INTRODUCTION TO QUALITY ASSESSMENT

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Agenda

• aim presentation
• introduction regulatory affairs
• introduction quality assessment
• specific issues
Aim presentation

• to summarize the basic principles of quality assessment in order to elaborate **discussion** between assessors / medicines agencies as a source of input to a harmonised approach to medicines assessment by all experts and member states in the European Union
Agenda

• aim presentation
• introduction regulatory affairs
• introduction quality assessment
• specific issues
Conclusion

• need for governmental control
• establishment national medicines agencies

► indeed necessary (cars, airolains, medical devices)?
Registration

**scope**

*global consensus*

license to trade a medicinal product manufactured by industry / on industrial scale (extemporaneous preparations are excluded from registration obligation)

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quality??

safety

*efficacy*
Harmonisation in EU: Dir 2001/83

• (2) The essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health

• (3) However, this objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community
Trade

► do you take this into consideration? If so, how?

► my approach to (quality) assessments
  - reasonable time frame
  - harmonised
  - consistent
  - transparent
  - risk based
EU approach to regulatory affairs

• company drafts MA dossier
  - paper assessment dossier by regulatory authorities
  - batch release synthetic medicines by company only
  - based on TRUST

► do you assess taking trust as the basis?
► need for re-consideration approach in view of globalisation trade in medicines / other cultures?
MA - dossier (CTD format)

- USA, EU, Japan
- human only
ICH?

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.

The purpose is to make recommendations on ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.

The objective of such harmonization is a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines whilst maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health.

scope: new drug products only, not generics
ICH parties

- European Union
- European Federation of Pharmaceutical Industries and Associations (EFPIA)
- Ministry of Health, Labor and Welfare, JP(MHLW)
- Japan Pharmaceutical Manufacturers Association (JPMA)
- US Food and Drug Administration (FDA)
- Pharmaceutical Research and Manufacturers of America (Pharma)
Basis EU assessment policy

directives, regulations, Ph. Eur.
guidelines, Q&As, database
EU jurisprudentie, EU farmacopees
pharmacopoeias member states
national policies / jurisprudence
open literature
regulatory expertise (whom?)
Agenda

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Function quality dossier (I)
global consensus: bridging
Bridging requirements generics

EU (approach differs from USA, Canada, Japan)

- identical active substance
- identical quantity active substance
- identical pharmaceutical form
- therapeutic equivalence demonstrated
  - eg bio-equivalence
  - eg in-vitro equivalence of drug disposition lung
Bioequivalence

- the rate and extent to which a pharmaceutical drug product is available at the site of (systemic) action

- systemic active substances with absorption phase: pharmacokinetic profile is measured by comparing
  - area under the curve (AUC), for absorbed dosage
  - maximum concentration (Cmax) for rate absorption
  - time to maximum concentration (tmax) for rate absorption
  - not Cmin
Bioequivalence

• equivalence tested in average population, not the individual;
• allergy (gluten!), applicability (children, elderly!) no issue

too large to swallow
CTD Module 3

- single assessor M32S & M32P? > general assessment!
- assessors team? > detailed assessment?

► assesssors team better? required?
Harmonised quality assessments

- stand alone attribute?
- part of benefit to risk assessment?

- my view: 3 pillar system

- is the lack of qualification for an impurity (proposed limit 0.5%) in a milligram based new life saving oncolyticum a major objection and thus reason to refrain from registration?
Consistent quality assessments

- based on EU policy only?
- based on national policies as well?

▶ my view: most common denominator principle is not a good approach. National policies should preferably be used as a basis for an EU policy.
Consistent quality assessments

use of a guideline

1. minimum requirement to be met; commonly things will be asked on top according the opinion of the expert?

2. normal requirements, in exceptional circumstances things can be asked on top or waved depending on the product particulars?

► my view 2); if you do not agree with a guideline then contact your QWP expert!
Consistent quality assessments

Q&A are meant to be followed

- my view: thus also if you personally do not agree
- my view: if you do not agree, you may wish to contact your QWP expert

opinion

- expert or member state?
- colleagues can take over or not?
- my view: harmonisation is already difficult enough with 27 member states…
Consistent quality assessments

jurisprudence

► every dossier assessed on its own merits, thus former decisions are not relevant
► would be nice, but we don’t have an archive
► would be nice, but it takes too much time
► I do not feel bound to former decisions

► my view: public health and trade will benefit from consistent assessments. This requires active control of jurisprudence and thus a good database system (ASMFs)
Transparent quality assessments

- assessment report is written
  - for the assessor?
  - for the home organisation?
  - for other quality experts in EU?
  - for CHMP members (general experts)?
Transparent quality assessments

- assessment report is written
  - as an archive to the assessor?
  - as an archive to the member state?
  - to show others the skills of the assessor?
  - to clarify the decisions taken?
Transparent assessments

- based on templates

► My view
- not copy-paste QOS with little comments
- but continuous application
  - Fact (what is in the dossier)
  - Discussion (consistent with guidelines? critical or non critical issue etc.)
  - Conclusion (accepted, other concern or major objection)
Transparent assessments

Peer review

► do you want to read 3 pages about how well everything is and than two lines with three questions?

► If the text is a full copy of the QOS, do you really believe words as perfect, excellent etc?

► do you have time to read e.g. 84 pages and 148 questions? Wouldn’t 30 pages be more than enough considering every assessor would have the QOS also at its disposal?

WORKSHOP!
Transparent assessments

- key stakeholders
  - other EU experts
  - industry
  - health care professionals
  - Patients

- feedback
  - accepted?
  - considered?
  - promoted?
Risk based quality assessment

- my view
  - level of control based on aspects like complexity of the active substance, route of manufacture
  - no full compliance check (police is not everywhere)
  - no consultancy function! (max. 30 questions)
  - scientific approach ≠ conducting science (only need to know questions, no nice to know questions)
  - better is nice, but no obligation for marketing
Make sure you (get to) know

- directives & regulations
- guidelines
- Q&As & database
- organisation EMEA (committees, working parties)
- role QWP, ICH, NtA, HMA
- how legislation is drafted in EU
- all relevant websites
- your national experts in working parties and committees (QWP)
Understand how policy is made

ASSESSORS HANDBOOK

Question, action item, stakeholders feedback etc.

ACTION

department
agency
ministry
QWP
MCRN
EDQM
KNMP
ICH
enz..
HMA

Directives
Regulations
Guidelines
Interpretations
Add Policy
QUESTIONS?