## 1 Purpose

The purpose of this Guideline is to provide a robust logic and guidance document to:

- Assist in the evaluation of actions required in the design, construction and operation of Packing Facilities.
- Assist in the clarification of health/hygiene and Good Manufacturing Practice (GMP) issues
- Be used as a tool to assist in the selection of equipment and facilities for packing operations.
- Encourage the use of the risk assessment model when considering both health and hygiene and GMP.
- Assign products to the most appropriate facilities (asset accommodation).
- Be used as a tool to encourage a consistent, rational, and defensible approach to decisions affecting the design of packing facilities and sitting of packing activities.

The application of a consistent and rational approach to facility design and operation is required and is of benefit to the business. However, it is recognized that the derivation of a single approach that can be applied anywhere is not practicable.

## 2 Scope

This guideline is designed to assist decisions on how to appropriately accommodate the packing of solid dosage forms starting from bulk-packed tablet product through to the finished pack for shipping. The focus of this document is on the technical issues that must be addressed.

## 3 Definitions

### 3.1 Beta-Lactams

A major class of antibiotics that includes pencillins, cephalosporins and carbapenems.

### 3.2 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.

### 3.3 Containment

The action of confining a chemical entity within a defined space.

### 3.4 Primary containment

Primary packaging
material(s) form the container/closure system for the product and therefore may be in direct contact with the product. Examples include HDPE bottles/caps, blister strip packs, tubes/caps for ointments.

### 3.24 Primary Packing Equipment

The hardware used to put the product into its primary container, e.g., the blister former or bottle filler.

### 3.25 Personal Protective Equipment (PPE)

Any equipment worn by an operator or technician to minimize exposure to a drug or substance, e.g., to provide protection to hands, eyes, skin or to prevent inhalation.

### 3.26 Potent

A compound that is biologically active at low doses.

### 3.27 Pressure Regimes

A subdivision of a series of rooms into defined air pressure regimes. The pressure regimes are cascaded, with the lowest pressure at the point of highest risk of loss of contaminant, to prevent airborne material transmission from process rooms into adjacent transit areas.

### 3.28 Respiratory Protective Equipment (RPE)

Equipment used as part of the strategy to control personal exposure to the product via the inhalation route.

### 3.29 Respiratory Sensitizer

A substance that can trigger an allergic reaction in the lungs or airways of a sensitized individual.

### 3.30 Risk

The combination of the severity of potential consequences, which could arise from a hazard and likelihood that these consequences will be realized.

### 3.31 Risk Assessment

The process used to evaluate whether or not the level of risk is tolerable. This is a three-step process:

1 Identification of the hazard
2 Assessment of the risks
3 Management of the risks

### 3.32 Secondary Packing

equipment that meet the requirements of GMP, safety and the needs of sourcing and asset strategies.

Manufacturing Strategy Group is responsible for designing strategies for the sourcing of individual products and for the provision of manufacturing assets consistent with the requirements of GMP and Safety.

## 5 Guideline

### 5.1 Background

Company product portfolio may includes a wide range of active materials. Effective use of those actives requires a clear recognition and understanding of the hazards, how to manage the associated risks and adequately control employee and patient exposure.

Experience has shown that:

- Historically there have been significantly different approaches taken to the management of containment and cross contamination reduction.
- Uncertainty and lack of clarity regarding requirements can result in inconsistent application of design and operation standards.
- A number of common questions affecting accommodation/control decisions have arisen from different areas of the Company. This has resulted in duplication of effort and the potential for application of inconsistent solutions.
- Decisions affecting packing operations have sometimes been based on hazard or perceived hazard, rather than risk. A specific example is products in the class “cytotoxic”. Whilst all products in this class “kill cells”, the mechanism of action and specific properties of individual products in this class may be different, and may require different solutions to accommodate them.
- Decisions affecting packing operations have sometimes been taken based on an inconsistent interpretation of GMP guidelines.
- Key factors affecting the design and operation of packing facilities and equipment (existing or new) should include:
- Operator protection
- Environmental protection
- Protection of patients in the community
- Product associated hazard and risk
- Company standards
- Engineering standards

to airborne substances at work.
In many cases experience and the risk assessment provides the information to give reassurance that adequate control of exposure of substances has been achieved.

If there are uncertainties about compliance with the OEL there are tools to help, e.g.,

- occupational hygiene monitoring of airborne concentrations. This should be done using the appropriate validated sampling and analytical methodology and occupational hygiene monitoring strategy.

Whilst risk assessment must be carried out locally to determine the potential for exposure, in general, the nature of packing activities is such that there should not be significant potential for airborne exposure if all operational controls are robust.

The OEL relates to exposure via inhalation. Where relevant, the potential for exposure via all routes should be considered, e.g., inhalation, ingestion, skin.

### 5.3.8 Can engineering designs achieve this OEL without PPE?

It is Company policy and a legal requirement in many of the Countries in which we operate that personal exposure must be controlled by means other than PPE, i.e., routine use of PPE is the last resort.

The rationale for this is sound and takes account of many factors, e.g.:

- Use of PPE does not prevent the spread of contamination
- The user may potentially be exposed when PPE is removed
- Other operators in the workplace who are not using PPE may be exposed.

The primary disadvantage to PPE is that is does not eliminate the hazard from the workplace and if it were to fail it results in exposure to the hazard.

Although the use of PPE should be considered the last resort for routine operation its use may be appropriate for some tasks, e.g., non-routine equipment maintenance or emergency responses to spills. The successful use of PPE relies on the equipment being properly chosen, used, cleaned, stored and maintained. Operators have to be trained in its use.

