GMO/ERA IN CLINICAL TRIALS

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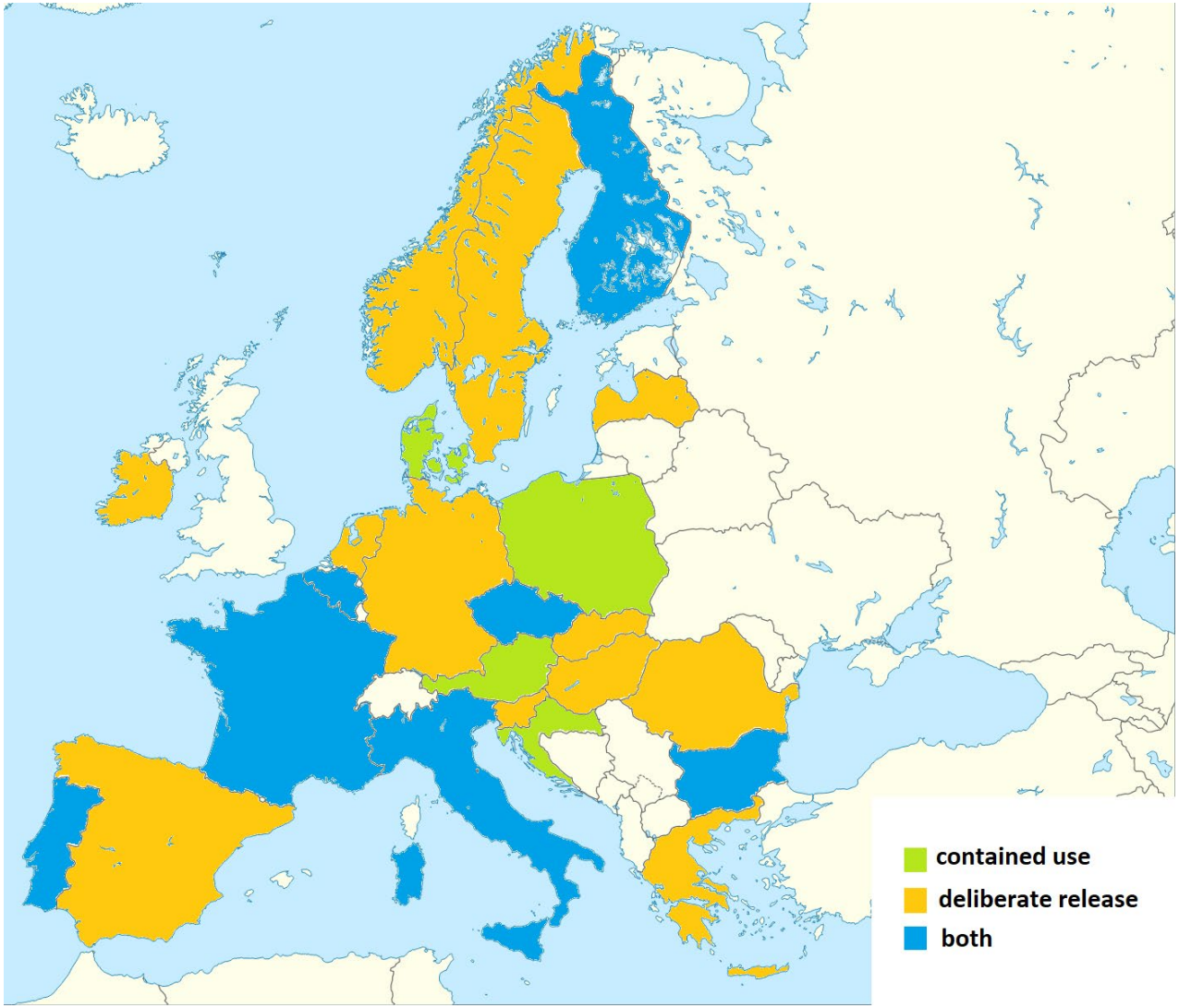
Disclaimer: I attend this conference as an individual expert, and do not represent the CAT. The views expressed here are my personal views, and may not be understood or quoted as being made on behalf of the CAT or reflecting the position of the CAT

