MANAGING REACTIVE CHEMICAL HAZARDS IN GAS SCRUBBER SYSTEMS

David Royle, Robert Fitch and Paul Gillespie, AstraZeneca, Macclesfield, Cheshire, UK

Vent gas scrubbers are routinely used to abate various substances from batch chemical processing using a range of scrubber fluids. However it is not just the particular pollutant which can end up in the scrubber, any other materials in use, particularly process solvents may be carried over into the scrubber. This may give rise to unanticipated chemical reaction hazards within the abatement system. A new risk based approach has been developed for use in process risk assessment meetings to cover a wide range of likely interactions within a scrubber system used in batch manufacturing process. This helps the process operator, accommodation manager, process engineer and process chemist to quickly understand the potential for interactions and impact. A case study will be presented where an incident arose from a scrubbing operation during manufacturing. Following an investigation into an exothermic decomposition within a scrubber system a compatibility matrix has been produced. This screening tool, as part of the risk based approach, is designed to identify when there is a possible interaction between process materials and scrubber solutions. The most appropriate scrubber liquor can then be selected to minimize the risk of unwanted chemical interactions taking place.

INTRODUCTION

Development pharmaceuticals are generally manufactured in multipurpose batch processing pilot plants. Due to the highly variable demands of new processes a high degree of flexibility is required from these manufacturing units. This need for flexibility extends to include abatement systems for vent gasses. Multipurpose plants routinely use off gas scrubbers to abate any various substances to within permitted limits and minimize the environmental impact of the manufacturing process. A range of scrubbing fluids can be used depending on the specific scrubbing requirements; a typical line diagram of a scrubbing system is shown in Figure 1.

Prior to operating processes in the pilot plant an individual Process Risk Assessment (PRA) is carried out. This risk assessment considers a wide range of potential hazards including chemical and operational hazards of the proposed process. It reviews the process against the pre-defined basis of safety for the pilot plant and also considers interactions with other activities in the area. If anything potentially falls outside of the basis of safety then suitable alternative procedures/modifications may need to be implemented.

Normal operation of the scrubber includes charging the scrubber with fresh liquor at the beginning of a campaign and confirming it is performing correctly by monitoring the liquor flow and column pressures. The scrubber is kept running throughout the whole manufacturing campaign where there is a scrubbing duty present. Sampling and analysis of the scrubber liquors between manufacturing batches is used to determine if the active component has been depleted and need replenishing. Finally at the end of the campaign, or when there was no longer a duty, the scrubber liquor is drained and the scrubber flushed with water to rinse the system.

DESCRIPTION OF INCIDENT

Prior to beginning a manufacturing campaign for a development compound, a solvent trial is undertaken to confirm the plant configuration is as expected and to check the integrity of pipework and equipment following any engineering work. In this particular case, the scrubber had been charged with dilute sodium hypochlorite solution ('bleach') ready for the solvent trial, as per the abatement requirements of the process to be run. The scrubber heat exchanger in the liquor recirculation loop was not connected at this time, as it had been removed for cleaning and replaced by a temporary line. The unit was removed under the site change control procedure and was due to be refitted before the first batch was manufactured, however the decision had been taken to proceed with the solvent trial without the heat exchanger due to there being no scrubbing duty and thus no anticipated cooling or process duty.

