Scale-up Basics for Formulators and Process Engineers

Bob Bornfriend
Alberto Culver, Melrose Park, Ill. USA

KEY WORDS: *scale-up, emulsion, equipment, batch processing, shear, mixing*

ABSTRACT: *This article aims to help novice formulators understand issues that arise from the scale-up of their recipes, and to remind experienced formulators of some of the less common pitfalls. It also focuses on the unique demands of process development for global implementation at multiple sites, specifically pertaining to the scale-up tasks for process engineers at multinational companies.*

A number of authors have written about scale-up processes for personal care products. One commonly referenced article by Dickey describes the importance of consistent tank geometry and provides a few approaches to calculating scalable mixer speeds.[1] Similarly, Yacko has presented on mixing and heat transfer considerations, as well as specific parameters and variables for cosmetic emulsions.[2] His work includes the often overlooked variable of shear on the physical properties of an emulsion as it is compounded and filled.

For those interested in modern technology for scale-up and mixing, simulation software[a] has evolved to an amazing degree to allow engineers to vary the parameters around different mixing systems and predict the results. These systems include models for turbulent flow (low viscosity liquids), laminar flow (high viscosity, non-Newtonian fluids such as emulsions), and combinations of different and multiple impellers on the same shaft, including the commonly used anchor mixer with side scrapers. Newer software[b] has even added a module for high shear devices such as homogenizers and mills for calculation of shear rates, pumping capacity and power consumption or torque.

Although continuous processes are efficient for making the same product again and again, they are inflexible to changes.

Equipment Variations and Their Effects

A unique challenge to multinational companies is the wide variety and design of mixing vessels around the world, challenging scale-up engineers to make the same product with the same specifications in all different types of configurations. Processes developed for US equipment systems may require substantial modification to accommodate equipment in Europe, Africa, Asia or Latin America. Formulators can find high-tech designs, indigenous copies of well-known manufacturers and unique local variants, all of which may require adapted processes. For example, although counter-rotating, side-scraped mixing equipment is common around the world for making emulsions, a process engineer might find configurations such as a mixer with a single sweep blade whose programmed reverse cycle uses the momentum of the fluid itself to impart the turbulence and shear necessary to produce the desired viscosity and droplet size.

Also possible are varying versions of counter-rotating mixers with design differences that can greatly affect process parameters. For instance, a counter-rotating mixer with a single drive motor (common to older designs) restricts the engineer to one speed for both sets of impellers and limits the amount of energy that can be input without splashing or potential aeration. Offset turbines coupled with a side scraper/sweep mixer present a different set of problems for scale-up. Since the turbine must fit in an area less than one-half of the tank's diameter, the impeller blades are short and do not reach the tip speeds necessary to develop the turbulence and shear for emulsion formation. They are also less effective in batch turnover when the product reaches a high viscosity, which then may require a recirculation loop to ensure complete homogeneity for a viscous product.

Of course, recirculation comes with its own set of problems such as aeration potential and cleanability. Aeration can occur when a recirculated stream is returned to the mix tank above the liquid level, dropping a distance through air. Cleanability is made more complex

[a] *Turbulent, Laminar, and Different Impellers are simulation software programs manufactured by VisiMix Ltd., Jerusalem, Israel.*

[b] *Rotor-Stator-Disperser (RSD) is a simulation software manufactured by VisiMix Ltd., Jerusalem, Israel.*

because the recirculation loop must be either separately cleaned or made part of an extended washout and sanitization procedure.

Finally, besides other mixer types, fully variable, large diameter turbine impellers may also be found within the same company.

Continuous, Semi-continuous and Batch Processes

Most commonly, batch processes are used to produce personal care products, although a small number of continuous or semi-continuous processes also are used. While continuous processes are efficient in making the same product again and again, they are generally inflexible in terms of process changes. Continuous processes are also formula-specific, so they tend to be concentrated on simple, low viscosity products or on product ranges with a single base. There are exceptions to this but they require a high level of technical support and expertise.

A particular challenge for multi-plant companies that produce emulsions using both batch and continuous processes is achieving the same droplet size in the inner phase, i.e. the oil phase. The same would be true for particle sizes of solid crystals formed in a liquid suspension, such as a pearling agent in a shampoo. This is due to the fact that a batch process delivers an average mix and shear effect that creates a wide distribution of particle sizes, while a continuous process acts consistently on a small portion of the batch at any one time, producing a narrower cut. The resulting differences can affect physical properties such as viscosity as well as the stability profile of the product. Therefore, it is prudent for the process engineer to evaluate the production of a new product via both processes—as if they were two different formulas—to avoid unpleasant surprises on start-up.

Fast Batch Processing

Some equipment systems are "fast batch" or batch processes that utilize a high energy device on a small volume of product to affect the emulsion or dispersion in a matter of minutes as opposed to hours. This technique can be used on an emulsion or gum concentrate that is later diluted to its final concentration using room temperature material streams, such as a heat sink, to remove thermal energy more quickly than standard jacket cooling.

The challenge for process engineers at an international company with multiple sites is to develop a process, regardless of type, that can be adapted to less sophisticated and less expensive conventional mixers. Lin recently published a book on this topic of fast batch processing and low energy emulsification.[3]

Pilot Vessel Size

Non-engineers such as formulators, project managers and those from operations often wonder what the proper size is for a pilot vessel to be scaled-up with some degree of reproducibility. There is no simple answer, as it will depend on the final production size, which can range from 200–20,000 L or more. Suffice it to say that if the pilot vessel is glass with straight walls and volume markings etched on the side, the vessel will not work for any size scale-up.

