HTA CG | MEMBER STATE COORDINATION GROUP ON HEALTH TECHNOLOGY ASSESSMENT

EU HTA Regulation for Health Technology Developers

SME Webinar
15 November 2024

Webinar Agenda

1. Governance and Role of HTA Coordination Group	Dr Roisin Adams, Chair of HTA CG
2. Joint Scientific Consultation (JSC) Process	Stephanie Said, Chair of JSC Subgroup
3. Letter of Intent Submission Process	Bela Dajka, European Commission Policy Officer
4. Joint Clinical Assessment (JCA) Process	Anne Willemsen, Co-Chair of JCA Subgroup
5. Methodologies and Procedures	Dr Beate Wieseler, Chair of MPG Subgroup

Chair of the webinar - Niklas Hedberg, Co-Chair of HTA CG

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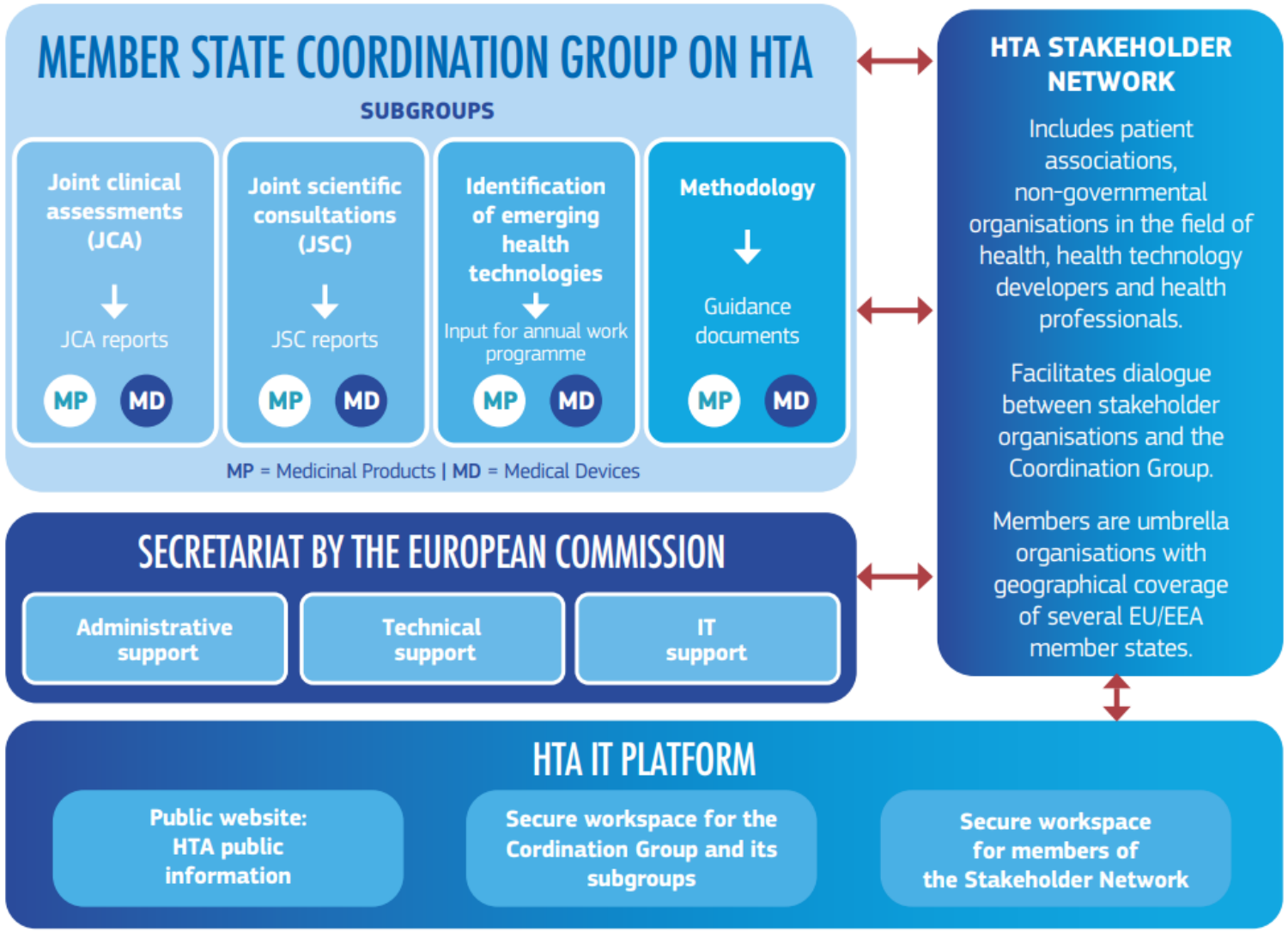
Governance and role of HTA Coordination Group