The solvent trial operations included heating, cooling, trickle purging and transferring material using nitrogen pressure, conducted with venting via the scrubber. The computer sequences that control the plant routinely select the scrubber vent route, even with processes that do not require a scrubber for an abatement duty. During processing the scrubber liquor low flow alarms were received and accepted following confirmation that the operating parameters, including flow, remained within the typical ranges specified by the operating procedure. The alarms were therefore assumed to be spurious. A number of hours later, the scrubber high temperature alarm activated, indicating that the scrubber liquors had reached 50°C. An initial check confirmed that the other scrubber operating parameters were still within their expected ranges. The high temperature alarm was thought to be connected to the fact that the heat exchanger was not in place and not related to
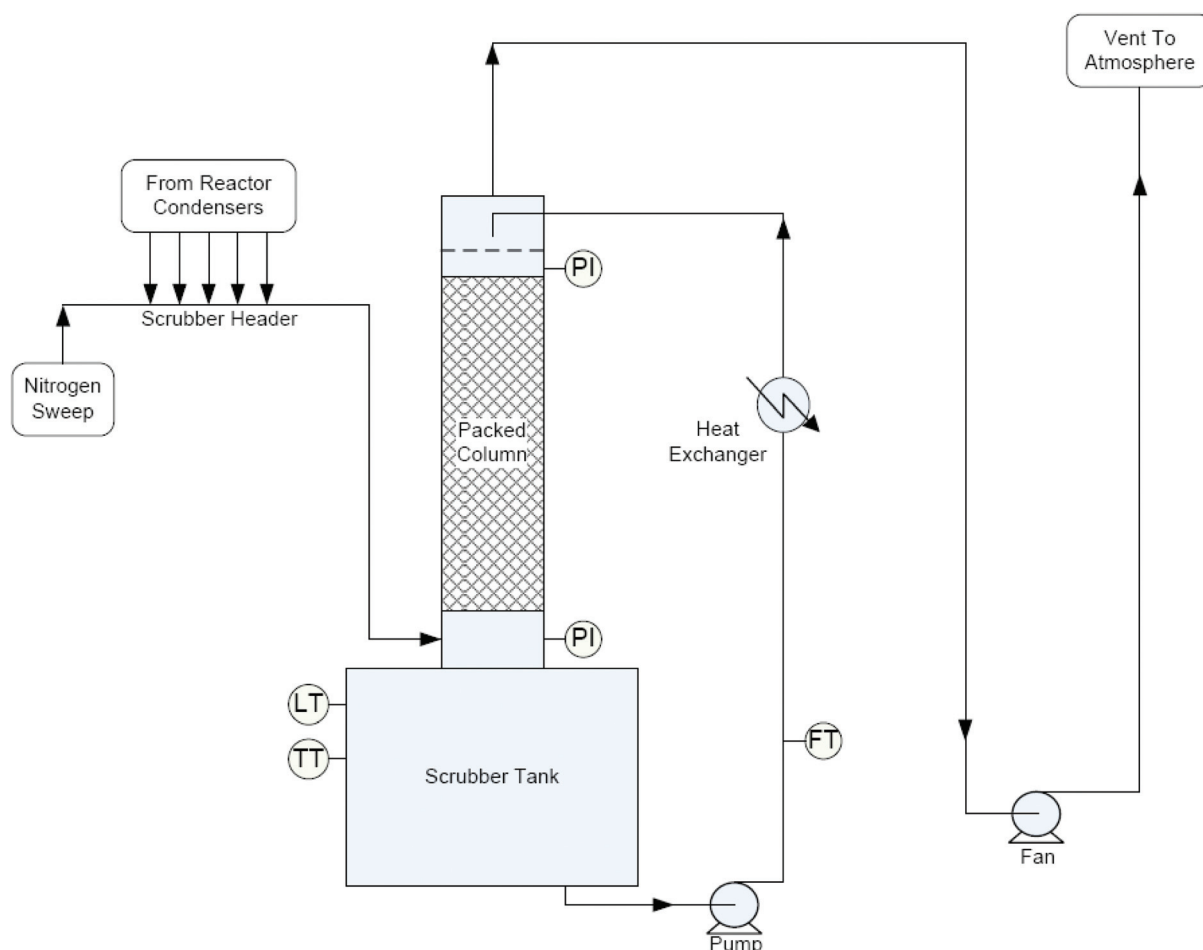
Figure 1. Typical gas scrubber line diagram

the ongoing activities in the plant. The temperature of the scrubber liquors was monitored and a peak temperature of 72°C was observed before the liquors began to cool. This can be seen from the temperature measurements taken in the scrubber during the solvent trial (see Figure 2). The issue was communicated to the incoming shift who observed the temperature of the scrubber liquor to have cooled to 62°C. Upon activation of a subsequent 'low differential pressure' alarm, the operational team found scrubber liquors leaking out of the scrubber fan housing and gas sampling point on the vent pipework, presumably due to foaming of the liquors. The scrubber pump and fan were immediately switched off and the solvent trial halted awaiting investigation into the issue. Samples of the scrubber liquor indicated that it was now ~pH 7 (ie. neutral), compared to strongly basic on charging.

