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GOOD PRACTICE GUIDE:

Operations Management

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Operations Management

Disclaimer:
This Guide describes how pharmaceutical operations are organized and operated to enhance the likelihood that development, production, storage, and distribution of products achieve the goal of ensuring finished product quality throughout the entire supply chain. ISPE cannot ensure and does not warrant that pharmaceutical operations organized and managed in accordance with this Guide will be acceptable to regulatory authorities and will achieve the goal of ensuring finished product quality throughout the entire supply chain. Further, this Guide does not replace the need for adjusting the organizations and systems to specific conditions of each individual supply chain.

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ISBN 978-1-936379-83-5

Preface

This ISPE Good Practice Guide on Operations Management has been developed and published by ISPE with the aim to provide to the industry a unique opportunity to integrate in a single document the complex body of knowledge required to all professionals involved in the highly regulated pharmaceutical market.

The Guide is intended to promote excellence and knowledge within the pharmaceutical operations enterprise and systems. The Guide addresses all operations along the supply chain from the selection of raw materials through the distribution of drug products to customers and ultimately patients.

The Guide is a reference source of good practices covering in the most structured way a wide variety of themes, subjects, problems and issues faced across the realm of pharmaceutical operations.

This Guide is solely created and owned by ISPE. It is not a regulation, standard or regulatory guideline document and products and processes designed and implemented in conformance with this Good Practice Guide may or may not meet US Food and Drug Administration (FDA), European Medicines Agency (EMA), or other global regulatory requirements.

This Guide is intended to be read in conjunction with other ISPE guidance, International Council for Harmonisation (ICH) guidelines, and industry recognized standards.

Acknowledgments

This Good Practice Guide was produced by a Task Team led by Marzio Mercuri (Polpharma Group) and Giuseppe Ravizzini (Recordati Group). The work was supported by the ISPE Operations Management Community of Practice (COP).

The Team would especially like to thank the ISPE Operations Management COP former Chair Gary L. Primes (PURE Bioscience, Inc.), current Chair Nick Davies (NDA Consultants), and Co-Chair Jim Curry (OpStat Group, Inc.) for their unwavering support of this document.

Core Team/Chapter Leaders

The following individuals took lead roles in the preparation of this document and each managed one or more chapter teams made up of writers and contributors.

Jim Curry	OpStat Group, Inc.	USA
Robert DiVasto, PE	Zavante Therapeutics Inc.	USA
Jim McKiernan	McKiernan Associates	Switzerland
Marzio Mercuri	Polpharma Group	Poland
Giuseppe Ravizzini	Recordati Group	Italy
Dennis Stamm	InnovaNet Group	USA

Chapter Writers and Team Reviewers

The Core Team wishes to thank the following individuals for their fundamental contribution during the preparation of this document.

Chris Abell	Pfizer Inc.	USA
Enric Jo Cardoso	Reig Jofre Group	Spain
Carrollynn Chang		USA
Alain Cruset	AC Consulting / ISPE France Affiliate	France
Nick Davies	NDA Consultants	USA
Kristin Fertig	Merck & Co., Inc.	USA
Zeljko Granosa	Pliva Croatia Ltd.	Croatia
Brian Guillett	NDA Consultants	USA
Theodore Iliopoulos	Abdi Ibrahim	Turkey
Niranjan Kulkarni	CRB Consulting Engineers	USA
Rodney Neal	Cyberwerks, LLC	USA
Brian Pochini	Genzyme	USA
Carla Reed	New Creed, LLC	USA
Gareth Sanderson	Novartis Pharmaceuticals	France
Patricia Seymour	BioProcess Technology Consultants, Inc.	USA
Marty Shelton	Shire Pharmaceuticals, Inc.	USA
Claus Weisemann	Luitpold Pharmaceuticals, Inc.	USA
Glen Williams	Biotechnology Consulting	USA

Other Contributors

The following individuals have given valuable contribution to the content of the Guide:

Terts Ashibi	Newleaf International Ltd.	United Kingdom
Wojciech Kisielnicki	Polpharma SA	Poland
Rey Ramos	Johnson & Johnson	Puerto Rico
Evelyn Santiago	Johnson & Johnson	Puerto Rico

The Team Leads would like to express their grateful thanks to the many individuals and companies from around the world who reviewed and provided comments during the preparation of this Guide; although they are too numerous to list here, their input is greatly appreciated.

Company affiliations are as of the final draft of the Guide.

Cover photos: iStockphoto.

