# From beaker to bucket: The safe scale-up of organic electrolyte materials

Argonne's Advanced Battery Materials Synthesis and Manufacturing R&D Program provide a critical junction that bridges the gap between the initial discovery and commercialization of new materials. The goal of the facility is to develop safe, scalable, and economic processes to produce kilogram quantities of material needed for industrial evaluation. This presentation will describe the main administrative and engineering measures undertaken during scale-up to assure safe transition from discovery to kilo scale syntheses of organic electrolyte materials for advanced lithium batteries.

**By Trevor Dzwiniel, Krzysztof Pupek, Gregory Krumdick**

## INTRODUCTION TO SCALE-UP

Although the hazards associated with lithium-ion battery electrolytes are well-known,[1] there is less attention paid to the hazards involved in large-scale synthesis of the battery electrolyte components. Electrolyte solvents and additives are normally organic compounds that are produced using a wide variety of chemical reactions. In general, the scale-up of any chemical reaction features many potential hazards that are not normally problematic in small-scale research operations.

*Trevor Dzwiniel is affiliated with the Energy Systems Division, Argonne National Laboratory, Argonne, IL 60439, United States*
*(Tel.: +1 6302521592;*
*e-mail: tdzwiniel@anl.gov).*

*Krzysztof Pupek is affiliated with the Energy Systems Division, Argonne National Laboratory, Argonne, IL 60439, United States.*

*Gregory Krumdick is affiliated with the Energy Systems Division, Argonne National Laboratory, Argonne, IL 60439, United States.*

This generates a common misconception or misunderstanding among both scientists and non-scientists about scale-up research: that scale-up simply involves building a bigger flask for the reaction and everything is known about the process.

Scale-up generally cannot be run as is a simple linear increase, meaning you cannot just multiply everything by 10 or 100 and get more material.[2] There are many physical phenomena that have a scale-dependent response: heat transfer, mass transfer, mixing/stirring, and in particular, the amount of time taken for each operation. Each of these phenomena may behave differently "on-scale" and dramatically affect the quality of the product. The main goal of scale-up research, or process development, is to transform a bench-scale process to a safe, effective, and reproducible process in large or commercial equipment without a noticeable change in the product attributes such as quality or performance.

Process development also investigates alternatives that can reduce costs, reduce waste, and improve process safety, yield and purity in addition to creating a better understanding of the fundamental characteristics of the process. Although a full Hazard and Operation Study (HAZOP) analysis for transfer into production equipment is beyond the scope of this paper,[3] here we propose a basic hazard analysis guideline for initial scale-up work from milliliter to liter scale processes.

## HAZARD ASSESSMENT

There first needs to be an analysis of the potential hazards of the process. The most basic study is that of the reagent chemical hazards: flammability, toxicity, and reactivity. Much of this information is readily available in the form of Safety Data Sheets (SDS) and National Fire Protection Association (NFPA) or Globally Harmonized System (GHS) rating systems. It is this information which may help determine the personal protective equipment (PPE), proper storage of chemicals, disposal concerns and other needs of the project.

The second stage of analysis involves the reaction hazards: mainly what happens when reagents are mixed. Commonly, this is an evaluation of the heat output of the reaction. This often goes unrecognized in small scale work, mainly due to the much more efficient heat dissipation rates in smaller volume round bottom flask relative to larger vessels. This means that a large exothermic process in a small scale will only cause a moderate rise in temperature. This same process in a larger vessel could be catastrophic. Again there are several excellent sources of information on reaction hazards,[4] albeit less well-recognized than an SDS. Several programs allow the process development chemist to identify reactions that are likely exothermic. Several databases and handbooks list potentially dangerous reagent combinations of reagents.

1871-5532/$36.00
http://dx.doi.org/10.1016/j.jchas.2013.11.006

Finally, there are multiple training courses and workshops that help train process chemists.

There are a number of commonly used reagent combinations that may be relatively innocuous on a small scale, but are prone to thermal runaway reactions. One infamous[5] example is N,N-dimethylformamide and sodium hydride. In such cases, other working alternative chemical reagents need to be determined.

