Safeguarding public health

MHRA

Roles of EMA and National Authorities

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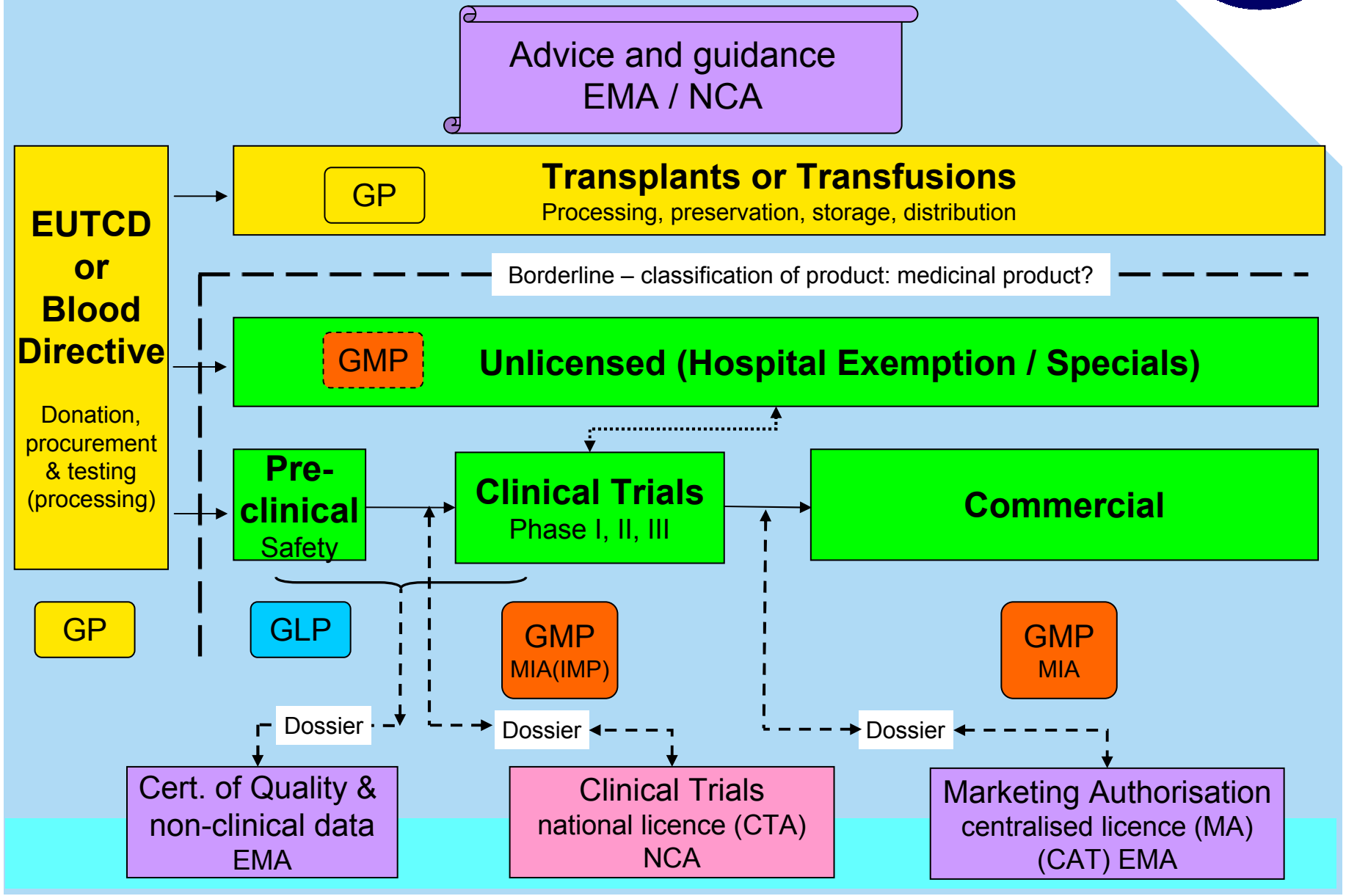
Presentation Outline

- Abbreviation glossary
- ATMPs – the regulatory setting
- EMA:
  - IWG
  - GMP Annex 2 revision
- NCA:
  - Advice and guidance
  - Inspections
  - Clinical Trial Authorisations
- Useful links

