Legislative Framework and Scientific Guidance in European Assessment

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Content of the presentation

- Scientific guidelines
- Other related documents
- The European Pharmacopoeia
- Web references

- **Scientific guidelines**
- Other related documents
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Legislation (1)

- Directive 2001/83(82)/EC on the community code related to medicinal products for human (veterinary) use is the main piece of legislation to be taken into account for assessment of MA dossier
- Annex 1 establishes scientific and technical requirements for the marketing authorisation of medicinal products
- Annex 1 also establishes how the information should be presented (format of the dossier)
- Further information on the format of the dossier is given in volume 2B (6B) of the Notice to Applicants (presentation and content of the dossier)

Legislation (2)

- Annex 1 Introduction:

  (4) *In assembling the dossier for application for marketing authorisation, applicants shall also take into account the scientific guidelines relating to the quality, safety and efficacy of medicinal products …*
- Applicable guidelines for any section of the dossier are listed in the CTD (currently applicable to medicinal products for human use)

Guidelines: definition (1)

- *A guideline is a **Community document** with explicit legal basis referred to in the legislative framework as intended to fulfil a legal obligation laid down in the Community pharmaceutical legislation. It **provides advice** to **applicants or marketing authorisation holders, competent authorities and/or other interested parties** on **the best or most appropriate way to fulfil an obligation laid down in the community pharmaceutical legislation**. In the case of scientific guidelines, these may relate to specific scientific issues reflecting a harmonised EU approach and based on the most up-to-date scientific knowledge.*

Guidelines: definition (2)

- ✓ Guidelines referred to in the legislation are applicable throughout the EU, irrespective of the procedure used (national, mutual recognition, decentralised, centralised)
- ✓ Guidelines are not legally binding (they are not legislation), but are expected to be followed, unless a justification is provided showing that the alternative approach used by the applicant is superior to what foreseen in the guideline

Different types of scientific guidelines

- Guidelines related to Quality, Safety and Efficacy
- Good Manufacturing Practice guidelines
- Maximum Residue Limits guidelines
- Pharmacovigilance guidelines
- Good Clinical Practice and conduct of clinical trials guidelines
- Herbal medicinal products guidelines
- Good Distribution Practice guidelines
- …

GLs related to Quality, Safety and Efficacy

- Referred to in Directive 2001/83(82)/EC
- Developed by CXMP Working Parties and/or (V)ICH and adopted by CXMP
- Published on the EMEA website

✓ Aim:

  – Provide a basis for practical harmonisation of assessment of scientific data in the dossier
  – Facilitate the preparation of dossiers for MA by the Pharmaceutical industry

Procedure for drafting a guideline (1)

- Main steps:
  - Inclusion in the relevant work program
  - Appointment of rapporteur
  - Development of the Concept Paper
  - Adoption of CP and public consultation (usually 3 months)
  - Adoption of draft guideline and release for public consultation (usually 6 months)
  - Collection of comments
  - Adoption of final guideline
  - Publication of final guideline

Procedure for drafting a guideline (2)

- ✓ The procedure was developed in order to be transparent and to give everyone (from pharmaceutical companies to single citizens), the possibility to express their views
- ✓ A published guideline should represent a document agreed by regulators, once adopted for public consultation, it is expected that no comments are received from Member States or regulators; people at competent authorities should have the possibility to comment before adoption (e.g. through their relevant working party member)

Publication of guidelines

- All scientific guidelines on quality, safety and efficacy are published together on the EMEA website, divided in categories to make their use easier, following the structure of the dossier
- For scientific guidelines published by EMEA (initiated from 2005), in order to increase transparency, an overview of comments is published upon finalisation, where the reasons for acceptance/not acceptance of any comment received during the public consultation phase are explained
- Every document published on the EMEA website is announced in the what's new section of the EMEA website; QWP documents are announced in the what's new section of the Inspections webpage of the EMEA website

Quality guidelines

- Developed by Quality Working Party (QWP) (Human and Vet, chemical products), Biological Working Party (BWP) (Human Biological Products) and Immunological Working Party (IWP) (Veterinary Immunological Products) and/or ICH/VICH
- Adopted by the relevant committees (CHMP/CVMP, HMPC, PDCO …)
- Published on the EMEA website

- Scientific guidelines
- **Other related documents**
- The European Pharmacopoeia
- Web references

