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The Secret Life of APIs: The Importance of Sociochemicology

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8 comments

When we produce a small-molecule active pharmaceutical ingredient (API), we have to pay close attention to its manufacturing process and quality systems, giving these much more scrutiny than we would for other synthesized chemicals. After all, APIs have the potential to improve our health or extend our life, where chemicals merely facilitate our lifestyles.

Thus, for API manufacture, we must have complete command of what we do. First-time quality has to be the way of life and our goal. Anything less than a quality-by-design (QbD) approach will add cost to the product.

Each chemical involved in the API manufacturing process is either a reactant, solvent, intermediate, or byproduct, and each has its own physical and chemical properties (for example, physical state, molecular weight, density, phase transition temperatures, solubility in water and other chemicals, viscosity, surface tension, and heat of formation). Some APIs are converted to a salt for easier dissolution, improved efficacy, and performance.

Each also has its own toxicity and toxic behavior when interacting with other chemicals. Since chemicals, like animals, have individual and collective behavior I call this behavior “sociochemicology.”

I'm not trying to oversimplify what all chemists and chemical engineers learn. However, we often seem to fail to account for the individual and collective behavior of constituents in our APIs. QbD becomes second nature when we understand and manage the behavior of chemicals that are used in the manufacture of active ingredients and formulations.

With this knowledge, we can manage, juggle, manipulate, maneuver, and even coerce behavior to develop a process that will produce quality product from the onset -- i.e., achieve the goals of QbD.

Such processes will be simple. We will have command of each reaction step and, collectively, for the whole process. In addition, the resulting process will offer the highest product yield.

Chemists and chemical engineers use sociochemical properties to select the desired chemicals for specific reactions. This information also allows us to have a safe starting point for reactions. We can use our knowledge and imagination to alter their behavior to our advantage. Understanding collective behavior of chemicals is important, because it allows us to handle them safely and properly in a process. It also gives us clues about how to manipulate and modify their relative

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amounts and reaction conditions to achieve the highest product yields, and the most economical and sustainable processes.

We can use sociochemicology to optimize process chemistry and operating conditions. Design of experiments should be used for optimization.

Reactivity and behavior can also be used to simplify addition point and method. Mutual solubility or lack of it, for instance, can facilitate phase separation or the removal of a desired product from the reaction mass. Solubilities also assist us in minimizing the number of solvents used. Process conditions can be used to influence reaction rate, flow, and solvent amount. Productivity, investment, and product cost are influenced. Physical state guides us to select the best flow control method. Clear liquid is the easiest to control, with gas being the hardest. Exotherm is best controlled using a heat exchanger vs. adding water/solvent or ice to the reaction mass.

Understanding of sociochemicology helps developers exploit unit operations to create economical, sustainable, and safe processes.

If we follow these basic principles, we have an opportunity to exceed regulatory guidelines in every step of API synthesis.

Additional reading:

- Malhotra, Girish: Chemical Process Simplification: Improving Productivity and Sustainability, ISBN: 978-0-470-48754-9, January 2011, John Wiley & Sons Inc.
- Malhotra, Girish: Focus on Physical Properties to Improve Processes: Chemical Engineering, Vol. 119 No. 4 April 2012, pgs. 63-66

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