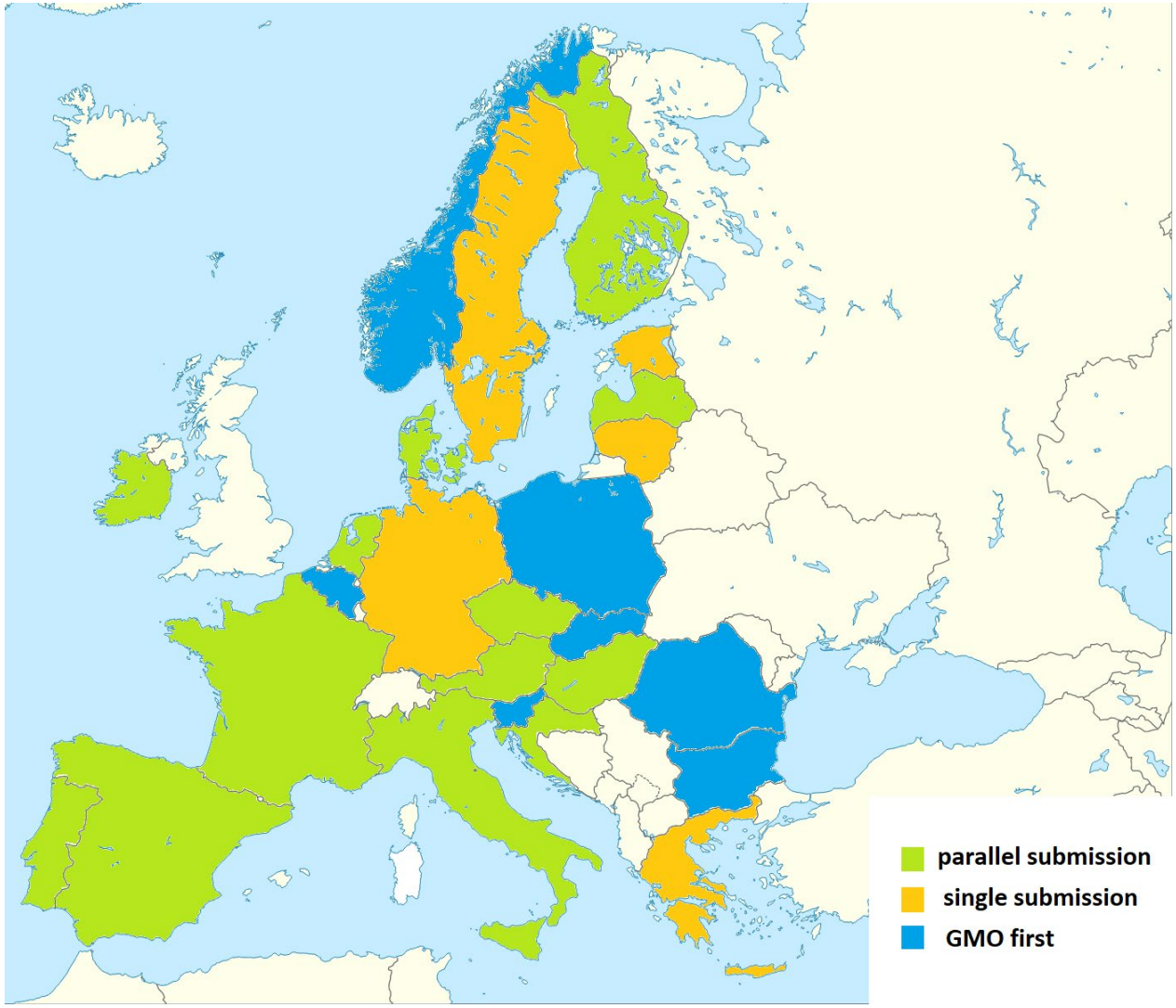
EU legislation

- **Contained use** (Directive 2009/41/EC), limited ERA, focused on containment measures
  - Class 1 – nor or negligible risk
  - Class 2 – Low risk
  - Class 3 – Moderate risk
  - Class 4 – High risk
- **Deliberate release** (Directive 2001/18/EC), ERA dossier focused on GMO technical dossier and environmental impact



