

K-TOPS® A Proprietary Intelligent Design Tool

1 THE MODULAR APPROACH TO MANUFACTURING MODELING

1.01 INTRODUCTION

Process modeling provides an appealing plan for the optimization of biopharmaceutical production. One of the main focal points of this appeal is the concept of tracking variable changes, programmatically, for effects on the model. Several different approaches to process modeling may be utilized depending on what effects are targeted.

A "micro-scale" approach to modeling is characterized by the requirement for stream physical characteristics and the modeling of unit operations physical phenomena. Typical targets of the micro-scale approach include elimination of pilot plant runs and acquisition of data details for particular unit operations (e.g., emissions, etc.).

A "macro-scale" approach to modeling is characterized by the requirement for overall process cycle times and monthly or annual financial data. Typical targets of the macro-scale approach include financial planning and summary schedule development.

Integrity of data input to a model is crucial to the reliability of data output from a model. This factor makes the choice of approach very important as, oftentimes, access to data for input is difficult to obtain on a micro-scale due to lack of details, and on a macro-scale due to lack of dependable summary data. An intermediate-scale approach to process modeling can be an attractive option when substantial unit operation physical characteristic details are not crucial. However, detailed scheduling optimization is required and time is of the essence.

With the speed of today's computer microprocessors and the ease of data sharing between software packages, intermediate-scale process modeling with typical software programs (e.g., Microsoft Office-based) is no longer an impossible task. In an intermediate-scale model, the critical data input factors are time, resource and equipment usages. These factors can be considered on a per step, per unit operation, and/or per product basis.

- A. Overview a typical biotech process diagram. Describe generic aspects of all processes that lend themselves to computer modeling. From a "macro" point of view, fermentation is the same as reactions. All separators behave similarly (centrifuges = filters = chromatography columns, etc.). Basically, if you can model one, then the others can be modeled from a unit ops standpoint.
- B. Introduce the concept of "process dynamic" which is a different space/time entity than single unit ops study. Expand this to also show how "business modeling" relates to other models as a spectrum.

Focus on the "process dynamic". How do you view the process so it can be modeled? A kitchen concept – a cookbook with many recipes, using the same "pots and pans" and taking

discrete amounts of times and materials. It can be viewed in three primary ways – from an equipment standpoint (equipment), from a product molecule standpoint (steps), and from a product interaction standpoint (resources, both direct contact, media/buffer/WFI/etc., and non-direct, steam, cooling fluid, people).

Process modeling (step-by-step) - Introduce specific event-type logic to make things unique.

The need to track variations in process operating philosophies can be a most formidable task in process modeling. Some examples of such philosophies are pooling of batches, splitting of batches, partial steady state operations intertwined with batch operations, etc.

- C. The modular approach to modeling allows for easy addition of procedures for handling operating philosophy difficulties. In this approach, a step is tagged with a variable that declares that a specific operating philosophy procedure be used when the scheduling procedure is run. Thereby, the operating philosophy dictates are being considered in parallel to the normal scheduling decisions.

Most importantly to this approach, alterations in operating philosophies can be easily handled without programmatic code changes. For example, pooling a different number of batches or moving a batch split to another unit operation can be handled by merely assigning, revising, and/or deleting step variables.

- D. Describe how step templates can be used to easily manage recipe data. Set-point data can be derived from knowledge of the equipment parameters and product quantities/concentrations. Also, equipment templates can generically incorporate chromatography columns.

Process modeling (unit op, by unit op) can incorporate scheduling logic to allow conflicts to be addressed/resolved.

- E. Describe how the various cascading resources can be analyzed. How are buffer tank volumes and quantities determined?
- F. Describe how CIP systems are determined.
- G. Describe how final central WFI systems are sized.
- H. How are flow spikes handled?
- I. In conclusion, modeling has the capability of having simple instructions in the micro-level as well as simple instructions in the macro-level which can resolve a very complicated process picture to aid in economic optimization, whether it be from resource optimization, equipment optimization, or people optimization.
- J. Once an optimized process is conceived, engineering data can propagate through various design tools to minimize the product speed-to-market. Critical documents/analyses can be utilized and generated quickly to move the project into and through the construction phase (constructability).