Roisin Adams
Chair of the HTACG
SME webinar, 15 November 2024

Governance

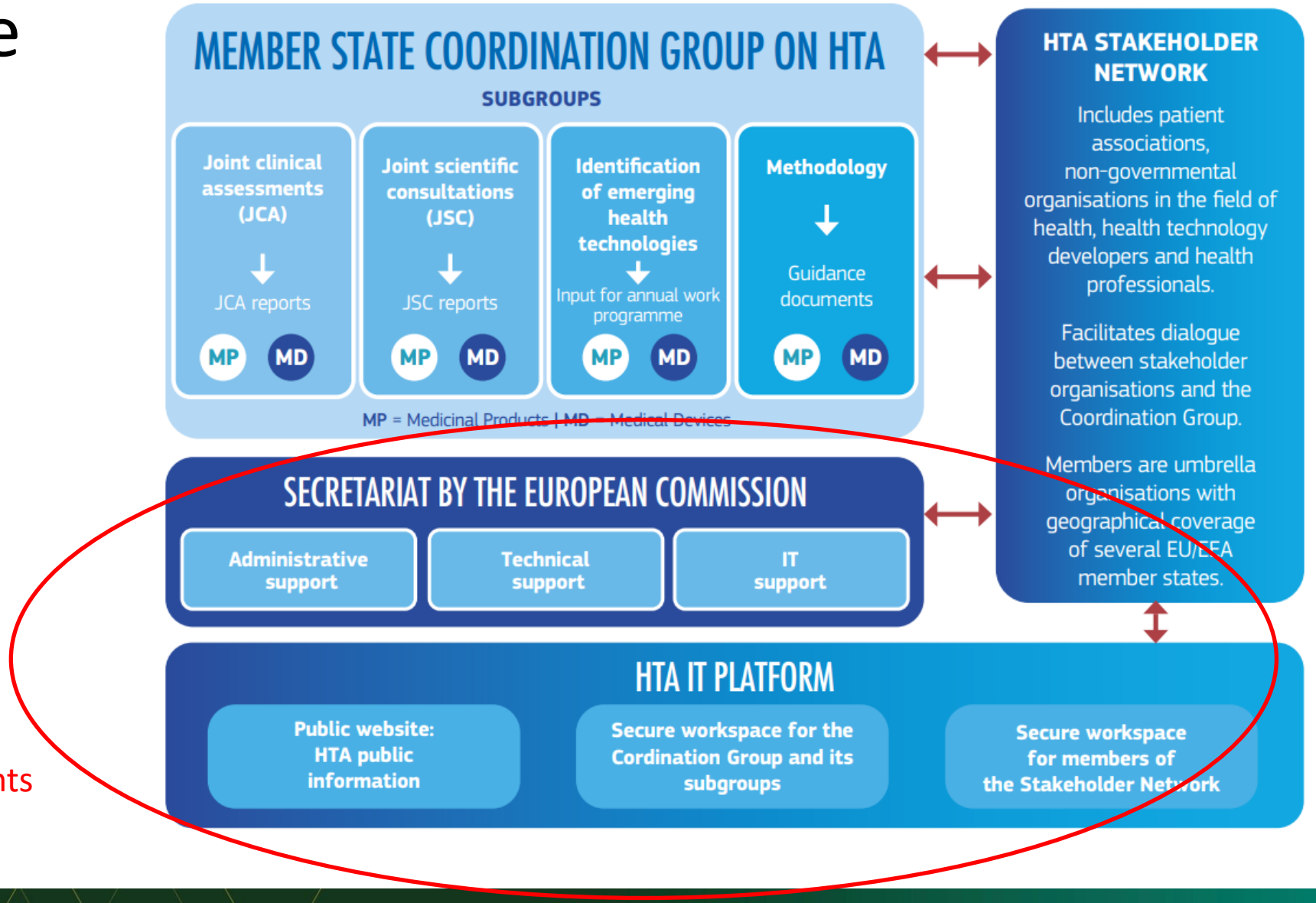

MEMBER STATE COORDINATION GROUP ON HTA
SUBGROUPS
Joint clinical assessments (JCA)
JCA reports
MP
MD
Joint scientific consultations (JSC)
JSC reports
MP
MD
Identification of emerging health technologies
Input for annual work programme
MP
MD
Methodology
Guidance documents
MP
MD
MP = Medicinal Products | MD = Medical Devices
HTA STAKEHOLDER NETWORK
Includes patient associations, non-governmental organisations in the field of health, health technology developers and health professionals.
Facilitates dialogue between stakeholder organisations and the Coordination Group.
Members are umbrella organisations with geographical coverage of several EU/EEA member states.
SECRETARIAT BY THE EUROPEAN COMMISSION
Administrative support
Technical support
IT support
HTA IT PLATFORM
Public website: HTA public information
Secure workspace for the Cordination Group and its subgroups
Secure workspace for members of the Stakeholder Network

HTACG – Role and Responsibility

Article 3: Member State Coordination Group on Health Technology Assessment

- MS shall appoint members and representatives and elect a Chair(s).
- Adopt all scientific and procedural guidance needed.
- Provide strategic direction
- Establish subgroups
- Decide and publish on an annual work programme
- Meet in joint configuration (MP & MD)

Governance



Applicant
HTD Interaction points

Information on work of HTACG and Subgroups

Member State Coordination Group on HTA (HTACG)

PAGE CONTENTS

The Regulation on health technology assessment (HTAR) established the Coordination Group on Health Technology Assessment (the 'HTACG') composed of Member States' representatives, mainly from HTA authorities and bodies.

The key tasks of the HTACG are to coordinate and adopt the joint HTA work carried out by its sub-groups within the scope of this Regulation and to adopt methodological and procedural guidance documents for joint work.

The HTACG also aims to ensure cooperation between the relevant European Union bodies (e.g. the European Medicines Agency), as well as appropriate involvement of stakeholder organisations and experts in its work.

