EUnetHTA 21 – Stakeholder Meeting

18 November 2022
14:00-15:30 CET

1. **Welcome from the Chair of the Consortium Executive Board (CEB) and objective of the meeting**

Niklas Hedberg, TLV

Upcoming stakeholder meetings

Meeting date	Objective
25 November 2022	EMA/EUnetHTA 21 bilateral in accordance to work plan
Spring 2022	EMA/EUnetHTA 21 bilateral in accordance to work plan
12 May 2023	5th General EUnetHTA 21 Stakeholder Meeting
8 September 2023	6th & final General EUnetHTA 21 Stakeholder Meeting
Fall 2023	EMA/EUnetHTA 21 bilateral in accordance to work plan

Housekeeping of today's meeting

Alzbeta Tuckova, ZIN

Information for attendees

Entering the meeting:

- Please ensure you have logged in with your **name, surname, organisation and country** *i.e. Juste Jurgutavičiūtė (ZIN, The Netherlands)*.
- You can rename yourself after you have logged in.
- Please do not switch your webcam on.

Information for attendees

Questions:

- To ask questions, you may post them in the Q&A box.
- Responses to all questions will be coordinated by the Chair and will be taken at the **end of relevant presentations or during the Q&A item.**
- Please note: for internal purposes this meeting will be recorded.

Information for attendees

Technical issues:

- If you experience problems with Zoom during the meeting, please:

  1. Go to www.zoom.com and search for help.
  2. Contact euenthta@zinl.nl or call Juste Jurgutavičiūtė on **+31 6 43 47 04 69** for support (You may wish to take a picture of these contact details).

Today’s agenda

Niklas Hedberg, TLV

Agenda

ID	Time	Description	Presenter/s
#1	14:00-14:10	Welcome from the Chair of the Consortium Executive Board (CEB) and objective of the meeting	Niklas Hedberg, TLV
#2	14:10-14:30	Update from the European Commission	Valentina Barbuto, EC
#3	14:30 -15:00	Update on status of deliverables a) Joint Scientific Consultations b) Joint Clinical Assessments c) Transversal Activities	Antje Behring, G-BA Roisin Adams, NCPE
#4	15:00-15:25	Q&A	Niklas Hedberg, TLV
#5	15:25-15:30	Closing remarks	Niklas Hedberg, TLV

2. **Update from the European Commission**

Valentina Barbuto, EC

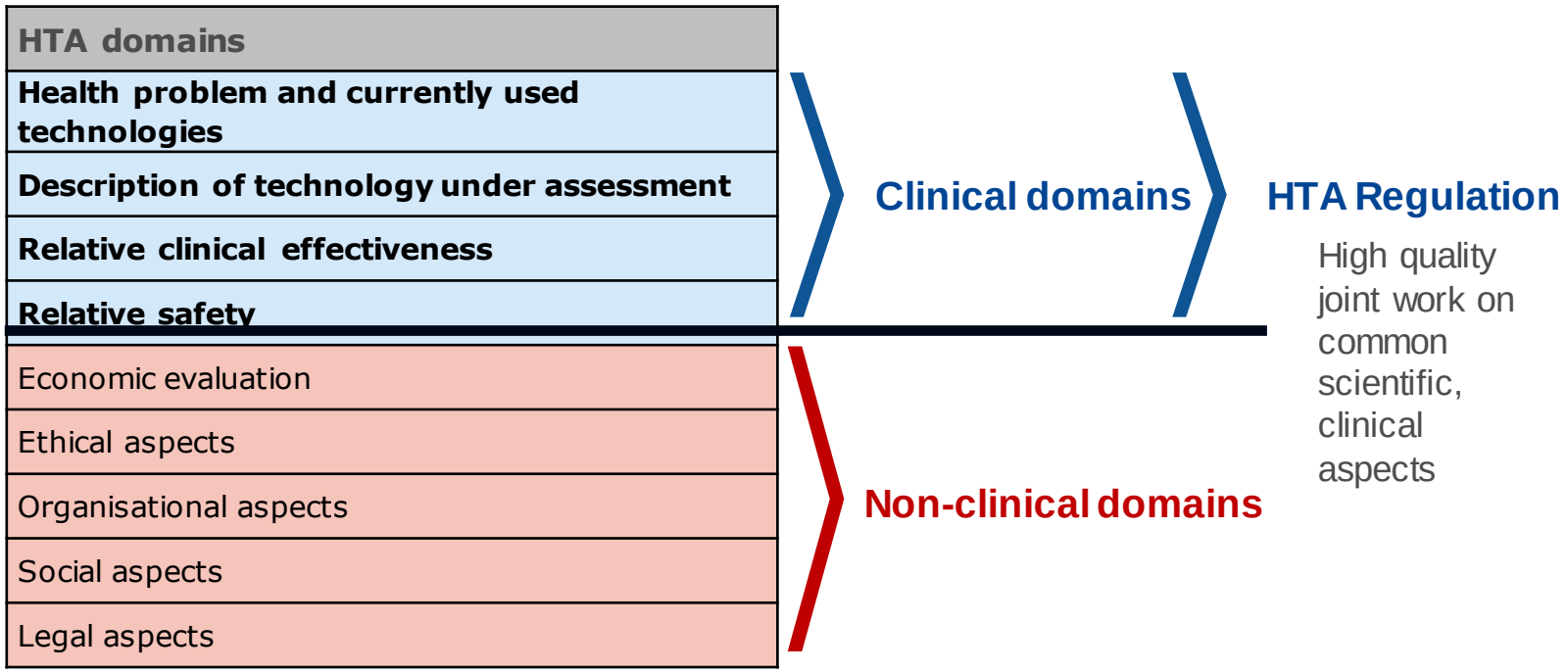
Update on the implementation of Regulation (EU) 2021/2282 on Health Technology Assessment

