Norwegian Medical Products Agency

Session 5

EU HTA REGULATIONS - STAKEHOLDER COLLABORATION TO IMPROVE PATIENT ACCESS

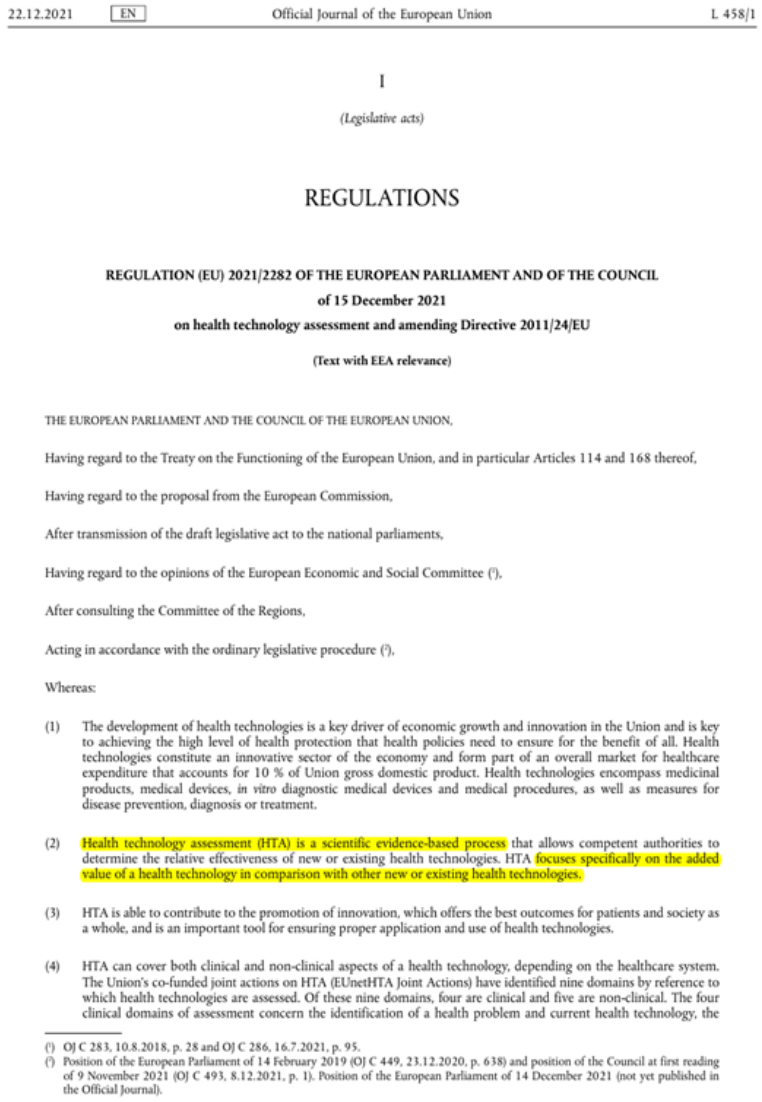
From Approval to HTA, 2025 and beyond

CDDF; Challenges, Advances, and Open Questions in Global Cancer Drug Development and Clinical Trials
3-5 February 2025

Anja Schiel, PhD, NOMA

2025, a new era begins…..

- Approval ≠ Access



I

(Legislative acts)

REGULATIONS

REGULATION (EU) 2021/2282 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 15 December 2021
on health technology assessment and amending Directive 2011/24/EU

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Articles 114 and 168 thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinions of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) The development of health technologies is a key driver of economic growth and innovation in the Union and is key to achieving the high level of health protection that health policies need to ensure for the benefit of all. Health technologies constitute an innovative sector of the economy and form part of an overall market for healthcare expenditure that accounts for 10 % of Union gross domestic product. Health technologies encompass medicinal products, medical devices, *in vitro* diagnostic medical devices and medical procedures, as well as measures for disease prevention, diagnosis or treatment.

(2) Health technology assessment (HTA) is a scientific evidence-based process that allows competent authorities to determine the relative effectiveness of new or existing health technologies. HTA focuses specifically on the added value of a health technology in comparison with other new or existing health technologies.

(3) HTA is able to contribute to the promotion of innovation, which offers the best outcomes for patients and society as a whole, and is an important tool for ensuring proper application and use of health technologies.

