Recent developments in ATMP Regulation in Europe

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Outline

EUROPEAN MEDICINES AGENCY

26 July 2018
EMA/493240/2018
Human Medicines Research and Development Support Division

Draft Agenda
Workshop on support to quality development in early access approaches (i.e. PRIME, Breakthrough Therapies)
26 November 2018, European Medicines Agency, London

Purpose

The European Medicines Agency (EMA) and the US FDA launched the PRIME and Breakthrough Therapy schemes, respectively, to strengthen their support for the development of medicines that address unmet medical needs with the aim to help patients to benefit from these therapies as early as possible. Experience to date has shown that Applicants face challenges to complete quality and manufacturing development and data requirements during accelerated development. In order to address/overcome these challenges EU and US FDA Regulators wish to support Applicants with guidance and risk-based flexibility regarding their pharmaceutical development programme including, e.g. product characterisation, specification setting, validation and stability testing as well as early identification of quality issues / attributes that are critical to the clinical use of the medicinal product. The aim of this workshop, which constitutes a joint collaboration between EU regulators comprising EMP, QWP, and international partners including US FDA, is to discuss between Regulators and Industry these quality challenges and scientific and regulatory approaches which could be used to facilitate development and preparation of robust quality data packages, to enable timely access to medicines for patients whilst providing assurance that patient safety and product quality are not compromised.

These general discussions will be further elaborated through a number of specific industry case studies (covering chemical molecules, biologicals and ATMPs) and a discussion of experiences to date from early access approaches.

The conclusions from the workshop will be captured in a report, which will be published. The development of further follow-up guidance may be considered.

People interested in participating are invited to register by sending an email to [redacted] by 31 October 2018. As the number of spaces is limited, EMA will allocate places per stakeholder group to allow attendance of a wide range of stakeholders.

- Joint EMA-FDA workshop on quality support to PRIME & Breakthrough
- Clinical trials GTP: interplay with GMO framework
- Q&A: Use of Out-of-Specification ATMP

Joint EMA-FDA workshop on quality support to PRIME & Breakthrough

Challenges

- **Timelines** (e.g. commercial manufacturing sites/description, validation data, stability, control strategy)
- **Innovation & complexity** (e.g. product characterisation, potency, comparability)
- **Global development** (e.g. comparability, manufacturing sites, batch release testing)

→ **Module 3 data requirements** in line with scientific guidelines and technical requirements according to the EU legislation

(**Annex I of Dir. 2001/83/EC**, *Chemical, pharmaceutical and biological information for medicinal products containing chemical and/or biological active substances*)

Regulatory tools outcome

Existing reg/proc tools*

PRIME scheme (support, frequent interactions, early Rapporteur appointment)
Scientific advice (including parallel scientific advice (FDA/HTA))
Managing deferral of data (recommendations, Annex II conditions, etc.)
Change management (PACMPs, life cycle strategy)
Alternative data sources (e.g. Prior knowledge)

PACMP 'with flexibility': level of detail, flexibility and possibility for adaptation/modification of the protocol
Regulatory follow-up on comparability: Tools to report comparability data from batches used to treat patients after licencing (i.e. variations/recommendations)

