



**EDQM – COUNCIL OF EUROPE CONFERENCE
CERTIFICATION PROCEDURE
1992-2012: 20 YEARS OF EXPERIENCE
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ABSTRACTS

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ABSTRACT 1

The Evolution of the European Pharmacopoeia and Its Impact On the Certification Procedure

Dr Marianne Ek, Chair of the European Pharmacopoeia Commission

The Certification Procedure started in 1992 as a pilot and was fully adopted in 1994. The manufacturer was requested to demonstrate that a substance could be adequately controlled by the monograph in the European Pharmacopoeia. In 1992 the procedure was open for substances which had a monograph in the 2nd edition of the European Pharmacopoeia. In the 2nd edition most of the monographs had only TLC as a test for related substances, and further the production of new monographs was slow at this point in time. Since then it has been an extensive evolution of the European Pharmacopoeia which have had an impact on the Certification Procedure. The modernisation of the European Pharmacopoeia, increased production rate of monographs, faster implementation of monographs and implementation of ICH Q3A impurity guideline by the general monograph Substances for pharmaceutical use in the monographs have been very important for the Certification procedure, which also have lead to a growing number of application for new and revised certificates. Other general monographs have also been of importance such as Products with risk of transmitting agents of animal spongiform encephalopathies.

ABSTRACT 2

New developments in Certification, place of the procedure within the European regulatory framework and an update on the EU Review

J.L. Robert, Chair of the Joint CHMP/CVMP Quality Working Party and Former Chair of the Certification Steering Committee

The presentation will provide an overview of the initial reasons for the establishment of the Certification Procedure and focus on its development over the years. Changes in the assessment policy in line with evolving regulatory requirements of the national competent authorities will be highlighted. The presentation will demonstrate that same standards are applied in assessing applications for a certificate of suitability, active substance master files and individual marketing authorisation applications.

ABSTRACT 3

Remember the Pioneers: Why did we invent the Certification Procedure?

Prof. Per Helboe, First Chair of the Technical Advisory Board (TAB) for the Certification Procedure

In the late 1980's the basic concepts of impurity testing in active substances was thoroughly discussed in Europe in the CHMP Quality Working Party (QWP). Also, the European industry was involved. The discussions concluded in an amended EU directive and a new CHMP guideline. As a result it should now always be documented that the specification of any active substance was sufficient to control all potential impurities. This requirement was even valid for substances described in the European Pharmacopoeia.

During discussions between QWP and the European Pharmacopoeia Commission it was realized that a new philosophy was needed in relation to impurity testing in the pharmacopoeia. This resulted in elaborating transparent monographs giving full information of the capability of tests in the pharmacopoeia to limit named impurities.

The new requirements could potentially result a substantial amount of extra work for both industry and licensing authorities in Europe. In order to draw full benefit of the new concepts of the pharmacopoeia and to facilitate the work on complying with the new EU requirements the certification procedure was invented. After a pilot phase from 1992 the procedure became fully official in 1994.

The transparent monographs and the certification procedure made the European Pharmacopoeia outstanding in the world as an essential contributor to the licensing process for medicines.

ABSTRACT 4

Where do we stand after 20 years of running the certification procedure?

Dr Wilhelm Schlumbohm, Assessor for the Certification Procedure and Former Member of the TAB, BVL, Germany

Already in the early 1990s attempts were made to establish a certification procedure. The relevant guidance document at that time was the EU Note for guidance „Requirements in Relation to Active Substances“ which requested that the suitability of the monograph should be principally demonstrated to the competent authorities. In collaboration between Ph Eur, regulators from NCAs and industry the pilot phase was started 1992. 20 assessors from 11 European countries were involved in the dossier assessments. Shortly after the adoption of the Resolution AP-CSP (93) 5 the scheme entered the official phase in April 1994. Since that time the original resolution has been updated several times; the scope of the procedure was enlarged to cover fermentation products and TSE risk materials. Reference to the Certificate of suitability (CEP) was included in the pharmaceutical legislation.

