Federal Institute for Vaccines and Biomedicines

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National Competent Authorities experience with Environmental Risk Assessment (ERA) before setting clinic trials

Procedure and experience in Germany

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Agenda

- **Legal basis:**
  - GMO legislation
  - Pharmaceutical legislation
- **Procedure in Germany**
  - Simplified procedure (integrated evaluation process and combined approval of the clinical trial and the deliberate release of the GMO)
  - Areas and activities covered by the release authorisation
  - ERA documentation
  - Contained use: timelines at local GMO authorities
- **Experience in Germany**

Legal basis

- **GMO legislation: German Genetic Engineering Act (GenTG)**

  → National implementation of Directive 2009/41/EC (‚contained use' directive) and Directive 2001/18/EC (‚deliberate release' directive) as amended

  → § 2 (3) of the GenTG excludes the use of GMO in human from the scope of this act

Regulation for the use of GMO in human

→ Pharmaceutical legislation

Legal basis

- **Pharmaceutical legislation: § 40 (1) of the Medicinal Products Act**

  → A clinical trial of a GMO-containing medicinal product may only be conducted, if unjustifiable harmful effects on the health of third persons and the environment are not expected.

→ **Environmental Risk Assessment (ERA)**

Procedure in Germany

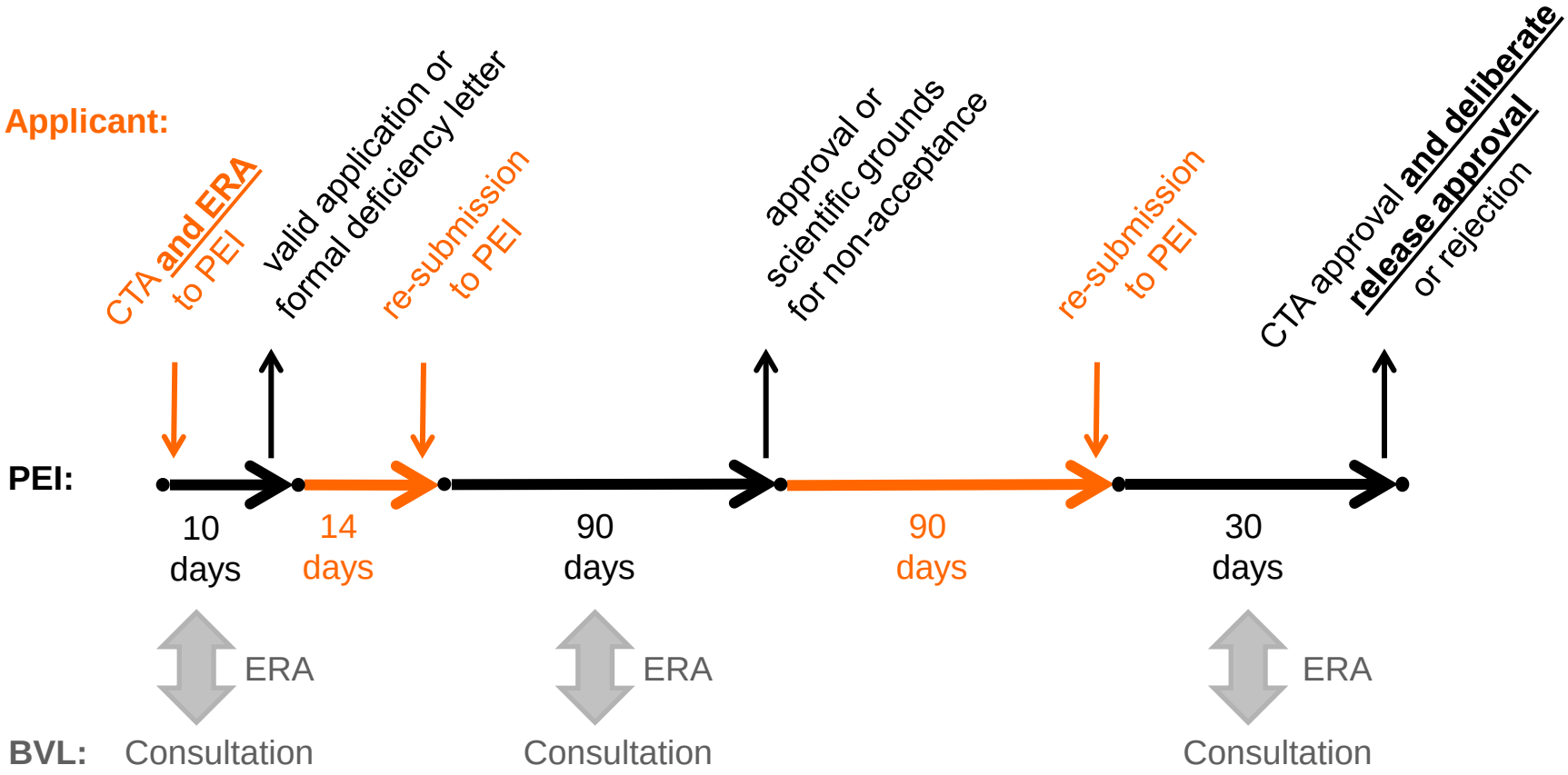
- **Integrated evaluation procedure: § 9 (4) of the Ordinance on Good Clinical Practice:**