The initial investigation focused on exploring the cause of the exothermic activity in the scrubber liquors causing the large temperature rise (the details of the actual investigation work undertaken is given in the following section). Meanwhile, the scrubber liquors were discharged

and a strong smell of organic solvent was noticed; this was later confirmed to be tetrahydrofuran (THF). This solvent had been used in the solvent trials and an inventory check following the completion of the trials showed a deficit of greater than 60kg. Some solvent carryover is expected during normal processing; however the subsequent investigation into how this significant quantity of material entered the scrubber system identified opportunities to review the plant control philosophy and changes to the computer control sequences have since been implemented to minimise the routes of carryover. On inspection of the scrubber, a small quantity of residual solids was found to be contaminating the internals of the equipment, however tests ruled out reaction or degradation of this solid as being a cause of the exotherm. A major concern was the potential impact of recirculating hot bleach on the mechanical integrity of the scrubber system. A thorough visual inspection, coupled with lab materials of construction compatibility tests with coupons of the scrubber liner gave confidence that there had been no significant damage to the equipment.
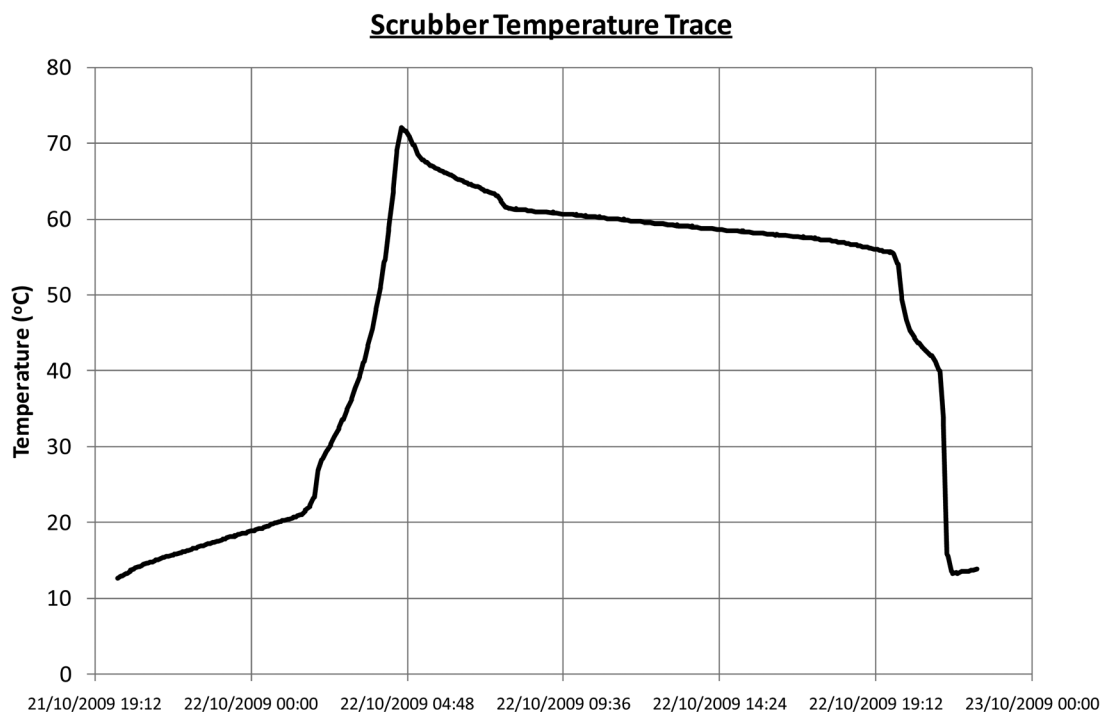
Figure 2. Temperature exotherm in scrubber tank

CHEMICAL HAZARD INVESTIGATION WORK

The initial investigation work focused on identifying the source of the temperature rise and the most obvious potential cause was from chemical reaction involving the scrubber liquor, especially as no external heat source was available. It is known that sodium hypochlorite is a strong oxidising agent and is inherently unstable, with the rate of decomposition related to factors including hypochlorite concentration, pH, temperature, impurities/contaminants, exposure to light and ionic strength of the solution. There are two main decomposition mechanisms (highlighted in many suppliers information/handling guides[1]):

$$3NaOCl \longrightarrow NaClO_3 + 3NaCl \qquad (1)$$
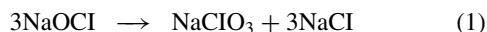
(1) is the predominant mechanism and generates sodium chlorate, the rate increasing with increasing temperature.

$$2NaOCl \longrightarrow O_2 + 2NaCl \qquad (2)$$
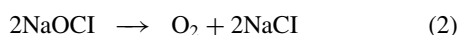
Mechanism (2) is catalysed by the presence of trace metals, such as Ni, Cu and Co and also light. This is a slow side reaction at ambient temperature to which over-pressurisation of storage containers have been attributed[2].

pH of aqueous sodium hypochlorite has a pronounced effect on its stability, the most stable having a pH in the range of 11.0 to 13.0. Sodium hydroxide (0.5 – 1.0% excess) is added to commercially produced bleach to maximise stability to temperature and light exposure. At pH > 9

OCl^- is the only component present, at pH 4 to 6 HOCl is the dominant species and at pH < 2 chlorine is the main component in solution.

