Federal Institute for Vaccines and Biomedicines

Paul-Ehrlich-Institut

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Press Briefing
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First clinical trial of a COVID-19 vaccine authorised in Germany

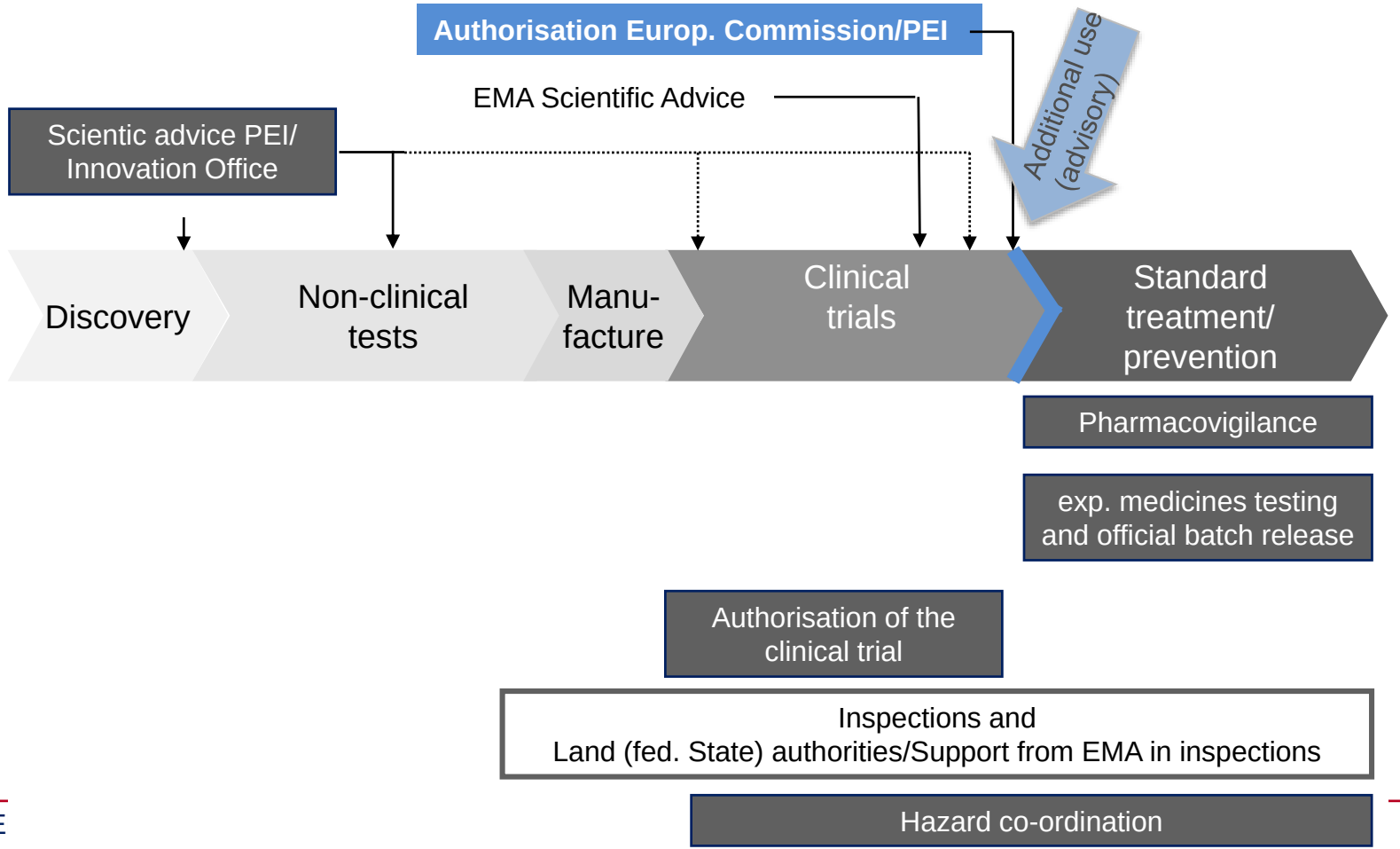
Professor Dr Klaus Cichutek, President

Das Paul-Ehrlich-Institut ist ein Bundesinstitut im Geschäftsbereich des Bundesministerium für Gesundheit

Agenda Press Briefing

- Role of the Paul-Ehrlich-Institut in vaccine regulation (Paul-Ehrlich-Institut)
- Basic principles of the authorisation of the clinical trial (Paul-Ehrlich-Institut)
- Study design (BioNTech)
- Outlook (Paul-Ehrlich-Institut)
- Questions

Paul-Ehrlich-Institut protects patients and supports medicines development

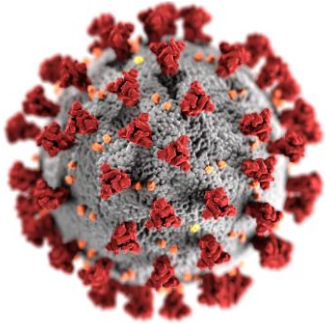


Advice from Paul-Ehrlich-Institut accelerates COVID-19-RNA vaccine development

- National scientific advice
  Early, across the entire path of development, uncomplicated
- Guidance to scientific advice from EMA (European Medicines Agency)
  In the late development phase → preparation for marketing authorisation application
- Research at PEI
  Safety and protection of vaccine platforms
- International harmonisation: EMA, WHO, ICMRA, HMA, …
- Advice to political bodies, public relations, …

