ALMAC

EU Regulatory Framework and Pathways

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Agenda

Regulatory procedures in Europe

Overview of Centralised Procedure

- Main features
- Timelines
- Procedural options
- Submission requirements

Regulatory procedures in the UK after Brexit

European Union – Regulatory Landscape

- 27 Member States (MS)
  - Three additional EEA countries
    - Norway
    - Iceland
    - Liechenstein
- Individual Regulatory Authorities
  - Each responsible for regulatory activities within their country
- European and national legislative implications

Clinical Trial Conduct in EU/UK

- Submit Clinical Trial Application (CTA) to Regulatory Authority in country in which propose to conduct trial
- Administrative, quality and clinical components
- Investigational Medicinal Product Dossier (IMPD)
  - Contains high level Chemistry, Manufacture and Control information on Drug Substance, Drug Product and Placebo
- No set timeline for assessment but approval process relatively short e.g. MHRA approval for Phase 1 study could be obtained in 14 days

EU Marketing Authorisation Procedures

There are four different routes to obtaining a Marketing Authorisation in the EU/EEA

1) **National Procedure**
2) **Decentralised Procedure (DCP)**
3) **Mutual Recognition Procedure (MRP)**
4) **Centralised Procedure**

EU National Procedures

Regulatory Application:

- One single application submitted to a single member state

Review Timeline:

- Highly variable

Output:

- One single Marketing Authorisation valid in that particular member state

EU Decentralised/Mutual Recognition Procedures

Regulatory Application:

- One single application submitted simultaneously to multiple member states

Review Timeline:

- Fixed

Output:

- Marketing Authorisations valid in multiple member states

Bundesinstitut für Arzneimittel und Medizinprodukte

Agenzia Italiana del Farmaco

Agence nationale de sécurité du médicament et des produits de santé

HPRA

EU Centralised Procedure

Regulatory Application:

- One single application submitted to European Medicines Agency (EMA)

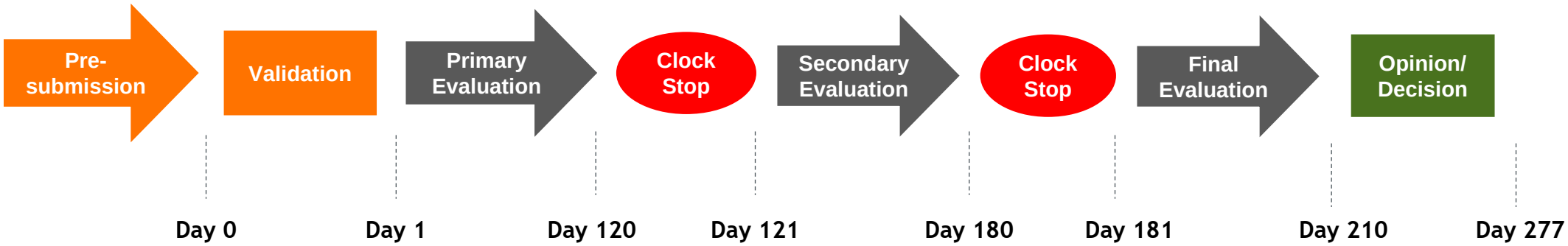
Review Timeline:

- Fixed

Output:

- One single Marketing Authorisation issued by European Commission valid in all EU member states and EEA countries