The bleach charged to the scrubber was 14–15% available chlorine which was then diluted with an equal volume of water (total volume ∼3000 Litres). The thermal stability of this solution itself was investigated in a Carius tube experiment (used for searching for exothermic activity and gas generation), with the results shown in Figure 3.

In this test no significant exotherm was observed on diluting the bleach solution with water, however a slow exotherm was observed on heating from 111°C, which could be seen from as low as 51°C in bulk, i.e. in a low heat loss scenario. The scale factor applied is based on a series of assumptions regarding reaction kinetics, the sensitivity of process safety tests and the natural cooling rates of plant vessels compared to lab scale, which all lead to a potential lowering of the onset temperature of thermal events on a larger scale. Appendix 1 gives more detail on the rationale behind the application of safety factors for small scale thermal stability tests used within AstraZeneca. The experimental test was carried out in the presence of mild steel and rust to address any impact they could have as potential impurities/contaminants. As stated earlier, all sources of external heating to the scrubber was ruled out by route cause analysis. Therefore it was concluded that the significant self heating of the hypochlorite solution from ambient temperature, in the presence of some destabilising agent(s), was the most likely cause.
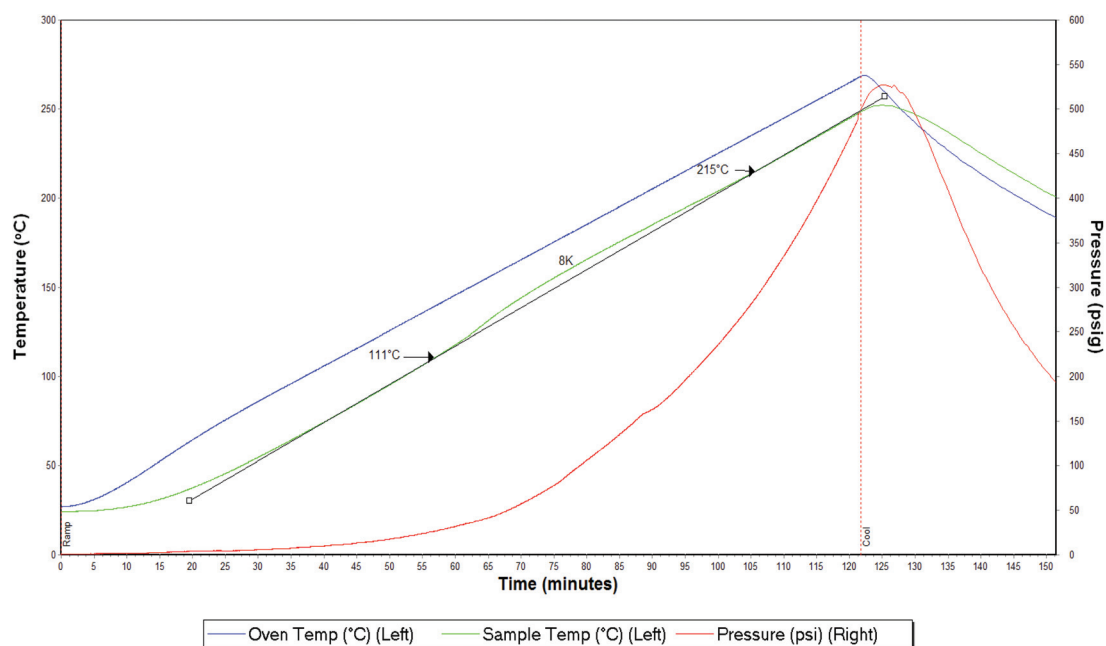
Figure 3. Carius tube test on diluted bleach

