Safeguarding public health

# Writing an Assessment Report

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# Programme

- Why we need Assessment Reports
- Writing style
- Deficiency points
- Potential Serious Risk to Public Health
- Targeted Assessment
- References

# Why we need Assessment Reports

# Legal requirement for Assessment Reports

- Article 21(4) of 2001/83/EC as amended
  - Competent authorities shall draw up an AR on the results of pharmaceutical and pre-clinical tests and clinical trials
  - AR to be updated whenever new information becomes available that is important for the evaluation of the quality, safety or efficacy of the product
  - Competent authorities shall make publicly available without delay the AR with reasons for their opinion after deleting commercially confidential information

# Types of Assessment Report

- Initial application & Type II variations
- MS conducts main assessment
  - National, MRP & DCP (RMS), Centralised (rapp/Co-rapp)
- MS relies fully or in part on assessment by another authority
  - MRP & DCP (CMS), Centralised (non rapp/co-rapp)
- Public Assessment Reports

# Purpose of the Assessment Report

- Explains why a MA & indications have been / can be approved or rejected by the RMS / competent authority
- Describes the benefit / risk considerations
- Provides an audit trail for decision making
- Establishes the SPC, package leaflet and labelling
- Outlines any conditions of the MA

# Purpose of the Assessment Report

- For the benefit of the reader - Who is the reader?
  - Assessors, Inspectors, Medical Writers, Management
  - CMS / CHMP members / CMD(h) members / EMEA
  - National Advisory Bodies / Boards
  - Applicant
  - Patients, Public, Industry, Healthcare Professionals (PAR)

# Writing Style

# Important Aspects of Writing Style

- Spelling
- Grammar
- Use Microsoft tools - spelling & grammar check
- Form complete sentences – don’t forget the little words – ‘the’, ‘a’
- Number and label tables & figures
- Limit abbreviations and three letter acronyms

# Important Aspects of Writing Style

- Stand-alone report
- Easy to read
- Critical evaluation
- Length – sufficiently detailed …. but concise – avoid waffle
- Summarise key data – but don't duplicate the dossier / QOS
- Avoid repetition
- Make conclusions & state if data are acceptable – need to state clear position for the reader
- Sometimes just comment on exceptions

# Report-Writing Process

- European templates & national templates
- Resource-efficient
- Can use cut-and-paste / pdf snapshots – legibility?
- Use previous assessments as basis for new assessment
- Take into consideration what we have allowed for similar products & how we have dealt with issues

# What Do We Find During Dossier Review?

- Acceptable data and supporting statements
- Mistakes, transcription errors, spelling/grammatical errors, inconsistency between sections
- Gaps/omissions
  - Not in line with legislation / mandatory requirements
  - Not in line with guidance
  - Aspects not discussed / sections of CTD not completed
  - Out of date information e.g. CEPs / ASMFs
- Inappropriate strategy/approach
- Compliance issues

# Deficiency Points

# Deficiency Points

- Raise points that add value to product evaluation
- Only raise points that affect the outcome of the assessment process or increase product quality
- Substantive issues that impact Quality, Safety and/or Efficacy
- Potential serious risk to public health or point for clarification
- Avoid raising minor points of clarification
- It is not the aim for a company to produce a perfect dossier
- Do not request a company to supplement their dossier solely to increase compliance with guidelines

# Preparing Deficiency Points - Considerations

- Clear & unambiguous instructions
- Concise & short sentences
- Good English and grammar
- Usually no need to include rationale for point
- Reflect:
  - mandatory requirements (….. must be provided)
  - expectations (….. should be provided)
  - recommendations (….. should be considered)
- May need ‘unless otherwise justified’
- Avoid ‘Please’ and ‘The applicant’

# Examples of the Format of Deficiency Points

- Updated stability data should be provided to support the proposed shelf life
- The limits for specified impurities should be tightened in line with batch and stability data
- A copy of the current Certificate of Suitability should be provided for …….
- Confirmation should be provided that the integrity of the sterilising filters is tested before and after use
- Representative certificates of analysis should be provided for the packaging components
- Further information should be provided on ……

# Potential Serious Risk to Public Health

# Potential Serious Risk to Public Health

- Guideline on exceptional cases where a MS can refuse to recognise a MA (MRP) / draft assessment report (DCP)
- MS needs to provide a detailed explanation for its position
- “A situation where there is a significant probability that a serious hazard resulting from a human medicinal product in the context of its proposed use will affect public health”
  - Serious: could result in death, be life-threatening, require hospitalisation or prolonged stay, persistent or significant disability or incapacity, congenital anomaly/birth defect, permanent or prolonged signs in exposed humans