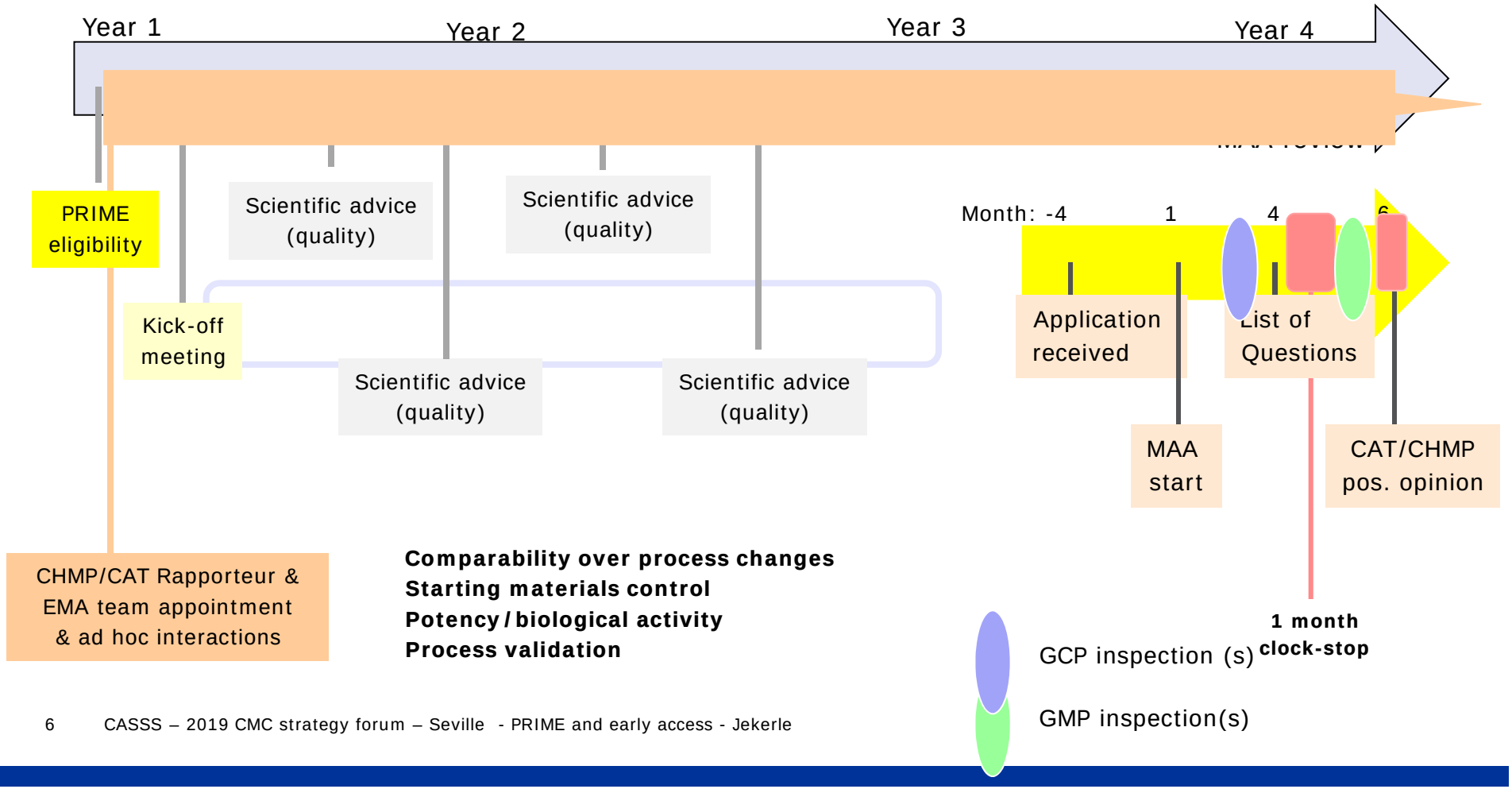
Reg/proc tools* to be explored

Regulators conclusions

- PRIME is a **support scheme** for development with the aim to achieve product quality that is not compromised
- **Global alignment** to answer similar challenges (FDA-EMA joined follow-up actions)
- **Flexibility** can be considered in terms of **when** the quality data comes in (partly post-authorisation) (& managed Annex II conditions, recommendations)
- Alternative data sources (e.g. platform/pilot scale data) can help build the case (see EMA Prior knowledge workshop: Meeting report - Prior knowledge workshop)
- **Risk-based thinking** to relate the available quality data vs. requirements
- Quality to be considered in the context of the **benefit/risk assessment**
- Meeting report drafted
- Presentations & Video Recordings: https://www.ema.europa.eu/en/events/stakeholder-workshop-support-quality-development-early-access-approaches-such-prime-breakthrough
- :

Example (ATMP)

support to PRIME product during pre-authorisation & MAA (on Quality)



Clinical trials with gene therapy medicinal products: interplay with GMO framework

Application of GMO framework

Slide: Courtesy of Rocío Salvador Roldán

Member States have national requirements for GMO in clinical trials

- GMO and Clinical trial applications can be Single, Parallel or Sequential procedures
- GMO legislation following either Deliberate release (DR) or Contained use (CU)

Repository of national requirements published in:

https://ec.europa.eu/health/human-use/advanced-therapies/gmo_investiganional_en

Slide: Courtesy of Rocío Salvador Roldán

European Commission

ATMPs: interplay pharma-GMO

Initiatives agreed with NCAs in 2018:

- **Good Practice on the assessment of genetically modified cell by means of retro/lentiviral vectors***:*
  - Streamlined approach to facilitate conduct of CTs agreed by all MS, except BG, HR, LT, LV, NL, PL, SL, SK and UK.
  - Common application form.
- **Q&A:**
  - Streamlined approach to clinical trials with gene therapy products that have already been granted a MA agreed by all MS, except BG, LT, LV, NL, PL and SK.

https://ec.europa.eu/health/human-use/advanced-therapies_en

Slide: Courtesy of Rocío Salvador Roldán

EMA Questions & answers document
Use of Out-of-Specification ATMP

- What is the pathway for the exceptional administration of out-of-specification (OOS) batches of ATMPs with marketing authorisation?
- Who should be notified and when?
- How should the manufacturer/importer/MAH notify the EMA of the OOS batch(es)?
- Are National Competent Authorities involved?
- Are there any other obligations or expectations ?
- What information should be provided to the patient?

https://www.ema.europa.eu/en/documents/committee-report/cat-monthly-report-application-procedures-guidelines-related-documents-advanced-therapies-march-2019_en.pdf