Account of the incident revealed that the scrubber liquors had a strong smell of THF and 66 kg of the solvent from the trial remained unaccounted for. This volume of THF relates to ~2.5% of the volume of the diluted bleach in the scrubber. The results of a subsequent Carius tube test on a sample of scrubber liquors with ~5 vol% THF added showed a large rapid exotherm from 70°C (Figure 4), and this could potentially occur from as low as 10°C under low heat loss conditions. Ingress of THF into the scrubber at ambient temperature could therefore explain the observed temperature excursion during the solvent trial. Un-stabilised THF was used in the Carius
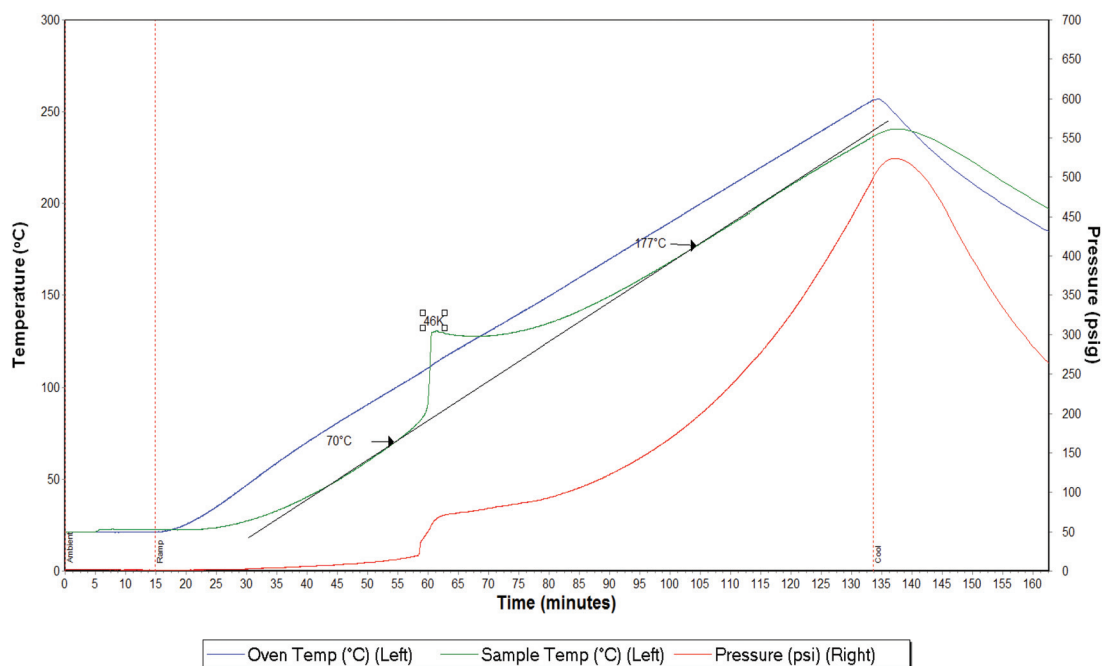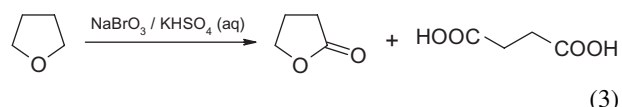

Figure 4. Carius tube test on diluted bleach +5 vol% unstabilised THF

tube experiments as this is likely to have been the case during ingress into the scrubber i.e. distilled and condensed THF would have entered the scrubber leaving the stabiliser in the source vessel. The Carius tube test indicated in Figure 4 was carried out in the presence of mild steel and rust as there was a likelihood the mixture would contact these materials. A test was repeated in the absence of these materials and showed no significant difference to the original test showing that the ingress of (unstabilised) THF alone was capable of producing the observed temperature excursion.

Testing of the scrubber liquors immediately after the incident showed them to be pH neutral. Therefore, an acidic material must have been present before or during the incident to neutralise the strongly basic bleach. The investigation found an amount of white solid in the scrubber but his had not been identified at the time of writing this paper. Interestingly a sample of this material was subsequently shown to be capable of neutralising the bleach liquors, i.e. it could be acidic. The results of a Carius tube test on a sample of diluted bleach, unstabilised THF and a small amount (20 mg) of the solid showed a very similar trace to the test in the absence of the solid but with a slightly lower ($\sim$8 K) onset temperature (see Figure 5). It is therefore feasible that the white solid contaminant in the scrubber could have brought about the neutralisation of the bleach solution noted in this incident. The change in pH of the scrubber liquor would also in turn increase the rate of decomposition of the bleach at ambient temperature. However, subsequent investigation revealed literature evidence[4,5] that oxidising agents can generate a variety of

ring opened products with cyclic ethers, equation (3).

$$\text{(structure: tetrahydrofuran)} \xrightarrow{\text{NaBrO}_3 / \text{KHSO}_4 \text{ (aq)}} \text{(γ-butyrolactone)} + \text{HOOC} \sim \text{COOH}$$

(3)

It was therefore postulated that the reaction between bleach and THF could produce succinic acid in a similar way either via NaOCl itself and/or with NaClO$_3$ – a decomposition product of NaOCl. In which case no additional acidic material would necessarily be needed to explain the observed neutralisation of the very basic scrubber liquor.

