RECENT EVOLUTION OF REGULATORY FRAMEWORK IN EUROPE – OPPORTUNITIES FROM UKRAINIAN PERSPECTIVE

CLINICAL TRIALS OF MEDICINAL PRODUCTS IN UKRAINE CONFERENCE
19 NOVEMBER 2015,
KIEV

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KNOWLEDGE / COMMITMENT / RESULTS

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TOPICS

- Evolution of Member States legislation and EU Directives implementation
- Authorization of clinical trials - knowledge transfer from Member States
- Ethical review and infrastructure of ethical boards - review of Member States approach and correlations with timelines
- Upcoming changes in the EU regulatory framework (Clinical Trial Regulation and Voluntary Harmonization Procedure)
- EudraVigilance concept and implications for non-Member States

EUROPEAN UNION LAWS – GENERAL INFORMATION*

I. Primary legislation – EU treaties - every action taken by the EU is based on treaties which have been approved voluntarily and democratically by all EU member countries.

A treaty is a binding agreement between EU member countries. It sets out:

- EU objectives
- Rules for EU institutions
- How decisions are made and
- The relationship between the EU and its member countries

II. Secondary legislation – the aims set out in the EU treaties are achieved by several types of legal act:

- EU Regulations
- Directives
- Decisions
- Recommendations, Opinions

*** source: www.europa.eu**

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EUROPEAN UNION LAWS – GENERAL INFORMATION*

- **Regulations** - binding legislative acts for the whole EU – directly applicable
- **Directives** - legislative acts that set out a goal that all EU countries must achieve and specific deadline – require implementation to local laws
- **Decisions** - binding on those to whom it is addressed (e.g. an EU country or an individual company) - directly applicable
- **Recommendations, Opinions** – not binding, no legal consequences

* source: www.europa.eu

EUROPEAN UNION DIRECTIVES RELATED TO CLINICAL TRIALS OF MEDICINAL PRODUCTS

- **DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**
  of 4 April 2001on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of **good clinical practice** in the conduct of clinical trials on medicinal products for human use

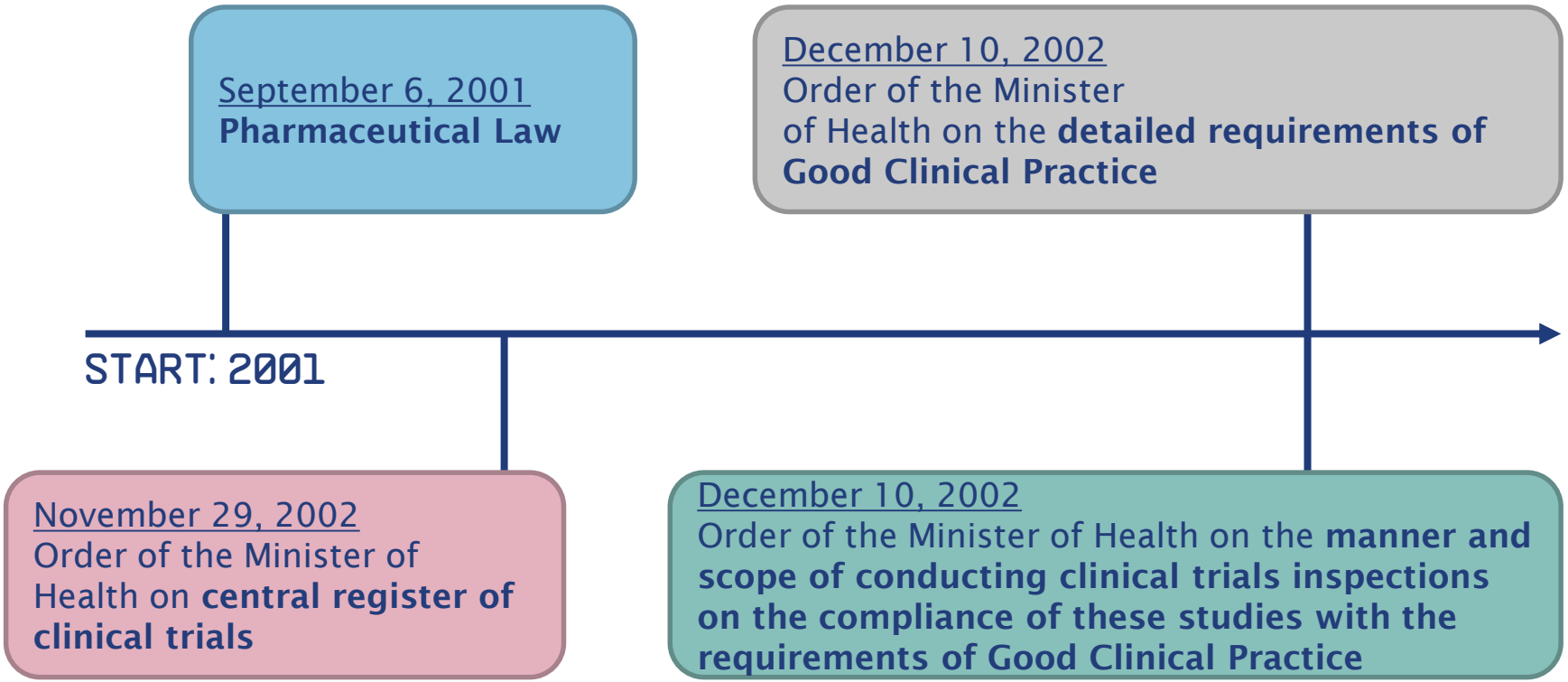
- **COMMISSION DIRECTIVE 2005/28/EC**
  of 8 April 2005 laying down principles and detailed guidelines for **good clinical practice** as regards investigational medicinal products for human use, as well as **the requirements for authorisation of the manufacturing or importation of such products**