Valentina BARBUTO
Policy officer, DG SANTE, Unit C2

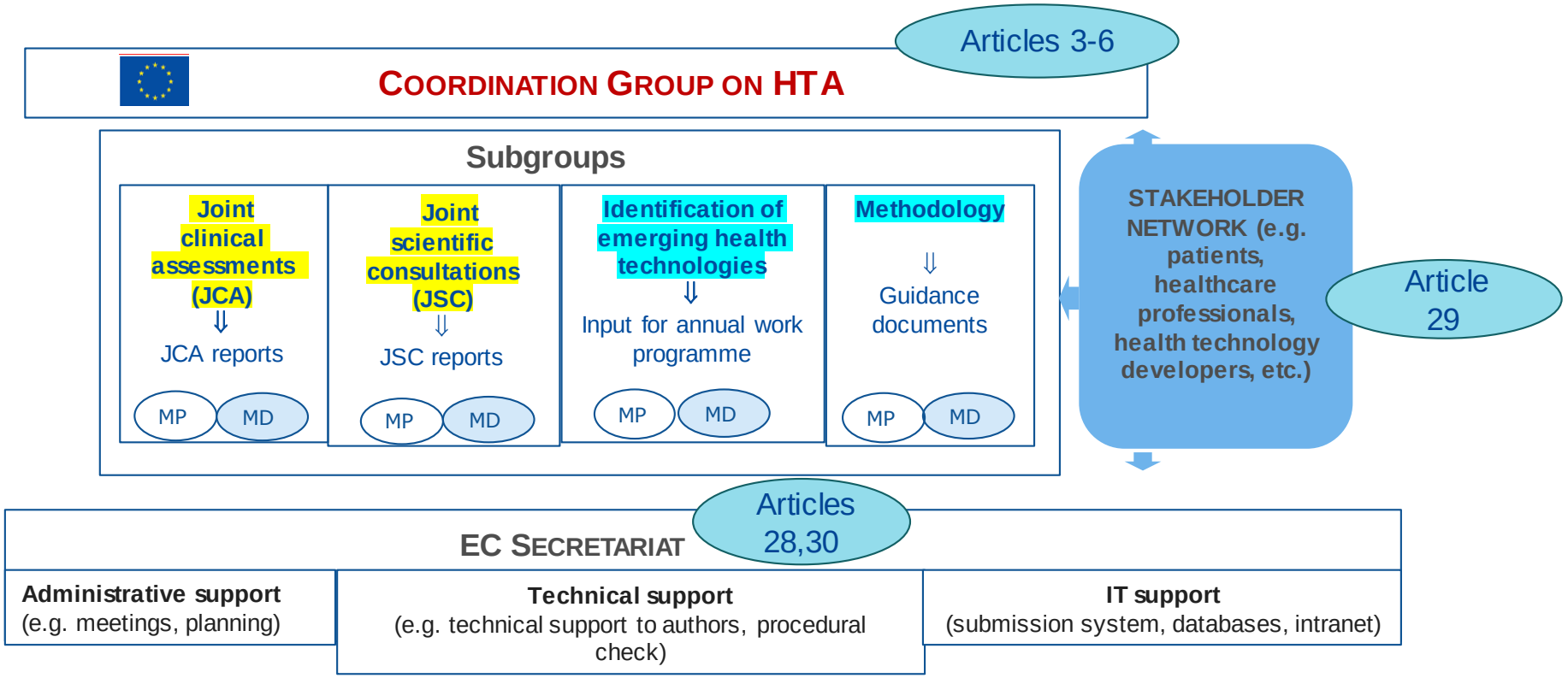
EUnetHTA 21 - Stakeholder meeting

18 November 2022

EU assessment **vs** NATIONAL appraisal



HTA Regulation: driven by Member States HTA bodies



MP = medicinal products, MD = medical devices

European Commission

HTA Regulation – Joint HTA & engagement with experts and stakeholders

1. Joint Clinical Assessments on:

- **medicines** (first 3 years: oncology medicines and ATMPs; following 2 years: + orphan drugs; after 5 years: full scope)
- **a selection of high-risk implantable medical devices**