Centralised Procedure Overview and Highlights



Clock stop one

Applicant response expected in three months

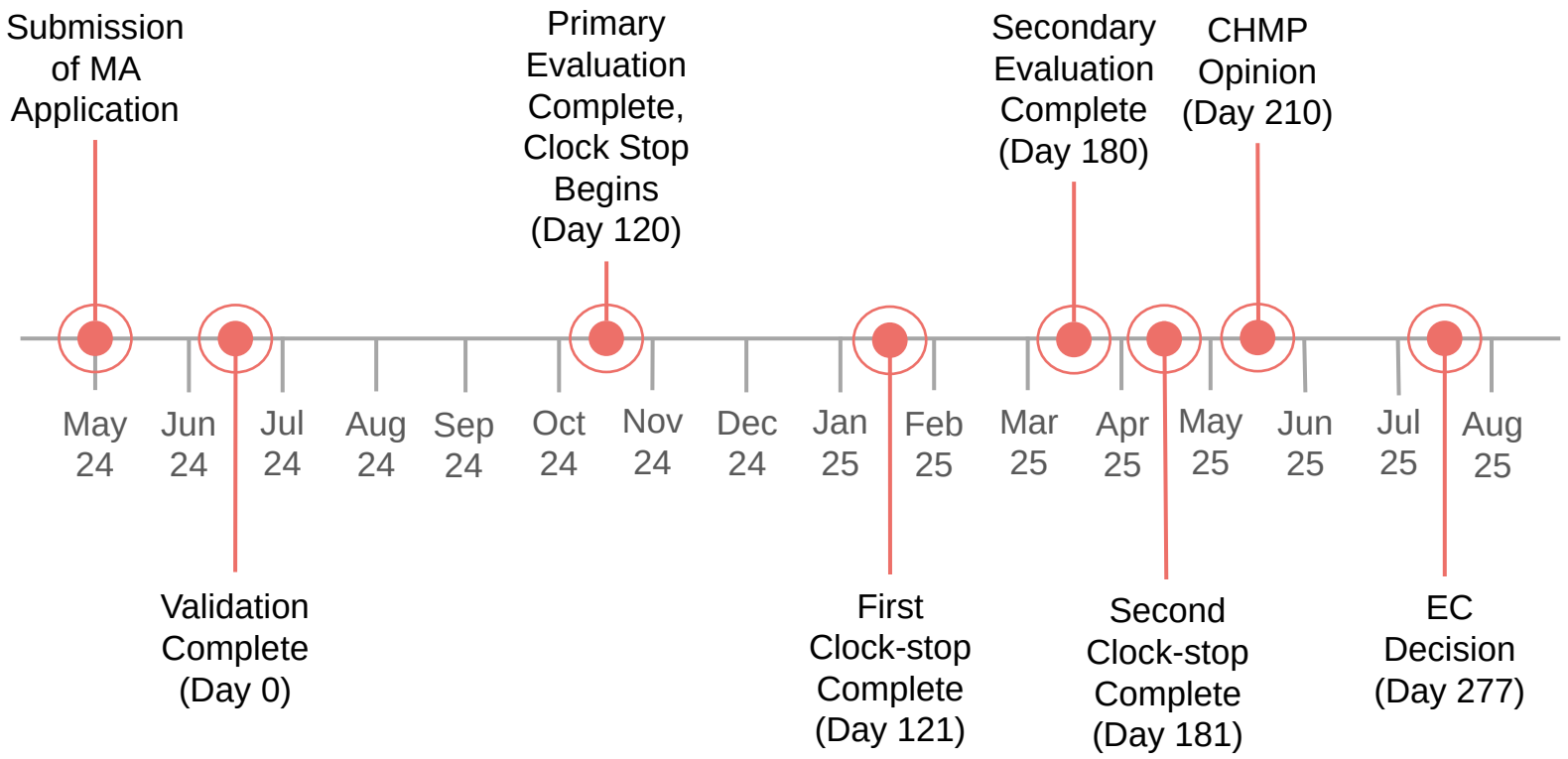
Clock stop two

Applicant response expected in one month

CHMP provides opinion by Day 210

EC issues opinion and grants Marketing Authorisation by Day 277

Centralised Procedure: Practical Timelines



Total timeline is about 15 months on average for standard assessment

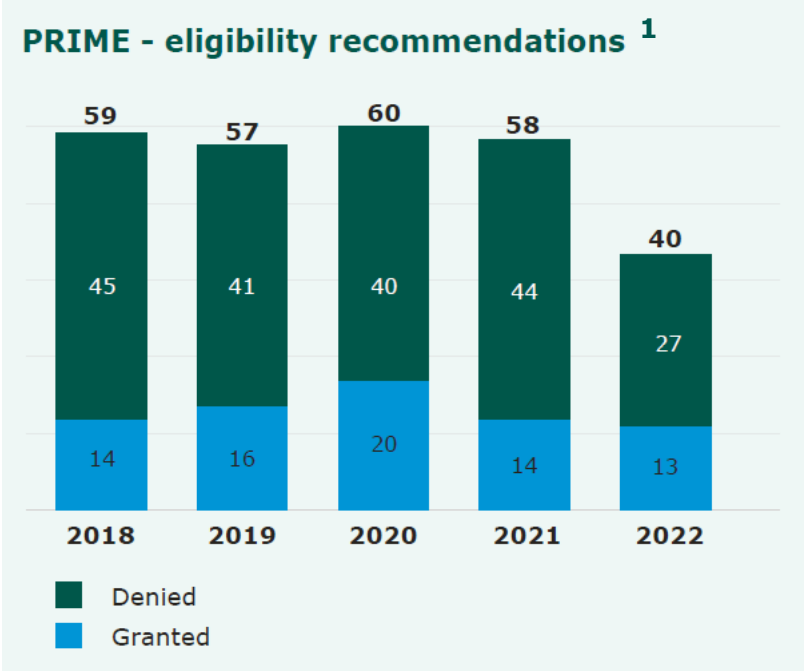
Shortened to 8 months on average for accelerated assessment

Special Assessment Pathways in US, EU and UK

FDA	EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH	MHRA
Fast Track Designation / Breakthrough Therapy Designation	Priority Medicines Scheme	Promising Innovative Medicine Designation
