

Final Concept Paper
Q3C: Impurities: Guideline for Residual Solvents
Dated and endorsed by the Steering Committee on 10 March 1994

Problem statement/Objectives

A general policy in limiting residual solvents (organic volatile impurities) qualitatively and quantitatively in drug products and excipient has not been defined globally.

Background/Status quo

At the second International Conference on Harmonisation in Orlando in October 1993, the subject of impurities enjoyed substantial interest and debate. The Expert Working Group on Quality is working to create a guideline on impurities and the pharmacopoeias have standards dealing with impurities. Toxicologists also have participated on the subject of impurities, with regard to toxicity of process-related impurities.

The issue remaining for resolution with regard to impurities lies in the area of limits on low levels of organic volatile, e.g., residues of solvents. So far, different limits are employed or are being considered among the regulatory agencies and the pharmacopoeias. Agreement on a single set of limits is highly desirable.

The pharmacopoeias have begun studies for harmonisation of their approach for the control of residual solvents. However it is preferable that other interested Parties participate in an effort to achieve agreement rather than the ICH Expert Working Group and the Pharmacopoeias reaching independent decisions which will have to be harmonised later through negotiation.

Impact

The list of residual solvents to be limited and the limits tolerated for these solvents in each of the regions differs (e.g. case by case decision by the Registration Authorities, different proposals of USP, Ph.Eur, and Japanese Pharmacopoeia). This leads to uncertainty and implies duplication of work for industry.

Time frame

Given that the first prospectives have been studied within the Pharmacopoeial Discussion Group it should be feasible to complete the topic and announce the results at the ICH3 Conference in November 1995.

Expert Group

The existing ICH Working Group on impurities composed of chemists and toxicologists would be an appropriate Forum with the addition of the experts of the pharmacopoeial bodies, i.e. the USP Committee of Revision, European Pharmacopoeia Commission and the Committee on the Japanese Pharmacopoeia.