Simulation Model of a Quality Control Laboratory in Pharmaceutical Industry

Andrea Costigliola∗,** Filipe A. P. Ataíde∗ Susana M. Vieira∗ João M. C. Sousa∗

∗Hovione Farmacêutica S.A., Lisboa, Portugal (e-mail: acostigliola@hovione.com, fataide@hovione.com)
,**IDMEC, Instituto Superior Técnico, Universidade de Lisboa, Portugal (e-mail: susana.vieira@tecnico.ulisboa.pt, jmsousa@tecnico.ulisboa.pt).

Abstract: Laboratories are critical components in drug manufacturing, and inefficiencies in laboratory management can have a major impact on the overall supply chain service level. The aim of this paper is to build a Discrete Event Simulation model of a Quality Control laboratory. To achieve this objective, a generic framework for information treatment and organization was built. In particular, information coming from different databases was organized into a single one that was used as input to a discrete event simulation model. The proposed model represents in detail the workflow of a quality control laboratory and it is intended as a support tool for planning, scheduling and decision making. The model was validated using real data, and it proved to be effective in the estimation of performance parameters such as, system throughput, equipment usage rate, system responsiveness and tasks processing times. Furthermore, the simulation model was tested with an alternative scheduling policy to evaluate how modifications on the system may improve its performance.

© 2017, IFAC (International Federation of Automatic Control) Hosting by Elsevier Ltd. All rights reserved.

Keywords: Computer Simulation, Discrete Event Systems, Modeling, Quality Control, Scheduling, Pharmaceutical Industry

1. INTRODUCTION

In the last decades, drug manufacturing evolved driven by external economic forces, patents expiration and increased competition. In order to maintain their competitive advantage, pharmaceutical companies organized themselves into complex organizations (supply chain and contract manufacturing networks), and started to be more concerned on achieving operational excellence through the optimization of the processes involved in drug manufacturing: chemical processes modeling, supply of raw materials, logistic operations, quality control, etc.

Pharmaceutical companies operate in one of the most competitive and regulated markets, and compliance with Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP) is mandatory for marketing any drug. Those regulations were introduced to ensure that every pharmaceutical product meets safety and quality requirements in a systematic fashion.

During its development life cycle, a drug must be constantly monitored with laboratory tests to assess its quality. In this scenario, quality control laboratories play an important role in the drug manufacturing process. Laboratory management is a complex task which involves resources (personnel and equipment) planning and scheduling, analysis prioritization, results evaluation and documentation.

Quality control laboratories are critical components in drug manufacturing and inefficiencies in quality control may delay obtaining results, affect negatively their quality and can have a major impact on the overall supply chain service level. The situation can be magnified in the case of a contract manufacturing organization, that produces goods under the brand of its clients and therefore has to deal with a large number of projects and materials.

Given the high mix of products and tests it is important to develop effective strategies for laboratory management. Laboratory information management systems (LIMS) used in pharmaceutical industry often lack of features essential (i.e. information on processing times, workflow) for planning, scheduling and stock management.

As pointed out by Juran and Godfrey (1999), quality control can be seen as a recursive process composed by three main tasks: quality planning, control and improvement. Thus, quality control is not only responsible for the execution of quality tests but also for the development and the improvement of methods to be used in the control process. Dedicated optimization methods for planning and scheduling, in addition with a generic framework for infor...
During its development life cycle, a drug must be con-

requirements in a systematic fashion.

ratory Practices (GLP) is mandatory for marketing any

Good Manufacturing Practices (GMP) and Good Labo-

cal processes modeling, supply of raw materials, logistic

of the processes involved in drug manufacturing: chemi-

complex organizations (supply chain and contract manu-

In the last decades, drug manufacturing evolved driven by

external economic forces, patents expiration and increased

that was used as input to a discrete event simulation model. The proposed model represents

built. In particular, information coming from different databases was organized into a single one

To achieve this objective, a generic framework for information treatment and organization was

1. INTRODUCTION

Laboratories are critical components in drug manufacturing, and inefficiencies in

control can be seen as a recursive process composed by

among several quality control laboratories, this study

Drug manufacturing and inefficiencies in quality control

ing, analysis prioritization, results evaluation and docu-

mation management can improve laboratory performances

and resource usage.

1.1 Related Work

In the pharmaceutical industry, laboratory management is

often done based on supervisors’ experience, rather than

with validated data driven models. Literature is short of

examples of generic optimization frameworks applicable to

pharmaceutical quality control laboratory management.

