Improved Scheduling Model for Biopharmaceutical Processes

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Abstract

The biopharmaceutical industry has been developing significantly with growing demand for therapeutic drugs. The concerned challenges associated with drug development and cost-effective manufacturing require a decision support system for improving the resource utilization. Several deterministic and stochastic approaches have been reported in the literature for scheduling a multiproduct facility for batch and continuous manufacturing of biopharmaceuticals using discrete-time and continuous-time representations. A comprehensive analysis of relevant literature models is presented in this work for continuous manufacturing of biopharmaceuticals, along with a discussion on some model deficiencies such as real-time storage violation, real-time violation of shelf-life, inadequate modeling of minimum campaign length, and products delivered before their due dates. The proposed model extends an earlier unit-specific event-based model (Kumar et al., 2021) with features including modified material balances, enhanced shelf-life and minimum campaign length (MCL) constraints, setup constraints based on product sequencing, and effective sales and penalty constraints for late deliveries. The shelf-life and MCL constraints are proposed to allow the campaign to continue over multiple events, based on four-index binary variables, in contrast to the literature models where they were based on single events which could result in sub-optimal solutions. A new binary variable is introduced for activation of initial setup in a unit. These improved features lead to better modeling in terms of handling of intermediate and final product storage without real-time violations of storage and shelf-life, with effective handling of initial setup in production tasks, and timely delivery of final products. Selected examples based on industrial data are adopted from the literature to validate the proposed improved model, the performance of which is compared with selected literature models (Vieira et al., 2017; Jankauskas et al., 2019; Kumar et al., 2021), yielding better results with higher profit, apart from overcoming the model deficiencies.

Keywords: Mathematical modelling, optimization, scheduling, biopharmaceuticals.

References

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