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600 N. West Shore Blvd., Suite 900, Tampa, Florida 33609 USA
Tel: +1-813-960-2105, Fax: +1-813-264-2816

www.ISPE.org

1 Introduction

1.1 Overview

The Pharmaceutical industry is under unprecedented pressure to deliver innovative health benefits at affordable costs. This means that Operations Management is also challenged to maximize the strategic benefit it provides to the company at an acceptable level of cost. As a key driver to delivering on this challenge, the industry has been adopting operational practices which should be understood as coming under the umbrella term of "Operational Excellence". The effectiveness of these approaches requires the use of practices, procedures, technics, tools, and relevant Key Performance Indicators (KPIs) across the entire organization.

Until the recent past, the competitive edge in the pharmaceutical industry was built and based on high margin policies, reduction of costs of manufacturing via standardization of processes and increases to manufacturing scales, and relying on technical issues such as front-end design of processes as keys to success.

The 21st Century has seen a change in the portfolio of the innovator company from small molecule blockbusters to a greater focus on specialized biotechnology products. Simultaneously, the use of generic drugs continues to grow, and there is relentless downward pressure on pricing of both generic and innovator products.

Thus the traditional ways of doing business are no longer acceptable and new, innovative ways of working are required. Change is now a constant in pharmaceutical operations. Innovative products, both proprietary and generic, must be developed and integrated into the supply chain while at the same time ensuring that current and legacy products are supported to meet fluctuating global demands and constantly evolving local and global legislative and regulatory expectations.

Efficiencies are needed in individual product manufacturing lines and across multi-plant supply chains to ensure that drug shortages are avoided and to meet the market pricing pressures.

For the purposes of this Guide, operations are defined as the transformative process within a series of activities, along a value chain extending from supplier to customer. Operations Management designs, operates, and improves supply chain systems for getting work done.

The *ISPE Good Practice Guide: Operations Management* aims to provide the pharmaceutical industry with a knowledge base to promote the use of best practices and operational excellence within pharmaceutical operations management.

The Guide addresses all operations along the supply chain, from the selection of raw materials through to the distribution of final product. Topics considered by this Guide include:

- Supply Chain Strategy and Management (see Chapter 2)
- Manufacturing Operations Strategy and Management (see Chapter 3)
- Key Performance Indicators (see Chapter 4)
- Continual Improvement and Innovation (see Chapter 5)
- Methods and Tools for Continual Improvement (see Chapter 5)

A case study (see Chapter 6 – Appendix 1) is also included.

1.2 Scope

The Guide addresses how specialty, bulk Active Pharmaceutical Ingredient (API), and drug product manufacturing systems are organized and operated in order to guarantee the production, storage, and distribution of products while ensuring drug product quality throughout the supply chain. All operations along the supply chain are considered, including:

- Sourcing of raw materials
- Manufacturing of the drug substance (also called the API) and the drug product
- Control over all quality components, the finished product, and critical intermediates process steps
- Adequacy of the manufacturing and control facilities in order to meet compliance and quality objectives
- Distribution of finished products

These responsibilities are achieved as a concept of supply chain. This means that suppliers are adequately audited, facilities are properly qualified, and processes validated, and the finished product checked for the compliance with the expected quality. For example:

- Quality Assurance (QA) is responsible for the compliance of the enterprise with all regulatory requirements.
- Maintenance is responsible for keeping the manufacturing facilities in an adequate state of qualification.

Both compliance and qualification require a multi-disciplinary approach which considers all functions (QA, Validation, Engineering, Manufacturing, Health, Safety, and Environment (HSE), and Logistics). Cooperation is needed between the parties involved to maintain an appropriate qualification and validation status of manufacturing assets and processes.

The manufacturing function is then driven by three major priorities:

- Sustained compliance with all applicable regulatory agencies, e.g.:
  - In the United States, the FDA and the Environmental Protection Agency (EPA)
  - In the European Union (EU), the EMA or REACH[1]
- Improved manufacturing performance and efficiency while maintaining control on costs
- Timely production according to demand

In order to fulfill its mission, the manufacturing operations function needs to coordinate with other functions of the pharmaceutical organization, in a spirit of teamwork and with shared objectives, including:

- Awareness of the products in development (to anticipate the future needs of manufacturing)
- Feedback to development based on manufacturing experience (to avoid future scale-up problems)
- Support to clinical supplies

[1] http://ec.europa.eu/environment/chemicals/reach/reach_en.htm