

## Robust Batch Process Scheduling in Pharmaceutical Industries: A Case Study

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**Abstract :** Batch production plants provide a wide range of scheduling problems. In pharmaceutical industries a batch process is usually described by a recipe, consisting of an ordering of tasks to produce the desired product. In this research work we focused on pharmaceutical production processes requiring the culture of a microorganism population (i.e. bacteria, yeasts or antibiotics). Several sources of uncertainty may influence the yield of the culture processes, including (i) low performance and quality of the cultured microorganism population or (ii) microbial contamination. For these reasons, robustness is a valuable property for the considered application context. In particular, a robust schedule will not collapse immediately when a cell of microorganisms has to be thrown away due to a microbial contamination. Indeed, a robust schedule should change locally in small proportions and the overall performance measure (i.e. makespan, lateness) should change a little if at all. In this research work we formulated a constraint programming optimization (COP) model for the robust planning of antibiotics production. We developed a discrete-time model with a multi-criteria objective, ordering the different criteria and performing a lexicographic optimization. A feasible solution of the proposed COP model is a schedule of a given set of tasks onto available resources. The schedule has to satisfy tasks precedence constraints, resource capacity constraints and time constraints. In particular time constraints model tasks due dates and resource availability time windows constraints. To improve the schedule robustness, we modeled the concept of (a, b) super-solutions, where (a, b) are input parameters of the COP model. An (a, b) super-solution is one in which if a variables (i.e. the completion times of a culture tasks) lose their values (i.e. cultures are contaminated), the solution can be repaired by assigning these variables values with a new values (i.e. the completion times of a backup culture tasks) and at most b other variables (i.e. delaying the completion of at most b other tasks). The efficiency and applicability of the proposed model is demonstrated by solving instances taken from Sanofi Aventis, a French pharmaceutical company. Computational results showed that the determined super-solutions are near-optimal.

**Keywords :** constraint programming, super-solutions, robust scheduling, batch process, pharmaceutical industries

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