EU legislation

- Different authority for Clinical Trial Approval and for DR/CU Application
- Now – GMO authority approval requested before CTA submission or some MS allows single coordinated submission procedure
- After CTR – GMO authority approval not a part of CTA submission, **but** CTR without a prejudice to DR/CU legislation
- No GMO specific functionality is currently foreseen for the EU Portal for submission of CT



Clinical Trials Regulation EC 536/2014

Article 91

Relation with other Union legislation

This Regulation shall be without prejudice to Council Directive 97/43/Euratom ([1]), Council Directive 96/29/Euratom ([2]), Directive 2001/18/EC of the European Parliament and of the Council ([3]), Directive 2004/23/EC of the European Parliament and of the Council ([4]), Directive 2002/98/EC of the European Parliament and of the Council ([5]), Directive 2010/53/EC of the European Parliament and of the Council ([6]), and Directive 2009/41/EC of the European Parliament and of the Council. ([7])

([1]) Council Directive 97/43/Euratom of 30 June 1997 on health protection of individuals against the dangers of ionizing radiation in relation to medical exposure, and repealing Directive 84/466/Euratom (OJ L 180, 9.7.1997, p. 22).
([2]) Council Directive 96/29/Euratom of 13 May 1996 laying down basic safety standards for the protection of the health of workers and the general public against the dangers arising from ionizing radiation (OJ L 159, 29.6.1996, p. 1).
([3]) Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC (OJ L 106, 17.4.2001, p. 1).
([4]) Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (OJ L 102, 7.4.2004, p. 48).
([5]) Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC (OJ L 33, 8.2.2003, p. 30).
([6]) Directive 2010/53/EU of the European Parliament and of the Council of 7 July 2010 on standards of quality and safety of human organs intended for transplantation (OJ L 207, 6.8.2010, p. 14).
([7]) Directive 2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of genetically modified micro-organisms (OJ L 125, 21.5.2009, p. 75).

Situation in EU

- Medicines with GMO falls under CAP (centralised authorisation procedure) evaluation by EMA, **but** ERA also assessed by national GMO authorities
- Definition of GMO can differ in MS (e.g. GM cell is not considered an organism) – need for harmonisation
- ICH considerations – outdated (2006, 2009)
- EMA guideline on ERA for GMO – 2007
- **Approach to GMO not harmonised**
- EC effort for harmonisation, but without changing the legislation („voluntary“ activity of MS)
- Directives 2009/41/EC and 2001/18/EC still applicable

GMO – Pharma Interplay, European Commission

- https://ec.europa.eu/health/human-use/advanced-therapies_en
- Good Practice Document for **AAV** vectors, v2, Dec 2020 + Common Application Form
- Common application form for viral vectors contained in investigational medicinal products for human use, v2, Dec 2020
- Good Practice document for GM human cells, v4, Dec 2020 + Common Application Form
- Oncolytic viruses: Considerations for the evaluation of Shedding, v1, Dec 2020
- A repository of national requirements

Conclusion

- Need for further harmonisation
- Legislation changes needed
- Encourage industry to bring this topic to EC level

Call for More Effective Regulation of Clinical Trials with Advanced Therapy Medicinal Products Consisting of or Containing Genetically Modified Organisms in the European Union

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CTIS

- CTIS trainings: https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support
- Strict timelines in CTIS submissions (e.g. 12 days in case of RFI), recommendation to go for pre-submission national SA

Thank you for your attention

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