ENVIRONMENTAL RISK ASSESSMENTS: EU CLINICAL TRIALS WITH GMO-BASED ATMPS

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16 DECEMBER 2016

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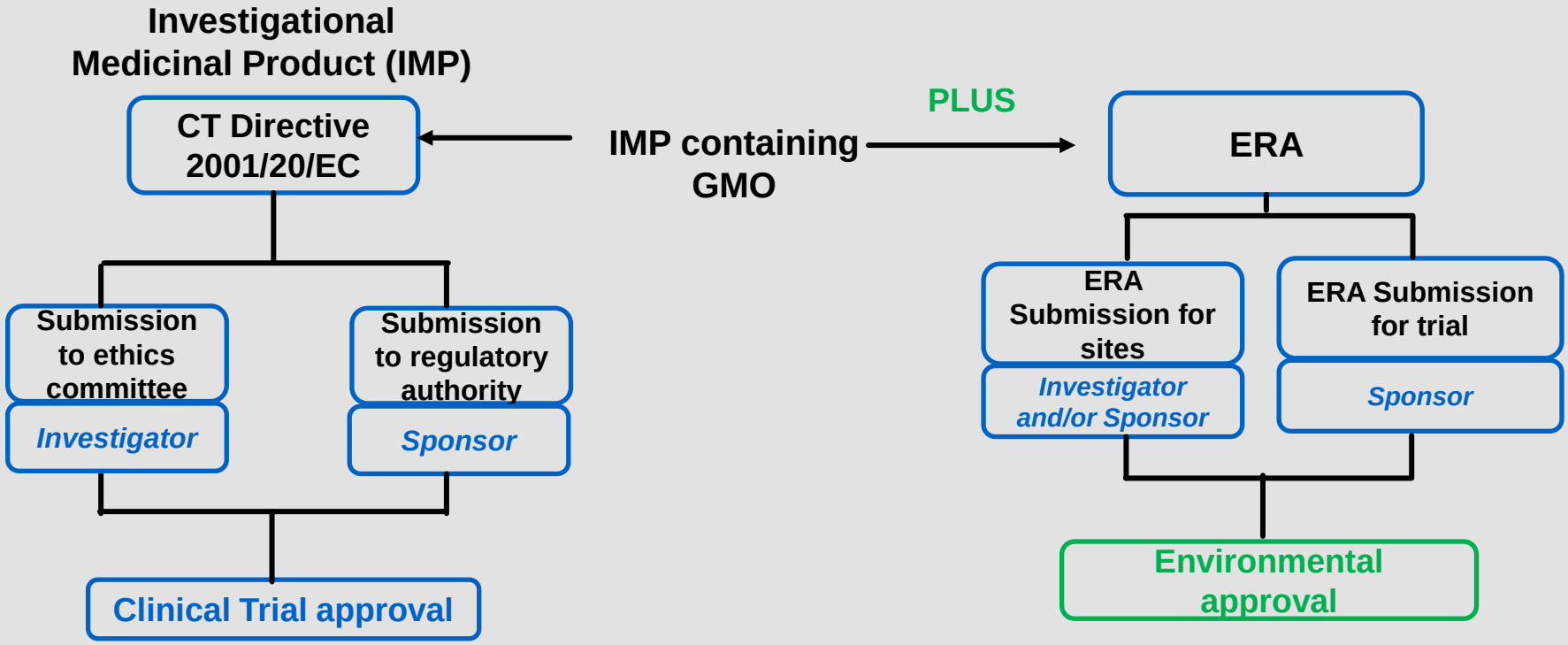
Pioneering science delivers vital medicines™

