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Session background and objectives

Research and evidence generation for medicines including new uses

- Source of topic: suggestions by platform participants, regulatory science research needs (RSRN), prioritisation by platform steering group

- Help researchers seek interdisciplinary collaborations, e.g. on pharmacology, safety experts, building a case
- Help addressing regulatory science research needs (RSRNs) related to the topic
- Promote approaching medicine regulators, EMA and Member state
- Promote using time until new EU pharmaceutical legislation may provide for EMA's scientific opinion on evidence by not-for-profit entities ('repurposing')

RSRNs related to evidence generation for uses of medicinal products

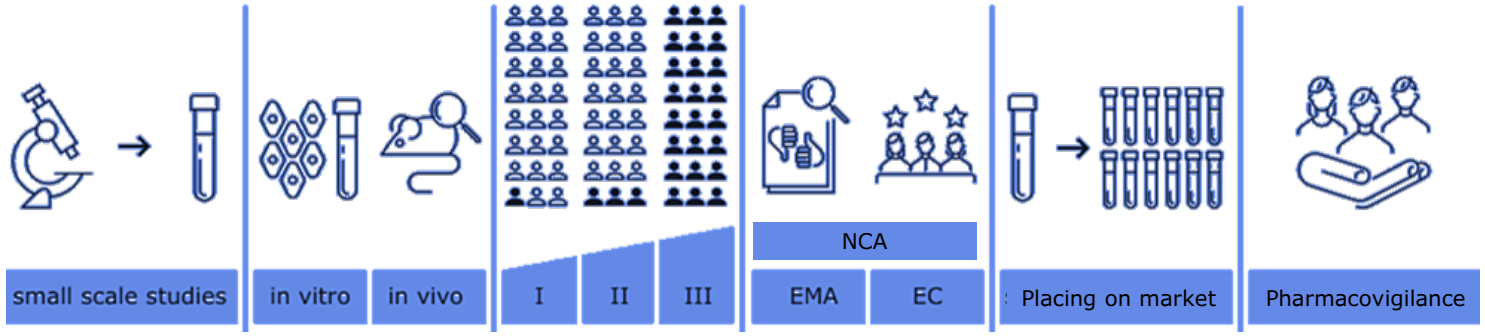
RSRN ID	Research need	Priority topic	Keywords	Domain of impact
Focus area: Going beyond current regulatory pathways				
RP1	Research on the impact of medical devices and medicinal product / medical devices combinations on the medicine's lifecycle and the regulatory system	1. Review and describe the evidence framework and methodological principles for generating scientific evidence underpinning medical devices, medicines and their combination (G)	• Medical device/drug combination • Combination product • Clinical trials • Regulatory framework	Human medicine

RSRN ID	Research need	Priority topic	Keywords	Domain
Focus area: Platform technologies and vaccines				
NT1	Research on mRNA-based medicines across therapeutic areas with a focus on oncology and rare diseases	1. Generate scientific evidence on efficacy and safety as determined by the type of mRNA (e.g., self-amplifying, trans-amplifying, circular) considered for future medicines in comparison to mRNA types used in authorised medicines (A; D; E) 2. Generate scientific evidence on how molecular	• Platform technologies • mRNA • Oncology • Rare diseases	Human and Veterinary Medicine

https://www.ema.europa.eu/en/about-us/what-we-do/regulatory-science-research/regulatory-science-research-needs

Need for generating evidence…

…on a particular medicine under investigation



Medicinal product research, develop-ment and evaluation

…on methods and their application in developments

Domain I:
Investigating and establishing tools and methods for specific activities in drug development

Domain II:
Investigating and establishing approaches for optimising evidence generation

Domain III:
Investigating and evolving the regulatory activities and system

This session

ulatory

- **pendent**
- approach
- emia leading
- Often multiple stakeholders
- Often publicly financed

“Research and evidence generation...”?

- “**Data**”: e.g., ‘raw’ observations or measurements

- “**Evidence generation**”: a deliberate (planned), methodologically sound, systematic process of producing data and analyses to accumulate evidence, e.g. with the purpose to support a claim for a new medicine or new use

- “**Evidence**”: data that are analysed and interpreted with a view to inform regulatory decisions; various types of evidence can be used

https://www.ema.europa.eu/en/about-us/what-we-do/authorisation-medicines/how-ema-evaluates-medicines-human-use

“...for new medicines and new uses”?