The new regulation will apply NOT EARLIER THAN from 28 May 2016:

- **REGULATION (EU) NO 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL** of 16 April 2014 **on clinical trials on medicinal products for human use**, and repealing Directive 2001/20/EC Text with EEA relevance

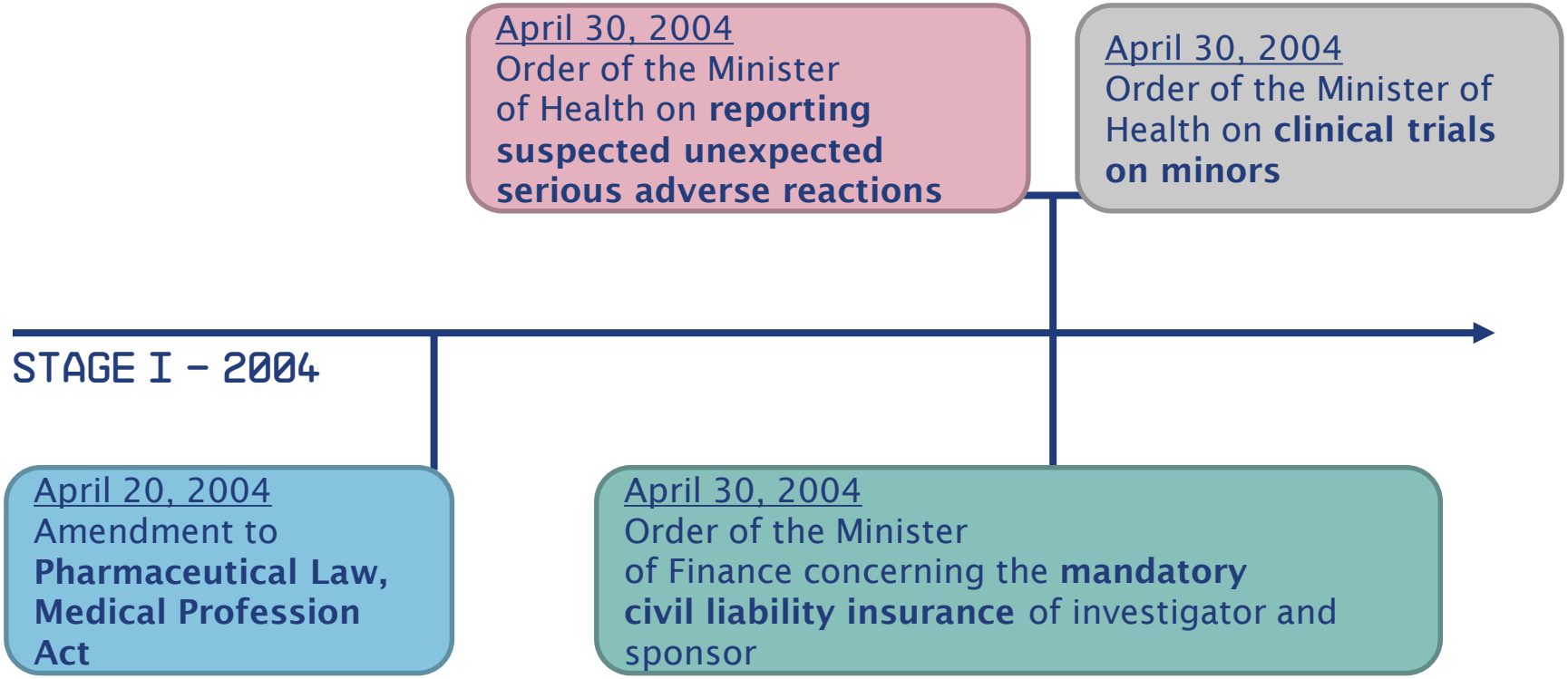
POLAND – ADJUSTMENT OF LOCAL LAWS TO EU STANDARDS

- Basic acts in scope of pharmaceutical law & clinical trials were adopted in year 2001 (before Poland became a member of EU)