(4) HTA can cover both clinical and non-clinical aspects of a health technology, depending on the healthcare system. The Union's co-funded joint actions on HTA (EUnetHTA Joint Actions) have identified nine domains by reference to which health technologies are assessed. Of these nine domains, four are clinical and five are non-clinical. The four clinical domains of assessment concern the identification of a health problem and current health technology, the

(1) OJ C 283, 10.8.2018, p. 28 and OJ C 286, 16.7.2021, p. 95.
(2) Position of the European Parliament of 14 February 2019 (OJ C 449, 23.12.2020, p. 638) and position of the Council at first reading of 9 November 2021 (OJ C 493, 8.12.2021, p. 1). Position of the European Parliament of 14 December 2021 (not yet published in the Official Journal).

2025, a new era begins but a difference remains

- Approval ≠ Access

- Clinical trial = Regulator

Efficacy (**B/R**)

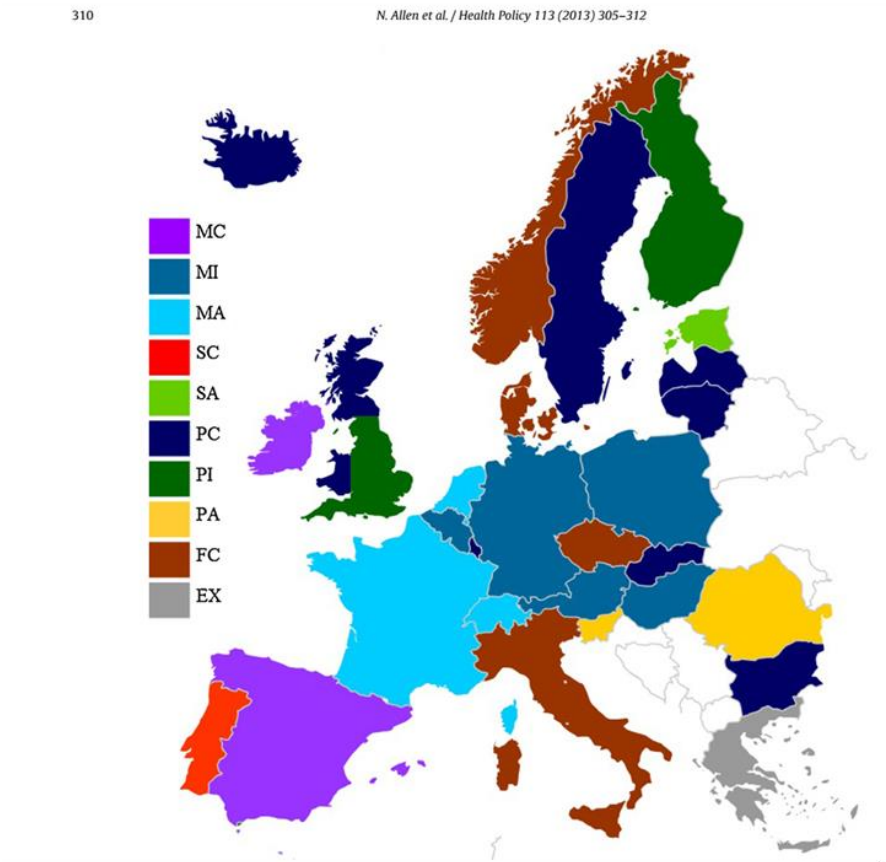
- Does it work in experimental setting
- Population selected
- Placebo or a selected comparator

- Real world = HTA

Relative Effectiveness (**C/E**)

- How does it work in clinical practice
- Patients as they come
- Many alternative treatments

2025, a new era begins but Europe is not united



Development of archetypes for non-ranking classification and comparison of European National Health Technology Assessment systems

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[c] Eli Lilly and Company, Erl Wood Manor, Windlesham, Surrey, GU20 6PH, UK