  → Authorisation of the clinical trial includes authorisation of the release of the GMO within the framework of the clinical trial.

  → Decision in consultation with the Federal Office for Consumer Protection and Food Safety (BVL, Bundesamt für Verbraucherschutz und Lebens-mittelsicherheit), which is the competent federal authority for the deliberate release of GMO in Germany.

Procedure in Germany

- **CTA procedure and timelines for ATMPs and GMO-based ATMPs:**



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What areas/activities with the GMO-based ATMP can be subsumed under the term „use of GMO in human"?

What is covered by the release authorisation?

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- Administration of the GMO-based ATMP to the study participants
- Shedding of the GMO-based ATMP into the environment
- Storage and in-house transportation of the GMO-based ATMP, contaminated waste and samples from study participants

  → close relationship with the administration of the GMO-based ATMP to the study participants (time, location)
- Reconstitution and preparation of the GMO-based ATMP for administration
- Decontamination and disposal of waste
- Routine diagnostic laboratory testing

What is **not covered** by the release authorisation?

- Manufacturing including manufacturing steps at the study site

  → Genetic Engineering Act; interaction with the local GMO authorities

- Transportation

  → Regulation on Carriage of Dangerous Goods

- Long-term storage of the GMO-based ATMP or contaminated materials at the study site

  → Genetic Engineering Act; interaction with the local GMO authorities

- Further activities with samples from study participants, in particular if they may allow replication of the GMO (e.g. biodistribution and shedding analyses) → usually performed at a central laboratory

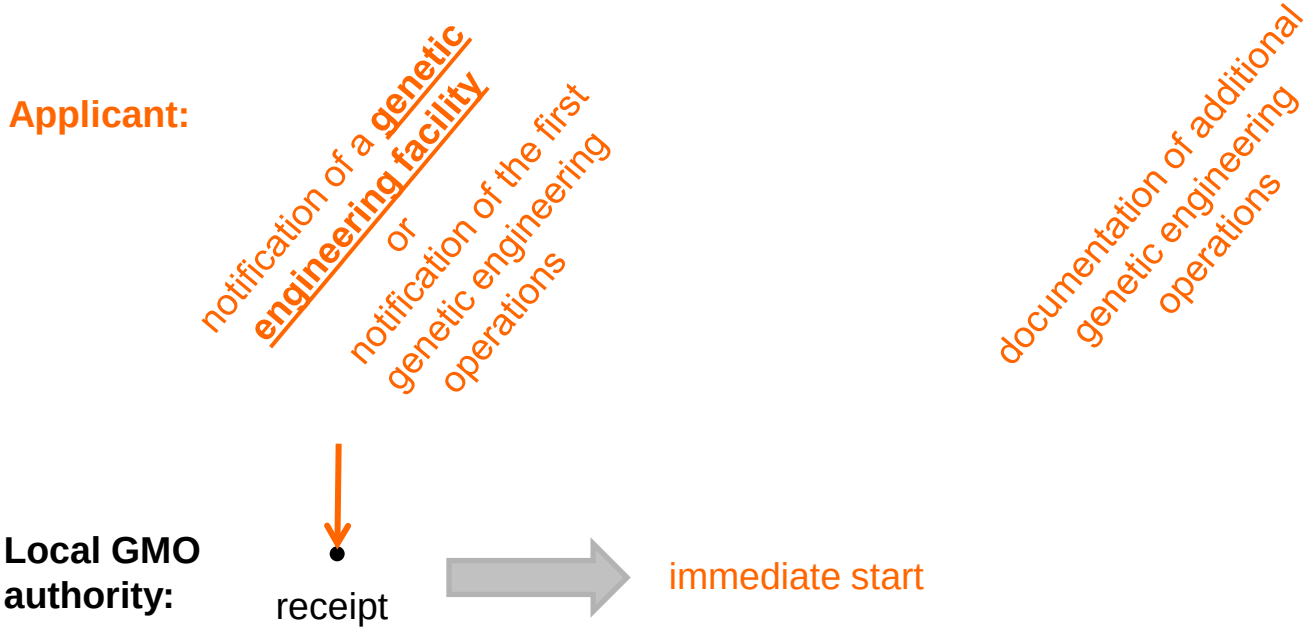
  → Genetic Engineering Act; interaction with the local GMO authority