DIRECTIVES IMPLEMENTATION IN POLAND

- DIRECTIVE 2001/20/EC



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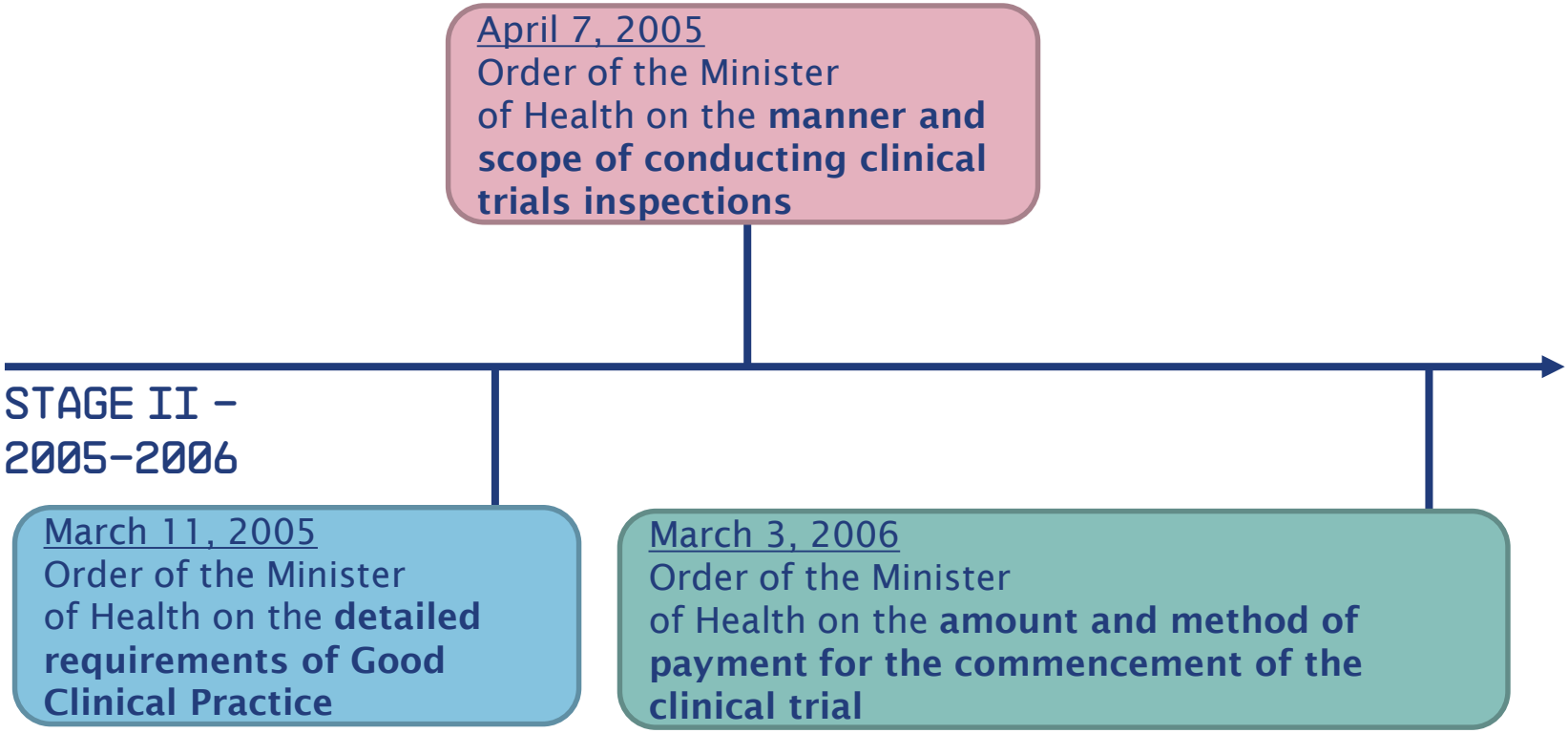
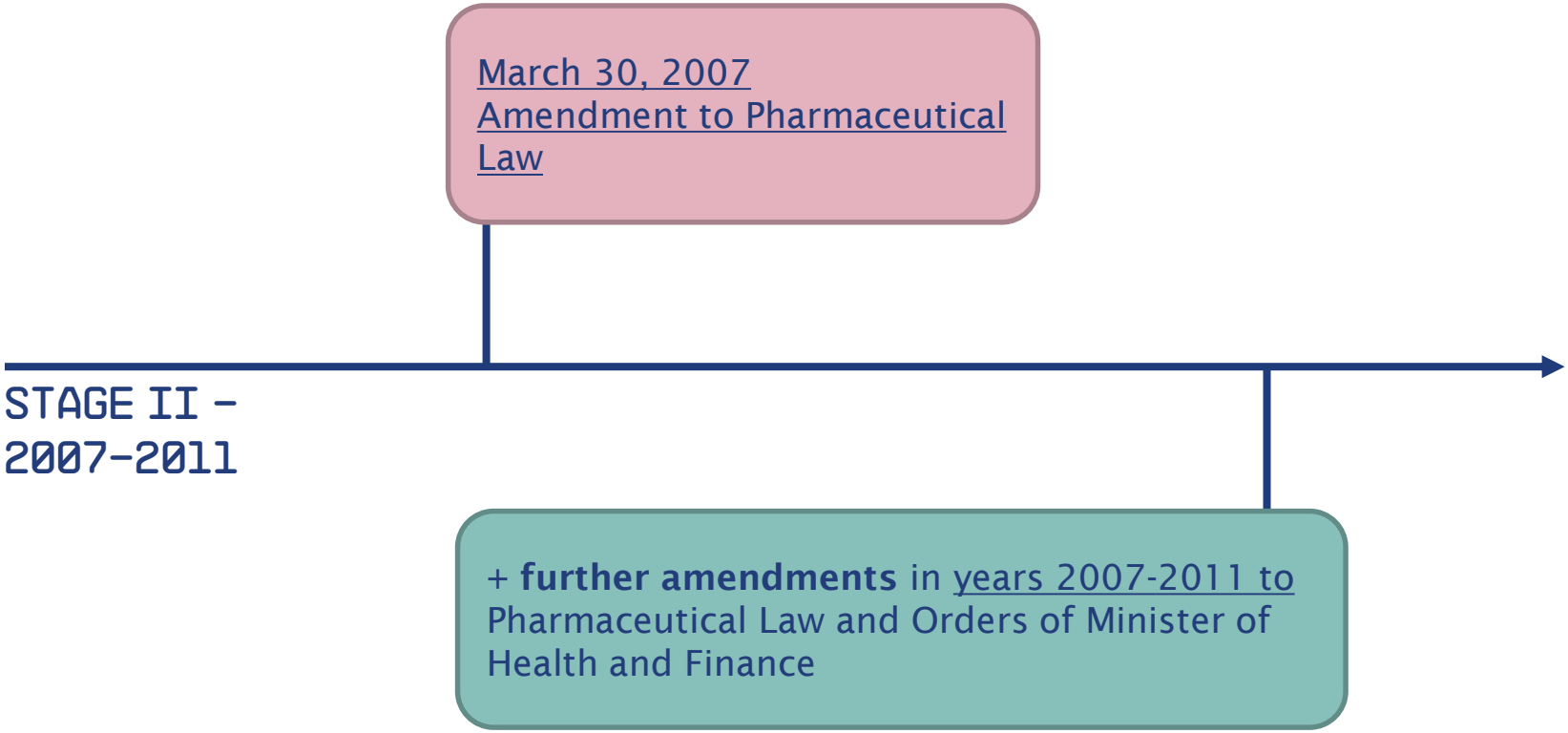


