Applications for Finished Pharmaceutical Product (FPP) Prequalification based on Technology Transfer (TT)

Introduction

The transfer of an FPP's ownership and its manufacture to another manufacturer requires the submission of a new application for FPP prequalification.

Transfer of Technology (TT) applications rely on transfer from a Sending Unit (SU) to a Receiving Unit (RU) of what is usually either a product approved by an SRA authority (according to the working definition[2]), or a prequalified product.

TT, as it is used in this document, implies complete transfer of the product and its components, including the approved API suppliers (some exceptions may be justified).

Changes that do not fit this definition are not considered in this document. Examples include the change or addition of a manufacturing site, where the overarching product responsibility has not changed or where only ownership of a product has changed, all other details remaining the same. Note that elements of TT may be required to support dossiers which do not represent complete transfer of technology.

This document provides a brief description of the PQTm assessment expectations specific to TT dossiers. Applicants are also reminded of the existing WHO TT guideline[1] reflecting the expectations of WHO inspectors.

In all cases, due to the specificity of such an application, PQT medicines should be contacted directly before any such submission is made.

Definition

Transfer of technology is defined as "a logical procedure that controls the transfer of any process together with its documentation and professional expertise between development and manufacture or between manufacture sites". It is a systematic procedure that is followed in order to pass the documented knowledge and experience gained during development and/or commercialization to an appropriate, responsible and authorized party. Technology transfer embodies both the transfer of documentation and the demonstrated ability of the RU to effectively perform the critical elements of the transferred technology, to the satisfaction of all parties and any applicable regulatory bodies.[1]

[2] Reference: WHO Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities TRS986 Annex 5

[1] Reference: WHO guidelines on transfer of technology in pharmaceutical manufacturing TRS961 Annex 7

Principles

For a TT dossier, information regarding the FPP (and its components) produced at the RU is considered the primary information for assessment, and information regarding the SU is considered supportive.

TT may provide assurances with respect to Bioequivalence (BE) and development of the FPP formulation and manufacturing process, but the resulting product is assessed and prequalified on its own merits. Exceptions to these requirements are indicated below.

Bioequivalence requirements

The bioequivalence requirements are decided on a case-by-case basis. A biowaiver may be possible taking into consideration product complexity and the demonstrated equivalence of the process (including multimedia comparative dissolution). The granting of a biowaiver has the expectation of identicality of quality information from the SU and RU. Consultation with PQTm is advised as to whether a biowaiver may be acceptable, and to confirm details of the comparative dissolution study. Note that the SU clinical/biobatch dissolution data is expected to be included if available.

Quality requirements

Since each TT dossier is unique, the provision of a comprehensive set of guidelines for such products is beyond the scope of this document. However, based on general quality requirements and the referenced WHO guidelines, the following quality expectations for TT dossiers are noted:

1. The SU and the RU are expected to jointly develop a protocol for the transfer of relevant information related to the manufacturing process from the SU to the RU, as well as the development of an equivalent process at the RU. See the referenced WHO guidelines[1] for expectations of the protocol contents.

2. The joint transfer report should be submitted with the above protocol, documenting execution of the protocol. These documents should demonstrate that the formulation, manufacturing process and specifications of the SU product (and its components) are adequately transferred.

In addition to the above, the following data should be provided by the RU on the transferred product:

1. The CTD API sections should be provided (as per normal requirements) and will be assessed according to the standard assessment procedures, i.e. API assessment depends on the API option used and its prior history (if any) in PQTm.

   In all cases, API specifications of the proposed FPP manufacturer (RU) are considered the principal API specifications of the dossier.

2. Full data on the FPP should be provided according to normal requirements (CTD FPP sections), including pharmaceutical development data (which the RU should have received). The usual batch requirements (size, number) apply for process validation, batch analysis and stability studies. Assessment of pharmaceutical development data will be abbreviated (in the case where the SU product is an SRA product or prequalified product); for example, API-excipient and API-API compatibility studies will be considered established.

[1] Reference: WHO guidelines on transfer of technology in pharmaceutical manufacturing TRS961 Annex 7

3. Where analytical methods are transferred (both for API and FPP specifications), in the case where the SU product is an SRA product or prequalified product, the information required is limited to the transfer report.

TT dossier requirements are applied on a case-by-case basis, including the use of risk management principles. Particularly close control of certain aspects will be required for certain formulations such as sterile products and complicated products (e.g. hot melt extrusion premixes).