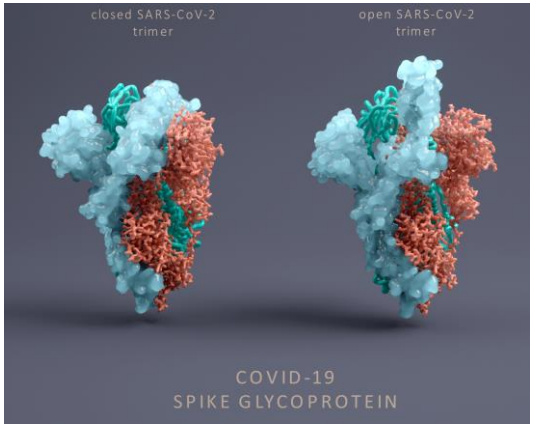
Authorisation of a Phase 1/2 Clinical Trial in Germany
Prerequisites

- Selection of a vaccine platform
  - Different RNA technologies
  - Clinical experience with RNA tumour vaccines for treatment are available
- Identification of the pathogen component that confers immune protection
  - From MERS Coronavirus research: Spike protein of SARS-CoV-2
  - Spike protein or component of spike protein becomes antigen (active ingredient in the vaccine)
- Modification the genetic information (plan) for antigen formation
  - RNA of modified spike proteins (pre-fusion conformation)
  - RNA of domain binding to cell receptor (RBD) of the spike protein



Authorisation of a Phase 1/2 Clinical Trial in Germany
Manufacture (GMP), Quality

- Manufacture of the RNA observing the quality assurance requirements
  - Synthesis by *in vitro* transcription with DNA as template
  - Large-scale manufacture (up-scaling) for Phase 1/2



- Formulation of the vaccine and filling
  RNA + LNP (lipid nanoparticles, water-soluble)

- Batch testing at the manufacturer
  - Identity of RNA (correct sequence)
  - Specification: Share of RNA and share of excipients in the vaccine

Authorisation of a Phase 1/2 Clinical Trial in Germany
Preclinical Tests

- Immunogenicity and dose in the animal (mouse) model
  - Creation of an immune response against the spike protein of CoV-2, i.e. RBD
  - Dosage (amount of RNA per dosage)
  - Vaccination regimen (one or two vaccinations, time interval?)

- Toxicology (rat) at repeated vaccine administration (on-going)
  - Platform data
  - Test for organ damage, local tolerabililty

- Pharmacology and pharmacokinetics (cell culture)
  - Formation of the desired antigen (spike protein i.e. RBD)

Authorisation of a Phase 1/2 Clinical Trial in Germany
Clinical Trial

- Aims: Safety, tolerability, immune response
  - Immunogenicity: Creation of an immune response against the spike protein i.e. RBD
  - Dosage (amount of RNA per dose)
  - Vaccine regimen determined (one or two vaccinations (time interval day 1 and 22))
- Pharmacovigilance (safety of the vaccine)
  - General tolerability (fever, headache, malaise,…)
  - Local tolerability (redness of the skin, haematoma;…)
- Pharmacology and pharmacokinetics, immune response
  - Evidence of antibodies
  - Ratio of neutralising to only binding antibodies
  - Balance of immune response (Th1 vs. Th2)
- Around 200 persons, no control arm

Authorisation of a Phase 1/2 Clinical Trial in Germany
Particular features of the clinical trial: Start of Part A

- Healthy adults 18 to 55 years in Parts A and B
- Risk persons in Part B (persons >55 years, healthy or with pre-existing diseases)
- Interim report before authorisation from PEI in the Part B study
- Around 200 persons in Part A, around 500 persons in Part B

- Cytokine profile in the blood
- Neutralising antibody, binding antibody
- No particular risks in the case of RNA vaccines recognisable
  (ADE and ERD; animal models at WHO level under discussion)

- Additional data on ADE and ERD in animals shall be submitted before Phase 2

On-going clinical trials world-wide
Preventive specific CoV-2 vaccines

Platform	Type of candidate vaccine	Developer	Coronavirus target	Current stage of clinical evaluation	Same platform for non-Coronavirus candidates
Non-Replicating Viral Vector	Adenovirus Type 5 Vector	CanSino Biological Inc./Beijing Institute of Biotechnology, China	COVID-19	Phase 2 ChiCTR2000031781 Phase 1 ChiCTR2000030906	Ebola
DNA	DNA plasmid vaccine Electroporation device	Inovio Pharmaceuticals, U.S.A.	COVID-19	Phase 1 NCT04336410	Lassa, Nipah , HIV Filovirus, HPV Cancer indications Zika, Hepatitis B
RNA	LNP-encapsulated mRNA	Moderna/NIAID, U.S.A.	COVID-19	Phase 1 NCT04283461	multiple candidate vaccines
Non-Replicating Viral Vector	chAdenovirus Type 3 Vector	Oxford Univ., UK	COVID-19	Phase 1	Ebola
RNA	LNP-encapsulated mRNA, saRNA	BioNTech, Germany	COVID-19	Phase 1/2	multiple candidate vaccines