Priority Review	Accelerated Assessment	Accelerated Assessment
Accelerated Approval	Conditional Approval	Conditional Approval
N/A	Exceptional Circumstances Approval	Exceptional Circumstances Approval
Emergency Use Authorization	N/A	Temporary Authorisation under Regulation 174

Priority Medicines (PRIME) Scheme

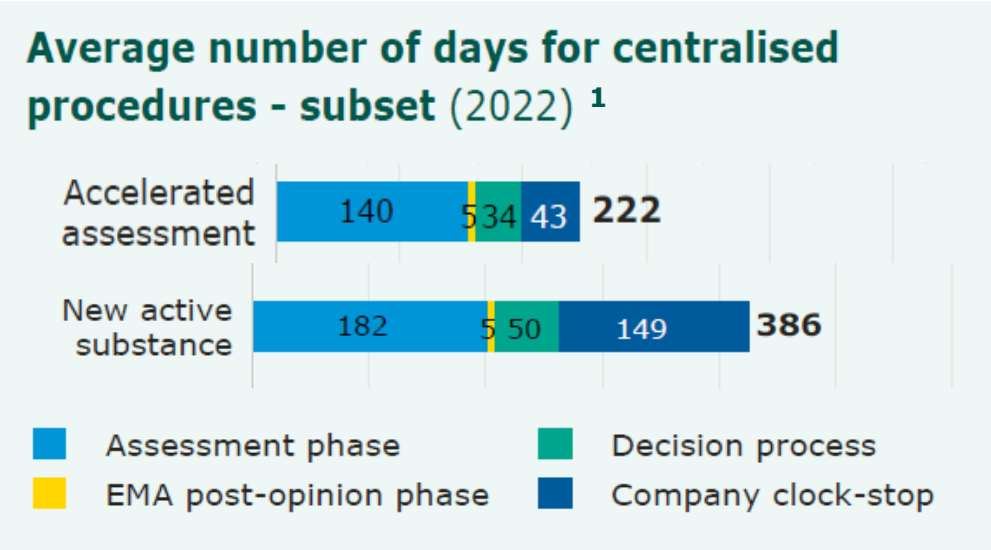
- EU equivalent of ‘Breakthrough Therapy Designation’ in the US
- Supports the development of medicines that target an unmet medical need
- The request is made based on preliminary clinical evidence
- Gives early engagement with the EMA
- Eligibility criteria are those of the accelerated assessment



