experienced an immediate rapid exotherm, raising the batch temperature to around 150°C. This effect was consistent with the laboratory findings, suggesting that water was held up in the column and returned to the batch when vacuum was broken. This then increased the rate of reaction by the mechanism described in section 6.3. Further monitored batches showed similar column problems and similar exotherms occurring during the reaction period, indicating that the distillation was not removing water effectively.

7.   CONCLUSIONS AND RECOMMENDATIONS TO THE TOLLER

From the safety data and data taken from the production plant, calculations were carried out to determine the size of distillation column required to remove water effectively from the 5 te scale plant reaction. The calculations did indeed reveal that the column currently in use on the toller facility was very much under-sized and was not fit for the duty expected. Therefore, the persistent temperature excursions would certainly continue if this column were left in place, with the inevitable safety concerns therefore remaining.

To ensure safe operation of the process and to help with future process efficiency, a number of suggestions were made to the toller:

- For the immediate future, the process could be run with a 4 hour DCEE addition which would lessen the impact of any thermal excursion and minimising the MTSR (maximum temperature of the synthesis reaction).
- An additional element of process control could be adopted to stop addition of DCEE if the rate of temperature rise started to increase. This would minimise the amount of DCEE accumulation and would again reduce the MTSR.
- The distillation column could be replaced with a column fit for purpose i.e. one that was correctly sized for duty. This would allow the process to be carried out as planned, with reduced cycle time and increased yield, therefore raising efficiency and increasing commercial viability.

7.1   REMEDIAL WORK AND RESULTS

The cost of the replacement column was too much for the toller to bear. However, the strategic importance of the product and efficiencies that would be achieved together with the risk to the business should an incident occur, were sufficient for the Syngenta business to sanction the cost of the project ($M's). This required several months lead time, during which the toller continued operation having adopted the other suggested process changes to ensure it could be run more safely.

The process changes showed an immediate improvement and although temperature excursions still occurred, they were much less frequent, less severe and eminently manageable. The column was put in place with one more design modification to improve

safety; a device was installed at the base of the column to prevent the contents of the column returning to the reactor should vacuum be lost. The process was then run as designed without incident and continues to run, incident free to this day.

8. SUMMARY AND CONCLUSIONS

This paper has detailed one technical example of the possible benefits of maintaining a good ongoing working relationship with a contract manufacturer. At the point of process handover, a comprehensive data package was provided to the toller. The data, particularly the safety data, did not include recommendations for scale up and did not include Process Risk Assessment (PRA) data. However, the exchange of information on handover included detailed discussions of every known process hazard and from the technical package, the toller was able to carry out their own PRA and arrived at a basis of safety comparable to that determined in-house.

As is often the case, scale up of the process highlighted problems which did not come to light in the laboratory or on the pilot plant scale. The problem was one that was not foreseen as it related to a maloperation, whereas the data handed to the toller related only to the desired process. Once the problem was highlighted, the good working relationship that had been built up with the toller, both during this campaign and from previous out-sourcing projects, helped both parties to work together to acquire all the necessary information to resolve the issue successfully.

Whilst this example is one of a successful working relationship between a business and a toller, in reality this is probably an unusual case and the outcome could have easily been much different. Questions one could ask:

- Would the relationship and the outcome have been the same if the toller had been in the Far East?
- If the suggested process changes had not been adopted, what action would the business have taken?
- If the remedial work had not been successful, how much more resource would the business give to solving the problem?
- If the advice given had resulted in an incident, could the business be liable?

In this case there were a number of factors which made it advantageous to have a closer relationship:

- The toller was the sole supplier of the product at that time
- The product was a "blockbuster" product in its first year of sales and therefore hugely important to the business to maintain security of supply

Having this close relationship provided the advantage that the business found out about problems at an early stage and were able to minimise the Business Interruption Risk (BIR). However, it is not always advantageous or desirable to have such a close relationship. The tendency with contract manufacturers is normally to leave them well alone.

After all, we have an only finite resource – which is why products are outsourced in the first place. It is ultimately the contractor's responsibility, it is their asset.

In the end it comes down to common sense and maintaining a balanced approach.

- When dealing with contract manufacturers, it is important to <u>share</u> as much information as possible at the start. This means obtaining as well as giving information – find out as much as possible about the manufacturers themselves, such as the standard and suitability of their manufacturing facility and particularly their level of understanding of the process risks and hazards.
- It can often be advantageous to have an ongoing relationship with the toller but the level of relationship will depend on the situation – when trying to avoid BIR and to maintain security of supply, a closer relationship will mean that problems are communicated earlier. However, it is important not to spoon-feed the toller and impose your way of thinking, it could lead them down the wrong path. Don't make the assumption that you know better – it is not always the case – and remember, they know their own kit better than you do. Closer relationships also require more resource, the one thing we wanted to free up in the first place.
- When dealing with manufacturers in developing countries, we need to accept that standards are not going to be as high as in the established manufacturing facilities in the Western World. We have a moral obligation to use the relationship during the contract to help them advance. However, there comes a point where we have to accept the standards and live/work with the remaining risk.

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