At the level of the Ph Eur the running of the scheme was further improved by introducing a Technical Advisory Board (TAB) and a Steering Committee. Internal guidance documents were drafted, and staff was recruited. In addition to the core business of assessment of new dossiers in order to issue CEPs, the activities were enlarged to cover revisions and renewals. Further activities dealt with the implementation of an inspection sector. EDQM established additional measures to smoothly run the scheme, e. g. the Technical Advice procedure and the One-to-one sessions. The certification procedure as it stands now can be regarded as a mature scheme which enforces the role of the Ph Eur as the reference in the European licensing system, facilitates updating and revision of Ph Eur monographs, and saves time and resources on both, the industry's and regulators' side.

ABSTRACT 5

Use of CEPs outside Europe: Health Canada's experience

Dr Amirthini Rajkumar, Health Canada

In 2004, the Therapeutic Products Directorate (TPD) of Health Canada initiated an exercise to explore the official and systematic use of the Certificate of Suitability (CEP) issued by the European Directorate for the Quality of Medicines and Healthcare (EDQM) in TPD's review process. CEPs have been accepted in TPD's review of the Active Pharmaceutical Ingredient (API) quality since March 2007 as part of a pilot implementation project. Currently a complete DMF is still required. However, when a valid CEP has been filed in the corresponding DMF, the restricted part of the DMF is not reviewed. The process leading to acceptance of CEPs by Health Canada and the expected benefits will be discussed along with Health Canada's experience to date and future plans.

ABSTRACT 6

Use of CEPs outside Europe: Therapeutic Goods Administration's experience

Dr Michael Pass, Therapeutic Goods Administration, Australia

The Therapeutic Goods Administration (TGA) is a division of the Australian Government Department of Health and Ageing, and is responsible for the regulation of therapeutic goods including medicines, medical devices, blood and blood products in Australia.

Applications to register a prescription medicine in Australia must be in CTD format and the technical data requirements have been closely aligned with those required for applications for marketing authorisation in the EU.

The TGA has historically taken a close interest in the EDQM's certification procedure from its inception in the early 1990's. The procedure was seen as having the potential to remove the need to evaluate a drug master file (DMF) for drug substances which are the subject of a Ph Eur monograph. By the late 1990s CEPs from the EDQM were generally being accepted in lieu of a DMF with minimal assessment by the TGA. This was formalised in 2004 with the publication of the 'Australian regulatory requirements for prescription medicines' which sets out (Appendix 11C) the verification steps needed to refer to a CEP or replace a DMF with a CEP for a drug substance. The EDQM certification procedure continues to allow the TGA to make substantial savings in evaluation resources, and sponsors are encouraged to make use of them in their submissions.

ABSTRACT 7

Inspections of API manufacturers: What is new? What are the new challenges to face? Opportunities of international collaboration

Mr Olivier Gross, Scientific Administrator, EMA

Active pharmaceutical ingredients (API) are an essential ingredient of a medicine and most APIs are produced outside the EU. In order to ensure their authenticity and quality the recently published EU Falsified Medicines Legislation Directive 2011 /62/ EU:

- Strengthens requirements for inspections of sites located within the EEA and in third countries manufacturing and wholesale distributing APIs
- Strengthens the rules on inspections and introduces Good Distribution Practice

To alleviate the additional inspections workload, the new legislation also builds on a wider international collaboration between the European Commission, the European Medicines Agency and the EEA national authorities competent for medicines, to ensure through a better use of resources a better inspectional coverage of API manufacturing and distribution sites both inside and outside the Union.

The feedback received from the inspectors participating in the International API Inspection Programme is shared to illustrate the ongoing international cooperation and its benefits.

ABSTRACT 8

Inspections of API manufacturers: Experience of the EDQM

Dr Thomas Hecker, Inspector, EDQM, Council of Europe

The presentation provides information about the regulatory framework and the implementation of an inspection program for Active Pharmaceutical Ingredients under the EDQM's Certification of Pharmaceutical Substances procedure. Information about the organisation, conduct and the outcome of inspections, supported by statistical data, will be delivered. The slides summarise the EDQM's experience in the field of API inspections and give perspectives for future work.