

1 Purpose

The purpose of this Guideline is to describe the process in place to ensure that drug products and drug substances are manufactured in a manner that minimizes patient risk through adulteration from products manufactured in the same manufacturing plant or facility.

2 Scope and Applicability

This Guideline applies to the manufacture of commercial or development products in Operations facilities. It also applies to the manufacture of commercial or NPI (New Product Introduction) products at contractors. It is applicable to all Operations and Research and Development sites involved in these activities.

The manufacture of development compounds in R&D facilities is out of scope.

3 Definitions

3.1 Limit of Detection (LOD)

The LOD is the lowest amount of a given substance in a sample that can be detected but not quantified with the selected analysis procedure.

3.2 Limit of Quantification (LOQ)

The LOQ is the lowest amount of a given substance in a sample that can be quantified with suitable accuracy and precision with the selected analysis procedure.

3.3 Cleaning Validation

Establishing documented evidence that a specified cleaning procedure will provide a high degree of assurance that it can be used to consistently clean a piece of equipment or a facility to a predetermined acceptable level of cleanliness.

3.4 Acceptable Carryover Quantity (ACQ)

The ACQ is the potential maximum allowable quantity of previous product, which may be carried over to any subsequent product during manufacture.

3.5 Therapeutic Dose

The therapeutic dose is the amount of active substance given to a patient to achieve the desired pharmacological effect.

Note: The therapeutic dose is expressed as a weight of active substance (usually mg or g) per day.

3.6 Nil Effect Dose (NED)

Based on human data, is the maximum (single or repeated) dose at which there are no observable pharmacological effects in man.

4.2 Drug Safety Review Committee

Is responsible for coordinating the evaluation of requests and based upon available information, providing recommendations and advice on sitting decisions to the requests. Committee shall try to provide timely advice according to the nature of the request and the production schedule.

The committee secretary is responsible for providing therapeutic dose information requested by sites/functions.

4.3 Other Functions and Departments

Other Functions and Departments (e.g. R&D and Supply Chain) are responsible for coordinating requests for any New Chemical Entities (NCEs) proposed for manufacture in Operations facilities and the application of committee recommendations.

5 Guideline

5.1 Introduction

A company which has a portfolio of products with a wide range of pharmacological potency, its manufacturing strategy usually involves the frequent use of multi-product facilities (both in-house and at contractors). Therefore, in reviewing sitting and accommodation options for one product the impact of that product's pharmacological potency must be considered when evaluating the potential impact of carryover of that product to other products manufactured in the same facility.

To assist Operations and R&D Functions with unusual or potent product accommodations (including accommodations at contractors) decisions, the Drug Safety Review Committee should exist to ensure that products (drug substance and drug product) are manufactured in a manner that minimizes patient risk through cross-contamination from products manufactured in the same equipment, manufacturing plant or facility. Committee is therefore a support mechanism for sites/functions to assist with difficult cleaning and product accommodation issues.

The committee comprises representatives from Supply Chain, Drug Safety, Compliance Management and members from Operations, R&D as appropriate.

For atypical product accommodations, usually involving highly potent products, Operations Sites and R&D Functions should refer to the committee for advice or endorsement of sitting decisions or product changeover proposals. Committee also provides a focal point for handling other contamination or general cleaning issues, or questions concerning company policy and procedure for cleaning.

5.2 Operating Principles for Drug Safety Committee

The head of the committee has the responsibility to set the meeting schedule as suits business needs. Although the primary purpose is commercial product manufacture, advice will be given, on request, with regard to the manufacture and sitting of development compounds, especially where these impact on Operations facilities. The committee secretary should maintain a database of medical information for