Members of the HTACG

The members of HTACG are designated by the Member States in accordance to Article 3(2) of the Regulation (EU) 2021/2282, following a request from the Commission. Observers from EEA countries are designated following a similar procedure.

As laid down in Article 3(8), the HTACG will provide expertise on HTA for both medicinal products and medical devices (the latter covering also in vitro diagnostic medical devices).

- Members and EEA observers of the HTACG – medical devices
- Members and EEA observers of the HTACG – medicinal products

Members of the subgroups

https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment/member-state-coordination-group-hta-htacg_en

IMPLEMENTATION ROLLING PLAN

2023-2024

REGULATION (EU) 2021/2282 ON HEALTH TECHNOLOGY ASSESSMENT

This rolling plan contains a list of key activities that the Commission has carried out or intends to carry out in preparation for the implementation of Regulation 2021/2282 Health Technology Assessment (the "HTAR"). The plan is subject to regular review to provide national authorities and stakeholders with the most updated information.

The HTAR entered into force on January 11, 2022. It will be applicable as of January 12, 2025.

Latest update: September 2024

Rolling plan available at: https://health.ec.europa.eu/document/download/397b2a2e-1793-48fd-b9f5-7b8f0b05c7dd_en

Thank you!

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HEALTH TECHNOLOGY ASSESSMENT

Joint Scientific Consultation Process

Stephanie Said
Chair of the JSC Subgroup

Governance JSC for Medicinal Products

Joint Scientific Consultations

	Health Technology Assessment
Secretariat	**European Commission**
Approval and decision adoption	**HTACG** (Member State Coordination Group on Health Technology Assessment) Members are national HTA authorities and bodies; and Ministry of Health
Technical work	**SG JSC** (Subgroup for Joint Scientific Consultations)
Legal basis	REGULATION (EU) 2021/2282: EU-HTA Regulation

Governance JSC for Medicinal Products

Joint Scientific Consultations in parallel with Scientific Advice

	Regulatory	Health Technology Assessment
Secretariat	**EMA**	**European Commission**
Approval and decision adoption	**CHMP** (Committee for Medicinal Products for Human Use) Members are national competent authorities	**HTA CG** (Member State Coordination Group on Health Technology Assessment) Members are national HTA authorities and bodies; and Ministry of Health
Technical Work	**SAWP** (Scientific Advice Working Party)	**JSC SG** (Subgroup for Joint Scientific Consultations)
Legal Basis	REGULATION (EC) 726/2004	REGULATION (EU) 2021/2282: EU-HTA Regulation

Legislation and Guidance documents

HTA Regulation

- Art. 3.7, 6.2 b
- Section 1 JCA. Art. 8.4, 8.5
- **Section 2 JSC. Art. 16-21**
- Art. 27.2, 30.3 k, 31.1 c

Commission implementing regulation

- Conflict of interest management: Adopted 25 Oct 2024
- Cooperation by exchange of information with the EMA: Adopted 25 Oct 2024
- **JSC Medicinal Products: to be agreed end of next week**
- JSC Medical Devices: ongoing public consultation

Guidance documents

- *Procedural guidance for JSC*
- *Guidance for the selection of JSC*
- *Guidance on the appointment of assessor and co-assessor*
- *Submission request template*
- *Briefing package templates*
- *Outcome document*

Key facts and key milestones

Number of JSC will be communicated in the work programme at the latest by 30 November of each year

- For 2025: ~ 10 JSC planned with the aim to continuously increase capacities in the coming years
- 2 request periods planned for 2025: 3.2.-3.3.2025 + 2.-30.6.2025

To apply: Request template must be submitted during a request period and justify eligibility and fulfilled selection criteria

Submission of Briefing package in case of selection:

- Briefing document template:
  - PICO (Population, Intervention, Comparator and Outcomes)
  - Post Licensing Evidence Generation (PLEG) only in conjuction with study design
  - Health Economic Assessment (voluntary cooperation)

Key facts and key milestones

Selection process will be laid down in the Guidance on JSC selection:

- Step-wise approach: Eligibility criteria → selection criteria → number of JSC scheduled for the request period

Feedback loop during the process: List of Issues (LoI) for HTD and Written response to LoI by HTD