System Process Archetypes

HTA Process Archetypes	M	S	P	F	E
	REG → HTA → CB	REG → HTA → CB	REG → HTA → CB	REG → HTA → CB	REG → CB
C (TV, EV → AP)	DC (CYP) NCPE (IRE) DGFPS (SPA) MOH DTC (MAL)	INFARMED (POR)	AWMG (WAL) PDL (BUL) IMPRC (ICE) CHE (LAT) LRC (LIT) MSS (LUX) CC (SVK) SMC (SCO) TLV (SWE)	SUKL (CZE) DKMA (DEN) NOMA (NOR) AIFA (ITA)	
I (TV, EV → AP)	HEK (AUS) INAMI (BEL) IQWIG (GER) OHTA (HUN) AHTApol (POL)		NICE (ENG) HILA (FIN)		
A (TV → AP)	HAS (FRA) CFH (NET) FDC (SWZ)	SAM (EST)	MoH (ROM) ZZZS (SVN)		
X (External HTA → AP)					GREECE LIECHTENSTEIN

Archetype Key: MC, MI, MA, SC, SA, PC, PI, PA, FC, EX

Choose your perspective

Societal perspective

- Medical costs borne by third-party payers and paid out-of-pocket by patients
- Time costs of patients in seeking and receiving care
- Time costs of informal (unpaid) caregivers
- Transportation costs
- Effects on future productivity and consumption
- Other costs and effects outside the health care sector

Health sector perspective

- Include all costs and benefits impacting a system of providers, payers and patients.
- Do not consider impact outside of the health system (e.g. long-term value to patients)
- Based on Direct Medical Costs reimbursed by a third party
- Can include out-of-pocket costs to the patient
- Can include current and future costs as a result of a pathway of care

Patient perspective

- Fees for consultation
- Bed day charges at the health facility
- Expenses on medicines, diagnostic tests,
- Travelling expenses to the health facility for the patient and accompanied persons for treatment,
- Amount spent on meal / food taken while waiting for treatment
- Time loss of the patient and the accompanied persons for seeking treatment
- Informal caregiving
- Pain and suffering

Your perspective and political mandate determine the methodology

Type	Unit of effect	Strength	Limitations
Cost–benefit analysis (CBA)	All effects measured in €	The net benefit (NB) is easy to interpret. When a new treatments extra benefits are worth more than the extra costs then NB > 0	• It is difficult to measure the value of all health outcomes (positive or negative) in € • Ethical aspects come into the discussion (Prioritisation, discrimination, the Pareto principle)
Cost-utility analysis (CUA)	Two effects (quality and length of life); reflected as quality-adjusted life years (QALY's)	Patient relevant outcomes involving both quality and length of life can be incorporated into the analysis. In theory the QALY measure is 'universal', allowing evaluation of very different decision problems with each other.	• QALY outcomes can be biased by method, indication and population • Society might value a QALY for different patient groups differently (and who should we ask, patients or healthy people form the street?)
Cost-effectiveness (CEA)	Effect measured in 'natural units'	There is one outcome and it is measured in its 'natural unit'.	• Only one outcome is considered for the effect conclusion (no context)
Cost-minimization (CMA)	No effects measured	Only cost data are needed	• Few treatments have truly identical outcomes • Still some evidence is needed to confirm the assumption of 'equality'

Assessment

Type	Unit of effect	Strength	Limitations
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Appraisal

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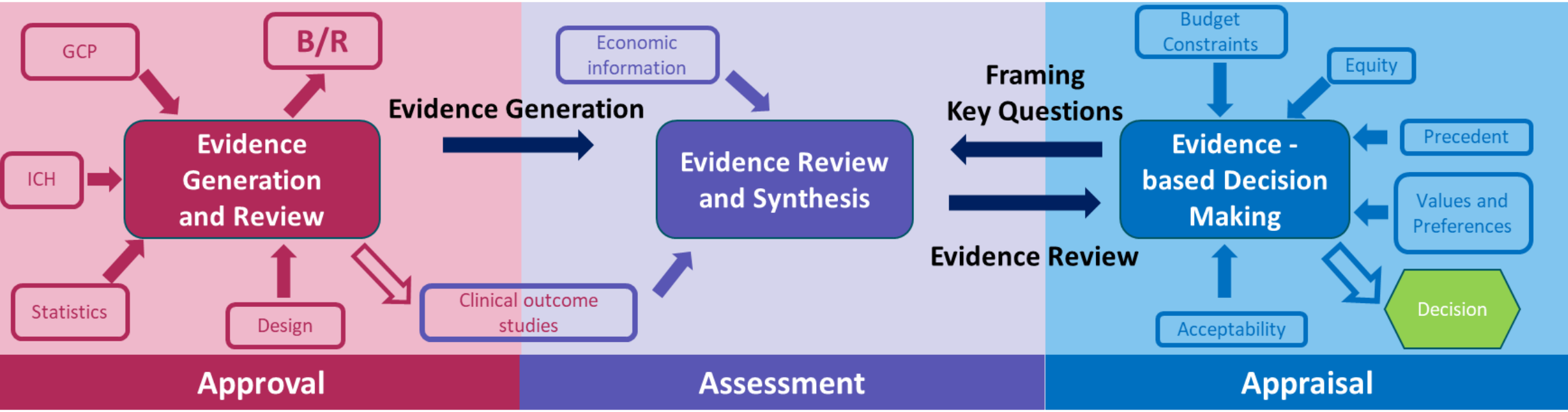
The Trinity

