

Cross contamination control strategy in multiproduct pharmaceutical manufacturing facilities

Viktorija Velkovska*, Meri Davcheva, Milkica Gligorova

Alkaloid AD, Blvd. A. Makedonski 12, 1000 Skopje, Republic of North Macedonia

Introduction

Multi product pharmaceutical manufacturing facilities offer flexibility, efficiency and cost reductions, because the same equipment is used for manufacturing different products. But such multiproduct manufacturing brings the risk of cross contamination. The term contamination means undesired introduction of impurities (chemical/microbial/foreign matter into or on to starting material or intermediate – during sampling, production, packaging or repackaging. While cross contamination is the contamination of a starting material, intermediate product or finished product with another starting material, intermediate product or finished product. One of the greatest challenges in multi-product facilities is the prevention of cross contamination.

The aim of this paper is to present the most effective strategies for cross contamination control in multi product pharmaceutical manufacturing facilities.

Cross contamination control strategies

A contamination control strategy should be implemented across the facility in order to assess effective prevention of cross contamination. The most effective ways to prevent cross contamination are described below.

Well-designed and operated facilities - Cross-contamination should be prevented for all products by appropriate design and operation of

manufacturing facilities. Production premises should be of suitable size (adequate space for orderly placement of equipment and production materials to prevent mix-ups and contamination), construction and location. The facility must have smooth surfaces, so it can be reduced accumulation of dust and should permit easy cleaning and maintaining. Airlocks should prevent particulate contamination of the different areas. The opening of more than one door at a time should be prevented with proper door interlock systems. The flow of materials and personnel through facilities should be well defined and designed in such way to prevent mix-ups or contamination (European Commission, Guidelines for Good Manufacturing Practice, 2014).

Personnel - Only well trained, suitably qualified and authorized personnel should have access into production, storage and product control areas. Personnel should be well trained for the specific manufacturing technologies used in the production processes, then for cleanroom practices, contamination control and performing cleaning. Personnel should wear appropriate protective equipment and clean body coverings. It should be avoided direct contact between operator's hands and starting materials, intermediate or bulk products, and also primary packing materials. Movement in clean areas, should be kept to a minimum and well controlled and defined (Pharmaceutical Inspection Convention Guide to GMP, 2018).

* vzdravkovska@alkaloid.com.mk

Equipment - Manufacturing equipment should be designed so that it can be easily and thoroughly cleaned. There should be written standard operating procedure for cleaning of each equipment. The cleaning process should be validated. If the equipment is difficult to clean, then it should be considered dedicating the equipment for manufacture of a single formulation of product. It is important that all the equipment, material used and the facilities should have cleanliness status labels. For every cleaning procedure should have records and should be performed checks in between batches. Where applicable should be used closed systems in production, so it can be prevented generation of dust and direct exposure of the product to the surrounding environment will be avoided, according to European Commission Guidelines for Good Manufacturing Practice (2014).

Validated cleaning procedures - Cleaning validation is a documented evidence that the cleaning procedure provides reproductive removal and cleaning of the previous product or detergents used for cleaning the equipment. Good cleaning procedures are fundamental. Manual cleaning is very subjective, as a result of operator-to-operator variability in the degree of cleaning. So the standard operative procedures for manual cleaning must include very detailed instructions for the cleaning procedures and the operators should be well trained for the cleaning procedure, to accomplish reproducible manual cleaning of the equipment. Cleaning procedures should be monitored at appropriate intervals after validation to ensure that these procedures are effective when used during routine production (Alley et al., 2017).

Heating, Ventilation and Air Conditioning (HVAC systems) - HVAC systems control airborne particles, dust and microorganisms through air filtration using high efficiency particulate air (HEPA) filters. Air must be controlled where product is exposed to the environment. The filtered air entering a production room can be turbulent or unidirectional (laminar). Laminar flow should be used in areas where there is excessive dust formation. The second important function of HVAC systems is maintaining room pressure. Clean areas must have higher room pressure than the surrounding areas. This means that when the door of the clean area is opened the air flow will be from the

“cleaner” area towards the surrounding areas. Pressure control devices should be linked to an alarm system set which will indicate reduction of pressure differentials below set limits, according to World Health Organization Guidelines on HVAC systems (WHO, 2019).

Additional measure to maintain the pressure differentials that should be taken in consideration is interlock door system that do not allow simultaneous opening of the doors in the production area.

Conclusion

Controlling of cross contamination in multi product pharmaceutical manufacturing facilities is very important. Cross-contaminated pharmaceutical products can be life-threatening for the patients. There are many cross contamination control strategies that should be implemented to prevent cross contamination: well-designed facilities, well-trained operators; having written standard operating procedures for handling and storing material and products, for cleaning of equipment and facilities; well designed and maintained HVAC systems; validated cleaning and decontamination procedures; preventing generation and dissemination of dust; using cleanliness status labels on equipment.

References

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