Maintenance Procedure for Q3C

This Maintenance Procedure has been developed by the International Council for Harmonisation (ICH) for revising the existing ICH guidance for industry Q3C Impurities: Residual Solvents (ICH Q3C) to include new solvents and revising existing permitted daily exposures (PDEs) for solvents already listed in ICH Q3C as new toxicity data for solvents becomes available.

Data and/or proposals pertaining to the revision of ICH Q3C with supporting information can be submitted directly to the ICH Secretariat at admin@ich.org. Information provided within a proposal should be based on significant toxicity data from studies such as repeat-dose toxicity studies, reproductive toxicity studies, genotoxicity studies, carcinogenicity studies and/or other relevant studies. Single-dose toxicity data alone are not sufficient. The toxicity data should be of sufficient quality to calculate a PDE.

The ICH Secretariat will share any proposals received with the Q3C Expert Working Group (EWG) Rapporteur and ICH Coordinators. The Rapporteur will facilitate the review of any proposals received by the EWG, and the EWG will make a recommendation on whether the proposal should be supported by the ICH Management Committee (MC).

If a proposal for maintenance is supported by the EWG, the ICH Secretariat will subsequently notify the ICH Coordinators and MC. The MC will then provide a recommendation to the Assembly on whether the EWG should be tasked with making the revision.

A revision will be considered only on presentation of new data or previously unrecognized toxicity data sufficient to result in a significant change, or because of convincing evidence that the existing data used to calculate a PDE are invalid. Minor changes in a PDE will not be considered. The Rapporteur, with the consensus of the EWG members, will assign data reviews to the EWG and request subsequent recommendations.

Based on the discussion, with requests for further information to the proposing group and/or individual as appropriate, the Rapporteur will prepare an assessment report based on the EWG's approval with a recommendation to accept, with or without modifications, or reject any proposed revisions.

After endorsement by the Assembly, either at the next formal meeting or by electronic endorsement, the recommendation of the EWG will be published in each region for public comment (*Step 3* of the ICH process). In addition, the proposal will be provided to each pharmacopoeia for their publication.

After closure of the public comment period, the Rapporteur may convene a meeting of the EWG or will rely on correspondence or teleconferencing to consider the comments and finalize the proposal for the revised ICH Q3C. The final recommendation for ICH Q3C and implementation is then forwarded to the Assembly for adoption in consultation with the MC. Implementation will follow regional practices. With approval of the ICH Assembly, the change will be provided to the pharmacopoeias at the regional/national level for publication.

When a new or revised PDE is recommended by the EWG, approval by the ICH Assembly is required. Once approval occurs, the information should be disseminated as quickly as possible to all ICH participants and other members of the chemical and pharmaceutical communities. It is recommended that the following actions should be taken by the Assembly to ensure rapid transmission of the new information:

- Publish relevant information on the ICH Web site
- Request publication of revisions by the pharmacopoeias of the ICH regions in their Forums or web sites
- Request that the members publish the new or revised PDE information on their respective web sites