# Potential Serious Risk to Public Health

- Cannot consider in isolation – risk-benefit assessment
- Quality: the proposed production and quality control methods cannot guarantee that a major deficiency in the quality of the product will not occur
- Safety: lack of evidence that all potential safety issues for the target population have been appropriately and adequately addressed
- Efficacy: data to support the proposed indication(s), target population(s) and proposed dosing regimen do not justify claims for efficacy; adequate proof of bioquivalence is lacking for generic application

# How Much Assessment Should We Do?

- Decision rests with each MS
- Must be able to meet obligations as RMS or Rapp/Co-rapp
- MS decision when acting as CMS:
  - (i) Full assessment of data
  - (ii) No assessment of data
  - (iii) Partial assessment of data
- Resource considerations
- Training opportunity

# Targeted Assessment

# Review of Full Data v Targeted Assessment

## UK Approach

- Review of full data
  - UK primary AR - National/OMRP, DCP (RMS), MRP & DCP (CMS) for new active, Centralised (rapp/co-rapp),
  - New assessors – above and IMRP & DCP (CMS)
- Targeted assessment
  - MRP & DCP (CMS) – including line extensions, new combinations, new indications, first generics
  - Accredited Assessors & Associate Assessors ready for accreditation

# Targeted Assessment

- Risk-based approach
- Maximises use of resources
- Assessment is based on RMS report
- In the spirit of mutual recognition and work-sharing

# Targeted Assessment

- Review RMS report and annotate with major concerns & relevant information / or prepare separate brief report - avoid minor points of clarification
- Also target and review based on properties of active substance, dosage form, manufacturing process or areas critical to product quality if not adequately discussed by RMS
- Full evaluation of SPC, PIL/technical leaflet, labelling & User Testing

# Key Concept of Targeted Assessment

Only refer to the submitted data if product quality can't be substantiated from the RMS report

# Preparation for a Targeted Assessment

- Consider the nature of the product under evaluation
- Identify critical aspects of the manufacture and control of the product (part of risk analysis)
  - Sterile products, modified release, topical products, transdermals, inhalation use
  - New or critical functional excipient
  - Inherently unstable active substance
  - Properties that may impact on product quality / performance
- Areas of Focus

# Areas of Focus (1)

| | |
|---|---|
| 1. Module 1 | - Suitabile legal basis and reference product<br>- Suitable licences for supply chain activities |
| 2. Synthesis of active | - Suitability of proposed starting material(s)<br>- Use of genotoxic substances / structural alerts<br>- Impurity control<br>- Carry-over of fermentation products<br>- Class I solvents |
| 3. MR products | - Dissolution limits / IVIVC / dose dumping<br>- Process validation (for specialised forms)<br>- Suitability of BE studies – multi-particulate/unit dose<br>- Comparability of commercial v clinical batches |
| 4. Sterile products | - Method of sterilisation<br>- Process validation<br>- Container/closure |

# Areas of Focus (2)

| | |
|---|---|
| 5. Unstable active | - Stability data for active / product<br>- Stress testing<br>- Analytical method for related substances |
| 6. Topical / transdermal | - BE, clinical study, *in vitro* methods<br>- Local tolerance<br>- *In vitro* release / in-process control<br>- Process validation (as necessary)<br>- Comparability of commercial v clinical batches |
| 7. Inhalation | - Particle size control & methodology<br>- Delivery device<br>- Process validation<br>- Comparability of commercial v clinical batches |
| 8. BE study | - Validation of bioanalytical method<br>- Suitability of test/reference products |

# Areas of Focus (3)

| | |
|---|---|
| 9. Novel ingredients | - As necessary to confirm suitability |
| 10. TSE-risk materials | - Appropriate TSE declarations |
| 11. Specifications | - Active – consider monographs, CEP, guidelines<br>- Product – consider BP/USP, guidelines |
| 12. First generics | - Impurity profile<br>- BE requirements – studies / acceptance criteria |
| 13. New combinations | - Physical/chemical interactions |

# References

# References & Key Documents

- Guideline on the Assessment Report for Mutual Recognition and Decentralised Procedures (Rev 3) – www.hma.eu/
- Templates – www.hma.eu/
- Guideline on the definition of a potential serious risk to public health in the context of Article 29(1) and (2) of Directive 2001/83/EC – Official Journal of the EU (2006/C 133/05)

# Closing Comments

- Consider purpose of the report and needs of the reader
- Stand-alone report with focus
- Critical review of dossier (not simply a summary)
- Raise points that add value
- Raise points on issues that affect the outcome of the evaluation (avoid minor points)
- Give careful thought to how points are written
- Maximise use of resources