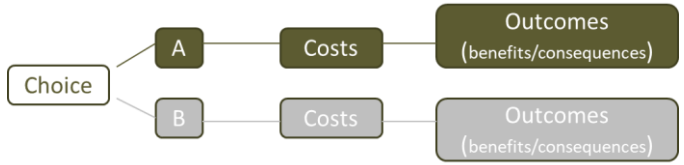


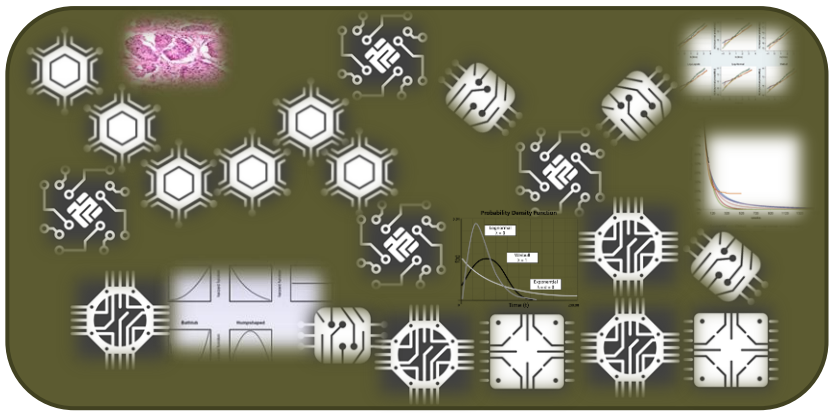
Adapted from Teutsch, S.; Berger, M. (2005) 'Evidence synthesis and evidence-based decision making: Related but distinct processes. *Medical Decision Making*, pp 487-489

How to get from approval to access (CUA)

The technology assessment

Clinical evidence with best/high **internal** validity (B/R)



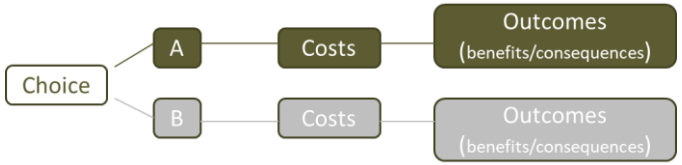


The Health economic decision
To pay or not to pay?
External validity

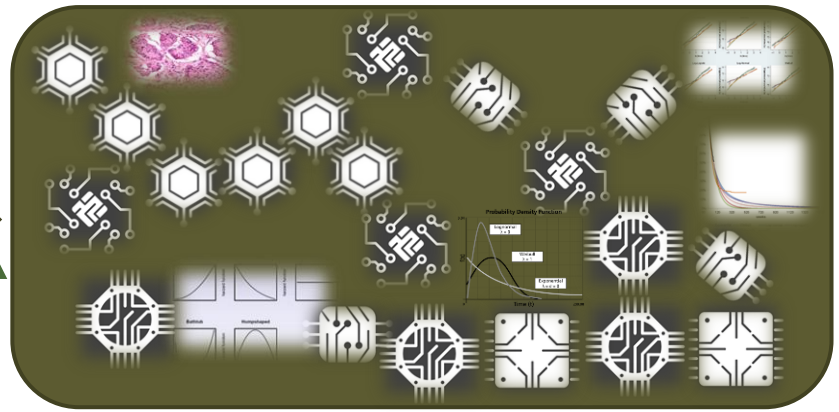
https://www.vecteezy.com/free-vector/technology-icons

