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Questions and answers on the template for the Qualified Person's declaration concerning GMP compliance of the active substance used as starting material and verification of its supply chain "The QP declaration template"

Draft

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Comments should be provided using this template. The completed comments form should be sent to qwp@ema.europa.eu

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QUESTIONS & ANSWERS: Template for the Qualified Person's declaration concerning GMP compliance of the active substance used as starting material and verification of its supply chain "The QP declaration template"

Submission of the QP declaration

1 Does the QP declaration template introduce new requirements for the declaration?

No, the QP declaration template does not introduce new requirements for the declaration. The information to be provided in the QP declaration template is necessary to comply with current regulatory requirements.

The template format clarifies that the QP declaration is underpinned by audit and verification of the Active Pharmaceutical Ingredient (API) supply chain.

2 Is the use of the QP declaration template optional?

No, this would not be appropriate.

The template has been developed, in light of experience, to provide a harmonised, comprehensive and clear format for the provision of data required for the QP declaration and to enhance the efficiency of the regulatory process.

3 Should a QP declaration be submitted when the API is registered with an EDQM CEP Certificate of Suitability?

Yes, a QP declaration is required for all relevant submissions, regardless of the means by which the data requirements for the API are met – either by an EDQM CEP Certificate of Suitability, Active Substance Master File (ASMF) or full details in the dossier.

4 Should a QP declaration be submitted for registered back up sites that are not routinely used?

Yes, a QP declaration is required for all registered API manufacturing sites and finished product manufacturing (EEA) / importation / batch certification sites that may use the API, even if the site is not routinely used i.e. no site may be excluded.

Redundant sites or sites for which a declaration cannot be provided should be deleted from the marketing authorisation by submission of a Type IA variation (Change code A.7).

5 Which functions should be stated for the finished product manufacturing sites listed in PART A.

The finished product manufacturing sites to be listed in PART A should be those where any finished product manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging.

A brief summary description to adequately identify the manufacturing activities undertaken at each site should be provided e.g. finished product manufacture.

If considered necessary for reasons of clarity, a flow-chart indicating all manufacturing and control sites involved in the manufacturing processes of the medicinal product and the API may also be submitted. For new applications, reference can also be made to Annex 5.8 of the Marketing Authorisation Application form.

6 Is it compulsory to underwrite all the subsections in PART E of the QP declaration or may these optionally be deleted?

Yes, this is required to give assurance that the QP has the opportunity to put the necessary GMP controls in place. No subsection of the Attestation in PART E may be deleted.

7 What will be the outcome if the QP declaration is deficient or incomplete?

The regulatory submission will either be refused (Type IA variations) or subject to a request for further information (Type IB and Type II variations, new applications and renewals).

In some cases, issues identified in the QP declaration may be referred by the assessor to the GMP inspectors for follow-up via a risk-based inspection programme.

Active Pharmaceutical Ingredient (API) manufacturing sites

8 Which API manufacturing sites should be subject to the QP declaration?

The manufacturing sites involved in the synthesis of the API are stated in the Module 3.2.S / Section 2C of the marketing authorisation dossier or ASMF.

In the case of an EDQM CEP Certificate of Suitability, the sites of production are stated on the certificate.

Only those manufacturing sites to be registered and used as sources of the API need be subject to the QP declaration.

It is necessary that the manufacturing sites to be registered as sources of the API include so-called "part-process sites" - where different manufacturing sites are used sequentially to manufacture / synthesise the API.

All these sites and their function should be stated in the table provided in PART A of the QP declaration template.

Those sites, given in Module 3.2.S / Section 2C or the EDQM CEP Certificate of Suitability, which are not to be used as a source of API for finished product manufacture should be clearly identified and stated. An assurance should be given that there are appropriate controls in place to ensure that API from these other sites is not to be used to manufacture finished products. This could be verified through the manufacturer's raw materials supplier approval process or approved supplier list (which will name only the API production sites covered by a QP declaration) and incoming checks.

9 Is a new QP declaration required if changes are made to the API manufacturing sites during regulatory review? e.g. the addition of new API manufacturing sites to Module 3.2.S / Section 2C of the marketing authorisation dossier or Active Substance Master File (ASMF)

Yes, because the QP declaration should reflect the final dossier.

The QP declaration will need to be revised to reflect changes made to Module 3.2.S / Section 2C and include any additional or new API manufacturing sites, including part-process sites.

10 Should manufacturing sites upstream from the API manufacturing sites, but before the finished product manufacturing site, e.g. micronisation sites, also be subject to a QP declaration?

Yes, all sites upstream of from the API manufacturing sites, but before the finished product, e.g. micronisation sites, should also be subject to a QP declaration.

Questions relating to auditing

11 What experience and qualifications are required for third party auditors?

The manufacturing authorisation holder responsible for GMP of the API must be satisfied as contract giver that the auditor is appropriately qualified for the task; this would be subject to contractual arrangements.

12 Can an audit report that has been prepared for another, unrelated manufacturer be used?

Yes, sharing of audit reports is encouraged if this is managed in a controlled manner. The QP declaration should still be provided and state who has conducted the audit and that arrangements are in place between the contract giver and contract acceptor.

13 Will the competent authorities request audit reports for review?

No, audit reports will not be routinely requested. But competent authorities may request audit reports for review where there are concerns either relating to the specific site or the processes implemented by the manufacturer to assure the quality of their APIs.

14 Does the audit of the API manufacturing site have to be completed at the time the regulatory submission (application for a new MA, renewal or variation) is made?

Yes, the QP declaration should indicate that an audit of the API manufacturing site(s) has been completed at the time of the regulatory submission. This is to provide assurance that appropriate checks and controls of the API have been implemented. It is not acceptable to provide an assurance that an audit will be conducted retrospectively.