Direct exchange: Discussion meeting with HTD

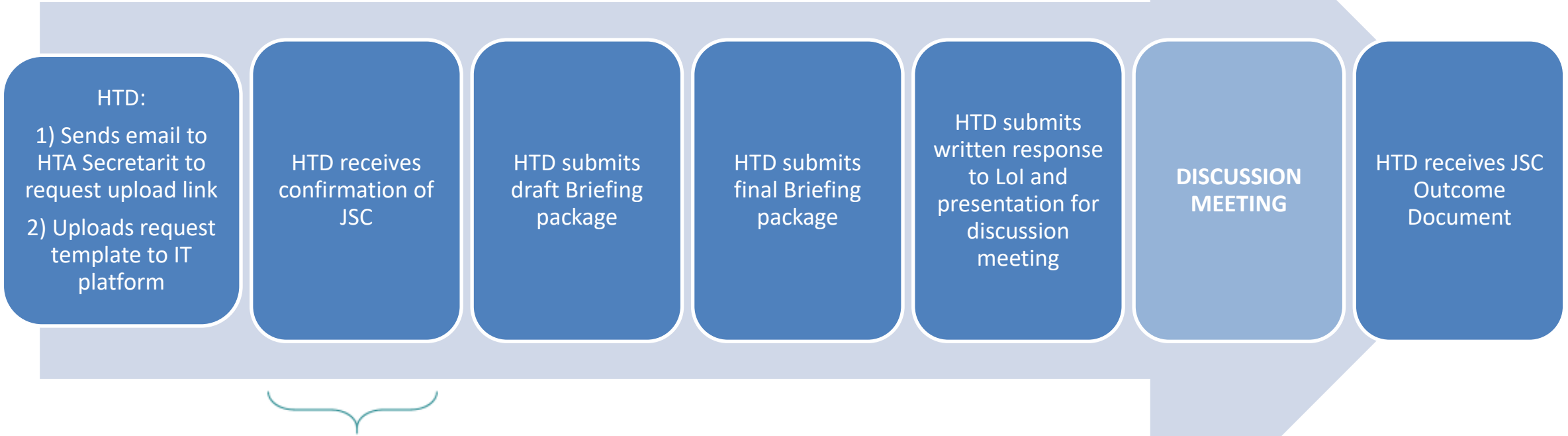
Outcome of the JSC procedure: JSC Outcome Document with common position + individual positions by MS in an annex (further specifications)

- Not legally binding but should reflect the state of the art of medical science at the time of the JSC

Process overview: HTD action points

During the request period

Duration: approximately 4.5 months, from the receipt of the draft Briefing package



- Within 15 working days after the end of each request period, the Coordination Group shall inform the requesting health technology developer whether it will engage in the joint scientific consultation

JCAs and JSCs: Practical information for HTDs

Webinar for health technology developers

15 November 2024

Bela Dajka, Policy Officer

Directorate-General for Health and Food Safety, European Commission

Submission of early information for JCA

- Possibility to send the EMA Letter of Intent to the HTA Secretariat
- Secure upload link via the HTA IT Platform

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Digital, EU4Health and Health systems modernisation
State of Health, European Semester, Health technology assessment

Joint clinical assessment of medicinal products: Submission of early information by health technology developers

After 12 January 2025, medicinal products falling under the scope of Article 7(2), point (a) of Regulation (EU) 2021/2282 (the HTA Regulation) will be subject to a Joint Clinical Assessment (JCA). Initially, the JCA will concern medicinal products with new active substances for which the therapeutic indication is the treatment of cancer as well as advanced therapy medicinal products. As of 13 January 2028, all medicinal products designated as orphan medicinal products and, as of 13 January 2030, all other medicinal products falling under the scope of Article 7 of Regulation 2021/2282 are also subject to JCA.

The EMA published guidance on 21 June 2024 to applicants/health technology developers on how to declare in the EMA Letter of Intent (via the Pre-submission request form) whether their application falls under the scope of the Health Technology Assessment Regulation ((EU) 2021/2282 Article 7) and, therefore, is subject to JCA. The Member State Coordination Group on Health Technology Assessment published a document entitled *"Scientific specifications of medicinal products subject to joint clinical assessments"* to support identification of products subject to JCA from 2025.

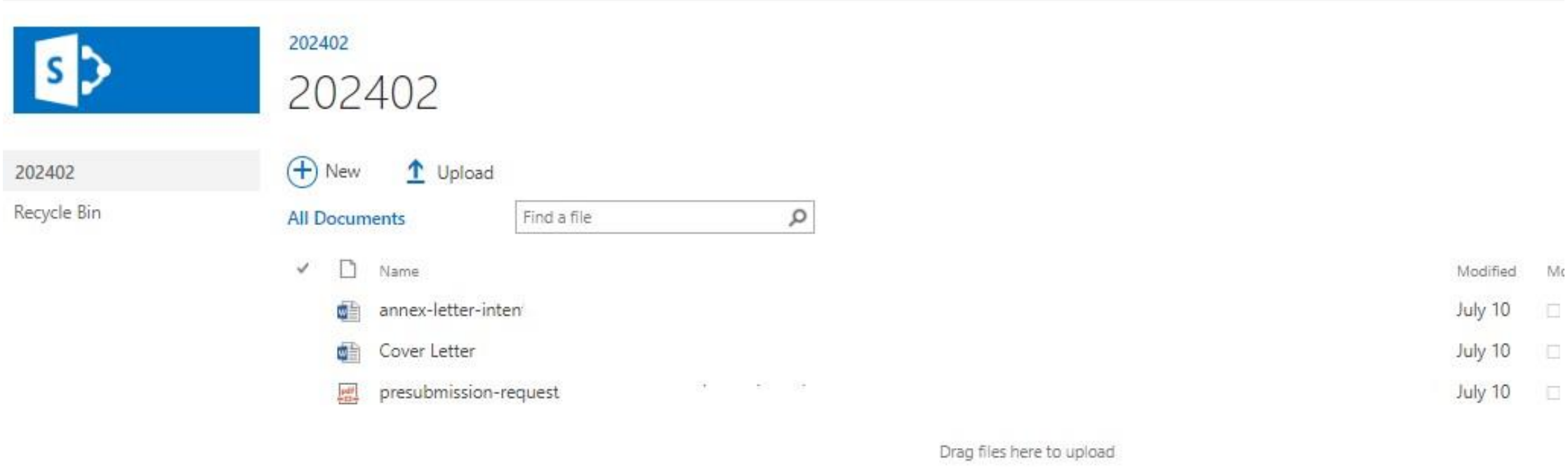
Pre-authorisation guidance

2.4.1.2 Declaring a product in scope of Joint Clinical Assessment (JCA) under the HTA Regulation (Regulation (EU) 2021/2282) in the Letter of Intent NEW June 2024