Klaessens et al. (1988) developed a simulation model that

consists of classes of objects (sample, sample generator,

planner, analyst and instruments) and applies concepts of

queuing theory to describe a laboratory organization. The

authors proposed two planning strategies: centralized (the

workload of a day is planned by the expert planner) and
decentralized (the analysts determine which samples are

Schäfer (2004) proposes a set of terms and definitions

can be used to model all components interacting

on the workbench (i.e. samples, instruments, sensors, re-

sults, information systems) and provides a description of

a schematic scheduling process applicable in quality

control laboratories. His approach comprises the following

steps: process description, information treatment, work-

plan generation, scheduling generation, execution, instru-

mental control and data storage.

Maslaton (2012) presents a two steps process towards the

optimization of a quality control laboratory. The first step

is related with resource planning, while the latter refers to

the scheduling of the laboratory. The author proposes to

organize information on products and raw materials

into groups, based on products similarities, define types

and number of tests for each group and estimate analysis

processing time for each test. Once the correct amount of

resources has been determined the second step of the

optimization process is the scheduling of the analyses.

To assign the best available resource to a sample/test, clas-

ical optimization algorithms can be used effectively. Boyd

and Savory (2001) applied a genetic algorithm for labora-

tory personnel scheduling. Their program maximizes the

value of a fitness function that measures how well a given

work shift scheduling of analysts and their skills matches

a set of work tasks. Similarly, Dudnikov et al. (2012)
developed a laboratory analysis planning system to sched-

ule analyses on the available resources. Their algorithm

considers two types of analyses (periodic and unplanned),

and creates a 24 hours scheduling considering only periodic

samples that is rearranged in case of unplanned samples.

1.2 Objectives

The objective of this work is to build a generic framework

for modeling and simulating a quality control laboratory

of a pharmaceutical company. In particular, the modeling

stage involves the study of the system and the design of

an integrated database that contains all the relevant

information that can be used for planning and scheduling.

Moreover, it uses concepts of Discrete Event System (DES)

and Petri net graphs theory for modeling purposes. See


A model of the real system is simulated using the academic

license of Simio simulation software (version 8.132). The

developed model will serve as basis for planning, schedul-

2. QUALITY CONTROL LABORATORY OVERVIEW

Hovione Farmacência S.A. is an international company

operating in the contract manufacturing business sector.

Quality control represents an important part of the drug

manufacturing process. With thousands of samples to

be analyzed every year, laboratories management can be
difficult and inefficiencies at quality control level may

affect negatively the overall supply chain service level.

Among several quality control laboratories, this study

focuses on a particular one, that is located in the Por-

tuguese facility of Loures (Lisbon). It is furnished with 70

equipment of 6 different types and employs 20 analysts

working on 3 work shifts. The six classes of equipment are

related with particular analysis techniques: High Perfor-

mance Liquid Chromatography (HPLC), Gas Chromatog-

raphy (GC), Particle Size Analysis (PSA), Karl Fischer

Titration, Differential Scanning Calorimetry (DSC) and

X-Ray Powder Diffraction (XRPD).

Typical tasks in pharmaceutical quality control laborato-

ries are analytical methods development and validation,
tests on final products, raw materials, in-process control

and stability analyses. Analytical methods must be de-

digned, developed and validated with the goal to rapidly

test a specific compound.

2.1 Laboratory Staff and Shifts

The quality control lab considered in this study is open

24 hours a day, 7 days a week. A reason for this is the

need to have always analysts available to support the

manufacturing process with in-process control tests. Other

types of tests (i.e. stability, development, validation) are

performed 5 days a week, from Monday to Friday. A total

of twenty analysts have been considered: six analysts work

on 12 hours rotating shifts, four analysts on two different

8 hours shifts, and ten analysts work 5 days a week on a

fix 8 hours shift. See table 1.

Table 1. Analysts Work Shifts.

<table>
<thead>
<tr>
<th>Work Shift</th>
<th>Days a week</th>
<th>Hours shifts</th>
<th>Analysts on Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shift 1</td>
<td>7</td>
<td>8:00-20:00</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20:00-8:00</td>
<td></td>
</tr>
<tr>
<td>Shift 2</td>
<td>5</td>
<td>8:00-17:00</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17:00-24:00</td>
<td></td>
</tr>
<tr>
<td>Shift 3</td>
<td>5</td>
<td>8:00-17:00</td>
<td>10</td>
</tr>
</tbody>
</table>

2.2 Analysis Work flow

Every day a high number of samples enters the laboratory
to be analyzed. According to the analytical technique

needed to analyze a particular sample, it flows to the

appropriate group of machines and it is scheduled to one

of the available machines. Independently from the analytical

technique used, an analysis starts with the preparation

of solutions and materials, and with the setup of the
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات