

Chapter 13

SELECTION AND SCHEDULING OF PHARMACEUTICAL RESEARCH PROJECTS

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Abstract This paper deals with the lead optimization phase of pharmaceutical research where a number of leads (molecules as a basis for potential drugs) are processed by different departments in order to optimize their biochemical characteristics. We depict each lead as a project and model the problem as a static multi-project selection and scheduling problem under resource constraints with the objective to maximize the weighted work performed. For solving the problem we propose two heuristics. We assess their performance in a computational study and we point out one dominant method. Furthermore we show the impact of problem parameters such as the extend to which projects can be crashed.

Keywords: Pharmaceutical R&D, Lead Optimization, Multi-Mode Resource-Constrained Project Scheduling, Heuristics.

13.1 Introduction

A vital task of pharmaceutical companies is the research and development of new drugs. The latter is characterized by long lead times, expensive and thus scarce resources, a high attrition rate, and a strong time-based competition due to the fact that the company which first gets a new compound patented will have a time-limited monopoly to produce and market the associated drug. In this

context it is crucial to select the right research projects and to schedule them in a proper manner in order to generate value.

The focus of this paper is twofold. First, we model the problem of selection and scheduling of pharmaceutical research projects. The problem arises in the lead optimization phase of a major European pharmaceutical company. We model it as a multi-project resource-constrained project selection and scheduling problem. Second, we propose two heuristic solution procedures. The heuristic methods are experimentally evaluated on a set of benchmark instances which has been generated based on real world data.

The paper is organized as follows: In Section 13.2 we provide a problem description and a brief literature review. Section 13.3 is devoted to the development of the integer programming model. The two heuristics are proposed in Section 13.4 and the experimental test and its results are reported in Section 13.5. Section 13.6 summarizes.

13.2 Problem Description

13.2.1 Drug Research and Development Process

The drug research and development process can be depicted by seven phases (cf. Figure 13.1). The first three phases are considered as research, the next three phases are considered as development, and the final phase is the marketing phase. The first six phases may take up to 15 years. In the sequel we give a brief description of the phases.



Figure 13.1. Drug Research and Development Process

Target Identification and Lead Generation Starting point of the drug research and development process is a disease for which the company wants to discover and develop a new drug. In order to cure the disease researchers look first for targets, biological elements of the human body which play an important role in the progression of the disease or its symptoms. The target identification phase comprises all activities concerned with finding such targets.

Within the next phase, lead generation, the goal is to find chemical compounds (molecules) which act on the target so that the disease can be treated. By using high-throughput technologies a large number of compounds, i.e. 60,000, is automatically generated and tested within a time span of two weeks. Molecules which show promising characteristics are called leads (because they will lead the way to new drugs).

Lead Optimization and Preclinical Studies The task of lead optimization is to optimize the characteristics of a lead in terms of its effectiveness to cure