- Typically, ‘use’ means a medicinal product with an authorised *indication*

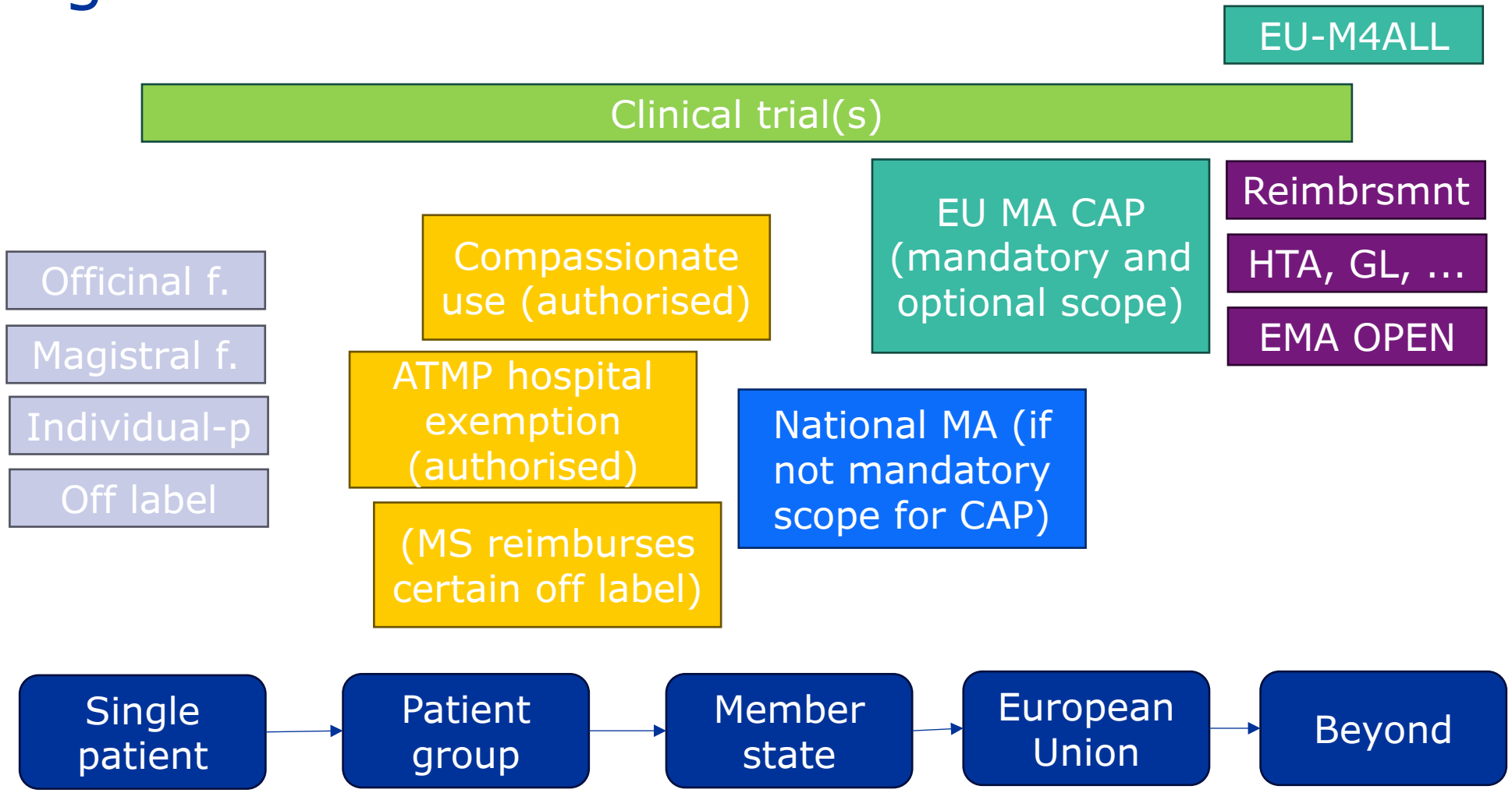
- Regulators scrutinise (“assess”) and describe the data
  - Assessment report(s)
  - Authorised “Therapeutic indication” =
    Summary of product characteristics (SmPC) section 4.1
  - SmPC sections 4.2 (posology) and 5 (data on pharmacological properties)

- ‘Indication’ does not imply that the medicine is the best option for all patients;
  “are there patients in the right decision context who prefer drug to placebo?”