DIRECTIVES IMPLEMENTATION IN POLAND

- DIRECTIVE 2005/28/EC - official EU deadline for implementation was 29 January 2006



DIRECTIVES IMPLEMENTATION

- General problems identified:

DELAYS IN IMPLEMENTATION TO LOCAL LAW

DISCREPANCIES IN LOCAL LAW BETWEEN MEMBERS STATES

In order to avoid it in the future, new EU law regarding clinical trials has a form of **regulation** which is a binding legislative act for the whole EU and is **directly applicable** (no implementation needed).

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CLINICAL TRIAL AUTHORISATION – MEMBER STATES GENERAL VIEW

REGULATORY AUTHORITY	ETHICS COMMITTEE
Submission to REGULATORY AUTHORITY possible **at any time (no fixed dates)**	Submission to CENTRAL ETHICS COMMITTEE for **particular EC session date**
APPROVAL EXPECTED after 60 days if no questions raised	**OPINION** EXPECTED after 60 days if no questions raised

*Process based on EU Directive 2001/20/EC implemented into local law – **assessment by one central Ethics Committee***

SUBMISSION & REVIEW PROCESS IN POLAND- AS EXAMPLE OF PROCESS FACILITATION

BEFORE MARCH 2011:

DELAYS IN APPROVAL OBTAINING

URPL review and assessment → **DRAFT** of DECISION prepared by URPL → Transfer of DECISION to **MOH for execution of the approval**

AFTER MARCH 2011:

DELAYS ELIMINATED

URPL review and assessment of Clinical trial → **FINAL DECISION** signed and executed by **URPL**

- ✓ *After changes in Polish legislation **2-step process of DECISION on CLINICAL TRIAL** (with Involvement of Ministry of Health) has become shortened to **1 step process**.*
- ✓ *Head of Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL) is issuing final decision on Clinical trial. Delays in obtaining of final decision are eliminated.*

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SUBMISSION & REVIEW PROCESS IN POLAND- AS EXAMPLE OF PROCESS FACILITATION

- In case NO QUESTIONS have been raised by Regulatory Authority

  and

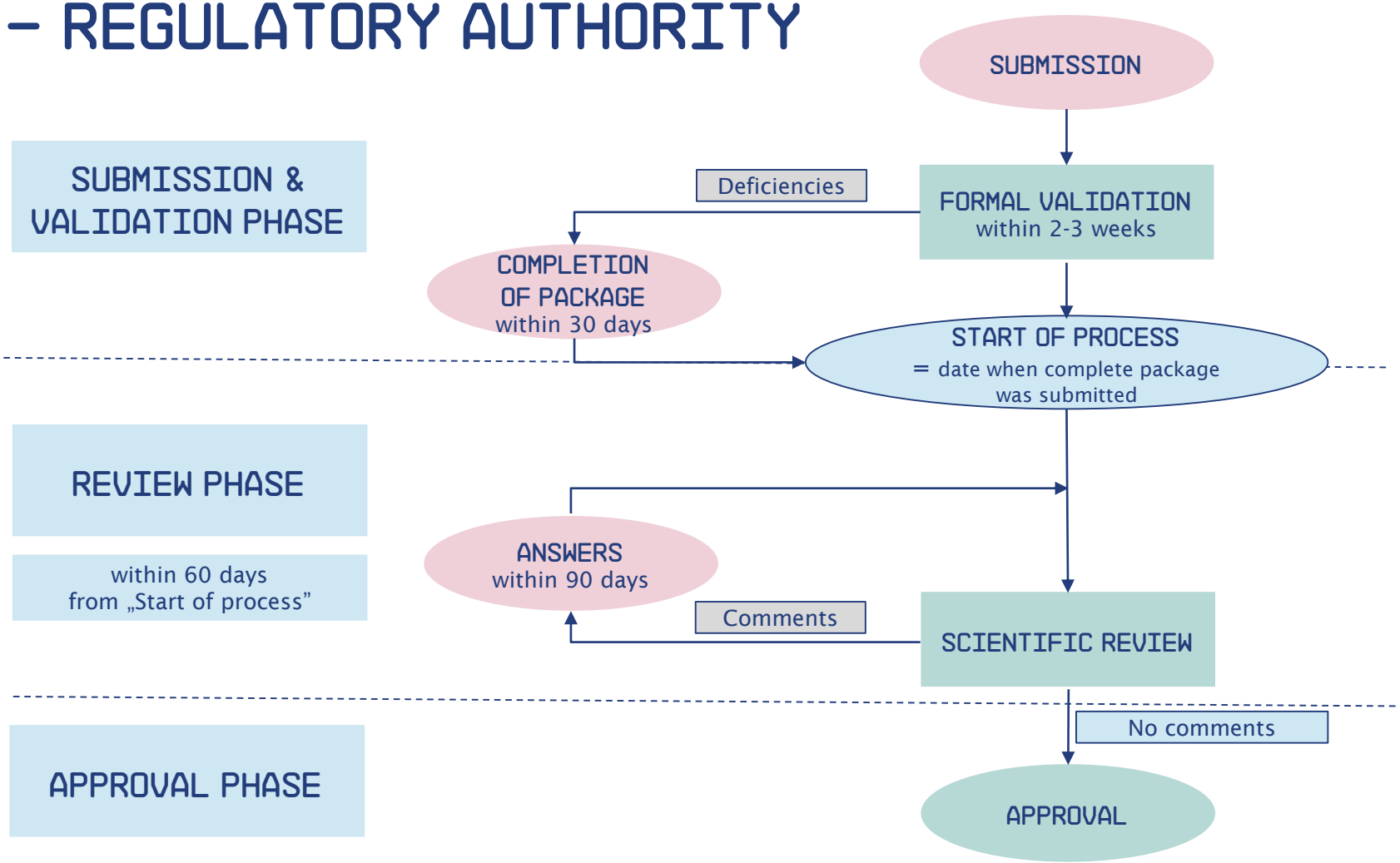
- 60 DAYS of assessment HAVE ELAPSED and no written decision has not been issued by RA