As of 13 January 2025, all medicinal products falling under the scope of Article 7 of Regulation (EU) 2021/2282, for which the applicant declares in its application for marketing authorisation that it contains a new active substance and the therapeutic indication is the treatment of cancer and those that concern ATMPs are subject to JCA. As of 14 January 2028, all medicinal products designated as orphan medicinal products and, as of 14 January 2030, all other medicinal products falling under the scope of Article 7 of Regulation (EU) 2021/2282 are also subject to JCA.

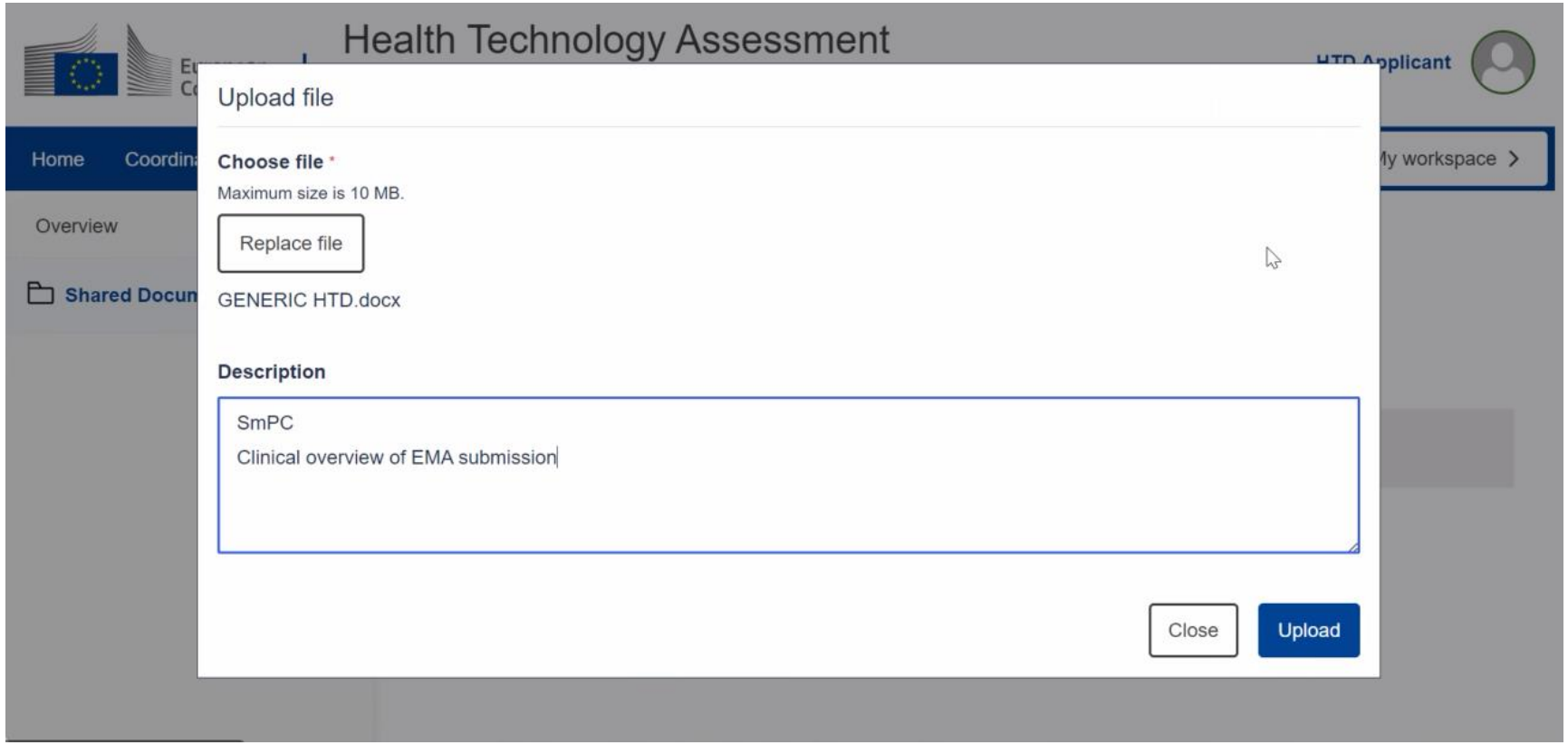
To facilitate and prepare the respective assessments, EMA and the secretariat of the Member State Coordination Group on HTA (HTACG) have agreed to use the same form for respective notifications. Therefore, on the basis of the type of submission for a marketing authorisation application and the planned submission time, applicants should declare in the Pre-submission request form whether their application falls under the scope of Article 7 of Regulation (EU) 2021/2282 and therefore is subject to JCA. This declaration shall be made alongside the request under section 1.1.1 (when selecting the indent "Intent to submit MA").