- ‘Indication’ describes the population that includes such patients

MA = marketing authorisation
CAP = centrally authorised medicinal product

Pathways for patient access – high-level overview



EudraLex – rules governing medicinal products in the EU

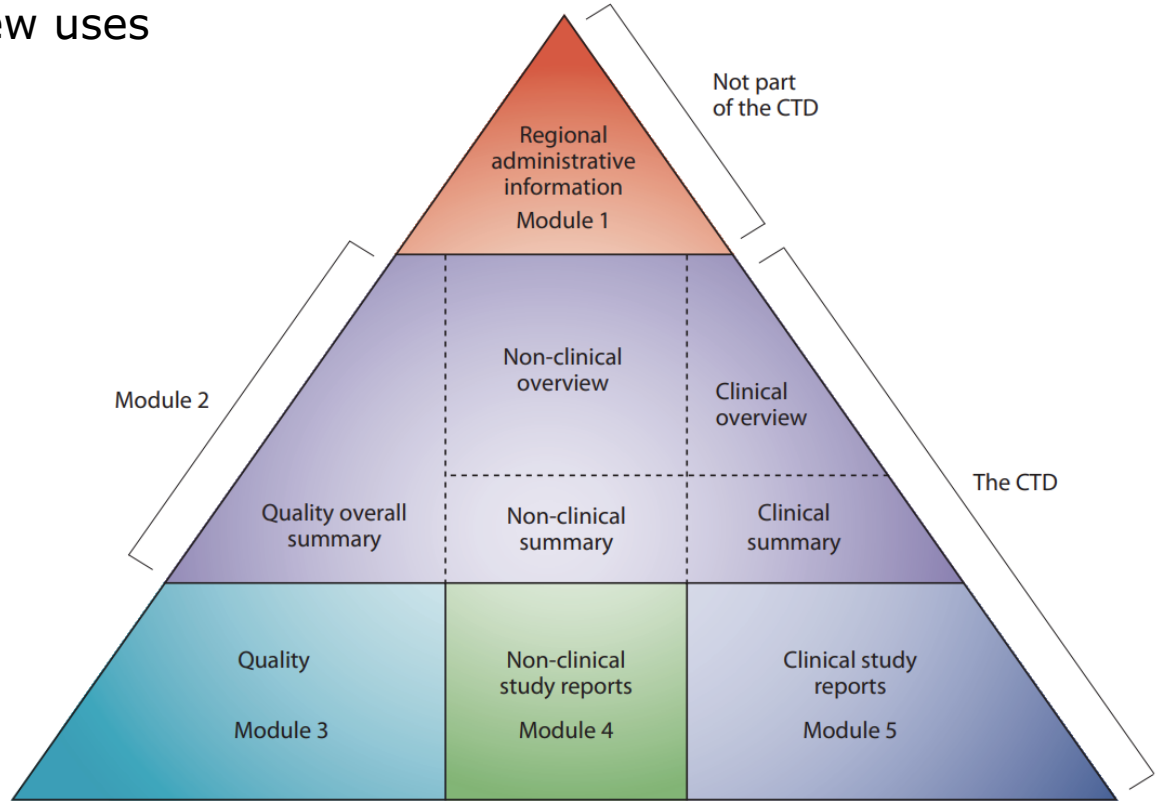
- Volume 1 - EU pharmaceutical **legislation** for medicinal products for human use
- Volume 5 - EU pharmaceutical **legislation** for veterinary medicinal products
- Volume 2 - Notice to applicants and **regulatory guidelines** for medicinal products for human use
- Volume 3 – EMA **scientific guidelines** for medicinal products for human use
- Volume 4 - Guidelines for good **manufacturing** practices for medicinal products for human use and veterinary medicinal products
- Volume 6 - Guidance to applicants for veterinary medicinal products
- Volume 7 - Scientific guidelines for veterinary medicinal products
- Volume 8 - Maximum residue limits
- Volume 9 - Guidelines for **pharmacovigilance** for medicinal products for human use and veterinary medicinal products
- Volume 10 - Guidelines for **clinical trials** for medicinal products for human use (CTA, safety reporting, quality of IMP, inspections, FIH, GCP)

Types of data in a dossier

Data to support new medicines including new uses

"Common Technical Document" (eCTD)

- Module 1 Administrative information
- Module 2
  - Quality overall summary
  - Non-clinical overview, summary
  - Clinical overview, summary
- Module 3 Quality data
- Module 4 Non-clinical study reports
- Module 5 Clinical studies reports