Individual experts

2. Joint Scientific Consultations

- HTA only
- in parallel with regulators

Individual experts

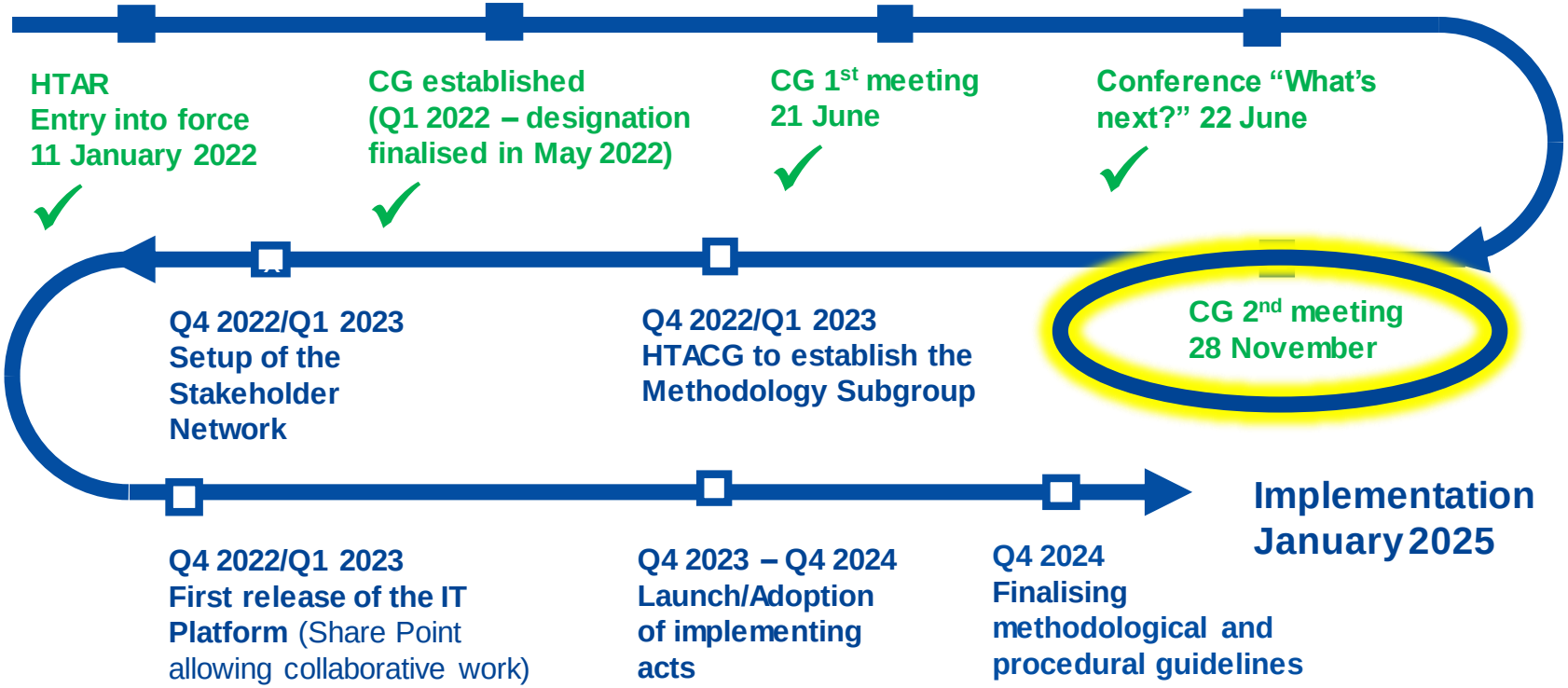
3. Emerging Health Technologies

4. Methodology

Organisations

European Commission

HTA Regulation
Implementation rolling plan



HTA Regulation: timeline

Adoption

December 2021

Entry into force

January 2022

Date of Application

January 2025

Joint Clinical Assessment Full Scope

January 2030

Preparatory phase

Implementation phase

- **Setting up the Coordination Group (EC)**
- **Setting up the Stakeholder Network (EC)**
- **Drafting implementing acts (EC)**
- **Drafting guidance documents (CG)**

Joint Scientific Consultations (JSC)

+

Stepwise build-up of

Joint Clinical Assessments (JCA) scope for medicines:

- From Jan. 2025: cancer drugs, ATMPs

(from date of application)

- From Jan. 2028: orphan drugs

(3 years after date of application)

eunethta

Service contract EUnetHTA21

European Commission

HTA Regulation: The Stakeholder Network

Open call for applications

to all eligible stakeholder organisations,
e.g. patient associations, consumer organisations, non-governmental organisations in the field of health, health technology developers and health professionals

Eligibility criteria:

- proof of engagement in HTA
- relevant professional expertise
- geographical EU coverage
- communication and dissemination capabilities

Organisations
to declare their membership and sources of funding

Representatives
to declare any financial or other interest

European Commission

The co-creation of a new system

Inclusiveness and transparency as key principles of the joint work

Commitment of all stakeholders essential to secure smooth implementation

- **STAKEHOLDER ORGANISATIONS** can apply to the stakeholder network
- **INDIVIDUAL EXPERTS** will be asked to provide input on JCAs and JSCs

Only two years left until application

European Commission

Any questions?

Contact details:

valentina.BARBUTO@ec.europa.eu

SANTE-HTA@ec.europa.eu

European Commission

Thank you for your attention

European Commission

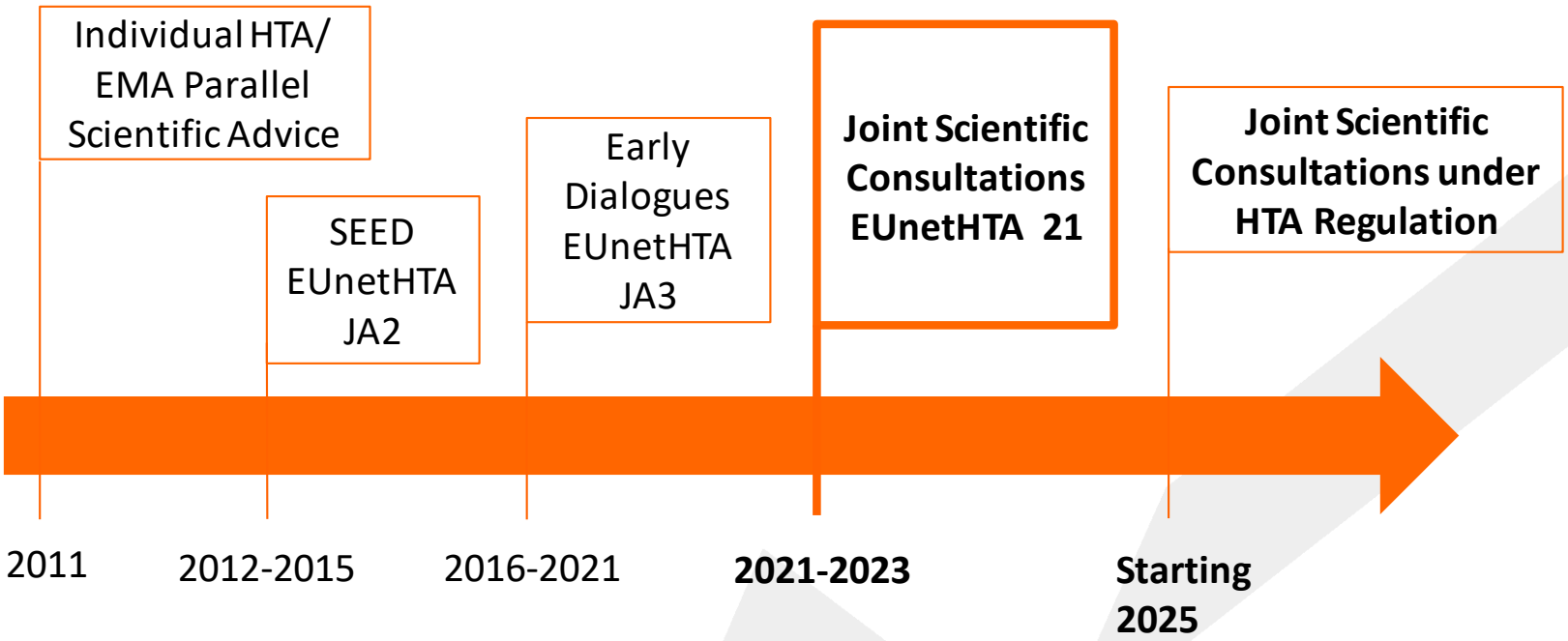
3. **Update on status of deliverables**

Antje Behring, G-BA
Roisin Adams, NCPE

3a. **Joint Scientific Consultations**

Antje Behring, G-BA

EUnetHTA history and joint consultations



EUnetHTA 21 JSCs Background

EUnetHTA 21 service contract

- **6 - 8 parallel EMA/EUnetHTA 21 Joint Scientific Consultations (JSCs)** planned until September 2023

Part of the EMA/EUnetHTA 21 work plan 2021 – 2023

- Joint EMA and EUnetHTA 21 activity: **Joint Scientific Consultation (JSC) for robust evidence generation**

➢ All EUnetHTA 21 JSCs are done in parallel with EMA

EUnetHTA 21 JSCs
What is new (compared to EUnetHTA JA3)?

- At least 6 participating HTA institutions in each JSC
  - Final deliverable (Final Written Recommendations) validated by 11 HTA institutions (EUnetHTA 21 Committee for JSC: CSCQ JSC)
- Open Call system
- EU HTA Regulation selection criteria applied, with a slight focus on oncology products, ATMPs and orphan drugs, as these will be the first candidates for evaluations – Joint Clinical Assessments (JCA)
- No focus on medical devices (MD)
- Post-launch evidence generation (PLEG) advice only in conjunction and when contextualized with clinical data from phase II/III pivotal trials
- No “Written-only” or “HTA-only” format
- Systematic involvement of patients and clinicians

EUnetHTA 21 JSCs
Open Call system

- 2 Open Calls for JSCs during EUnetHTA 21 project phase
  - Open Calls completed and 8 products have been prioritized

1st Open Call for parallel EMA/EUnetHTA 21 JSCs: 8 Nov - 7 Dec 2021

3 products selected: 2 oncological and 1 non-oncological products - 3x First in class (FC), 2x Orphan designation (OD), 1x PRIME

- 1st batch JSCs: JSC 001 – 003 completed

2nd Open Call for parallel EMA/EUnetHTA 21 JSCs: 6 June - 31 Aug 2022

5 products selected: 3 oncological and 3 non-oncological products - 5x First in class (FC), 2x Orphan designation (OD), 2x ATMP, 1x PRIME and 1x SME

- 2nd batch JSCs: JSC 004 started in October, JSC 005 will start beginning of December

Selection Criteria for JSCs according to EU HTA Regulation Art. 17 (3)

a. Unmet medical needs (no treatment or only unsatisfactory treatment available);

b. First in class;

   First representative of the class of substances for the disease in question, and have a unique mechanism of action. There must be no authorised substance in this class for the disease in question.

c. Potential impact on patients, public health, or healthcare systems;

d. Significant cross-border dimension;

e. Major Union-wide added value; or

f. Union clinical research priorities

There is no prioritisation or ranking of selection criteria in the regulation, nor do all criteria have to be met.

Further elaboration by EUnetHTA 21: https://www.eunethta.eu/jscfaq/

Expert involvement for JSCs during EUnetHTA 21

Who can get involved?
Based on requirements from the HTA Regulation

As external experts

(no stakeholder participation in JSCs)

- ➢ Patients (or close carers) affected by the disease or condition
- ➢ Clinical experts

- ▪ Speaking on their own behalf
- ▪ Able to provide input beyond the borders of their own Member State

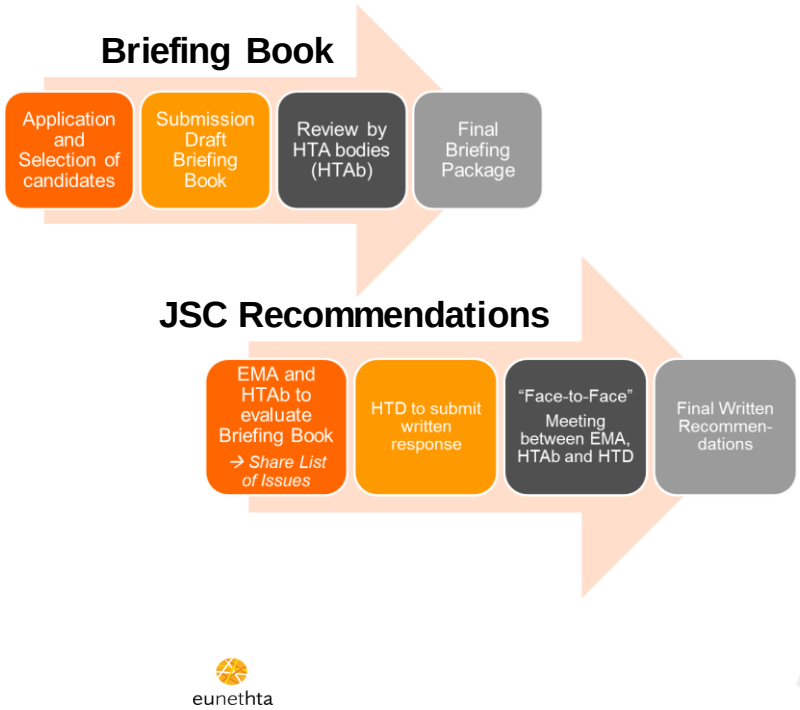
- ➢ Must complete the Declaration of Interest (DOI) form and the EUnetHTA21 Confidentiality Agreement (ECA)
  - ▪ The documents are reviewed by the EUnetHTA21 Conflict of Interest Committee (COIC)
  - ➢ Exceptional cases defined in the guidance e.g. for rare diseases

More information can be found here:

https://www.eunethta.eu/coic/

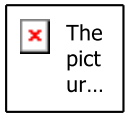
When are patients & clinical experts involved in EUnetHTA 21?