How to get from approval to access (HTAR/JCA)

The technology assessment



Clinical evidence with best/high **internal** validity (B/R)



HTAR

CHMP

The Health economic decision
To pay or not to pay?
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How to get from approval to access

The technology assessment

Clinical evidence with best/high
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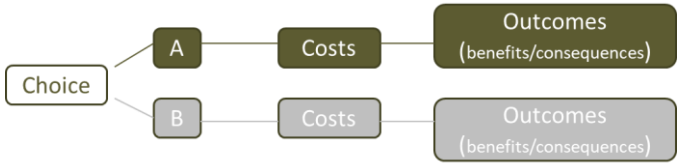

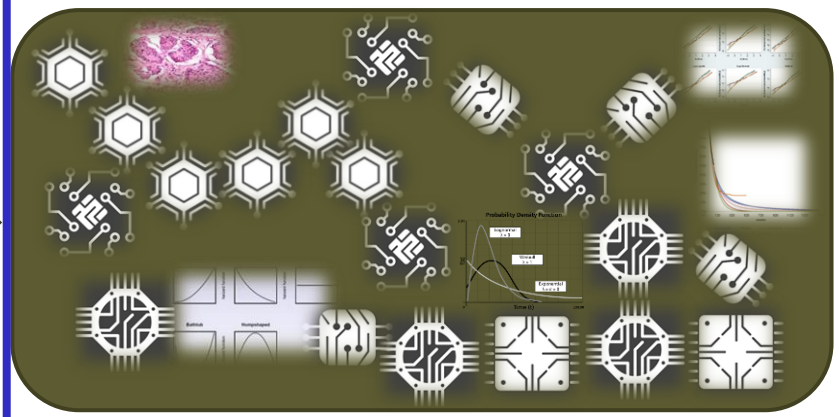

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How to get from approval to access

Clinical evidence with best/high **internal** validity (B/R)

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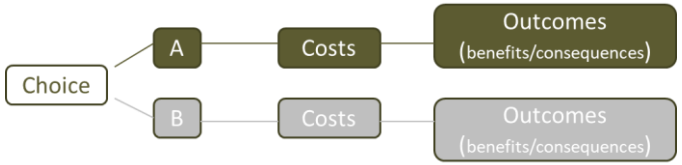

