

Progress Update

Health Canada's Use of the European Directorate for the Quality of Medicines and Healthcare's Certificate of Suitability and the Signing of a Memorandum of Understanding

As previously announced, the Therapeutic Products Directorate (TPD) of the Health Products and Food Branch (HPFB) of Health Canada has undertaken an exercise to consider the option of using Certificates of Suitability (CEPs) issued by the European Directorate for the Quality of Medicines and Healthcare (EDQM) of the Council of Europe in lieu of conducting a portion of the in-house quality assessment of drug substances.¹ It is anticipated that incorporating CEPs into TPD's evaluation of drug substances will lead to a reduction in both review times and in the number of chemistry-related deficiencies noted in the first cycle of review.

Findings from the confidence building exercise have established that the key principles underlying the review practices of EDQM and TPD are comparable. The HPFB and EDQM have therefore agreed to sign a memorandum of understanding that will facilitate cooperation and information exchange with regard to the use of CEPs.

As a consequence, this announcement serves to provide guidance and encourage the filing of CEPs for Active Pharmaceutical Ingredients (APIs) used in drug products reviewed by the Directorate pursuant to Division 8, Part C of the *Food and Drug Regulations*, with the exception of highly complex substances.² This exercise will allow for greater familiarity in the use of CEPs by TPD.

In accordance with Health Canada guidance and long-established practice, Drug Master Files (DMFs) may be filed with TPD in support of Division 8 submissions. Currently, TPD conducts an assessment of the 'closed' part of a DMF as part of the DMF review; the open part being reviewed as part of the submission.

As of this notice, if a CEP is filed in conjunction with a DMF for the same API, producer, site, and manufacturing process, only the open part of the DMF will be evaluated by TPD. The closed part of the DMF, containing details of the manufacture, will not normally be reviewed. For sterile APIs and APIs that have the potential of being contaminated with adventitious agents of human, animal or micro-organism origin, TPD will review the manufacturing processes and controls. In exceptional cases, the EDQM review report may be requested.

¹ This exercise is presently limited to CEPs certifying that the chemical purity and microbiological quality of a manufacturer's drug substance is suitably controlled by the monographs of the European Pharmacopoeia.

² For example, enoxaparin sodium

It is important to note that the provision of a CEP does not at present replace the option of filing a DMF. In filing a CEP, the following authorizations and attestations are to be submitted concurrently:

- Letter of access authorizing TPD to refer to a DMF in support of a submission (no change);
- Written authorization for TPD to examine the EDQM confidential review report for the drug substance, should the need arise;
- Written assurance that there have been no changes in the manufacturing method following the granting of the CEP, or its last revision, by EDQM; and
- Written assurance that the manufacturing process described in the Canadian DMF is identical to the one evaluated by EDQM.

Following further experience with the use of CEPs in TPD's review process it is expected that guidance on the full implementation of CEPs will provide drug submission sponsors with a new option of referencing a CEP in their submission, rather than referencing a DMF. Guidance will be developed in consultation with stakeholders.

Questions or comments related to this project or notice should be directed to:

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