1. European Medicines Agency Annual Report 2022

Accelerated Assessment

- EU equivalent of ‘Priority Review Designation’ in the US
- CHMP opinion in 150 days instead of 210 days
- Justification based on major public health interest
  - Unmet needs
  - Therapeutic innovation
  - Major impact on medical practice



1. European Medicines Agency Annual Report 2022

Conditional Approval

EU equivalent of ‘Accelerated Approval’ Program in the US

Additional clinical data required but benefit to public health of immediate availability outweighs risk

Valid for one year on a renewable basis

- Required to complete ongoing or new studies
- Completion of studies = conversion to Marketing Authorisation

Exceptional Circumstances Approval

The Marketing Authorisation may be granted subject to specific obligations e.g. additional studies or advice in Product Information

Comprehensive data cannot be provided e.g. extremely rare indications

Reviewed annually to assess the risk-benefit balance

Will not normally lead to the completion of a full dossier and become a ‘normal’ Marketing Authorisation

Orphan Drug Designation

Designation NOT Authorisation

Granted by EMA in certain circumstances:

- Life threatening / chronically debilitating disease
- Prevalence in EU ≤ 5 in 10,000
- No satisfactory treatment already approved or the new treatment will be of significant benefit

Designation provides benefits:

- Procedural and marketing
- Financial

EU Marketing Authorisation Application Submission Strategy

- **Product type may influence EU submission route**
- **Mandatory for Centralised**
  - New active substances for:
    - Oncology, Diabetes; Neurodegenerative, Autoimmune and Viral disorders; AIDS
  - Biotech products
  - Advanced Therapy Medicinal Products
    - Gene Therapy
  - Orphan Medicinal Products

EU Marketing Authorisation Application Submission Strategy

- **Optional for Centralised**
  - New active substances
  - Significant therapeutic, scientific or technical innovation, or in the interest of patients
  - Certain paediatric products
  - Generics or hybrids of Centralised products
- **Conditional/Exceptional/PRIME/Accelerated procedures**
  - Mostly only available via the Centralised route

EU Centralised Procedure Activities 2023[1]

1. European Medicines Agency Human Medicines Highlights 2023

Project Orbis

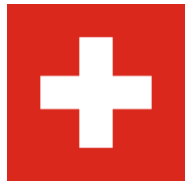
- Project Orbis is a multinational review programme for cancer products. The following countries can be involved:


UK


Brazil


USA


Israel


Switzerland


Canada


Singapore


Australia

- It’s coordinated by the FDA, but each national authority makes it’s own final decision on what is approved.

Marketing Authorisation Applications in the UK

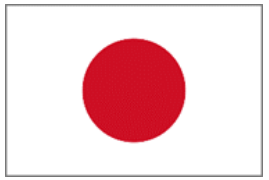
- Great Britain can no longer be part of any EU MA procedures – including the Centralised Procedure
- Currently, Centralised Procedure MAs are still valid in Northern Ireland, but this will change on 01 January 2025
- Going forward, Northern Ireland will generally be aligned with Great Britain for the approval of medicinal products
- ‘UK only’ labelling required on packs

Marketing Authorisation Applications in the UK

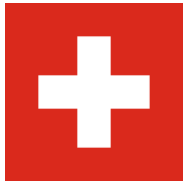
- International Recognition Procedure is the new way to get a UK MA approved, based on approval from another country's regulator:

EU

USA



Japan



Switzerland

Canada

Singapore

Australia

- Depending on the complexity of the application, it has a 60 or 110 day timetable, plus a single clock stop of another 60 days to answer questions

Summary

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Questions