Reflection Papers

- *A reflection paper may be developed to communicate the current status of discussions or to invite comment on a selected area of medicinal product development or a specific topic. It can provide a framework for discussion or clarification particularly in areas where scientific knowledge is fast evolving or experience is limited. A reflection paper does not provide scientific, technical or regulatory guidance, but may contribute to future development of such guidelines, or related documents.*

Questions/Answers

- *The EMEA has developed "Questions and answers" or "Frequently asked questions (FAQ)" documents to provide additional public information on topics of particular interest. They are intended to briefly communicate, in easily comprehensible language, requirements, practices or interpretations responding to the most frequent questions in a specific area.*

✓ Q/As are adopted by CXMP, but they are not subject to public consultation

Other EMEA documents

- Public statements
- Recommendation and procedural advice
- …

QWP documents

- Guidelines (public-provide guidance)
- Questions/Answers (public-provide guidance)
- Reflection Papers (public-do not provide guidance)
- Entries in the quality database (not public-reflect agreement at QWP level)
- …

✓ All these kind of documents have a different purpose; It is better to have in mind from the beginning what the document will be, using the right template from the beginning saves time and resources

Quality database (1)

- The quality database contains information on decisions adopted at QWP meetings on specific issues
- Every adopted decision which is not addressed by current guidance documents is recorded in the database
- It is an important tool for assessment of quality, in particular to avoid that divergent decisions are taken for similar cases by different Member States or at different points in time

Quality database (2)

- The database should be available to all quality assessors in the EU/EEA but not available to pharmaceutical companies
- QWP is working on a more user friendly version of the quality database which should be ready by the end of the year
- For the time being, it will not be possible to publish the database with a secure access, so access to the database for quality assessors which are not QWP members should be ensured by the relevant QWP member

- Scientific guidelines
- Other related documents
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Legislation (3)

- Annex 1 Introduction:

  (5) *With respect to the quality part (chemical, pharmaceutical and biological) of the dossier, all monographs including general monographs and general chapters of the European Pharmacopoeia are applicable.*

Scientific guidelines vs Ph. Eur. (1)

- EMEA scientific guidelines and European Pharmacopoeia monographs and chapters are complementary:
  - guidelines provide advice on the best or most appropriate way to fulfil legal obligations
  - the European Pharmacopoeia sets standardised specifications for pharmaceutical preparations, their constituents and containers

Scientific guidelines vs Ph. Eur. (2)

- EMEA quality guidelines can be cross-referred in Ph. Eur. texts, to avoid repetition and facilitate updating, in particular in areas where the technical and scientific knowledge is rapidly evolving
- The General Notices (1.2) of the Ph. Eur. state:

  *"**References to regulatory documents**. Monographs and general chapters may contain references to documents issued by regulatory authorities for medicines, for example directives and notes for guidance of the European Union. These references are provided for information for users for the Pharmacopoeia. Inclusion of such a reference does not modify the status of the documents referred to, which may be mandatory or for guidance."*

QWP Q/As vs Ph. Eur.

- It has been agreed that Q/As related to application of the Ph. Eur. are published on the QWP Q/As document on the EMEA website
- The QWP Q/As document already includes Q/As on
  - Harmonised Ph. Eur. Chapters 2.6.12, 2.6.13 and 5.1.4
  - Ph. Eur. Monograph on Tablets
  - Harmonised Ph. Eur. Chapter Uniformity of Dosage Units

- Scientific guidelines
- Other related documents
- The European Pharmacopoeia
- **Web references**

- Pharmacos – EUDRALEX (for pharmaceutical legislation, notice to applicants, good Manufacturing Practice etc)

  http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/pharmleg_en.htm
- EMEA home page (What's new etc)

  http://www.emea.europa.eu/
- EDQM Home page (for Ph. Eur. etc)

  http://www.edqm.eu/en/Homepage-628.html

- EMEA – Inspections webpage (shortcuts to QWP, PAT, GMP etc)
  http://www.emea.europa.eu/Inspections/index.html
- EMEA website: scientific guidelines list
  http://www.emea.europa.eu/htms/human/humanguidelines/background.htm (H)
  http://www.emea.europa.eu/htms/vet/vetguidelines/background.htm (V)
- EMEA website: QWP Questions/answers
  http://www.emea.europa.eu/Inspections/QWPfaq.html
- EMEA website: procedure for drafting guidelines
  http://www.emea.europa.eu/pdfs/human/regaffair/2414304en.pdf

Thank you for your attention!

Any question?