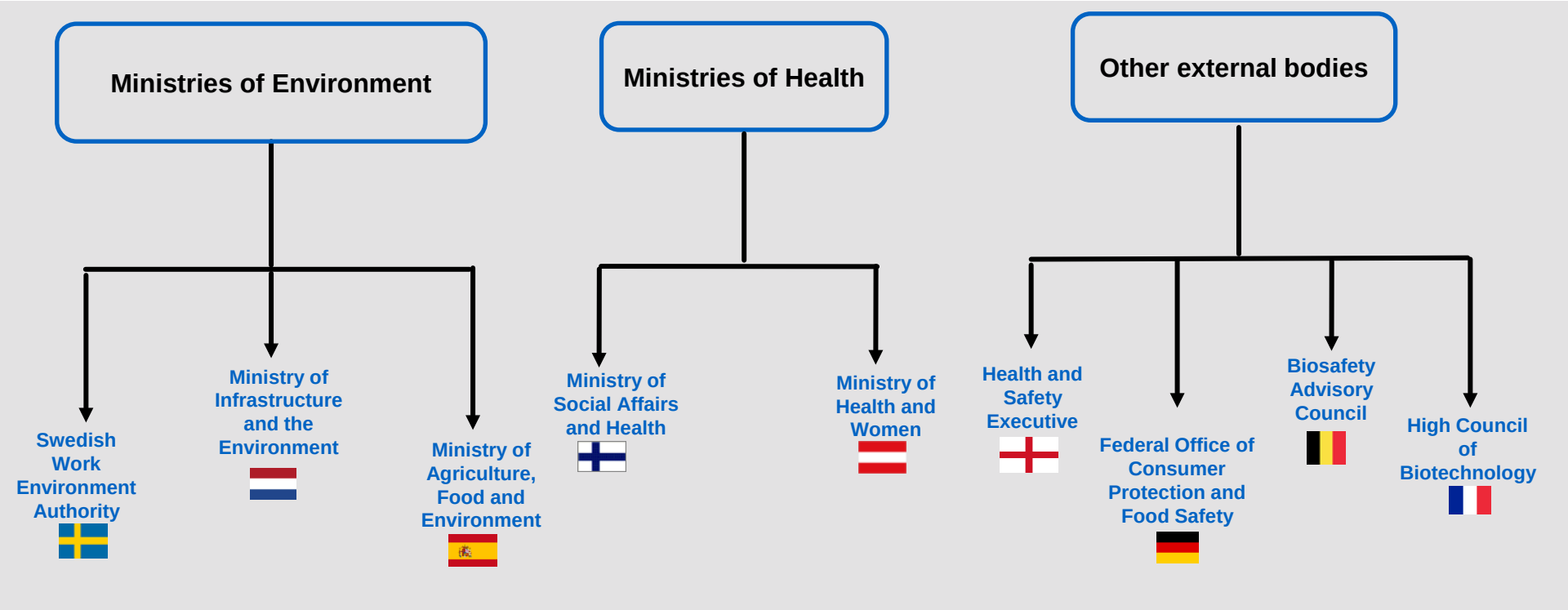
SIMPLIFIED DEFINITIONS

- Genetically Modified Organism (GMO)?
  - An organism, e.g virus, plant, in which genetic material has been altered “unnaturally”
- Environmental risk assessment (ERA)?
  - To identify potential harmful effects of GMOs and assess need for specific protective measures
- Contained Use (CU)
  - GMO considered to be used in an controlled or contained setting
- Deliberate Release (DR)
  - GMO considered to be in wide use with fewer, or no, containment measures

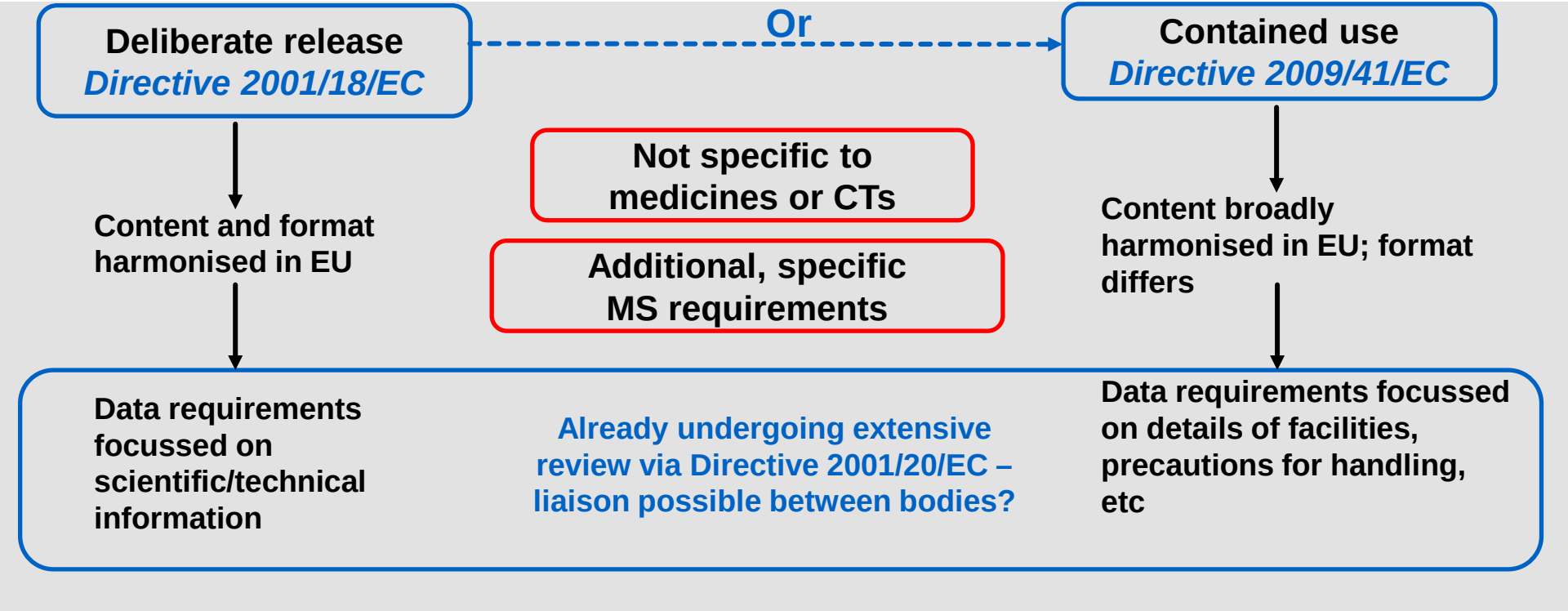
EU GMO LEGISLATION REQUIRES A CASE-BY-CASE EVALUATION OF RISKS TO HUMAN HEALTH AND THE ENVIRONMENT