ERA documentation

- **§7 (4) of the Ordinance on Good Clinical Practice:**
  - ERA in accordance with Annex II of Directive 2001/18/EC (Deliberate Release Directive)
  - Technical dossier supplying the information required by Annex III of Directive 2001/18/EC
- Information on storage, in-house transportation of GMO and waste etc. to have sufficient information on all areas/activities covered by the release authorisation
- Part B SNIF application form to be published on the homepage of the EU commission (http://gmoinfo.jrc.ec.europa.eu/gmo_browse.aspx)

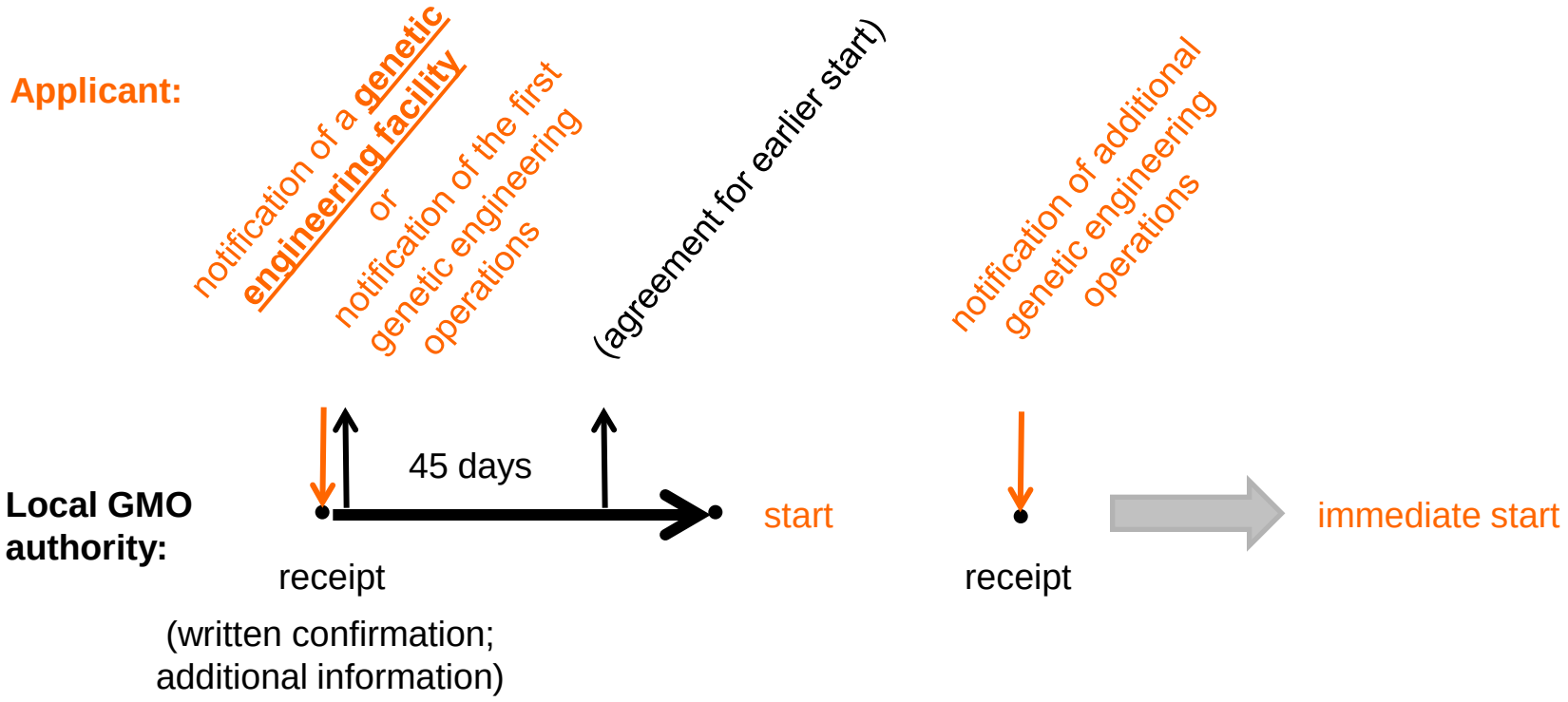
Contained use: timelines of local GMO authorities

