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The Applicability of Cleaning Validation

Cleaning validation is primarily applicable to cleaning of process manufacturing equipment in the pharmaceutical industry. The focus of cleaning validation is those cleaned surfaces that, if inadequately cleaned, could potentially contaminate the product subsequently manufactured in that same equipment. This primarily covers product contact surfaces in the cleaned equipment—these are the surfaces that directly contact the next product.

This includes the interior surfaces of vessels, agitators, piping, hoses, pumps, and other items that directly contact the manufactured product, and thus can directly transfer residues to the next product. There are some applications where indirect residue transfer may occur. Some examples of indirect transfer are clear. The reflux condenser in the organic synthesis of an active ingredient may not directly contact the next manufactured product; however, the refluxing solvent does contact the condenser surfaces and could potentially carry residues from the condenser surfaces to the solvent containing the active ingredient.

A more controversial example of indirect transfer involves the interior surfaces of a lyophlizer (or freeze dryer). The possibility exists that residues left on shelves (for example) could potentially transfer by an airborne route from the shelves to the manufactured product. Such a transfer has not been demonstrated in real life cases. However, because the products manufactured in a lyophilizer are usually parenteral products, some companies have been asked by regulatory authorities to validate the cleaning of lyophilizers, while others have chosen to pursue cleaning validation for other reasons.

Other types of cleaning cannot be validated because of the frequency of performing the identical cleaning procedure (SOP). For example, for clinical trial materials or for drugs made infrequently (every year or two), it is doubtful that the exact same cleaning SOP would be used three successive times in order to obtain three PQ runs. In such cases, the cleaning process cannot be validated; however, it is still necessary to determine that the equipment is suitably cleaned for the manufacture of the next product. This calls for cleaning verification, and involves performing tests similar to those done for the three PQ runs in cleaning validation, except that the tests are performed for each and every cleaning event.

Still other types of cleaning do not require either validation or verification. For example, cleaning of the outsides of tanks and the cleaning of walls and floors is required under GMPs. There should be SOPs defining those cleaning processes. However, those processes are not critical, and therefore do not require validation.

The applicability of cleaning validation should be written into a facility's Cleaning Validation Master Plan to define clear situations which require validation, but to permit professional judgment in cases which may require considered reflection.