Pre-submission workspace

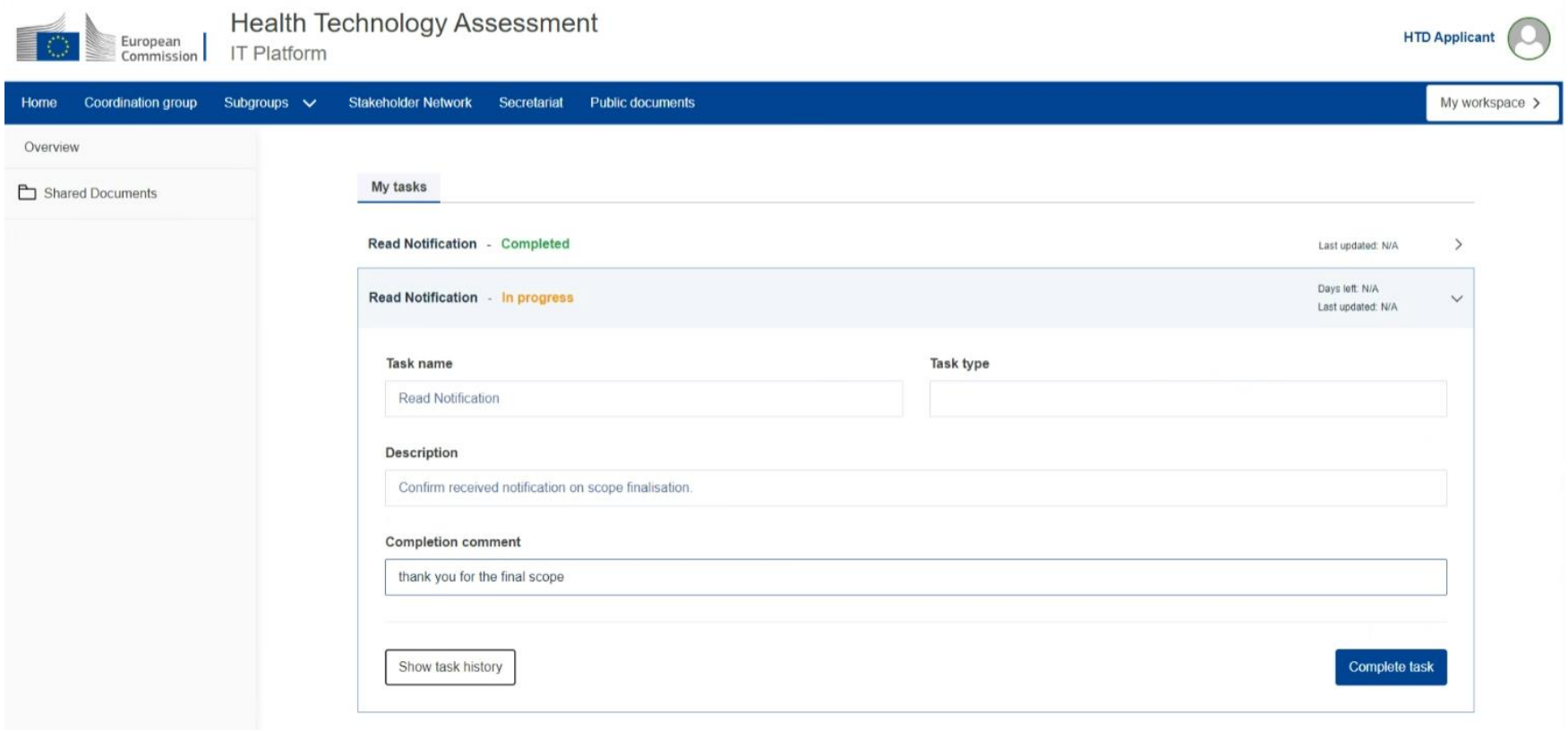


European Commission

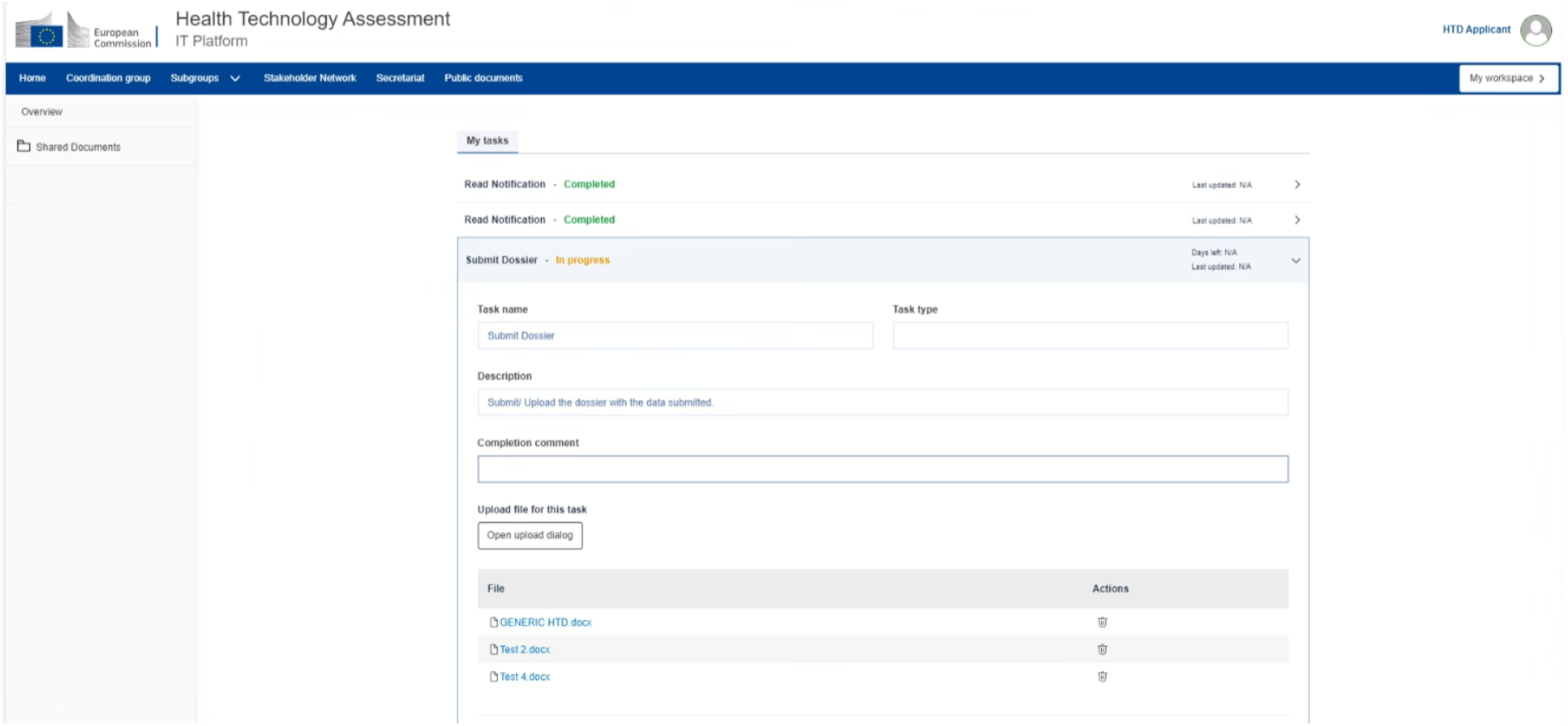
Start of JCA


Health Technology Assessment
HTD Applicant
Home
Overview
My workspace
Upload file
Choose file *
Maximum size is 10 MB.
Replace file
GENERIC HTD.docx
Description
SmPC