Joint Scientific Consultation (JSC) process



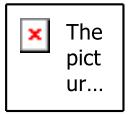
- Interview or written statement before List of Issues
  - At the latest **before the Face-to-Face meeting**
- Review and provide feedback on List of Issues
- Participation in Face-to-Face meeting with company
- Final Written Recommendations to be shared with experts

Relevant Documents for JSC expert involvement during EUnetHTA 21



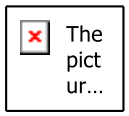
1. Briefing package/Briefing Book for JSC

- Contains all information provided by the company for the consultation (e.g. development plan) and the questions to EMA and HTA organisations



2. Input template for external experts for JSC

- Contains questions about the specific disease, e.g. relevant symptoms and current treatment limitations
  - As a written statement of the expert or filled out by the Assessor during an interview



3. Final Written Recommendations for JSC

- Final output document of the procedure
  - Contains the recommendations of the HTA institutions
  - **Includes the full expert contribution as an annex**
  - Patients will not be named, but an anonymized description of the patient(s) will be included. Clinical experts can be named upon approval.

Expert recruitment for JSC 001 – 003
Experiences gained so far during EUnetHTA 21

JSCs Year 1 EUnetHTA 21	Expert involvement	
	Patients	Clinical experts
JSC 001	1x Patient European level 2x Patient national level via interview	1x Clinical expert input on SOC national level 2x Clinical expert national level via written statement
JSC 002	1x Patient European level 2x Patient national level via interview	1x Clinical expert input on SOC national level 2x Clinical expert national level via written statement
JSC 003	2x Patient national level via interview	1x Clinical expert European level 1x Clinical expert input on SOC national level 2x Clinical expert national level via written statement

- National expert recruitment not within the remit of the EUnetHTA 21 guidance document for patient and HCP involvement

Expert recruitment for EUnetHTA 21 JSCs
Experiences gained so far during EUnetHTA 21

- Expert recruitment always within tight timelines
- If you are contacted by the JSC Secretariat a response in a timely manner is much appreciated
- Challenges of expert recruitment – patients and HCPs: collaboration of JSC Secretariat with other HTA organisations and also EMA to find experts

➢ At the moment we are in the process of building a functional network of contacts: sources, e.g. EUnetHTA 21 stakeholder repository, EMA eligible patient organisations etc.

➢ Differences in EMA vs. EUnetHTA 21 COI policy

Your help and support upon initial contact is much appreciated!

Thank you in advance!

THANK YOU!
Any questions?