  and

- EC opinion is FAVOURABLE

CLINICAL TRIAL CAN BE COMMENCED

SUBMISSION & REVIEW PROCESS IN POLAND – REGULATORY AUTHORITY



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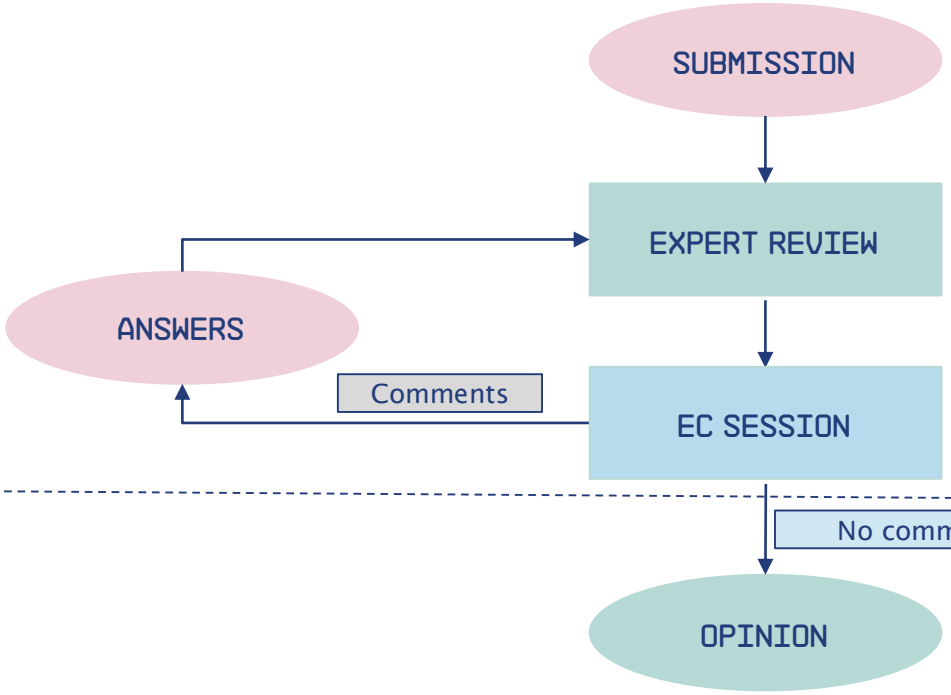
SUBMISSION & REVIEW PROCESS IN POLAND – ETHICS COMMITTEE

SUBMISSION & REVIEW PHASE

60 days per law
approx. 30 days in practice



APPROVAL PHASE

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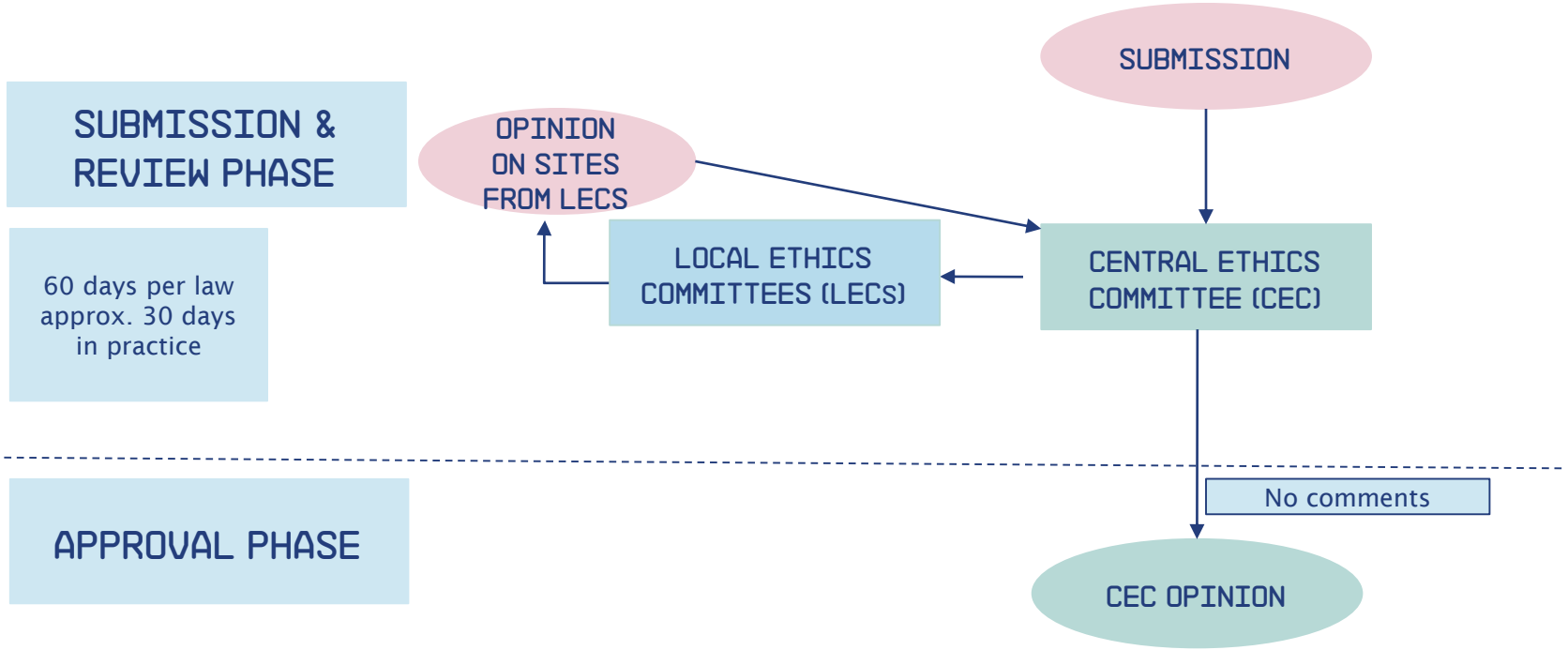
SUBMISSION & REVIEW PROCESS IN POLAND – ETHICS COMMITTEE