Clinical overview of EMA submission
Close
Upload

Notification after finalisation of assessment scope

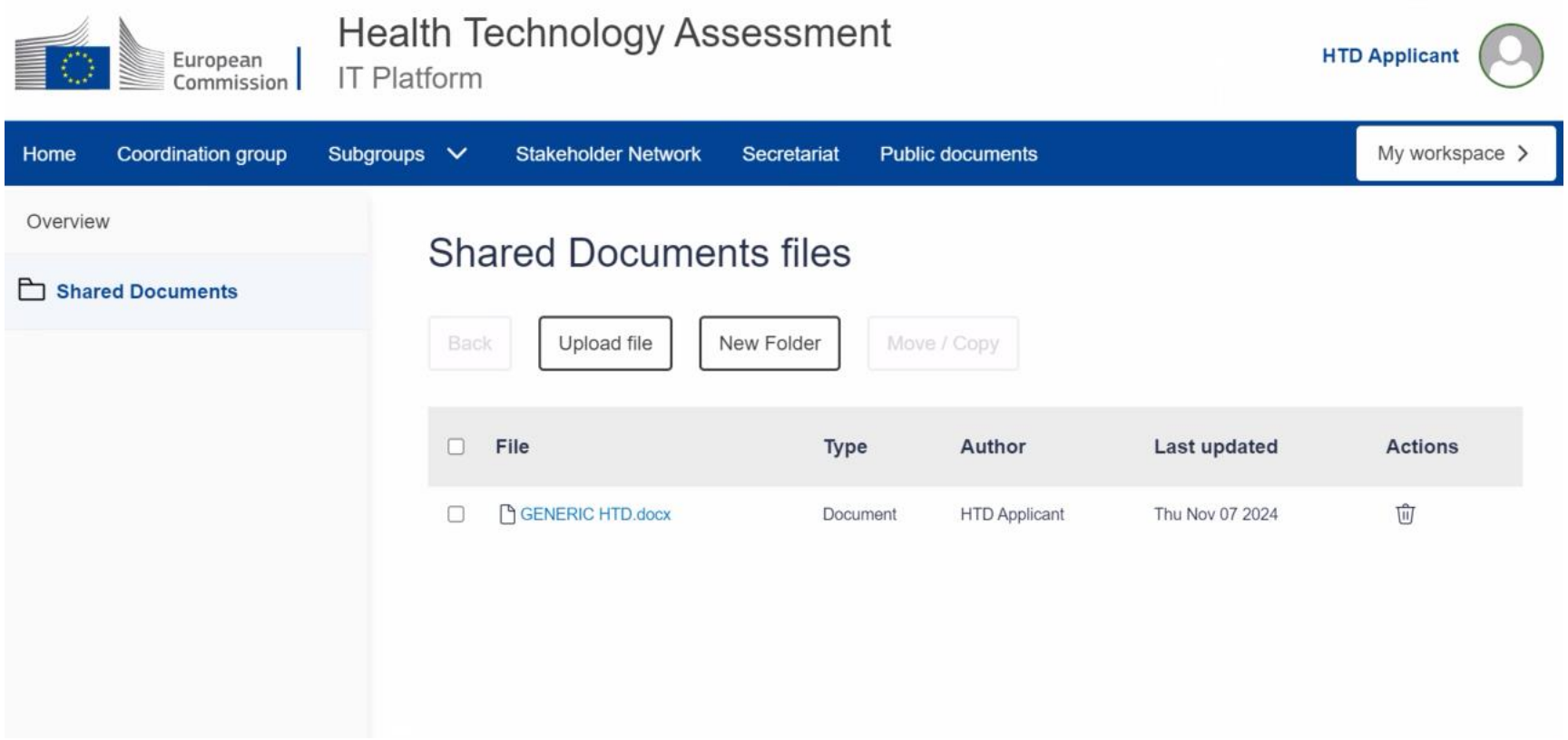


Notification for dossier submission



European Commission

JCA workspace



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Joint Clinical Assessment Process