EUnetHTA 21 JSC Secretariat
EUnetHTA21-JSC@g-ba.de

3b and 3c. **Joint Clinical Assessments & Transversal activities**

Roisin Adams, NCPE

HTA in the EU context

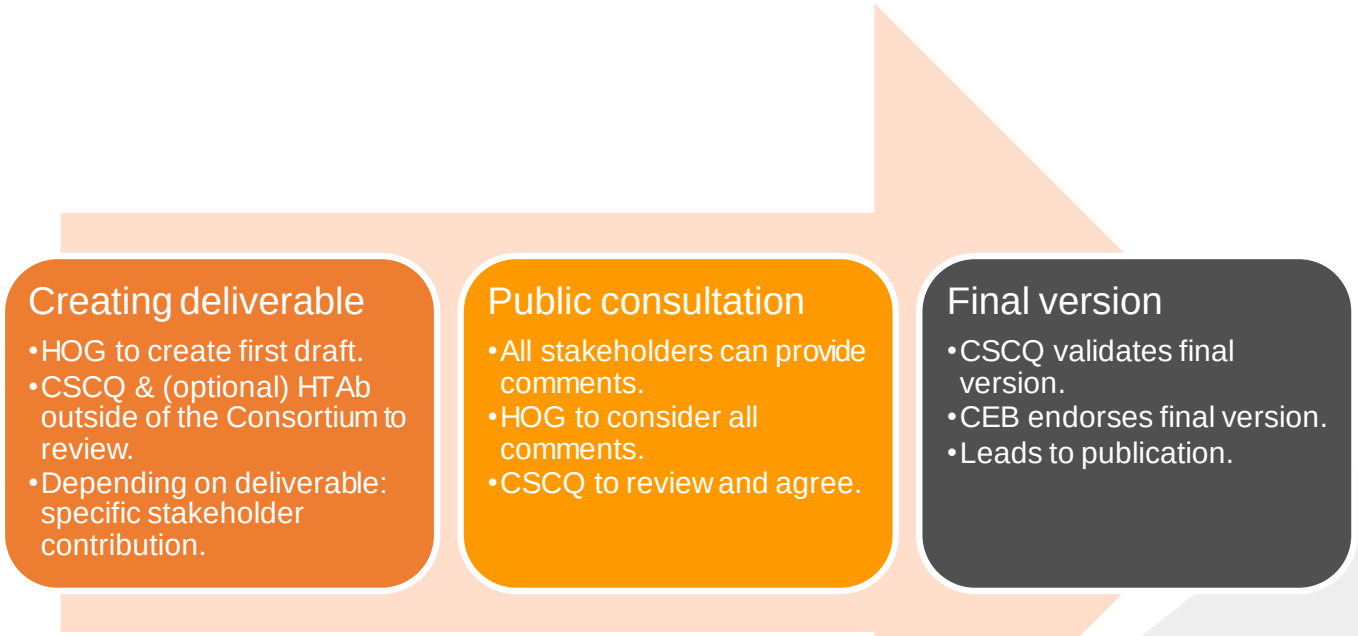
Joint Clinical Assessments

Joint Scientific Consultations

Horizon Scanning/ Emerging Technologies

Voluntary Cooperation

Process flow for deliverable production



Progress of EUnetHTA 21 deliverables

https://www.eunethta.eu/jointhtawork/

Deliverable	Title	Status
D5.3.1	*Selection criteria (co-)assessor JCA*	*Published*
D5.3.2	*HTA body technical expert working groups*	
D4.2	*Practical Guideline – Scoping Process*	
D4.3.2	*Methodological Guideline – Direct & Indirect Comparators and Comparisons*	
D4.7.1, 4.7.2	*Framework for JCA of high risk MD*	
D4.7.3, 4.7.4	*EUDAMED data reporting template/Guidance for EUDAMED-based TISP process*	*In progress*
D4.5	*Practical Guideline Applicability of Evidence*	*In progress – publication expected in December 2022*
D4.6	*Practical Guideline Validity of Clinical Studies*	*Finalized by EUnetHTA 21. Publication expected in November 2022, pending EC review*
D5.1	*Submission Dossier Template Guidance*	
D7.1	*Practical Guideline HTD and HTA interaction*	
D5.2	*JCA report template Guidance*	
D7.2/7.3	*Patient and HCP guidance & templates for interaction*	
D4.4	Practical Guideline Endpoints	Public consultation closed (1/11/2022)
D6.2/6.3&6.4	JSC briefing book template & procedural guidance	Ongoing – public consultation in August 2023

Collaboration with Regulators

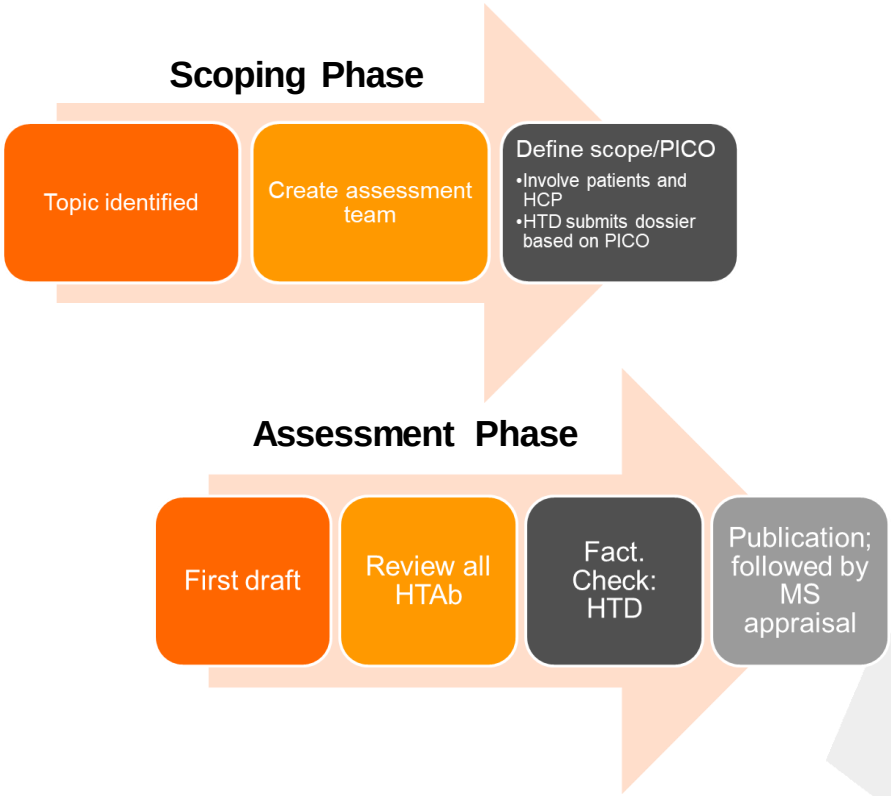
Contribution through the joint EMA/EUnetHTA21 work plan

Joint scientific consultation on evidence generation, including PLEG Exchange of information on the respective assessments of medicinal products by regulators and HTA bodies Continuous optimisation of regulatory outputs	Study methods and guide-lines of real-world evidence, including for registries Methodologies for engage-ment of patients and HCPs Extrapolation / evidence transfer as tool to support assessment in smaller populations	Generation of patient relevant data / information to support decision making Practices in the context of companion diagnostics Horizon scanning and preparedness of HTA and regulatory systems

- Oversight through biannual EMA/EUnetHTA 21 bilaterals (most recent on 17th June 2022)
- In addition, exchange on selected EUnetHTA 21 deliverables