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DOCUMENTATION REQUIREMENTS SPECIFICS

IMPD	Required only for Investigational Medicinal Products which are not authorised in EEA and US. For Authorised products Summary of Product Characteristics is sufficient
Certificates of analysis	Required: • In exceptional cases, when unexpected impurities are detected • Only for representative batches of the Investigational Medicinal Products
Manufacturing Authorisation and GMP certificate	Required for the Manufacturer which is responsible for batch release on the EU territory (not all manufacturers involved in manufacturing process)

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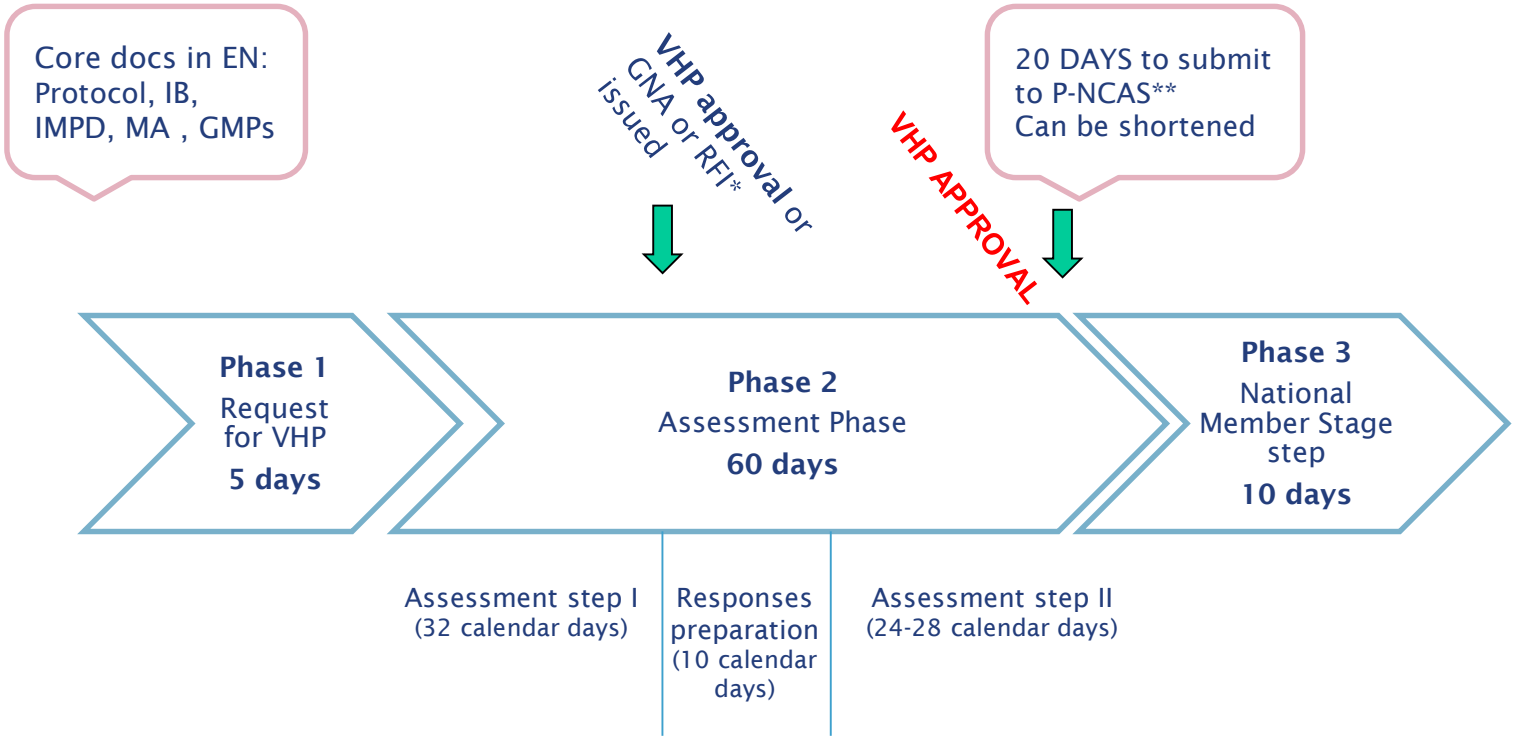
VHP SUBMISSION PROCESS- VOLUNTARY EU CENTRALISED ASSESSMENT