To corroborate this a Carius tube experiment on a sample of 14% bleach solution diluted with an equal volume of water and unstabilised THF (5 vol%). The pH of the mixture was measured before and after the THF addition and after heating to 120°C. A small increase from pH 13.5 to 13.8 was observed after adding the THF. After heating to 120°C (to complete the reaction exotherm) the pH had fallen to 5.0. Hence this supports the postulation that an acidic species is generated during the interaction of hypochlorite and THF that is capable of neutralising the bleach solution. Further work would be required to confirm that this was succinic acid or other breakdown products.

The leakage of scrubber liquor from the fan housing and gas sampling point mentioned in the account of the incident raised concern that chlorine gas may have been generated. However a pH of $\leq$4 would have been necessary for this to occur. This is supported by the observation that no smell of chlorine was observed in the vicinity at the time. The likely mechanism for the decomposition is therefore
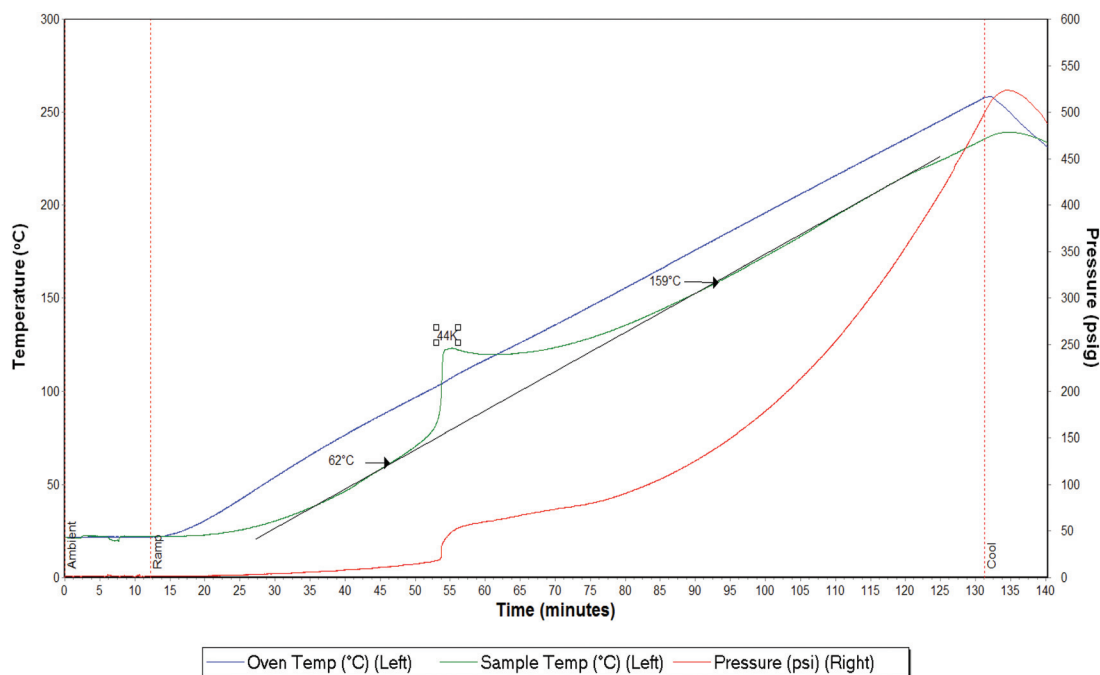

Figure 5. Carius tube test on diluted bleach +5 vol% unstabilised THF + scrubber solid

via equation (1) and (3) above. THF boils at ~65°C and the observed leakage was probably due to liquid boiling and frothing as the temperature rose.

Realistically, the solvent trial should have been more rigorously assessed and the potential interaction of THF and sodium hypochlorite would have been acknowledged and considered in more detail. Simple replacement of the scrubber liquor with water would have been the inherently safe option. One of the conclusions of the investigation therefore focussed on how to address these potential interactions in a more rigorous and effective manner.