Abbreviation Glossary

- ATMP - Advanced Therapy Medicinal Product (GT, SCT, TEP)
- CAT - Committee for Advanced Therapy
- EMA - European Medicines Agency
- EUTCD - EU Tissue and Cells Directive (2004/23/EC)
- GLP - Good Laboratory Practice
- GP - Good Practice (Quality System under Blood & EUTCD)
- GT - Gene Therapy
- IWG - EMA's GMP Inspectors Working Group
- MA - Marketing Authorisation
- NCA - National Competent Authority e.g. MHRA, PEI, Afssaps
- SCT - Somatic Cell Therapy
- TEP - Tissue Engineered Products
- VHP - Voluntary Harmonised Procedure

ATMPs - the regulatory setting



EMA - IWG

- Scope:
  - Maintain / update EU GMP
  - Harmonise inspections practices between NCAs
  - Maintain Mutual Recognition Agreements
  - Maintain the Community database (EudraGMP)
  - Interact with other bodies: FDA, PIC/S, WHO
- Participants: 44 NCA members, Commission
- Observers: EDQM, MRA partners, PIC/S, EU accession countries
- Others e.g. FDA, ICH, WHO
- Links to other EMA bodies: QWP, BWP, CHMP, CAT, industry
- Four 3-day meetings per year

EMA: Annex 2 revision overview

- Revision complete but not yet published
- Key guidance changes:
  - Scope – clarification of start points of GMP
  - Depth of guidance
  - Principle of Quality Risk Management (ICH Q9)
  - Interface with EUTCD / Blood Directive
  - Reference to GMP Annex 1
  - Dedicated facilities
  - Short shelf-life products

NCA – advice and guidance

- Early engagement!
- Areas:
  - Product classification, 44 requests since 2008
  - GMP: manufacturing facilities / Quality Systems
  - Manufacturing licence type(s) required
- Type of advice:
  - Regulatory / classification - free
  - Scientific - chargeable

NCA – Inspections

- All ATMP manufacture requires an appropriate manufacturer's authorisation under medicinal product legislation
- All inspections are conducted by the local NCA
- In UK there are 4 types of authorisation:
  - For clinical trial products - MIA(IMP)
  - For products with a Marketing Authorisation - MIA
    - Currently only 1 ATMP with an MA
    - Inspection triggered by EMA
  - Unlicensed products (i.e. exempt from holding an MA):
    - Hospital Exemption – specific for ATMPs
    - Manufacturer's Specials – available for all pharmaceuticals to supply special clinical need unmet by a licensed product

NCA – Hospital Exemption

- Purpose – to foster early stage product development
- For medicinal products in scope of ATMP regulation
- Prepared on **non routine** basis
- Prepared according to specific **quality** standards equivalent to ATMPs with centralised MA
- Scheme for manufacture **authorised by the NCA**
- Prepared and used in **same** Member State (no 'export')
- Used in a **hospital**
- Used under exclusive **professional responsibility** of a medical practitioner
- To comply with individual prescription for a **custom made product** for an individual patient
- **Traceability, quality pharmacovigilance,** standards equivalent to ATMPs with centralised MA

NCA – Clinical Trial Authorisation

- Required in each MS where a CT is to be conducted prior to trial commencement
- Always a national competence
- All ATMPs are covered by the CT Directive
- Timings for ATMPs and GMOs:
  - 30 days: initial assessment (extra 90 days if consult external committee)
  - 30 days: further information from applicant
  - 30 days assessment of further information

NCA – CTA: VHP

Key features:

- Heads of Medicines Agencies CTFG initiative
- Single application, consolidated set of questions, approvable in a number of Member States
- Sponsor can decide not to submit nationally if a MS raises a specific condition not acceptable to the sponsor
- Currently no fees payable during the VHP phase
- Only core documents required, (e.g. Protocol, IB, IMP Dossier, manufacturer's authorisations, labelling)
- Fixed timelines for Sponsor and Member States
- Addresses many criticisms of Clinical Trials Directive

NCA – CTA: VHP

- Launched March 2009, now at version 2
- 3 phases:
  - Request by sponsor
  - Assessment → letter of approvable CT
  - National CTA application, submit ≤21 days, approval ≤10 days
- Experiences:
  - 65 applications received of which there are 2 ATMPs
  - 1 negative outcome
  - 2 withdrawn
  - 1 not submitted nationally to any MS

Useful links

- EMA – What's new in Inspections:
  - http://www.emea.europa.eu/Inspections/WhatsNew.html
- Commission 'Latest News on Pharmaceuticals':
  - http://ec.europa.eu/health/documents/new_en.htm
- GMP Volume 4:
  - http://ec.europa.eu/health/documents/eudralex/index_en.htm
- MHRA – advice form and how we regulate ATMPs:
  - http://www.mhra.gov.uk/Howweregulate/Advancedtherapymedicinalproducts/index.htm

Questions / Discussion