Ask the Experts

Batch Processing

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Q. How do I avoid safety problems when scaling up a reaction from the laboratory to the plant?

Many chemical engineers face the challenge of establishing effective safety and process envelopes for manufacturing based solely on information derived from the laboratory. The critical transition from lab to plant demands both a broad perspective of the entire process and rigorous attention to detail. Getting it wrong can have significant penalties in terms of safety, time, cost and quality.

In 1997, working in the custom synthesis fine-chemical industry, I experienced such a problem. A six-step process had already been successfully run at the 1-L scale. It would now be scaled up to 1,000-L scale in a manufacturing facility.

All was well until step four, when the key reagent was added. This reagent had a reaction heat of 250 kJ/mol, a molecular weight of 85 g/mol and a density of 0.8 kg/L. From the literature, the development team knew that the process could evolve hydrogen during the reagent-addition phase (2 L of hydrogen/mol of reagent), but this event had not been observed under laboratory conditions.

The process was duly released to manufacturing, and the addition of the reagent was carried out as per a standard scale-up calculation method. The computation called for the addition rate of the reagent used at the bench or laboratory scale to be reduced by a factor of three for any given larger-scale experiment. In our work, following this rule resulted in a reagent-addition time of 90 min, which ensured that the resulting exotherm could be controlled and that the reaction performed correctly.

However, the team observed significant hydrogen evolution during the addition, and the nitrogen inertization was increased to the maximum rate of 800 L/min. Shortly thereafter, an alarm was received from the bulk nitrogen storage tank. The chemical engineering team went to investigate the scene.

The crew discovered that the nitrogen volume supplying the entire the manufacturing facility was falling rapidly. They quickly took inventory of all the manufacturing processes that were running at that time and identified one reaction in particular that was excessively consuming nitrogen. They immediately shut down the process. Subsequently, the engineers determined that the reaction responsible for excessive nitrogen consumption was evolving over 1,000 L of hydrogen during the 90-min addition period.

A detailed review of the process revealed that the required 1 vol.% maximum safety level for hydrogen in the headspace of the vessel would require that the hydrogen evolution remain below 8 L/min. This low rate would ensure compliance with the lower explosive limit (LEL) of hydrogen (or 4%) and the mandated safety factor of 25%. In the 1,000-L reactor at the given addition rate, the reaction evolved over 11 L/min of hydrogen.

To enable the reaction to be performed successfully and safely, the reactor size was scaled down by six-fold so that the correct addition rate could be achieved (based upon inertization). Six batches had to be run in a 160-L reactor to ensure that the maximum hydrogen evolution would not exceed the critical capacity of the nitrogen plant. The scaled-down process evolved 160 L of hydrogen/batch, resulting in an addition time of 25 min to keep below 8 L/min of hydrogen evolution.

Our solution to the problem resulted in a significantly longer campaign time and commercial penalties, due to late delivery of the finished product. However, the lessons we learned were invaluable.

First, we found that it is generally true that for large-scale campaigns, vessels with volumes or capacities greater than 1,000 L have lower overall addition times, but only if they are limited by heat transfer.

Secondly, this experience improved our understanding of the impact of gas evolution as scale increases. We now incorporate gas-measurement equipment into the vent of a reaction calorimeter to measure the actual evolution of flammable gas from processes prior to scaleup. Today, modern systems such as microreactors coupled with in-silico modeling programs (i.e., programs that design reactions) can quickly facilitate scaleup effects to be quantified and understood at a low risk.

Finally, we experienced, firsthand, the value of a concept we call right-to-left thinking — downstream-to-upstream and vice versa (*CEP*, Nov. 2002, p.7). In this case, the process would have improved exponentially had both the manufacturing team and the laboratory-and-development team possessed an in-depth understanding of the capabilities of the manufacturing facility. However, neither team understood the true "envelope" of the inertization system.

Remember, processes rarely improve upon scaleup. But during the transition from laboratory to manufacturing, the ability to understand and characterize potential problems ensures superior safety as well as realistic and achievable commercial commitments. Processes will take a different and likely, optimal course, if all technical staff involved in developing, scaling up and manufacturing the product possess a full and comprehensive understanding of manufacturing-plant operational parameters.

A broad perspective from team members at both ends of the operation can tremendously alleviate the potential for safety, time, cost and quality penalties. In my experience, the time to develop this broad understanding is a highly worthwhile investment.