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Gender equality in women's health

the forgotten priority

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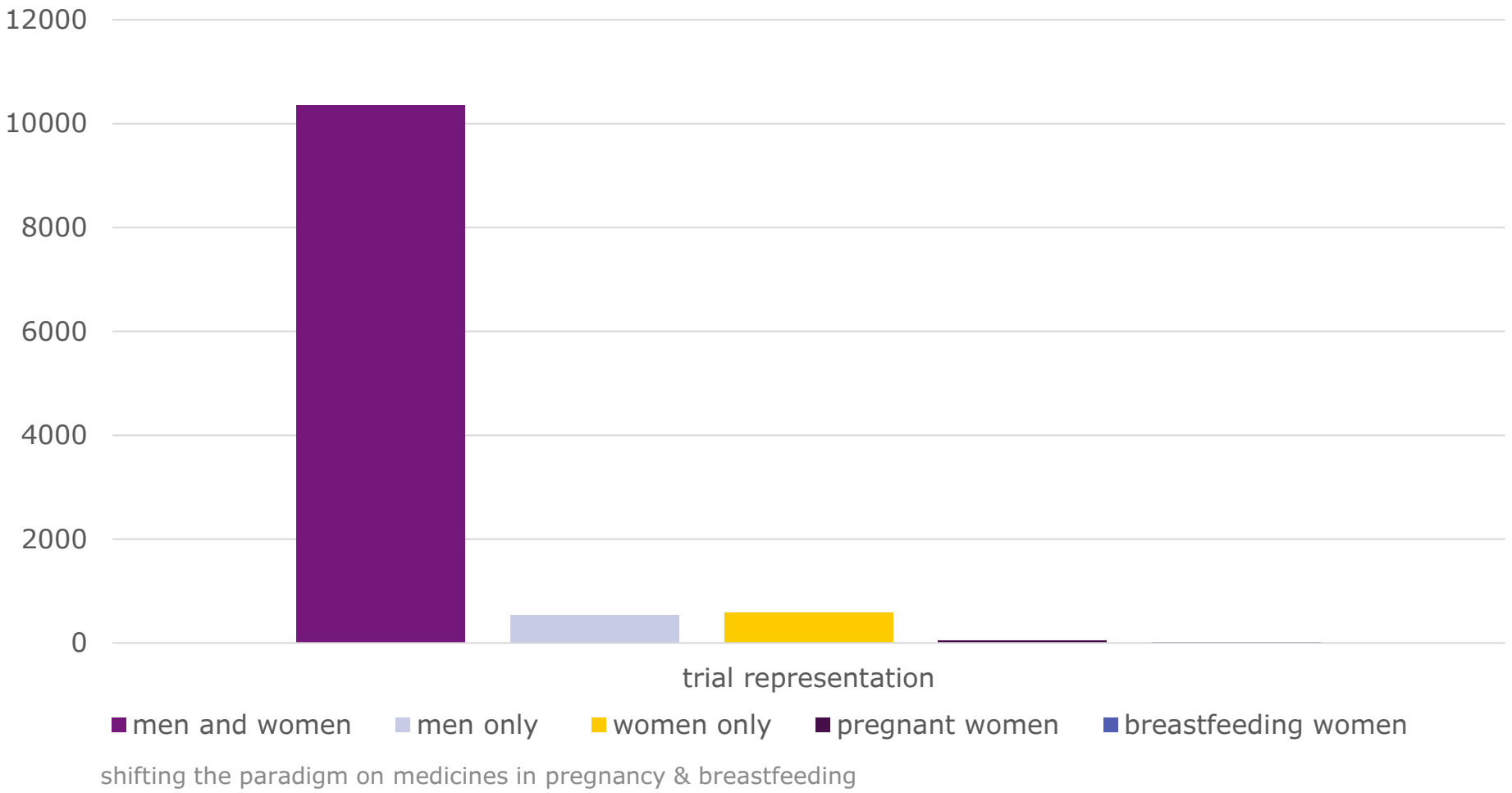
Are women under-represented?

