

Excipient Manufacturer's Perspective

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The presentation will discuss the types and scale of processes used in excipient manufacture and what types of residual solvents can typically be present for some excipients. It will be stressed that elimination of residual solvents from excipients is many times not possible without significantly changing the quality and performance of various excipients. Additionally, many of the excipients are primarily produced for other markets where the residual solvent levels are considered to be irrelevant. Therefore, in a number of cases, the residual solvents present in standard excipients may exceed the limits established in the ICH and USP guidelines for those solvents.

It is important for everyone in both industry and the regulatory community to realize that this is perfectly acceptable and that the ICH and USP guidelines do not preclude these materials from being used in drug products. It simply is necessary when this occurs for the user of the excipient to take these levels of residual solvents into consideration in their calculations or testing when determining if the finished dosage form meets the Residual Solvent requirements outlined in the General Chapter.

The USP General Chapter (as well as ICH Q3C) refers to the controls on the finished dosage form and does not place any requirements on the excipient manufacturer. It will be necessary however to inform the excipient users of what the residual solvent levels are in the excipient so that the user can make the appropriate determinations on how they need to handle their compliance to the Residual Solvent requirements for that finished dosage form. The General Chapter gives multiple mechanisms for how this can be handled.

A key point that we want to cover in this presentation is to educate the industry so that everyone understands that the residual solvent limits listed for certain solvents in the General Chapter do not constitute any type of specification for what an excipient must meet to be useable in pharmaceutical products. It will also be stressed why the reference to the General Chapter in excipient monographs that was proposed and then later retracted by USP would have created unnecessary confusion about what actually is required for the excipient itself and why it was necessary for this proposal to be retracted.

From an excipient manufacturer's perspective, the only impact of the implementation of the USP General Chapter should be that there will have to be improved communication concerning residual solvent levels in excipients.

The presentation will cover mechanisms for how this type of information can be shared between the manufacturer and the user since many times this type of information may be competitively sensitive and considered confidential. For this communication to happen appropriately, users will need to develop improved relationships with their suppliers to insure trust. Additionally, more efforts will be needed to evaluate equivalency of one manufacturer's excipient vs. the excipient from another manufacturer during excipient qualification exercises since residual solvent levels will typically be different from one supplier to another. This will not typically be identified through standard compendial testing and specifications. The functional differences which could potentially occur due to differing residual solvent levels will need to also be assessed before using alternative suppliers in drug formulation.