Process for patient and clinical expert involvement

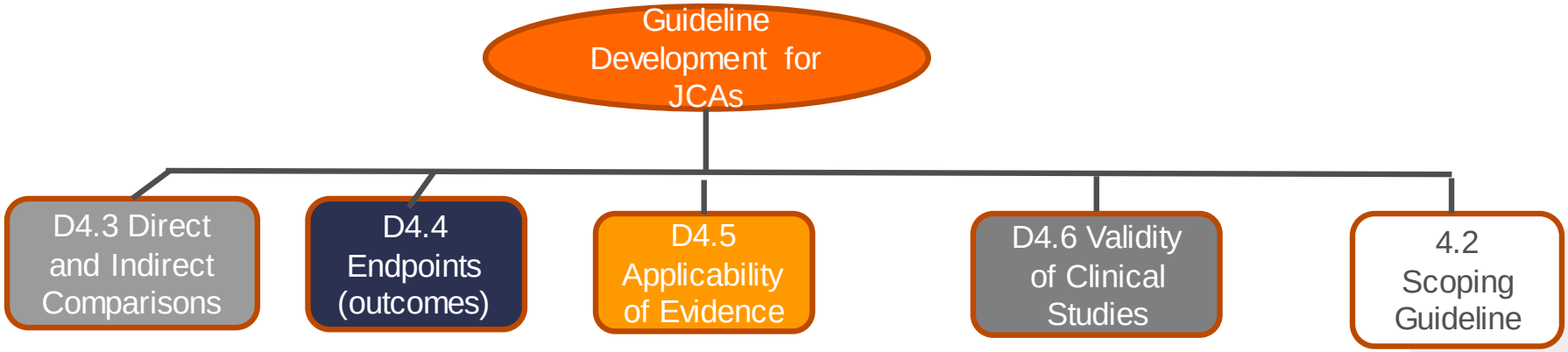
When are patients & clinical experts involved in EUnetHTA 21?
Joint Clinical Assessment process (JCA)



- When **defining the PICO**
  - By means of online questionnaire
  - Interviews with external experts may be conducted
  - External experts may participate in the PICO consolidation meeting
- During the assessment phase they answer questions the Assessor and Co-Assessor may have
- National procedure is not in remit of HTA Regulation
  - but the EUnetHTA 21 guidance highlights where this could take place

Deliverables on methodology

EUnetHTA21 Deliverables: Methodology



D4.3 - Methods of Direct and Indirect Comparison

Fundamental assumptions

- Synthesis of relative treatment effects
- Similarity, homogeneity, consistency
- Fixed and random effects