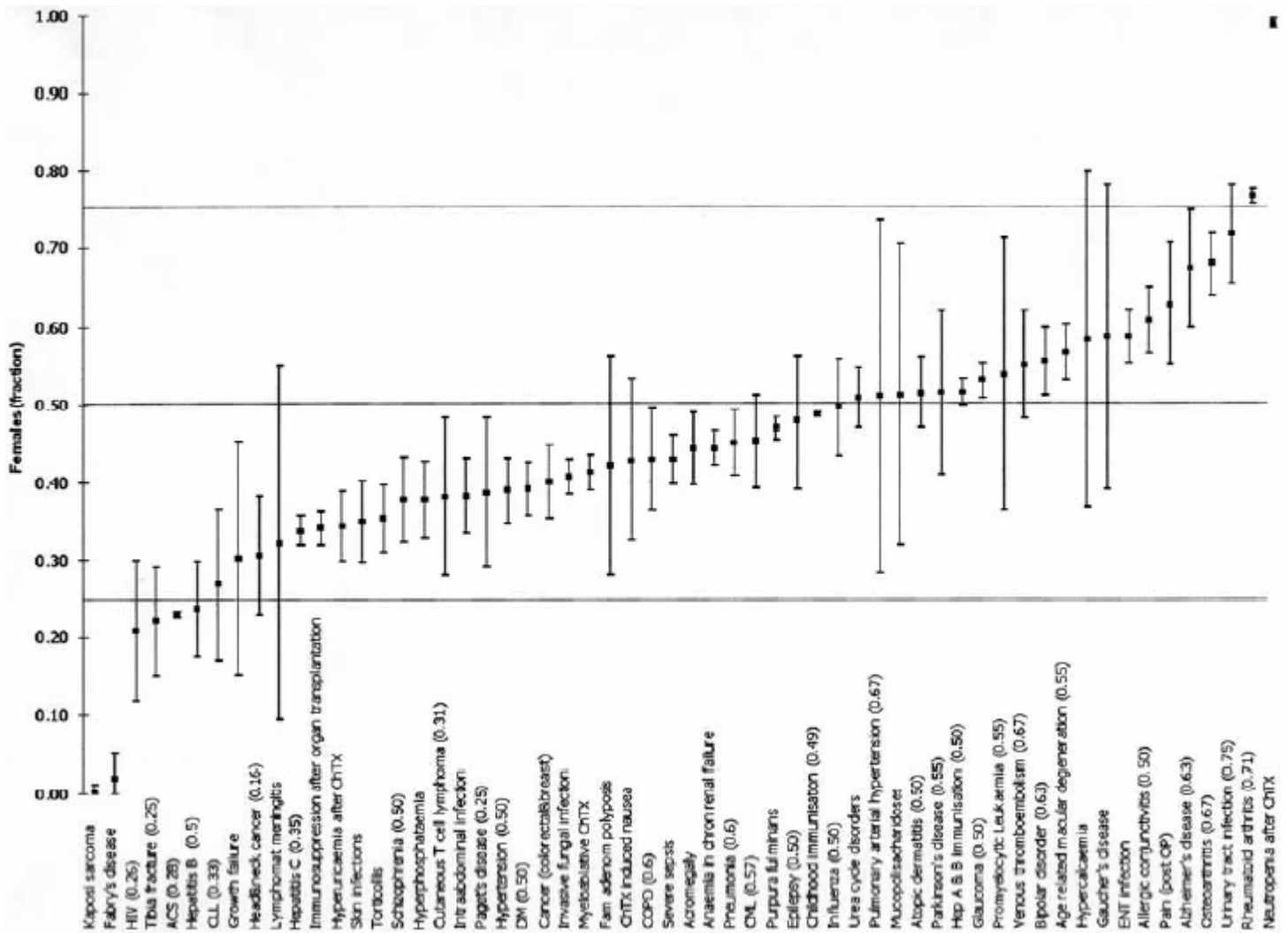
- Directive 2001/20/EC and clinical trials regulation (CTR): represent the anticipated user population
- Inclusion of women in clinical trials: facts and figures
  - All women
  - Pregnant and breastfeeding women
  - EMA actions to ensure appropriate inclusion
- Achievements to date, ambitions going forward