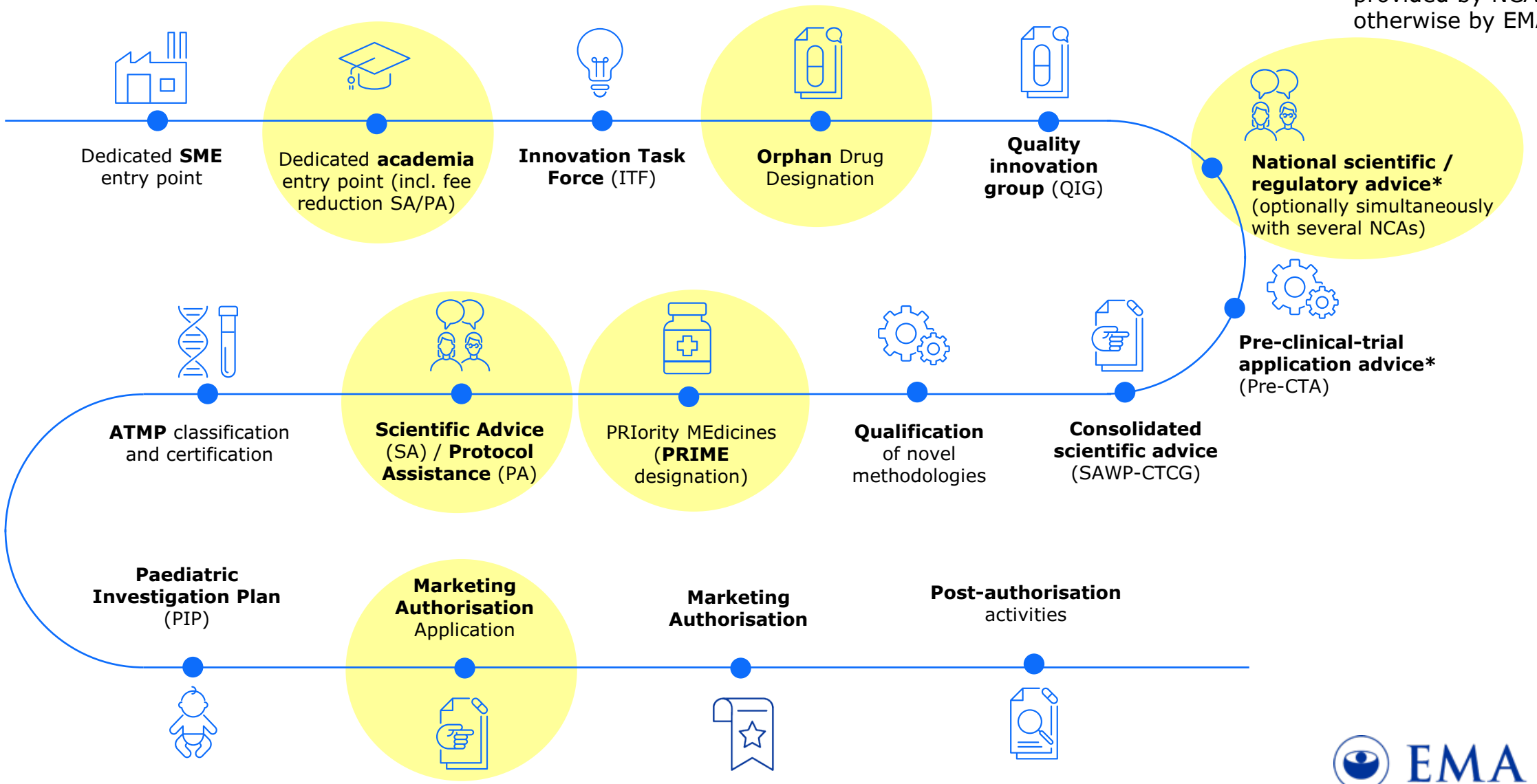


The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

Options to interact with EMA and NCAs* across the medicine life cycle

NCA = National competent authority of EU Member state

* indicates option is provided by NCAs, otherwise by EMA



[Orientation document]

Issues noted by regulators discussing with developers of new medicine uses

- Main endpoints not as typically used for regulatory evaluation
- No pharmacokinetic data collected, scarce rationale for dosing (posology)
- Sample size of trials, overall or for subgroup
- Trial design does not ‘isolate’ treatment effect (includes no internal control)
- Funding of trials limited to specific region or durations
- (Unclear approaches for commercial partnering)