*GNA – Grounds for Non-acceptance
RFI – Request for Information
**P-NCAS – participating national Competent Authorities

EUDRAVIGILANCE SYSTEM

- Electronic exchange of suspected adverse drug reaction reports

EUDRAVIGILANCE SYSTEM

EARLY DETECTION	· Strict reporting timelines · Acceleration of the communication for safety reporting · Standarisation of secure data transmission
SAFETY ASSESSMENT	· Continual monitoring of the benefits and risks of medicines · Risk management facilitation · Safety monitoring across the EU
TRANSPARENCY	· Clear legal obligations · Public access to reports of suspected side effects · Extended Medicinal Product Dictionary (XEVMPD)

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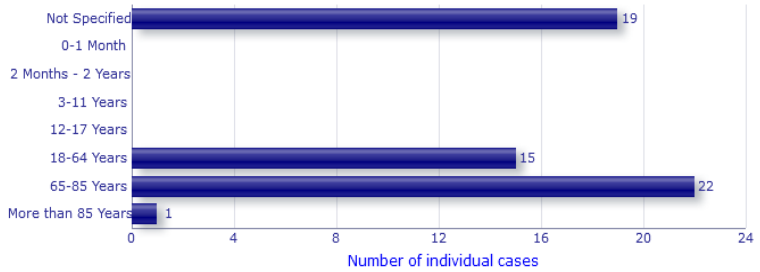
EU DATABASE FOR SUSAR REPORTS

Number of Individual Cases | Number of Individual Cases By Reaction Groups | Number of Individual Cases for a selected Reaction Group | Number of Individual Cases for a selected Reaction

The number of individual cases identified in EudraVigilance for **X** [redacted] is **57** (up to Oct 2015)

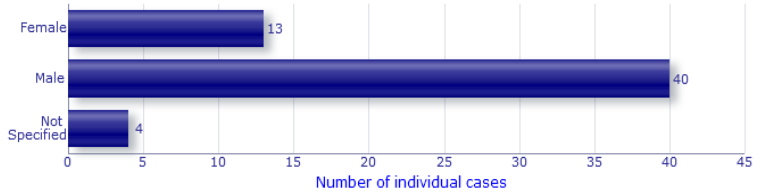
Number of individual cases by Age Group

Age Group	Cases	%
Not Specified	19	33.3%
0-1 Month	0	
2 Months - 2 Years	0	
3-11 Years	0	
12-17 Years	0	
18-64 Years	15	26.3%
65-85 Years	22	38.6%
More than 85 Years	1	1.8%
Total	**57**	**100.0%**



Number of individual cases by Sex

Sex	Cases	%
Female	13	22.8%
Male	40	70.2%
Not Specified	4	7.0%
Total	**57**	**100.0%**



* source: www.adrreports.eu/en/index.html

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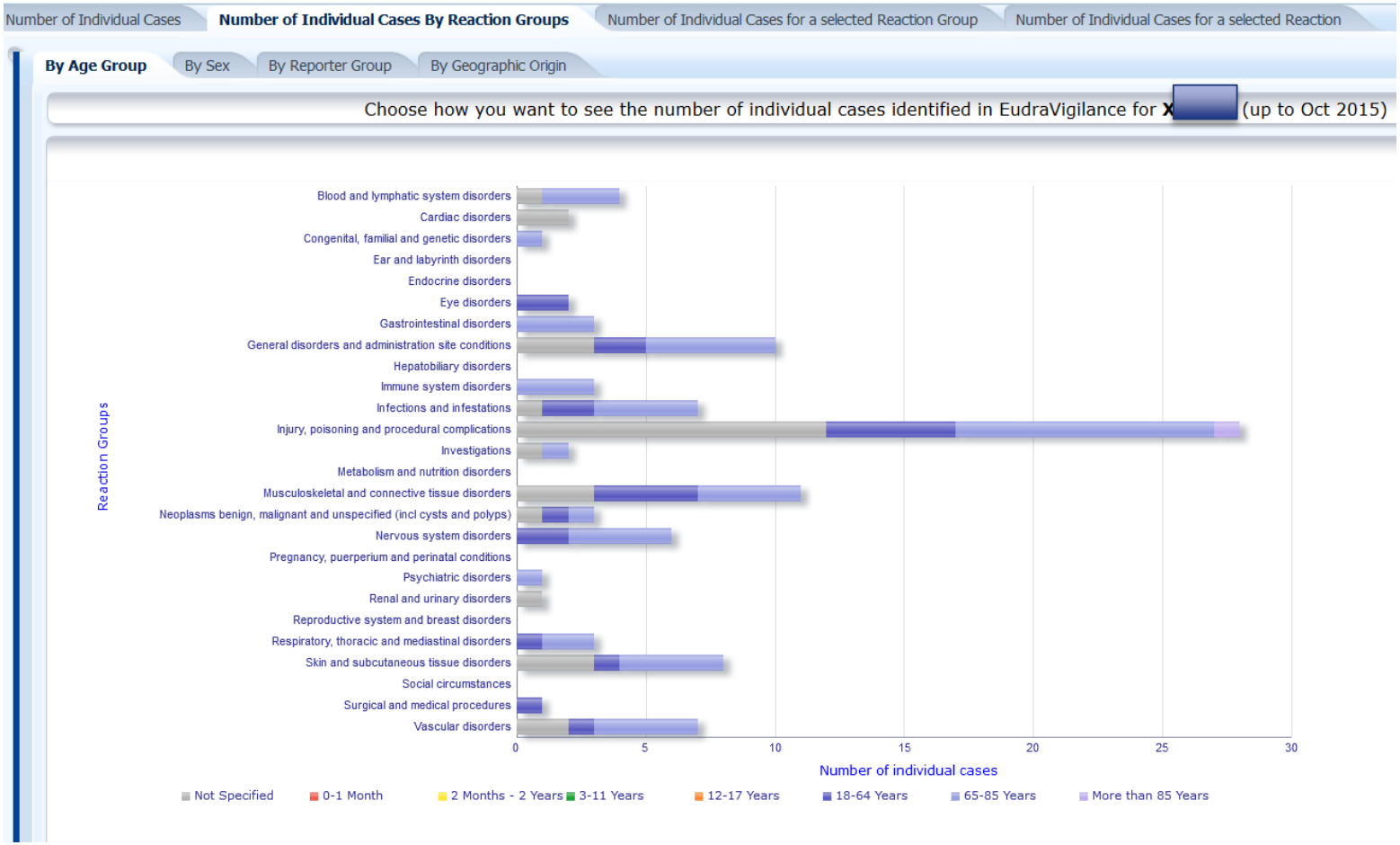