### 5.3.9 Choose appropriate technology to minimize the use of PPE

In solids handling, gloves and Respiratory Protective Equipment (RPE) are typically the most common type of PPE.

In general, there are four situations where the use of PPE is useful and appropriate.

1. When it is not technically feasible to control exposure by other means.

2. For emergency procedures such as cleaning major spillages.

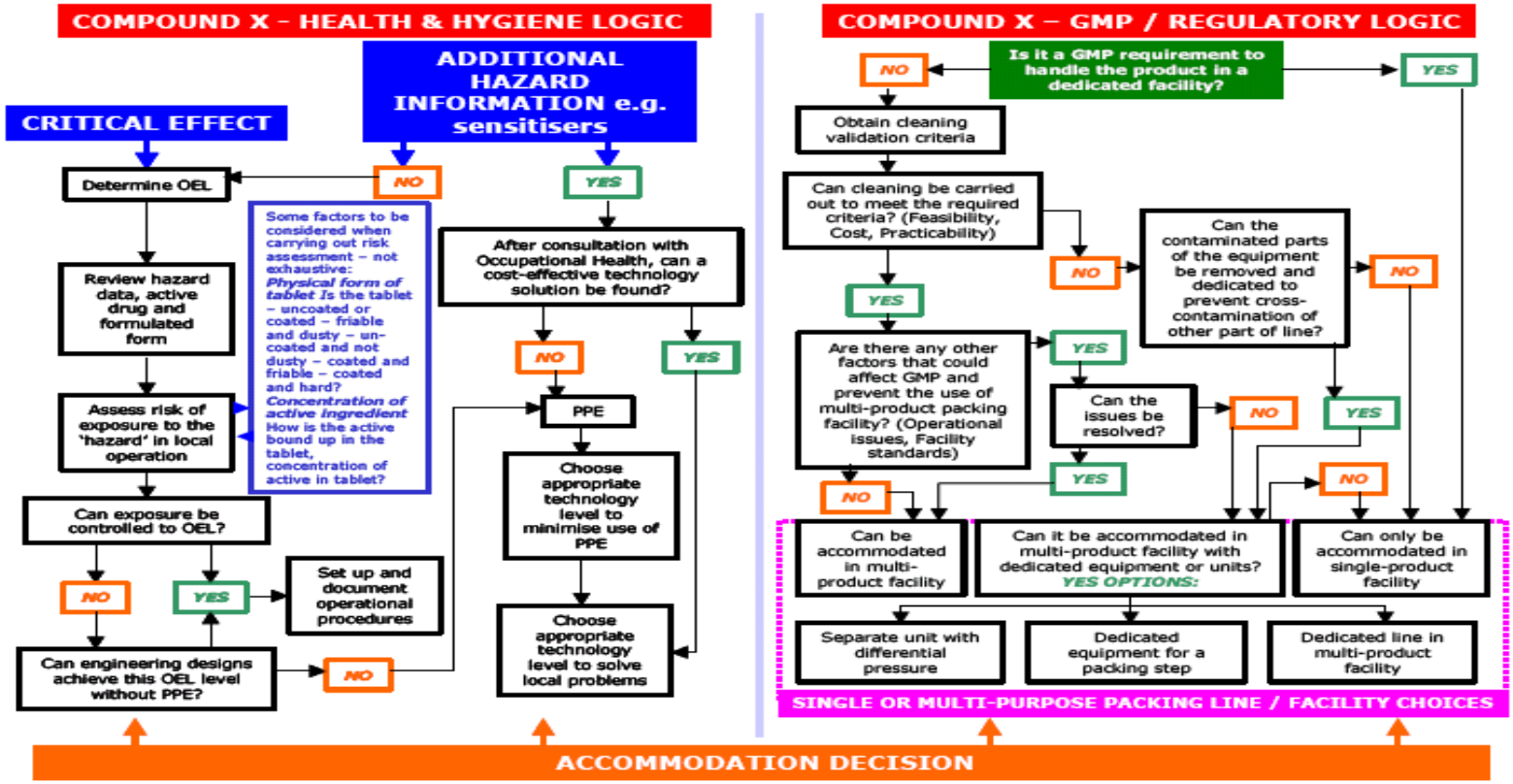
3. For maintenance work where containment is breached.

4. Where the risk assessment has shown an immediate risk that needs control

# 6. Appendices

## 6.1 Appendix 1 Logic Diagram to enable packing decisions using both Health / Hygiene and GMP / Regulatory data



### 6.2.5 Floor Finishes

Floor finishes should allow easy cleaning, e.g., coved finishes in primary packing areas.

A number of different floor finishes can be considered which are consistent with the usage and standard of cleanliness required, e.g., vinyl, resin, resin terrazzo, sealed concrete etc.

### 6.2.6 Packing Facility Operation: Temperature, humidity, air flows and pressure differentials

There are no general regulatory requirements for the monitoring of temperature, humidity within a packing facility. It is likely that these will monitored at a frequency for operational control of the HVAC system.

There may be, as a result of a specific product requirement of monitor and record humidity and temperature. This should be carried out up to the point where the product is being sealed into the primary container, e.g., a moisture-sensitive product is likely to have local control of humidity and this will be monitored from the tablet hopper to the tablet being sealed it the primary container.

Generally the packing hall should be at a positive pressure to ambient to give air flows from the packing hall to the outside and into technical spaces and be negative with respect to surrounding corridors to give air flows from the corridors into the packing facility. Air flows from primary packing cubicles, if provided, should cascade out into the general packing space unless there is a concern to contain particular products, in which case the direction of air flow should be into the cubicle, or the cubicles provided with an effective air lock.