Inclusion of women in clinical trials: facts and figures



Out of 11477 trials,

- 10,351 (**90.2%**) included men and women
- **9.8%** were men or women only
- 42 (**0.4%**) included pregnant women
- 13 (**0.1%**) included nursing women



- Women were slightly underrepresented in some, and slightly overrepresented in other conditions
- Not clinically meaningfully so
- No clinically relevant pharmacokinetic differences

Further data analysis and literature review:

- Narrative on biased gender inclusion goes back >40 years
- Biased inclusion may occur to some extent but not such that it is clinically meaningful
- PK differences between men & women routinely explored – rarely leads to differences in dosage recommendations.
- Transparency: included in the EPAR, SmPC section 5.1
- …which does not mean there are no underrepresented populations in clinical trials

Clinical Trial Information System (CTIS)

Backbone of the Clinical Trials Regulation, launched in 2022

- A single clinical trial application for up to 30 EU/EEA countries
- Used by sponsors to submit applications and Member States to approve and supervise clinical trials
- Public, searchable database increases transparency and enables patient enrolment
- Facilitates multinational trials to address key health issues
- Improves access to clinical research data
- Supports the EU to remain a competitive clinical research hub globally

The power of data: finding a clinical trial for me

Search for clinical trials – CTIS website

- **Trial Map** developed to empower patients and healthcare professionals
- Integrated with CTIS public portal
- Easy access to information on clinical trials by geographical region and disease area
- Provide your feedback or suggestions

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- …which does not mean there are no underrepresented populations in clinical trials
- Who are missing: pregnant and breastfeeding women

Why?

Is it OK to experiment on pregnant women?

Examples that have shaped our thinking, guidelines, and laws

Product	Indication	Impact on child
Thalidomide	Nausea, sleeplessness	Phocomelia, heart defects, etc.
Diethylstiboestrol (DES)	Threatened miscarriage	Vaginal adenocarcinoma, infertility
Isotretinoin	Acne	Miscarriage, cleft palate, heart defects, etc.
Valproic acid	Epilepsy, migraine, bipolar disorder	Spina bifida, neurodevelopmental disorders, etc

Risks in clinical practice

Disease	Impact on pregnancy	Impact on child
Diabetes mellitus	pregnancy loss, prematurity	Macrosomia, heart defects, NTDs, etc, metabolic syndrome
Asthma	prematurity, preeclampsia	SGA, birth defects?
SLE	Pregnancy loss, preeclampsia, thrombosis	Heart defects
High fever	Pregnancy loss, chorioamnionitis	NTDs, cardiac defects?
Epilepsy	Pregnancy loss, preeclampsia, prematurity	Foetal distress, SGA, respiratory distress syndrome, birth defects?