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ENHANCEMENT OF THE EUDRAVIGILANCE SYSTEM (2017)

- simplified reporting, better quality data and improved searching, analysis and tracking functionalities
- change from a national to a centralised system for reporting ICSRs in the EU
- the reporting of non-serious cases of suspected adverse drug reactions to EudraVigilance
- enhanced collaboration between EMA and the World Health Organization (WHO)

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THANK YOU

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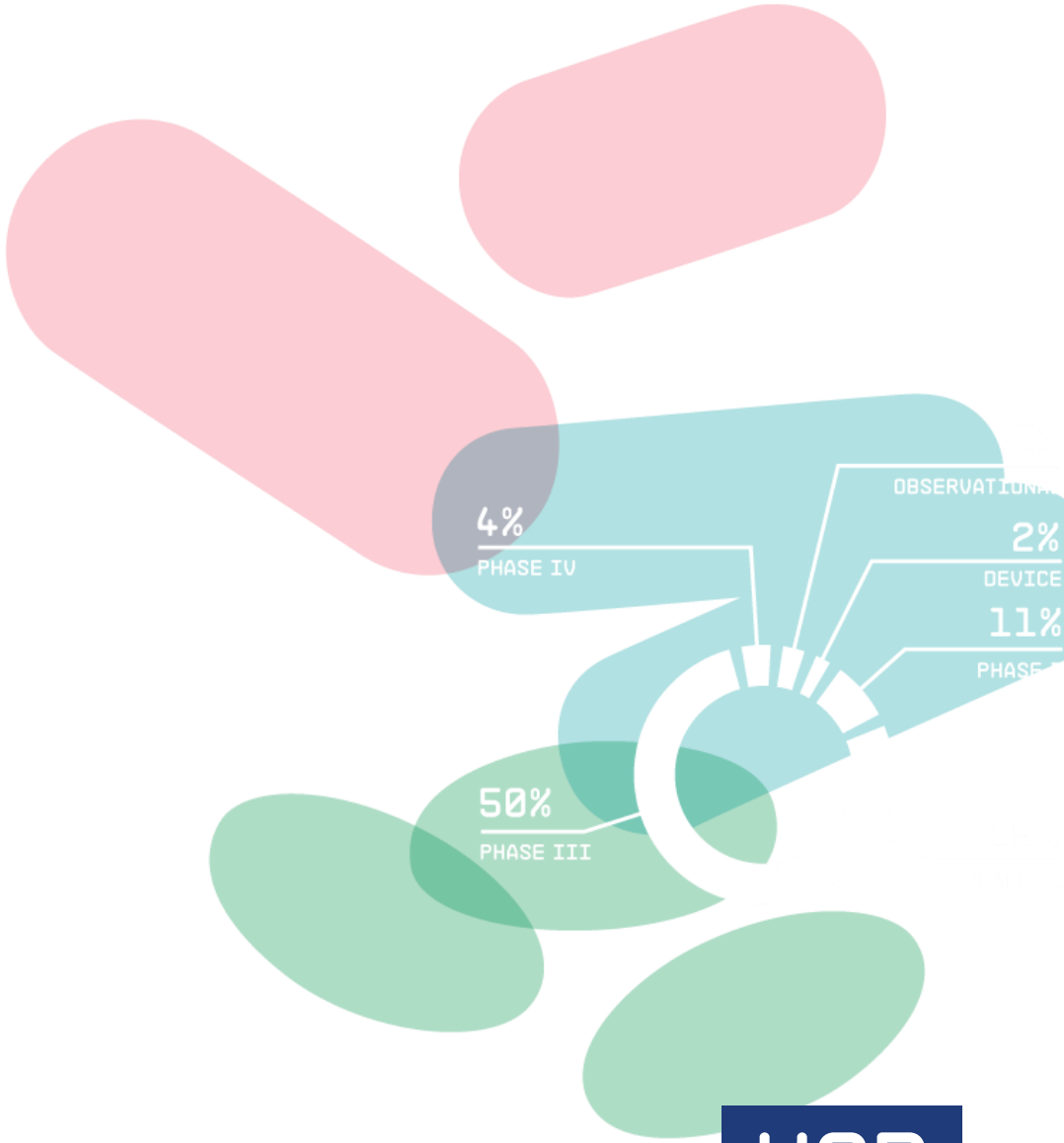

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