Some equipment manufacturers do offer small volume, scaled-down versions of their production units, and these can be a good start. Remember that small vessels do not allow the engineer to evaluate the step of product discharge and transfer if the product is scooped rather than pumped. It also does not allow the engineer to monitor the effect of the transfer operation on the physical properties of the product.

One way in which some companies try to cut corners is by scaling up in a production vessel but cutting the batch size so as to not waste as much product. This is penny-wise and pound-foolish because the value of the trial will be diminished as well. Since the batch-to-tank volume ratio will not be the same as in production, the mixing parameters may change. Additional problems may include aeration due to the product level occurring at the same level as the mix impeller, hot zones at the jacket wall—i.e. exposed surfaces of the heating jacket, and similar issues. The risk is a batch that is one-off with a process that is one-off and that needs further development at first production.

Filling

Another overlooked scale-up factor is filling. Too often, the pilot work is considered complete if the bulk product from the mix tank meets the desired specifications; however, scale-up is not complete until the product is in the final container. Filling can cause shear sensitive emulsions to lose or gain viscosity. Even the type of filler can have different effects. Common types of liquid fillers include overflow liquid, servo pump (e.g., gear and lobe pumps), peristaltic, gravimetric (e.g., timed gravity), piston/volumetric and net weigh. The latter would include fillers that utilize mass flow meters to measure specified weights/masses to the nozzles.

The main contributor to viscosity changes is the inherent restriction to flow. This can be caused by orifices, tubing size reductions, elbows, check valves, etc. Speed of filling is also a factor. A low speed in-line filler generally creates less turbulence and therefore less shear than a high speed rotary filler within any one type. Diving nozzles usually require less velocity per fill cycle than nozzles that squirt the fluid under pressure from a height above the bottle neck. All of these variables must be considered for scale-up since low shear fillers can produce a significantly different packaged product than high shear fillers.

Many manufacturers have multiple filling lines with different filler designs, and it can be a scale-up nightmare if they are all used to fill the same product in the same plant. It is sometimes possible to compensate for low shear fillers by adding a mild shear device to the transfer operation, equalizing the total shear seen by the product by the time it is packaged. This can range from a simple orifice plate inserted into the transfer line, to an in-line homogenizer or mill. The transfer operations must be considered as well. Pressure drops caused by multiple pumping (such as from mix tank to hold tank, to head tank to filler) all add to the cumulative effect of shear on the product. Moreover, short transfer lines using large diameter pipe or hose will add less shear than long lines using dozens of feet of hose or piping. It is common to find hoses snaking around a production floor to connect different tanks in different areas, along with multiple size reductions, to accommodate valves, connectors and hoses of different diameters.

Another practical reason to include filling as part of the scale-up trial is that the most innovative product is of no commercial value unless it can be packaged. Many stability studies are performed with hand-filled samples, which may or may not be representative of the commercial product. In addition, the profit margin of a newly commercialized product can become unfavorable if the filling line must be slowed to a quarter speed to accommodate the product. Therefore, the formulator and engineer should know the effects of the filler performance on the product and vice versa.

Formulator/Process Engineer Relationship

One last piece of advice is to foster a close and collaborative relationship between the product formulator and the process engineer. When the formulator involves the engineer at the early stages of product development, the engineer can offer advice and suggestions for optimizing the benchtop process to make modifications that could improve the robustness of the process or make it easier to manufacture reproducibly. This is especially critical on OTC products, as it is not easy to modify the process after it has been validated.

Similarly, when the project progresses to the pilot stage and plant scale-up, the formulator can see how the recipe transforms to the real world and suggest constructive modifications. This collaboration is also invaluable when troubleshooting production problems after start-up, as the formulator may be able to offer insight based on lab work, including failures, that led to the final recipe and procedure. In short, taking a team approach to both the development and scale-up stages can pay big dividends and ensure a successful new product launch.

To get a copy of this article or others from a searchable database, log on to www.CosmeticsandToiletries.com/magazine/pastissues.

References

Send e-mail to ct_author@allured.com

1. DS Dickey, Don't get mixed up by scale-up, *www.chemicalprocessing.com/articles/2005/519.html* (Accessed Dec 13, 2010)
2. D Yacko, Scale up and processing of cosmetic formulations, *SCC Continuing Education Course,* Chicago (June 2009)
3. TJ Lin, *Manufacturing Cosmetic Emulsions: Pragmatic Troubleshooting and Energy Conservation*, Carol Stream, IL: Allured Business Media (2010)

C&T

Lab Practical: Formulation Considerations for Scale-up

- Keep manufacturing plant capabilities in mind when designing a formulation process; make it robust enough to survive different configurations of mixers, pumps, in-line devices and fillers.
- Consider the variety of processing systems that might be used globally.
- Take transfer and filling steps into account for potential changes to product properties.
- Evaluate the effect of the product on the filler, not just vice versa.
- Perform scale-up qualifications in the proper size tank to deliver real scalability; it is not recommended to use partial batches to predict full-scale manufacture.
- Use a formulator/process engineer team approach at all stages of development and commercialization.