SGA – small for gestational age
NTD – neural tube defects

Balancing treatment needs with uncertainties about risk

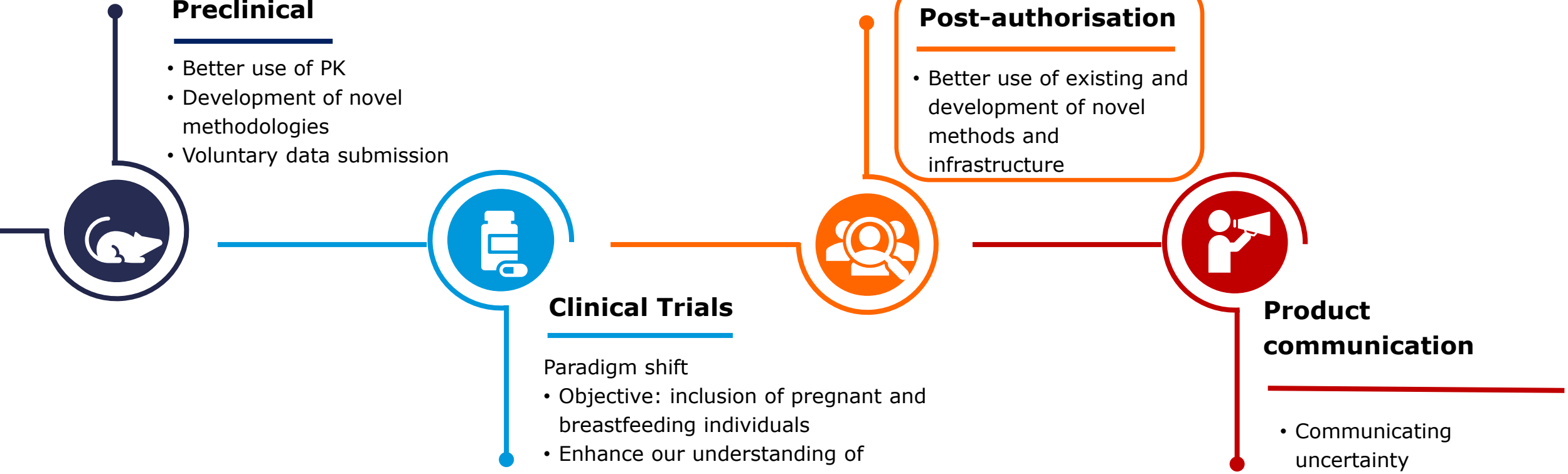
- A healthy child starts with a healthy mother

Exclusion from clinical trials is not automatically ‘being cautious’:

- Novel treatments may be better than current standard of care
- Disease may have a negative impact on the pregnancy
- Is it better to experiment in an uncontrolled setting?

Achievements to date, ambitions going forward

Strengthening benefit-risk information throughout product life cycle



Preclinical

- Better use of PK
- Development of novel methodologies
- Voluntary data submission

Clinical Trials

Paradigm shift

- Objective: inclusion of pregnant and breastfeeding individuals
- Enhance our understanding of benefit/risk antenatally
- Obtaining the benefits while protecting the women

Post-authorisation

- Better use of existing and development of novel methods and infrastructure

Product communication

- Communicating uncertainty
- Stakeholder engagement
- Content and communication skills

EMA efforts on PSURs, signals, PASS

HMA
Heads of Medicines Agencies

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9 December 2013
EMA/816292/2011 Rev 1*

Guideline on good pharmacovigilance practices (GVP)

Module VII – Periodic safety update report (Rev 1)

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shifting the paradigm on medicines in pregnancy & breastfeeding

1 EMA/653036/2019 DRAFT FOR PUBLIC CONSULTATION
2 4 December 2019

3 Guideline on good pharmacovigilance practices (GVP)
4 Product- or Population-Specific Considerations III: Pregnant and
5 breastfeeding women

Identification of pregnancy adverse drug reactions in spontaneous reporting systems: a novel algorithm developed in EudraVigilance

Cosimo Zaccaria[1], Loris Piccolo[1], María Gordillo-Marañón[2], Gilles Tourailleˡ[1], Corinne de Vries[1]

Annex 2 to the Guide on Methodological Standards in Pharmacoepidemiology

Guidance on methods for the evaluation of medicines in pregnancy and breastfeeding (2nd Edition)

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21 March 2024
EMA/127507/2024
Committee for Medicinal Products for Human Use (CHMP); Pharmacovigilance Risk Assessment Committee (PRAC)

