4.2.6 Personnel should not be a source of contamination.

4.2.7 Directional airflow within production or packing areas should assist in preventing contamination. Airflows should be planned in conjunction with operator locations, so as to minimize contamination of the product by the operator and also to protect the operator from dust inhalation.

4.2.8 HVAC air distribution components should be designed, installed and located to prevent contaminants generated within the room from being spread.

4.2.9 Supply air diffusers of the high induction type (e.g. those typically used for office-type air-conditioning) should where possible not be used in clean areas where dust is liberated. Air diffusers should be of the non-induction type, introducing air with the least amount of induction so as to maximize the flushing effect. (See Figs 9–11 for illustrations of the three types of diffuser.)

4.2.10 Whenever possible, air should be exhausted from a low level in rooms to help provide a flushing effect.

4.3 Unidirectional airflow

4.3.1 Unidirectional airflow (UDAF) should be used where appropriate to provide product protection by supplying a clean air supply over the product, minimizing the ingress of contaminants from surrounding areas.

4.3.2 Where appropriate, the unidirectional airflow should also provide protection to the operator from contamination by the product.

4.3.3 Sampling of materials such as starting materials, primary packaging materials and products, should be carried out in the same environmental conditions that are required for the further processing of the product.

4.3.4 In a weighing booth situation, the aim of the design using UDAF should be to provide dust containment.

4.3.5 A dispensary or weighing booth should be provided with unidirectional airflow for protection of the product and operator.
4.3.6 The source of the dust and the position in which the operator normally stands should be determined before deciding on the direction of unidirectional flow.

Example: In Fig. 12 the dust generated at the weighing station is immediately extracted through the perforated worktop, thus protecting the operator from dust inhalation, but at the same time protecting the product from contamination by the operator by means of the vertical unidirectional airflow stream.

4.3.7 The unidirectional flow velocity should be such that it does not disrupt the sensitivity of balances in weighing areas. Where necessary the velocity may be reduced to prevent inaccuracies during weighing, provided that sufficient airflow is maintained to provide containment.

4.3.8 The position in which the operator stands relative to the source of dust liberation and airflow should be determined to ensure that the operator is not in the path of an airflow that could lead to contamination of the product (Fig. 13).

4.3.9 Once the system has been designed and qualified with a specific layout for operators and processes, this should be maintained in accordance with an SOP.

4.3.10 There should be no obstructions in the path of a unidirectional flow airstream that may cause the operator to be exposed to dust.

Fig. 14 illustrates the incorrect use of a weighing scale which has a solid back. The back of the weighing scale should not block the return air path as this causes air to rise vertically, resulting in a hazardous situation for the operator.

Fig. 15 illustrates a situation where an open bin is placed below a vertical unidirectional flow distributor. The downward airflow should be prevented from entering the bin, and then being forced to rise again, as this would carry dust up towards the operator’s face.

Fig. 16 shows that a solid worktop can sometimes cause deflection of the vertical unidirectional airflow resulting in a flow reversal. A possible solution would be to have a 100 mm gap between the back of the table and the wall, with the air being extracted here.
4.3.11 The manufacturer should select either vertical or horizontal unidirectional flow (Fig. 17) and an appropriate airflow pattern to provide the best protection for the particular application.
Figure 12. Operator protection at weighing station

Figure 13. Operator protection by horizontal airflow
Figure 14. Operator subject to powder inhalation due to obstruction

UDAF, Unidirectional airflow.

Figure 15. Operator subject to powder contamination due to airflow reversal in bin
Current Good Manufacturing Practice (cGMP) Compliance (for Directional Airflow Devices)

The area of cGMP compliance covers many aspects of the devices specification. One of the most potentially serious areas of concern to a
visiting regulatory inspectors the risk of cross contamination. There are three different possibilities:

<table>
<thead>
<tr>
<th>Containment category</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound OEL μg/M³</td>
<td>&gt;100</td>
<td>1-100</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

- Airborne cross contamination
- Structural cross contamination
- Operator borne cross contamination.

Categorization of Compounds

Most of the theory of compound categorization was developed in the USA. Companies such as Eli Lilly and Syntex who pioneered the application of differing containment devices realized that categorizing their compounds into three or four simple groups made the engineers and pharmacists focus on the relevant technology rather than an ‘over engineered’ solution. As pharmaceutical compounds all have differing characteristics, the operator exposure level (OEL) based categorization in Table 6.5 outlines a simple categorization.

Some compounds are dermal or respiratory sensitizers which means that certain workers will be more susceptible to an adverse reaction. Other compounds may have a cumulative effect. The examples given in Table 6.6, therefore, are guidelines.

Principles of Bulk Dispensing

The modern dispensary facility in a pharmaceutical plant must be capable of:

- Dispensing raw materials to a registered formulation that will be manufactured into a product for either pharmacy or hospital use. The
exception to this is a dispensary for research and development, or clinical trials of a product where other considerations may apply.

- Providing records that enable a complete audit trail of all the materials dispensed. This must include both pharmaceutical materials and packaging components. However, packaging components are usually dispensed and reconciled at the beginning and end of a packaging operation in a separate area. Here we will not consider these aspects further.

In today’s modern plant there will probably be a ‘stock control’ and/or a warehouse management system in place. These are also manufacturing facilities which use ‘factory management systems, sometimes referred to as MRP systems (material resource planning).

At all times regulations under the Health and Safety Executive, MCA and FDA (if applicable) must be strictly followed. In addition all rules pertaining to Good Manufacturing Practice (GMP) must be obeyed. Standard operating procedures (SOPs) are subject to the ‘validation procedure‘ and all documentation relating to this must be kept secure.

My special thanks to askaboutvalidation group.

Durga prasad