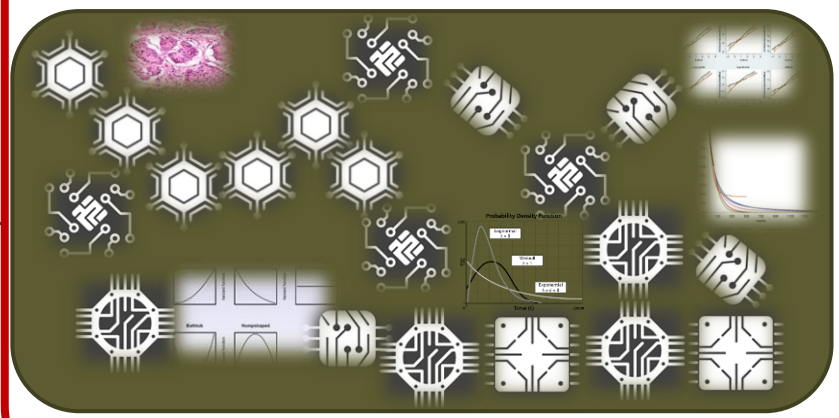

The Health economic decision
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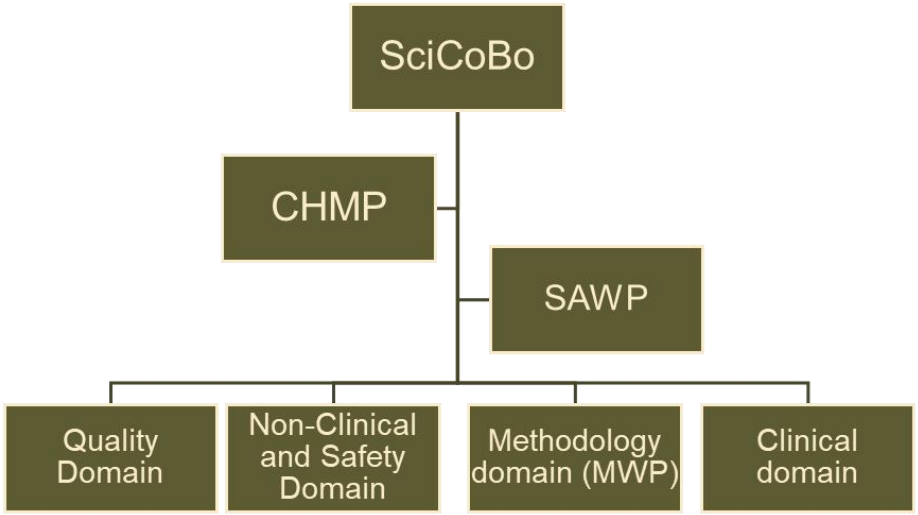
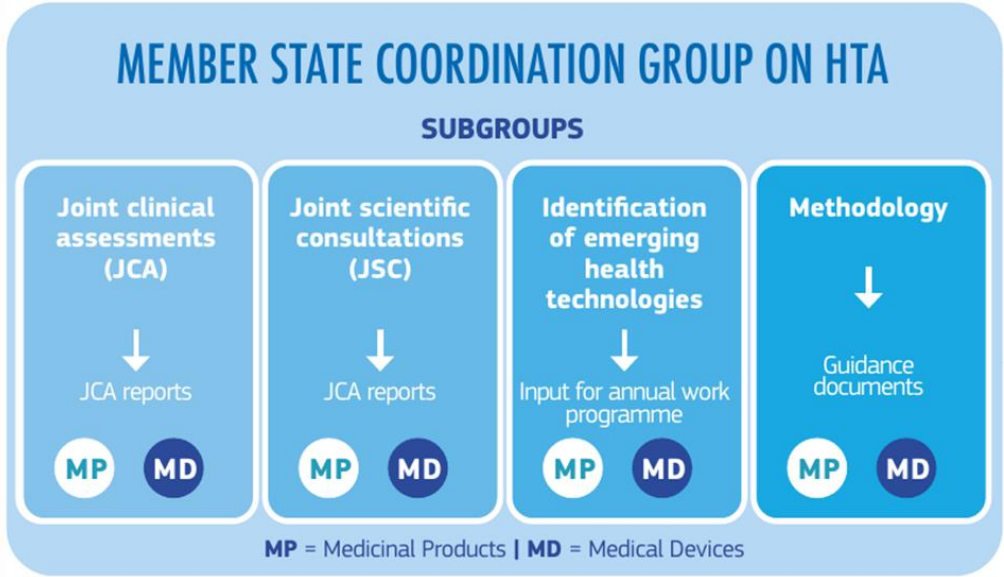
2025, a new era begins with new players

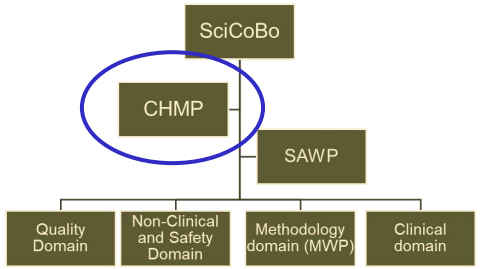
- The HTAR system mirrors, to some extent and wherever useful, the regulatory system

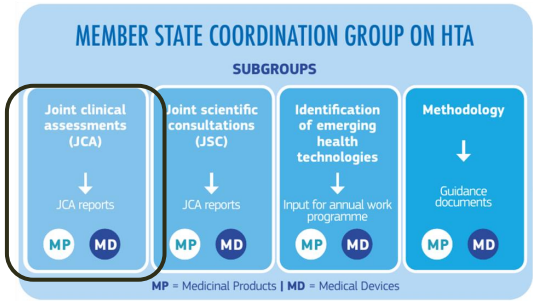




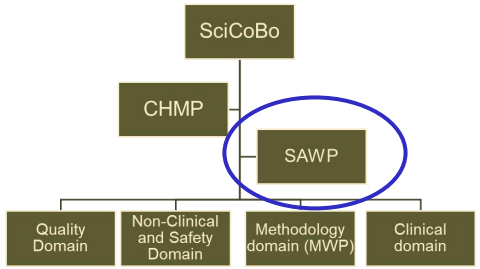
2025, a new era begins with new procedures