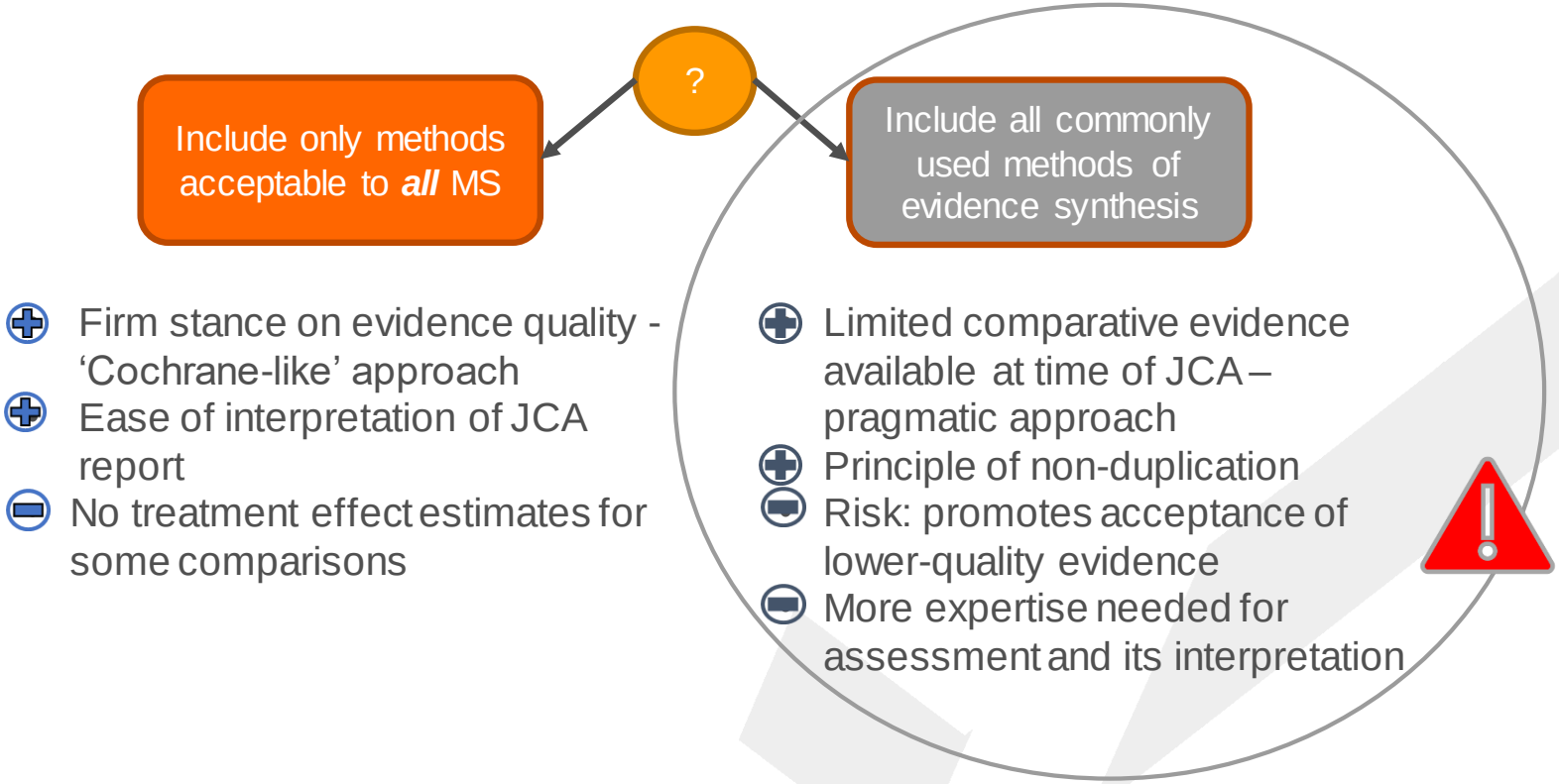
“Established” methods

- Pairwise meta-analysis, typically frequentist
- Bucher ITC
- More general NMA

“Emerging” methods

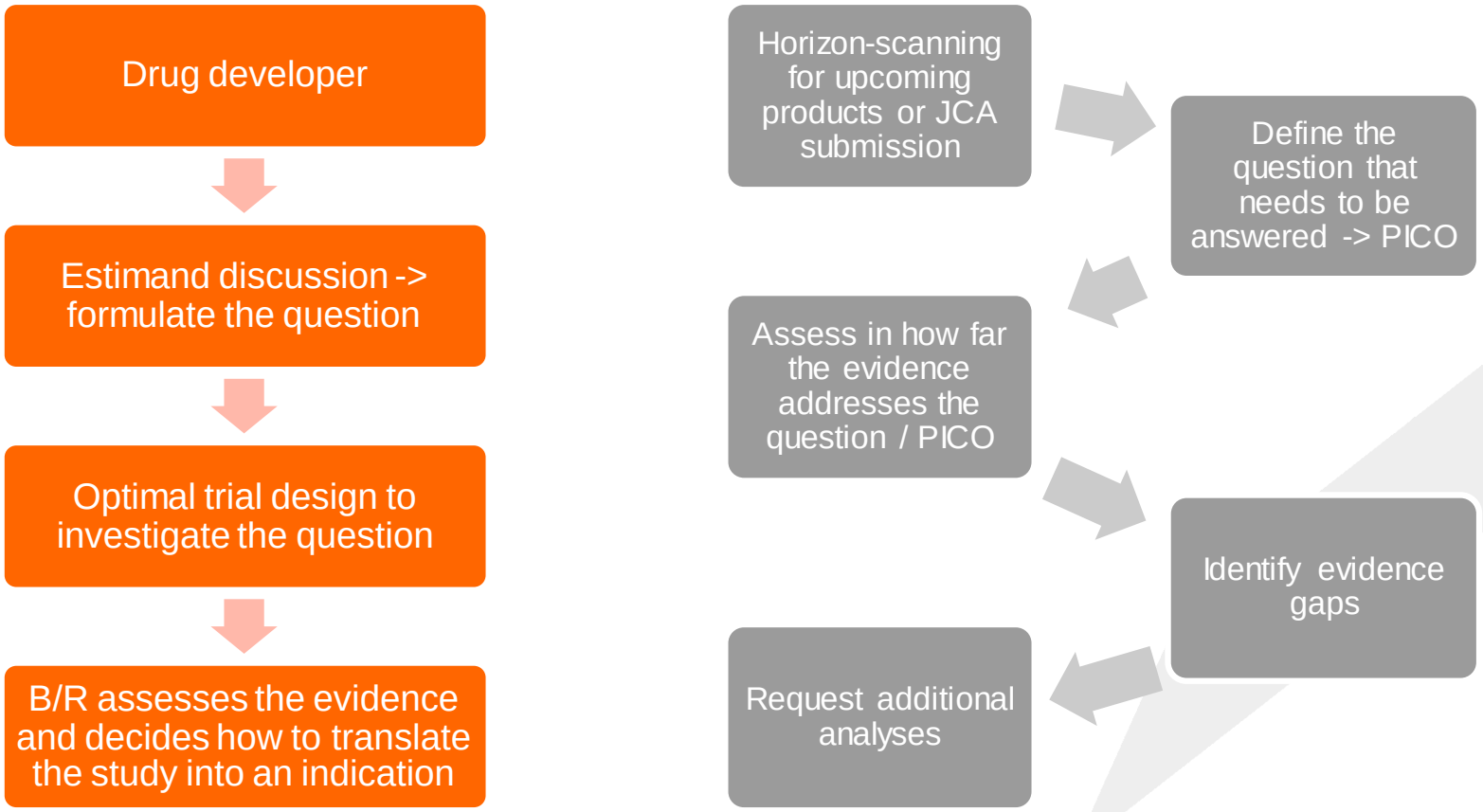
- Connecting disconnected networks - single armed studies
- Population adjustment - MAIC/STC
- Flexible survival models
- Sparse data – rare events, few studies
- Bayesian methods – incorporating external (prior) information

D4.3. Key Question - Acceptability of methods in JCA



How do we formulate our question in HTA?

Process of defining the questions



Anja Schiel, NOMA

PICO's don't just emerge out of thin air!

Population: they change with new drugs entering the market, they are defined by national treatment preferences, clinical guidelines and access (reimbursement or not)

- Mapping the landscape and keep updated on changes during the development phase

Intervention: it is your drug after all…

- It helps to have optimised your posology

Comparator: same as populations, they change with new drugs coming to the market, reimbursement decisions etc

- Mapping the landscape and keep updated on changes during the development phase
- Plan from day 1 how to support the external validity exercise

Outcomes: the least variable, clear preferences,

- Primary endpoints are for regulators to plan the study, HTAs look at all endpoints!

Anja Schiel, NOMA

Take home message on PICOs

- Prepare early
- Use the JSC process to begin to define your PICOs (PLEASE!)
- Use opportunities to interact with national bodies early to understand more on comparators.

JCA in EUnetHTA21

- We received no JCA submissions from HTDs for pharmaceutical products.
- 2 JCAs from HTDs for medical devices.

Status of JCA production in EUnetHTA 21

- 2 JCA for Medical Devices
  - JCAMD001: The Optilume® Urethral DCB Catheter is used to treat men ≥18 years of age with bothersome urinary symptoms associated with recurrent anterior urethral stricture.
    - Patient organisation & healthcare professional questionnaires closed. Thanks for your input!
  - JCAMD002: Saluda Medical Evoke® Spinal Cord Stimulation System as an aid in the management of **chronic intractable pain** of the trunk and/ or limbs
    - the patient organisation & healthcare professional organisation questionnaire is online
      - https://www.eunethta.eu/get-involved/online-questionnaires/ (until December 14; the earlier the better)
      - Also searching for individual patients & clinical experts
- Pharmaceutical JCA
  - Mock exercises to be conducted, to test the developed procedures and guidelines

THANK YOU!
Any questions?

4. **Q&A**

Niklas Hedberg, TLV

5. **Closing remarks**

Niklas Hedberg, TLV

Thank you