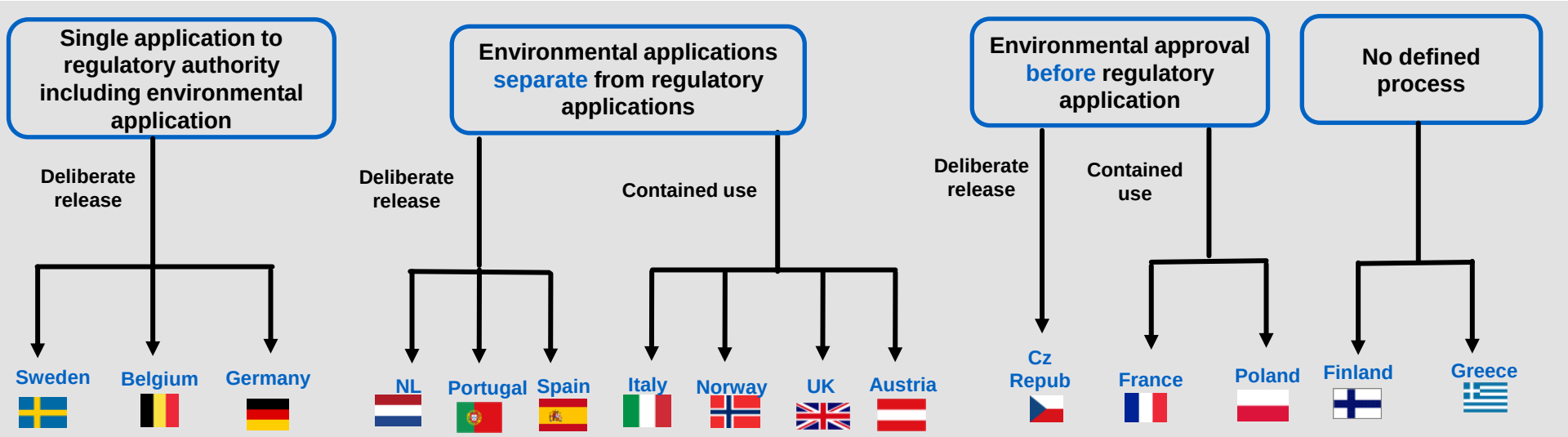
APPROPRIATE ENVIRONMENTAL BODY RESPONSIBLE FOR ERA VARIES ACROSS MEMBER STATES



DATA REQUIREMENTS FOR ERA VARY IN EACH MS: POSSIBILITY FOR REGULATORY/ENVIRONMENTAL BODIES TO COLLABORATE?

