

**ICH Concept Paper: Proposal for the Preparation of a Quality Guideline on  
Pharmaceutical Development**

**Type of Harmonization Action Proposed**

It is proposed that a new tripartite guideline be developed that would describe, at a high level, the harmonised contents of Section 3.2.P.2. (Pharmaceutical Development) within the Quality Module of the Common Technical Document. By this it is meant that a guideline should be developed to describe 'what' is to be discussed in Section P.2 but the guideline generally would not define the 'how' – the details of the studies that should be carried out. Additionally, this guideline will focus on principles of quality by design, and discussions of risk management will be incorporated into the appropriate sections of the guideline.

**Statement of the Perceived Problem**

CTD-Q provides a Section 3.2.P.2 for the applicant to include information on pharmaceutical development studies that were carried out to establish that, for example, the dosage form, formulation, manufacturing process and development, container closure system, and microbiological attributes are appropriate for the product described in the application. These are generally 'one time' studies that the applicant carried out in the course of the development of the drug product and are part of a background and context of scientific information that assists the CTD reviewer in understanding the critical-to-quality attributes of the drug product and its manufacturing process. Currently, only the EU has a guideline (Note for Guidance on Development Pharmaceuticals) that describes what might be included in Section P2. It has been agreed within the CTD-Q IWG that a guideline would be beneficial as currently there is not a consistent approach for providing and evaluating this information across the three regions. Potential topics to be addressed within P2 are illustrated below and could include sections on

Drug substance

- Key physicochemical characteristics
- Compatibility (with excipients and packaging materials)

Excipients

- Key physicochemical and/or biopharmaceutical characteristics

Drug Product

- Rationale for type of product
- Formulation development
- Overages
- Physicochemical and biological properties and their impact on product quality (risk analysis)
- Performance testing

Manufacturing Development

- Critical to quality manufacturing steps and process controls and their contribution to or interdependency with final product quality (risk analysis)
- Choice of sterilisation method
- Relationship of manufacturing performance and controls to end product testing (risk analysis)

Container closure system (and delivery devices)

Microbiological attributes

### **Issues to be Resolved**

Scope: what is included from e.g.,

- New chemical entities
- New biological entities
- Solid oral dosage forms
- Oral liquids
- Parenterals
- Topicals
- Inhalation
- Others?

OR

- Follow scope of Q6a and Q6b?

The types of studies and information that should go in this section so as to be acceptable in the three regions.

Discussions are also proposed to determine the role of this section in the overall assessment process. This understanding will help frame the contents of the guideline.

The primary purpose of this section is to provide information on how development data have been transformed into knowledge of the manufacturing science and technology thus helping reviewers to gain a better understanding of product and process attributes that can influence product performance and product quality.

Another key goal will be to develop a guideline that will help route field investigators through the inspection process so they can focus their inspections on the critical process steps and controls.

Initially, the Pharmaceutical Development section of CTD-Q will be used as regulatory submission document with a historical perspective. However, the knowledge and science-based discussion included within Pharmaceutical Development is intended to be applicable over the lifecycle of the product and may need to be updated as new information on the manufacturing science and technology become available. Specific topics to be addressed would be those described in the relevant sections of 3.2.P.2 of CTD-Q.

### **Background to the Proposal**

During the development of the CTD-Q format document, there was consensus among the six parties to consolidate the information described above within a single section in the registration dossier. However, the CTD-Q guideline describes the format of the section, not its content. The IWG has discussed which one of the CTD sections would most benefit from a guideline that would address content, where such a guideline does not already exist. Section P.2 was considered to be the most valuable, and this guideline will address the contents, at a high level, of this section.

It is proposed that this guideline be developed and implemented in phases. While elements of risk management and the application of this guideline during the inspection process will eventually be included, initial guideline development will focus mainly on those issues that need to be addressed for the first regulatory submission and its review process. Sections on risk management and integration of the inspection process will require close linkages with the EWG on Risk Management when that group is established.

### **Type of Expert Working Group and Resources**

A new Quality EWG should be formed that is based on the CTD-Q IWG. This is because it would be extremely beneficial if several of the EWG members were those involved in the development of CTD-Q. Additionally, as it is the intent of this guideline to reflect the needs of an integrated quality system (review and inspection), ultimately it will be necessary for the composition of the EWG to include industry and regulator members with inspection experience. To keep the size of the EWG manageable, it is suggested that the core group comprise two members from each of the ICH parties and the overall EWG be comprised of not more than three representatives from each of the ICH parties and one representative from each observer. It is recommended that the third member, that is one with manufacturing/inspection experience, be one of the members of a parallel EWG, ideally Risk Management (assuming adoption of the topic).

### **Timing**

Completion of Concept Paper	November 2003
Adoption of topic by ICH Steering committee	November 2003
First EWG	Spring 2004
Step 2 document	Mid 2005
(dependent on progress by Risk Analysis EWG)	

*Question to all parties: Should this concept paper be extended to include an Appendix that could constitute a first draft of the P2 guideline?*