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Product Volume & API Process Optimization: Connecting the Dots

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13 comments

To the uninitiated, active pharmaceutical ingredients (APIs) look like wiggly, leafless branches, but they can treat diseases. Selected chemicals are reacted to produce the desired effect. The manufacturing processes can be complex. Our job is to create processes that are as simple and environmentally friendly as possible and result in products that meet quality specifications all the time without much interference.

The most important factor in any API business process is the volume of product required to meet global demand. It determines manufacturing process design, equipment selection, and asset utilization, and it influences the overall supply chain.

Traditionally in the chemical industry, product volumes are large enough to warrant producing large quantities at multiple plants. However, pharmaceutical APIs present a different scenario. This needs to be understood and explained.

Since active ingredient dosages can vary from fractions of a milligram to a few hundred milligrams, the total amount of API needed can vary from a few hundred to thousands of kilograms per plant per year. We have to recognize that one kilogram of active ingredient at 100 percent formulation efficiency will produce 1 million tablets with a 1mg dose. Pharma's API needs are very different from the need for fine and specialty chemicals. There are limited numbers of active ingredients that are needed in millions of pounds per year.

Consider an API with a global need of about 20,000kg per year. With the right process and equipment, this could be made at a single plant. However, the reality is very different. This product could be produced at multiple sites while it is still under patent. When it becomes generic, many companies could be producing it, so production per site can be even lower.

If the active ingredient is to be produced at more than one plant, there will very likely be equipment that does not suit the process chemistry. As a result, the process must be adjusted to fit the equipment. Raw material and solvent costs, supply, usage, and handling will be different at each site. Processing conditions and the physical state of raw materials will impact the time it takes to produce the same quality product. Isolation of reaction intermediates and side products will also be different.

It is very likely that the process yield will be different; most likely, there will be processes that are inefficient and unsustainable. Since there will be product campaigns, the regulatory compliance workload will increase. Equipment cleaning and cGMP compliance will be a challenge. One can comfortably conclude that the factory costs will be different at each site. Since the processing conditions will be different at different plants, companies will have to rely on repeated analysis at

different stages of production to ensure quality. In other words, they will be relying on the outmoded Quality by Analysis that still rules at most pharmaceutical facilities.

Producing this API at a single plant would result in a much more efficient process, offering benefits in areas such as raw material costs, handling, and supply chain control. It would use significantly less solvent, would simplify regulatory compliance, and (if the process were properly designed) would result in a quality product. The process dynamics of a single plant will be simpler, and the profits will be much higher.

Rhetorical question: Why does pharma persist in manufacturing APIs in different facilities?

My next post will discuss which physical properties can be exploited to optimize API processes and how.

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