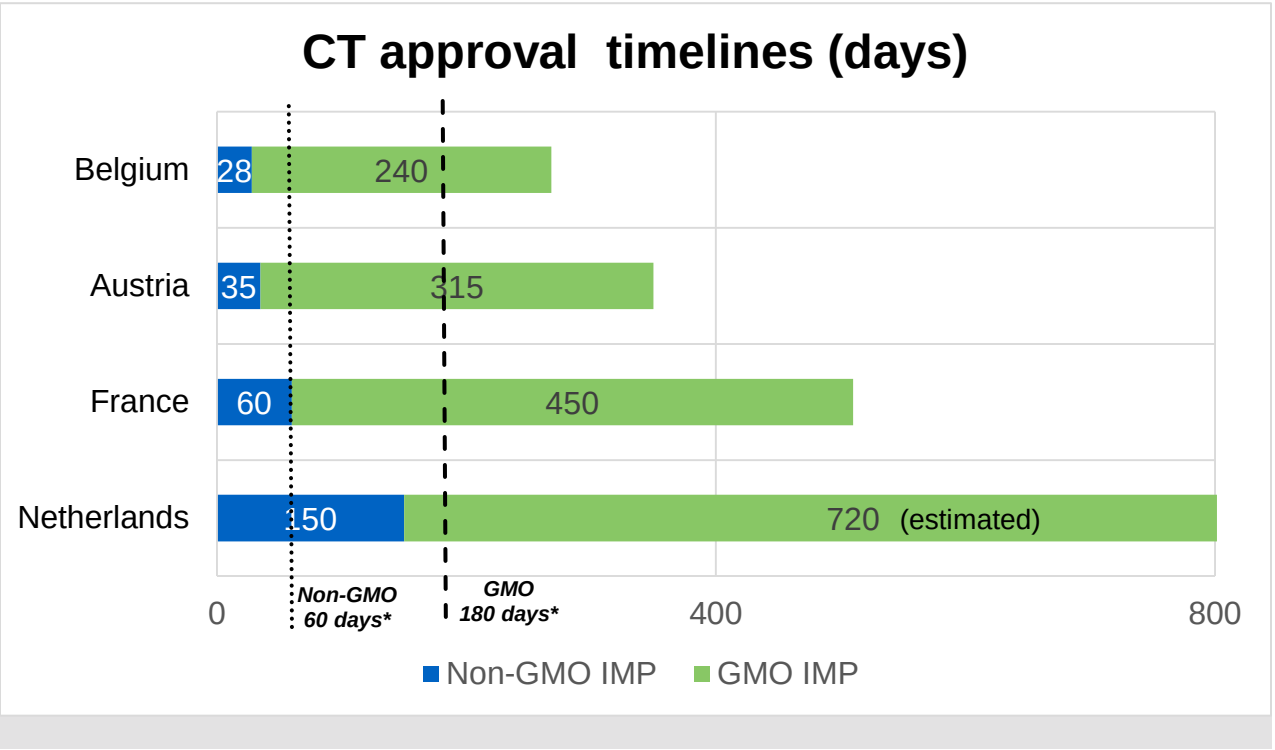


CHALLENGES OF DIVERSE TIMINGS AND PROCEDURES FOR ERA ACROSS MEMBER STATES



Environmental approvals for each site will also be needed
Significant issue for investigators

ERA APPROVALS DELAY INITIATION OF GMO IMP CLINICAL TRIALS BEYOND 2001/20/EC TIMELINES*



Unlike 2001/20/EC, no defined Q&A process for ERA

- **Multiple rounds of questions**
- **Unpredictable timings**
- **Questions - and data required - change from trial to trial**

Needs significant resources – from Sponsor and investigators

FUTURE CT REGULATION WILL NOT ADDRESS ERAS AND IS LIKELY TO RAISE ADDITIONAL ISSUES FOR GMO IMP TRIALS

Clinical Trial Regulation (CTR), due Oct 2018, will harmonise CT applications across EU

- **Single dossier submitted to all MSs**
- **Defined content for scientific, technical and ethical aspects of study**
- **Harmonised electronic submission and assessment process**

ERAs not addressed by CTR!

- **No harmonisation for ERA data, procedures or timings**

Potential new challenge of CTR

- **How could a single CTA be used in each Member State for GMO IMPs?**

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OPTIONS TO RESOLVE ERA CHALLENGES OUTSIDE OF CTR

- Preferred option
  - Co-ordinated ERA with one dossier via one central point - as for Marketing Authorisation Applications
- Minimum option
  - Harmonised data template, procedures and timings across Member States
- Since clinical trials already undergoing regulatory scrutiny
  - Cooperation between environmental and regulatory bodies within a Member State

PROTECTION OF HUMAN HEALTH AND ENVIRONMENT VERSUS PATIENT ACCESS TO INNOVATIVE THERAPIES

- Important to improve patient access to these GMO ATMPs
- Important to ensure environmental risks from innovative technologies are understood and controlled
- Clinical trials also subject to separate assessment by regulatory authorities
- Stakeholders urgently need to recognise issues and engage in resolutions to optimise development of these therapies