Concept paper on revision of the Guideline on Risk Assessment of Medicinal Products on Human Reproduction and Lactation: from Data to Labelling

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EMA efforts on PSURs, signals, registries, PASS

- Registries have limited impact
- Few PASS make it into labelling
- So far, no signals on pregnancy from EUDRAVIGILANCE
- PSURs: limited data on pregnancy
- Negligible post-authorisation data on breastfeeding

Strengthening benefit-risk information throughout product life cycle

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ICH E21: pregnant and breastfeeding individuals in clinical trials

- Scientific and regulatory principles to ensure appropriate inclusion
- In principle, consider pregnancy & breastfeeding for all products with WOCBP in the anticipated user population
- Considerations regarding data collection on dosing, clinical efficacy and safety:
- Trial design
- Timing of inclusion
- Strategies for generating data
- Impact of the treatment modality
- Strategies for timing of preclinical testing
- Considerations for the use of prior knowledge to inform assumptions for foetal exposure and metabolism
- For public consultation until 15 September 2025 – please submit your input

WOCBP – women of childbearing potential

conceptION
SAFETY EVIDENCE ECOSYSTEM

C NSIGN

ADEPT
Antiseizure meDication Exposure and Pregnancy and neonaTal outcomes research
Specific Contract implementing FWC EMA/2020/46/TDA/20

What about older medicines?

- Most medicines used in pregnancy and breastfeeding are off-patent
- Unless contra-indicated, if authorised for use in adults it's authorised for use in pregnancy and breastfeeding
- EMA Framework contracts to generate data where needed
  - translational sciences: NAMs for reprotox; medicines and breastfeeding
  - epidemiology: compare and contrast risk-benefit of off-patent medicines in pregnancy

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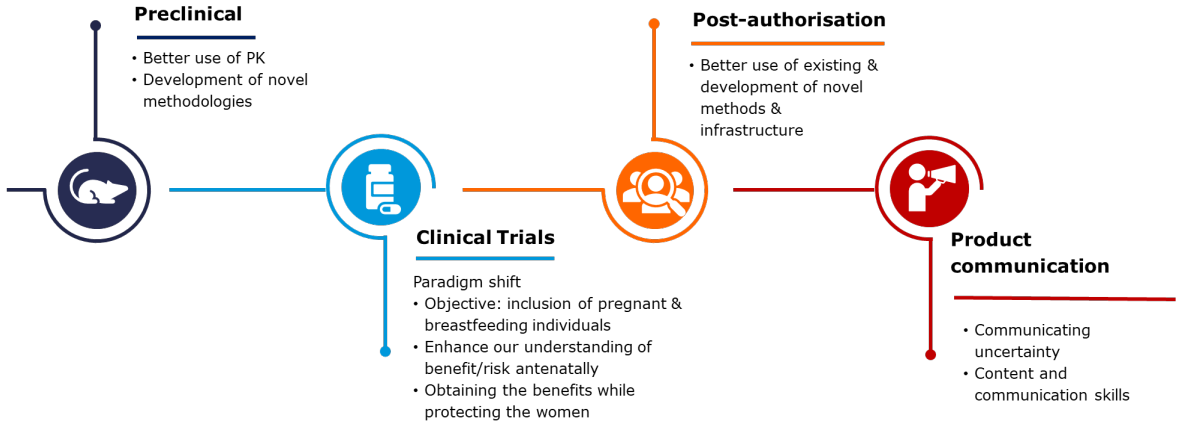
Opportunities going forward: shifting the paradigm together with our stakeholders

- Capitalise on Clinical Trials Information System (CTIS)
  - structured protocol and results data
  - trial map to enable inclusion for all
- Continuous and structural evaluation post-authorisation: studies built on existing infrastructure in the EU, resulting in benefit-risk information sufficiently robust for labelling
- Continued work across the product life cycle, in liaison with other regulators globally
- Stakeholder engagement through various channels



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Thank you

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