DEVELOPMENT AND USE OF COMPATIBILITY MATRIX

In order to minimise the risk of a re-occurrence of this incident, the accommodation team required an effective mechanism to review potential interactions in the scrubber system, ideally without introducing the requirement for

an experimental chemical compatibility screen for every process. The intention was to provide a clear and concise resource to primarily be used as a screening tool to identify likely interactions. A suitable solution was identified by using literature data to compile a matrix of known compatibility issues between a variety of solvent types and the most frequently used scrubbing fluids. This led to the construction of the compatibility matrix shown in Figure 6. The matrix is constructed from a number of literature sources which are illustrated in Figure 7.

If evidence of an unfavourable interaction was identified from multiple sources, the box is coloured red and the user is advised to seek guidance from a chemical hazard assessor. If indirect or conflicting evidence of interactions was found, the box is coloured amber and the user is advised to check the specific sources of information for additional details. If no interactions are known, the box is coloured green and no further action is required. In the vast majority of cases the literature information relates to

Scrubber Liquor chemical compatibility chart					
Solvent Type	Caustic (inc Proklenz one)	Citric Acid	Hypochlorite	Dil. HCl (≤6% w/w)	Water
Alcohols	AMBER	GREEN	RED	AMBER	GREEN
Aldehydes	RED	RED	RED	AMBER	GREEN
Alkanes	GREEN	GREEN	GREEN	GREEN	GREEN
Amides	GREEN	GREEN	RED	AMBER	GREEN
Amines (aliphatic)	GREEN	RED	RED	AMBER	GREEN
Aromatics (hydrocarbons)	GREEN	GREEN	AMBER	GREEN	GREEN
Carboxylic Acids	RED	GREEN	RED	GREEN	GREEN
Diols	AMBER	GREEN	RED	AMBER	GREEN
Esters	RED	GREEN	GREEN	AMBER	GREEN
Ethers	GREEN	GREEN	RED	AMBER	GREEN
Furans, Pyrans	GREEN	GREEN	RED	AMBER	GREEN
Halogenated (hydrocarbons)	AMBER	GREEN	GREEN	AMBER	GREEN
Heterocycles	GREEN	GREEN	RED	AMBER	GREEN
Ketones	RED	GREEN	RED	AMBER	GREEN
Nitriles	RED	RED	RED	AMBER	GREEN
Sulfoxides	RED	RED	RED	AMBER	GREEN

RED	Known ineractions possible: Seek advice	
AMBER	Some evidence of interactions possible: Seek advice	
GREEN	No anticipated issues	

Figure 6. The chemical compatibility matrix

Material Compatibilities Search Table

Solvent Type	Caustic	Citric Acid	Hypochlorite	Dil. HCl	Water	Proklenz (KOH)
Alcohols	1 2 / 3 4	1 2 / 3		1 2 / 3 4		1 2 / 3 4
Aldehydes	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Alkanes	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Amides	1 2	1 2		1 2		1 2
Amines (aliphatic)	1 2 / 3 4	1 2 / 3	6	1 2 / 3 4		1 2 / 3 4
Aromatics (hydrocarbons)	1 2 / 3 4	1 2 / 3 4	7	1 2 / 3 4		1 2 / 3 4
Carboxylic Acids	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Diols	1 2 / 3 4	1 2 / 3 4	6	1 2 / 3 4		1 2 / 3 4
Esters	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Ethers	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Furans, Pyrans	1 2 / 3 4	1 2 / 3 4	5	1 2 / 3 4		1 2 / 3 4
Halogenated (hydrocarbons)	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Heterocycles	1	1		1		1
Ketones	1 2 / 3 4	1 2 / 3 4		1 2 / 3 4		1 2 / 3 4
Nitriles	1 5 / 3	1 2 / 3 4	6	1 2 / 3 4		1 5 / 3
Sulfoxides	6	6		6		6

1 = CHEMWATCH Chemical Compatability Chart www.chemwatch.net
2 = CRC Chemical Compatibility Chart
3 = EPA-600/2-80-076. Chemical Compatibility Chart. April 1980
4 = Vanderbilt Chemical Compatibility Chart
5 = CHA ZZ05047 or other CHA evidence
6 = Bretherick's Handbook of Reactive Chemical Hazards
7 = Brookhaven National Laboratory - Chemical Storage and Compatibility Table

Figure 7. The chemical compatibility matrix citing literature

the concentrated reagents, whereas the chosen scrubber liquor is most likely to be used diluted with water. Hence in the situation where an unfavourable interaction is identified, either through a more detailed review of the literature data or experimental testing, any risks can be assessed and managed appropriately. If the incompatibility cannot be safely managed, the matrix can be referred to for selecting an alternative scrubbing liquor.