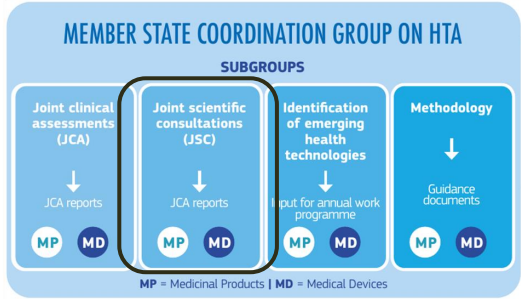
- Joined clinical assessment (JCA)
  - 12/01/2025 implementation date
  - Oncology and ATMP products must undergo JCA
  - Instructions, templates and additional information can be found here (link)
  - Close collaboration with EMA is built in
  - Patient involvement is built in





- Joined scientific consultations (JSC)
  - In parallel with EMAs Scientific advice working party or HTA only
  - Request periods in 2025
    - 3 February to 3 March 2025 for medicinal products only
    - 2 to 30 June 2025 for medicinal products and medical devices
  - Selection criteria can be found on above mentioned website





2025, a new era begins, all problems solved?

- Inequalities
  - The HTAR can’t remove inequalities.
    - To address that problem also the Pharma Legislation needs to be changed
  - Inequalities cannot be solved by the JCA.
    - Despite the JCA being available to all MS shortly after approval each MS still needs to receive a HTA submission by the developer to start the assessment. Multiple MS report that they receive submission for HTA (if at all) often years after approval. JCAs would be outdated by then.
    - The JCA only describes the analyses provided to address the additional evidence needed to answer questions on relative effectiveness that are formulated in form of the PICO(s). The JCA will describe whether the provided analyses are in line with methodological guidelines published by the HTAR CG. The acceptance of these analyses as basis for a reimbursement decision is still a national mandate.

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    - **The different PICOs are the result of inequalities in the European landscape!**
    - Uptake of the JCA is voluntary (but all MS have committed to do so) and depends on the national mandate and requirements

2025, a new era begins, all problems solved?

- Communication
  - The HTAR puts in place tools for increased early dialogue
  - JSC is a multi-Stakeholder process that has proven to improve the understanding of commonalities and differences between the Stakeholders but also among the Stakeholders
  - It can (but only on a voluntary basis) include discussions on Health Economic methods like CUA. Not all MS do health economics and some MS will not participate in that part of a discussion

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  - Capacity might not match the demand
  - A wish for more flexibility in the request process has already been expressed by the industry

2025, a new era begins, all problems solved?

- The patient voice
  - The HTAR makes Patient involvement mandatory, both for JCAs and JSCs
  - Aligning existing national processes and regulations (conflict of interest) has proven difficult. Some MS might have to change their legislation to enable patient participation as currently foreseen
  - Who (individual or patient organisations) can be the patient voice is still not fully settled

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  - Patient organisations and representatives have expressed concerns about the (unpaid) workload, lack of proper communication on the degree of involvement and lack of training.
  - Several patient organisations have provided training courses independently to be prepared

2025, a new era begins, all problems solved?

- No, while the HTAR hits the ground running, this is still learning by doing.
- No test JCA has ever been performed, the earlier REAs generated under the EUnetHTA umbrella have helped but are no real indicators. Few MS have been involved in those as EUnetHTA did not cover all of Europe
- In the interim period JSCs were conducted differently than what is now foreseen procedural wise. The experience level of the MS differ greatly (some MS having been involved since the start of joined EMA-EUnetHTA advices in different formats, other MS having only been observers or not participated at all until now)
- Timelines for JCAs are tight both for Industry and HTA-bodies

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- Timelines for JCAs are tight both for Industry and HTA-bodies
- The HTAR needs to be a learning system, reduce requirements and workload where appropriate, match processes to the needs of those involved and be willing and flexible enough to change processes to match the intentions of the HTAR

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