Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

# Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products – an update

Christiane Niederlaender, CAT Member
MHRA

# Background

Current

CPMP/BW/3088/99 Nfg on the quality, preclinical and clinical aspects of gene transfer medicinal products (2001)

Scope of Revision (Concept Paper, 2010)

- to reflect the significant development and experience gained
- to consolidate, update and cross-reference available GT guidelines and recommendations
- to encompass the requirements related to the introduction of the new legislation (i.e. 1394/2007, amended 2001/83/EC)
- to cover development genetics, production, purification, characterisation, quality control and comparability in the quality aspects of gene therapy medicinal products
- to provide general considerations as well as specific considerations in quality, non-clinical and clinical aspects of specific classes of gene therapy medicinal products

# Revised guideline

- Cross-competency guideline
- Structured in accordance with eCTD
- Fewer cross-references to other guidelines
- Broad input from regulators and additional experts
- Longer - written with requirements of SMEs and academia in mind
- Aims to be comprehensive and aims to ensure that correct data are included any MAA in the quality, non-clinical and clinical parts.
- Future proofing: field under constant development and guidance should be applicable to any novel product as appropriate

Consultation from 20/05/2015 to 31/08/2015

# Specific points

- applicable to all GTMPs, but most information on viral and nucleic acid vectors
- Sections aimed at different types of vectors are kept separate
- Information on bacterial vectors included but not as extensive
- Modified eukaryotic cells are in the main covered by other guidelines
- Term ‘therapeutic sequence’ used to reflect diversity of approaches
- Quality part with extensive section on development genetics and vector considerations

# Consultation responses


- Responses received from 28 different stakeholders – across industry spectrum
- General comments and specific comments on individual passages of the text
- Comments and questions on scope
- Quality section the longest = most comments
- Specific comments mainly requiring clarification and editorial

# General Comments

- GL aimed at products at the stage of MAA

  Separate guidance is under development:

  “Guideline(s) on requirements for documentation for ATMP investigational medicinal products in clinical trials”

  To be published for consultation 2017

- Clarification about product types covered, status of gene editing technology
- Glossary to be added

- ERA and GMO requirements out of scope
- Further International Harmonisation outside of EU currently out of scope
- Lots of requests to describe / identify suitable methods – no change

# Quality

- General information
  - Vector design
  - Development genetics
- Drug substance
- Drug Product
- DS and DP:
  - Process development and validation
  - Analytical Method, Validation and Reference Standards
  - Stability
  - Adventitious agents

**Comments:**

✓ Definition Drug Substance and Drug Product
✓ Vector / Cell line history
✓ Sequencing requirements
✓ Status of complexing materials
✓ Surrogate assays

# Non-clinical

General overhaul of the sections to give a much clearer focus for the requirements

- General principles: control groups
- Cross reference to the results from quality
- animal species/ model selection
- Proof of concept studies
- Biodistribution
- Vector Shedding

**Comments:**

- ✓ Animal models, use of data from homologous models
- ✓ RBA in non-clinical development; use of NC data / experience from same vector with other transgene
- ✓ Expectation for dose finding experiments
- ✓ Timing of NC testing vis-à-vis clinical trials

# Clinical

Section expanded, focus on:

- Pharmocokinetic studies:
  Shedding studies, dissemination, expression products
- Pharmacodynamic studies
- Clinical safety
- Pharmacovigilance

**Comments:**

✓ Guidance on methods for long-term follow up

✓ Dose finding: dose and dosing schedule justification

✓ Removed some repetitious sections

# Future Timelines:

- Drafting group currently finalising amendments in response to consultation comments
- Presentations to Working Parties and Committees: early 2017
- Aim for adoption of new Guideline: end of Q1 / 2017