Also a part of the reaction hazard assessment is an analysis of the products and byproducts. If a gas is produced in the reaction, there is always the concern of adequate venting to prevent over-pressurization of the reaction vessel. Here, a process development chemist may look at ways to avoid a gaseous byproduct or devise a process whereby the gas is generated slowly, perhaps by controlled addition of the reagent. Other waste stream concerns should also be addressed. Benzene may be produced in the waste stream when using a reagent such as phenyl magnesium halide. If 4-methylphenyl magnesium halide is used instead, the more innocuous toluene will be the byproduct.

The reaction work-up must also be considered as part of the reaction hazard assessment, especially since these steps may be the most exothermic event of the synthesis. Although it is relatively easy to pour a 20 ml reaction into a beaker filled with ice, this is both impractical and dangerous to do with several liters of material. The process chemist must therefore develop an entirely new quench procedure prior to scale-up.

## HAZARD MITIGATION

After the assessment and identification of reaction hazards, the process development chemists must then work on mitigation of these hazards. In concert with optimizing the process for yield and chemical purity, new methods may need to be developed to replace unsuitable bench scale techniques.

The simplest form of process development may be the identification and replacement of unsuitable organic solvents. Several common laboratory solvents such as hexane and diethyl ether are very seldom used in multipurpose pilot plants due to a combination of very high flammability and ability to accumulate static charge.[6] When these liquids are transferred, the accumulated static charge can cause a spark, igniting the solvent vapor. Simple replacements for hexane and diethyl ether are, respectively, heptane and methyl-tert-butyl ether, although several other solvents may be more suitable.

Similarly, highly reactive reagents are undesirable in a process and can often be replaced. Pyrophoric chemicals in particular are likely targets to replace; it is worthwhile to investigate non-pyrophoric alternatives such as lithium diisopropylamide. Similarly, it may be worthwhile to investigate alternative starting materials or other synthetic routes to avoid high energy reactions such as oxidations and reductions.

However, if the reagent hazards cannot be mitigated, the development should focus on conditions and procedures to minimize the hazard. In particular, controls for exothermic events should be in place, such as controlled slow addition of an active reagent. Associated with this is chemical accumulation, where one reagent is added but does not react until a higher temperature is reached. This is particularly infamous with Grignard reagents, where a typical procedure may be to add the reagent slowly at a low temperature and slowly warm to ambient. Often, there is little to no reaction at the low temperature, causing a situation where all the reagent is present but unreacted; a large potential energy source. As the mixture is warmed, at some temperature the reagents begin to react; if vigorous enough, this can lead to a thermal runaway. Determination of the minimum reaction temperature at which the Grignard reagent react upon addition is thus an important factor in safe scale-up. Again, for true large-scale processes, additional calorimetric data should be obtained and several additional factors considered.[7]

However, in initial scale-up work from milliliters to liters, less complicated and expensive equipment may be sufficient. Several simplified reaction calorimeters are now commercially available and are well-suited for work in preliminary scale-up development. Although not as accurate as a full-fledged calorimeter such as the Mettler Toledo RC1, the smaller versions generally give values of ±10% of the "true" heat of reaction. Especially in early development, the minor inaccuracy is well worth the increased cost and complexity of a full calorimeter. Initial process scale-up is greatly enhanced by this data.

Although calorimeters are normally used to estimate the heat production on a large scale, it is worth considering the reverse: that on a small scale, the corresponding amount of heat released is much smaller, thus safer, so small scale reactions should always be used to develop a thorough understanding of the process. This also partially explains why process development is rarely encountered except as on-the-job training in scale-up chemistry; you do not usually need a calorimeter for gram scale syntheses. A last point is that the process should always be discussed with others prior to scale-up.

## CASE STUDY

A good example of process scale-up is demonstrated by the scale up project recently completed at the Material Engineering Research Facility (MERF) located at Argonne National Laboratory. This compound, called RS2, is a redox shuttle and was also initially developed at Argonne.[8] A redox shuttle is an additive used for overcharge protection, to keep the batteries from starting on fire. The way they work is to shunt electrons between the cathode and anode, preventing an overvoltage condition. If the voltage gets too high, the battery could go into thermal runaway and potentially catch on fire. For years, several battery manufacturers wanted samples for testing and analysis of the materials performance in commercial cells. However, the amount needed for these tests was unavailable; the process, which performed well on 1 g scale used in the discovery stage and initial testing, was unable to provide larger amounts due to the complexity and constraints of