- **Safety level 1 (S1)** classified GMO (§ 8, 9 and 10 GenTG): **notification**



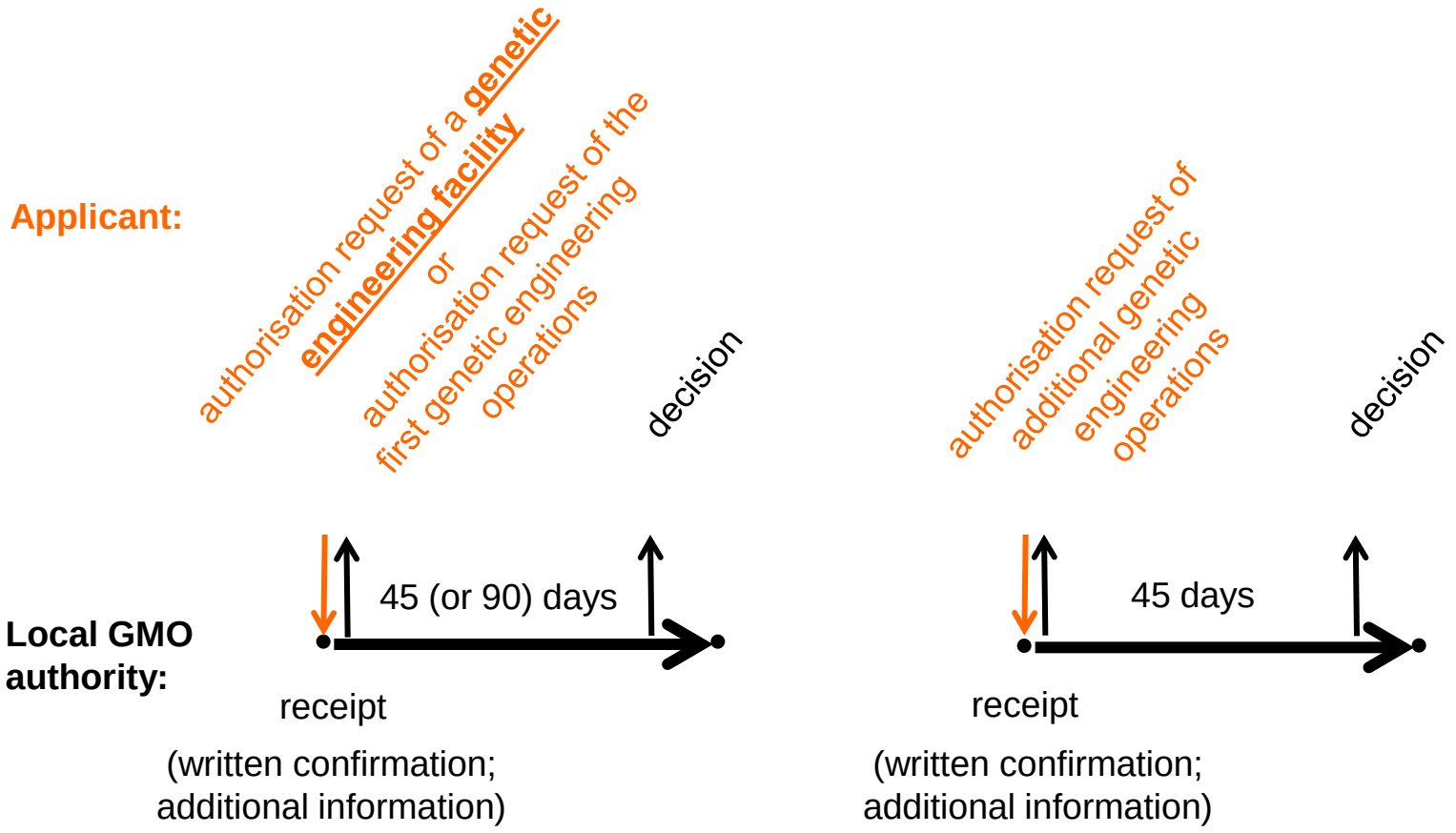
Contained use: timelines of local GMO authorities

- **Safety level 2 (S2)** classified GMO (§ 8, 9 and 10 GenTG): **notification**



Contained use: timelines of local GMO authorities

- **Safety level 2 (S2)** classified GMO (§ 8, 9 and 10 GenTG): **authorisation**



Experience in Germany

Number of CTA (2010-2016)	Classes of GMO
12	Replication deficient viral vectors
14	Replication competent viral vectors / viruses
25	Genetically modified human cells
05	Genetically modified bacteria

Experience in Germany

- **No delays** for approval of clinical trials with GMO-based ATMPs due to ERA evaluation

- **No rejections** of clinical trials with GMO-based ATMPs due to unjustifiable harmful effects on the health of third persons or the environment

- For GMO-based ATMPs **additional risk minimisation measures** (e.g. for protecting vulnerable thirds with close contact to the study participants) may be requested **(approval with conditions)**

Thank you!