

## Total Optimization Plant Simulation Qualifications Document

### 1 Definition

K-TOPS® is a dynamic event-based simulation tool used to analyze and optimize client processes during any phase of a project. A quick modeling effort based on production capacity parameters allows for the generation of timelines (Gantt Charts) and resource histograms, determines the bottlenecks within the process or support systems, and determines the impact of debottlenecking solutions. K-TOPS® was developed by our engineers using Visual Basic with an Excel interface.

### 2 Applications - Phases

Simulation-based modeling and optimization can be applied at any phase of a project. Four examples of phases where K-TOPS® has been used:

#### 2.01 Grass-Roots Design

A grass-roots design has virtually all degrees of freedom available at the onset, but economic and spatial restrictions soon present limitations to the design flexibility. Based on a desired production capacity, the process is modeled to optimize the usage of equipment and support systems. "What if" scenarios can be developed to determine potential bottlenecks. These scenarios include capacity increases, batch sizes, multi-product capability, process variations, or other reasonable considerations. During value engineering, a K-TOPS® analysis tests the feasibility of various options.

Proposals of optimized debottlenecking solutions for prioritized future plant can be incorporated into the initial design allowing for the desired process flexibility and minimizing overall capital cost.

#### 2.02 Critique of an Existing Design

Often, critique of an existing design through the use of simulation-based modeling and optimization is desired. Three examples point out the incredible value these efforts can provide:

- Plant capacities have been increased by 50% with only a 10% increase in capital cost by selectively debottlenecking the process while also making the process more operable.
- Simulation-based modeling and optimization can also demonstrate that the required increase in capacity can be achieved with a significantly smaller plant expansion. Saving of tens of millions of dollars have been realized.
- Support area optimization can typically result in an increase of production capacity by 30%.

#### 2.03 Capacity Analysis of an Existing Process

Modeling an existing process allows for quick analysis of existing bottlenecks and provides a range of solutions to debottleneck the process and increase capacity. These solutions may include additional capital

equipment, but may also just involve an adjustment of certain operations within the process timeline in order to optimize the usage of the most bottlenecked equipment.

#### **2.04 Capacity Analysis of Contract Manufacturing Sites**

The decision to outsource production is a desire to generate product quickly and cost-effectively. K-TOPS<sup>®</sup> ensures a fast and effective solution to determining the best contract manufacturing facility for your product. By combining a knowledge of the desired process and the available equipment and utilities at various contract manufacturing sites K-TOPS<sup>®</sup> can provide an analysis of each site. These analyses can be used to determine which contract manufacturer to use, and to confirm the expected capacity. It can identify areas where additional equipment (process, process support, and/or utilities) is required in order to achieve the desired production capacity as well as identify the capacity with no equipment changes.

### **3 Applications - Industries**

Simulation-based modeling and optimization can be applied to any type of process. Some key industries where K-TOPS<sup>®</sup> can be used:

- **Biotech.** Our biotech knowledge of processes such as mammalian cell culture, microbial fermentation, and vaccine processing, incorporating unit operations such as fermentation, chromatography, ultrafiltration, centrifugation, fractionation, as well as critical utility awareness is an area where unique solutions are found using K-TOPS<sup>®</sup>. These solutions ensure a robust economical operation for single or multi-product facilities for current and future operations.
- **Pharmaceutical.** Our pharmaceutical knowledge of processes encompasses solid dosage, vial filling, oral liquids, ointments and parenterals, as well as packaging for these operations. Critical operations for vial filling such as compounding, filling, capping, vial washing, depyrogenation and sterilization are identified in K-TOPS<sup>®</sup>. For solid dosage, granulation, blending and tableting or capsule filling are modeled. The evaluation of multiple lines and products is critical as well as the understanding of the utilities and support systems.
- **Critical Utilities.** Critical Utilities, such as Water-For-Injection, Purified Water, Clean-In-Place, and Clean Steam are essential to the production of many facilities and can become the limiting factor to facility production capacity. A K-TOPS<sup>®</sup> evaluation focused on critical utilities will help ensure that short-term and long-term production requirements are met.

### **4 Conclusion**

Simulation-based modeling and optimization has provided manufacturers with an invaluable program to maximize their plant capacity while minimizing capital cost. Whether utilized as a stand-alone analytical tool for plant optimization, or as a keystone activity in the design and construction of a new facility, this technology has delivered speedy analysis of processing difficulties faced by manufacturers.

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