The compatibility matrix now forms part of the standard pre-accommodation assessment conducted by a process engineer familiar with the process and equipment. Once the process solvents have been defined by the development chemist and the scrubbing requirements have been identified from emissions calculations, the matrix is consulted to check for potential interactions. References to the matrix within the PRA meetings has prompted both queries from the accommodation team to the process safety assessors with regards to clarification and testing of identified intreactions, as well as challenge to decisions regarding the choice of scrubber liquor.

CONCLUSION

Exothermic decomposition of sodium hypochlorite solution in the presence of unstabilised tetrahydrofuran has been identified as the most probable cause of the unexpected temperature rise in the gas scrubber system. The THF had entered the scrubber system from the process vessels via solvent carryover mechanisms. This incident led to a thorough review of potential contamination routes for both solids and liquids and corrective measures to plant operation and control philosophies have been implemented.

Additionally, the incident identified a gap in the chemical reaction hazard assessment process that is carried out prior to manufacturing all development products, i.e. potential interactions between the process solvent and the scrubber liquor. This has been addressed through the introduction of a compatibility matrix to allow the accommodation team to identify potentially unfavourable combinations of solvents and scrubber liquors. This allows any risks to be either managed or designed out. The screening tool has been successfully integrated into the PRA and

minimises the risk of undesirable chemical interactions in the scrubber system.

APPENDIX 1: AVOIDANCE OF SELF-HEATING FOR LIQUIDS BASED ON NATURAL COOLING

Avoidance of self-heating based on natural cooling for non-viscous liquids is assessed based on the Semenov model using conservative assumptions regarding reaction kinetics, the sensitivity of process safety screening tests (or analysis of the recorded self-heating rates in Adiabatic calorimeters) coupled with conservative application of measured cooling rates of pilot plant and Large Scale Laboratory (LSL) vessels. Presented below are the values used for the parameters from which critical runaway temperatures can be calculated:

Ambient temperatures:
- Ambient UK/Sweden: 25°C
- Ambient India/outsourcing: 35°C

Plant heat losses:
- LSL 50 mW/kg/K (measured)
- Large pilot plant vessel 10 mW/kg/K (measured)

Reaction activation energy:
- 50 kJ/mol (conservative value)

Assumed sensitivity of screening instruments:
- Differential Scanning Calorimeter 20 W/kg
- Thermal Screening Unit 10 W/kg
- Carius 5 W/kg

Application of Adiabatic calorimeter data:
- No unique heat output value can be associated with the test onset
- Actual heat output should be calculated.
- Heat capacity for sample: literature value if available otherwise 2.0 J/g/K for organics
- Assessment of critical runaway temperature on a case-by-case basis (to include evaluation of autocatalysis)

USE OF SIMPLE SCALE FACTORS

Provided the test onset is above the value stated in the table below, thermal runaway can be avoided by setting the operating temperature below the screening test onset temperature with the subtraction of scale factors listed below. However safe plant operation at higher temperatures or reactions with lower test onsets can often be demonstrated by:

- Operation in higher heat loss equipment (e.g. smaller, higher heat-loss vessels)

- More detailed analysis/testing of the decomposition kinetics, (to include evaluation of autocatalysis)
- Use of alternative time-based (TMR) basis of safety (with specified remedial action).
  - DSC 100K
  - TSU 80K
  - Carius 60K

MINIMUM SCREENING TEST ONSETS TO UNIVERSALLY PREVENT SELF-HEATING AFTER SUBTRACTION OF STANDARD SCALE FACTOR

At onset temperatures of up to ~5–10 K lower, there may still exist a safe operating temperature limit with the use of a larger scale factor.

Table of standard scale factors

Plant:	UK/Sweden LSL	Bangalore LSL	UK/Sweden Pilot Plant	Bangalore Pilot Plant
DSC	105°C	120°C	150°C	175°C
TSU	90°C	105°C	130°C	150°C
Carius	75°C	90°C	115°C	135°C

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