- 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

A system of containment, which prevents the escape of a chemical entity into the immediate working environment. It involves the use of closed containers or safety cabinets along with secure operating procedures.

### 3.5 Secondary containment

A system of containment, which prevents the escape of a chemical entity from a system of primary containment into the external environment or into other working areas. It involves the use of localized extract booths or rooms with specially designed air handling, the existence of airlocks and secure operating procedures. In many cases it may add to the effectiveness of primary containment.

### 3.6 Critical Effect

This is the first significant adverse effect(s), which occurs as the dose increases from zero. It is determined after consideration of all the available data. For

 

## 5.3 Health and Hygiene

The sub-sections below follow the health and hygiene logic diagram, i.e., the left hand side of the diagram as shown in Section 6.1 Appendix 1.

### 5.3.1 Critical Effect

The critical effect is the first or most significant adverse effect encountered on exposure to a chemical.

The critical effect is determined after consideration of all the relevant information and is used in the Occupational Exposure Limit (OEL) setting process.

- A no-effect dose or low effect dose is established for the critical effect
- Uncertainty factors are applied
- All judgments are made on a case-by-case basis
- Where there is a gender specific effect, the OEL derived for this effect will be applied for both sexes. Segregation will be avoided.

### 5.3.2 Determine the OEL

OELs are specific to the active ingredient and are agreed by a panel of experts (Toxicology and Regulatory Group Manager, Clinical Occupational Health Representative, Occupational Hygiene Representative, Manufacturing Department Representative, Occupational Toxicology Manager and Co-opted members form R&D).

### 5.3.3 Review hazard information

The material safety data sheets (MSDS) provide a summary of information about the hazards of the material. One section of the safety data sheet gives the OEL. The hazard is the potential of the material to cause harm

### 5.3.4 Additional hazard Information

In some cases there may be additional information about the hazard that requires further advice from occupational health professionals to assist decision makers, e.g., potent skin sensitizer.

### 5.3.5 Assess risk of exposure to the “hazard” in local operation.

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

It is very important to make a clear distinction between “hazard” and “risk”. Experience has shown many examples of decisions affecting operations being based on hazard or perceived hazard, rather than risk. These are an issue for the company.

Risk assessment and risk management is a three step process (see Figure 1).

 

Consider the use of differential pressure regimes to minimize the possibility of cross-contamination.

2) Dedicated Equipment: Dedicating equipment for a particular step, e.g., change parts, may address issues regarding the feasibility of cleaning or concerns over cross-contamination.

3) Dedicated Line: Certain product classifications, e.g., beta-Lactams, may dictate the use of a dedicated line.

### 5.4.7 Can the cleaning criteria be met for some stages of the packing operation?

It is possible that parts of the process may be sufficiently easy to clean that the cleaning validation criteria can be met. This could lead to a hybrid situation whereby part of the equipment, or an individual line or unit, may be dedicated but other unit(s) or pieces of equipment are acceptable for multi-product use. If the answer is No then the logic confirms the use of a single product facility.

### 5.4.8 Can the contaminated equipment be isolated to prevent cross contamination of other parts of the facility?

In connection with the step above, and if the contaminated equipment or unit can be isolated to prevent cross-contamination, then it will be possible to review the options for placing the product into a multi-product facility with dedicated equipment, line and/or units.

### 5.4.9 The product can only be accommodated in a single product facility

This is the least flexible option regarding facility use but demands of operator protection, cleaning and GMP may dictate its use.

 

### 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.

 