Anne Willemsen
Co-Chair of the JCA Subgroup
SME webinar, 15 November 2024

Regulatory

EMA

Regulatory approval

- Does technology X work?
- Does the benifit of technology X outweigh the risks?
- Are there any additional needs for technology X post-licencing?

Single licensing system; one EU legislation

Health Technology Assessment

HTAR

In JCA: relative assessment of Technology X vs. Technology Y (and others)

- How does it compare to what we already have (fewer harms, in whom etc)

Relative effectiveness and relative safety

Clinical domain only!

- No value judgements
- No conclusions on added value or reimbursement
- Common methodology and approach

National

Appraisal phase

- e.g. cost effectiveness to be added
- Other considerations?
- Weighing arguments; decision making/reimbursement advice

JCA should be given due consideration in national decision-making

Scope of HTAR

➢Medicinal Products

- From Jan. 2025: JCA on oncology and ATMPs
- From Jan. 2028: + JCA on orphan drugs
- From Jan. 2030: full scope JCA
- Includes Type II variations, once a JCA has been conducted on the initial indication
- See Scientific specifications of MP subject to JCA for details

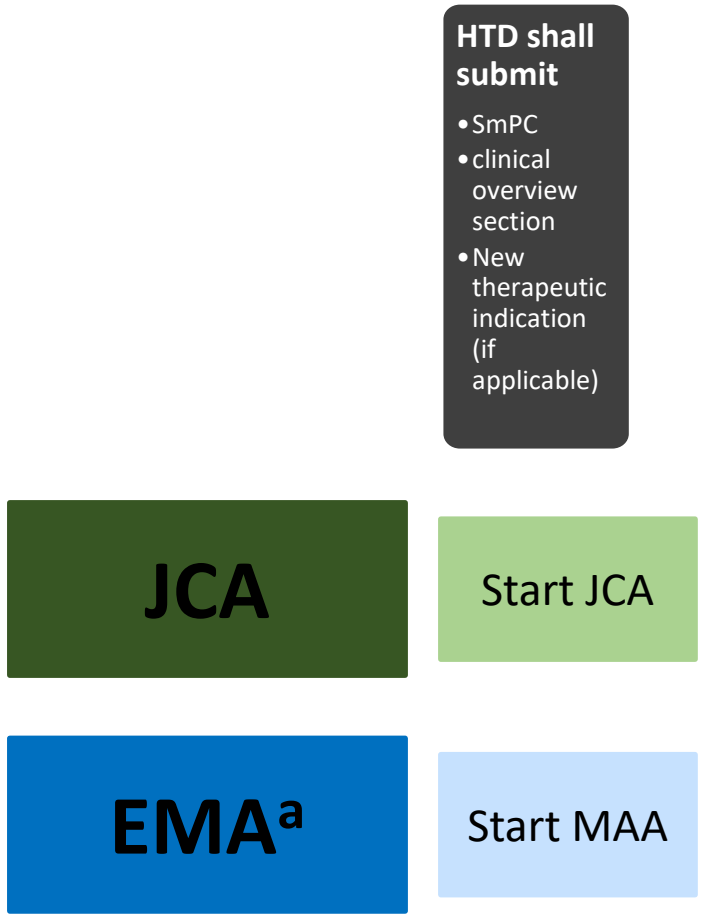
➢Medical Devices

- High risk MD, Type IIb, III and IVD

Joint Scientific Consultation (JSC)	Joint Clinical Assessment (JCA)
DEFINITION	
- Scientific advice - provided jointly by HTA bodies - Can be in parallel with regulators - To HTD on the clinical development	- Joint HTA reports, produced by 2 EU MS - On HTD submission dossier - HTD cannot submit data again on national level - Focussing on the **clinical domains** - **Without value judgements** - MS to give due consideration
AIM	
To generate evidence that satisfies the needs of HTA bodies during their assessment and ultimately facilitates patient access	To avoid duplications of work at the national level, increase consistency and quality of assessments and ultimately facilitate patient access
RELEVANT ARTICLES IN THE HTA REGULATION	
Art. 16 – Art. 21 Covering principles of JSC; Requests for JSC (& selection criteria); Preparation of JSC; Approval of JSC; Format and template for JSC	**Art. 6 – Art. 15** Covering annual work plan; Health technologies subject to a JCA; Initiation & PICO development; Obligations of HTD; Assessment process; Obligations Member States; Update of JCA

JCA timeline in parallel to EMA

a) Standard procedure for New Chemical Entities
b) Type II variation (Extension of Indication) and accelerated procedure
c) re-initiation of JCA or update of JCA without a new scope
d) Update of JCA with a new scope



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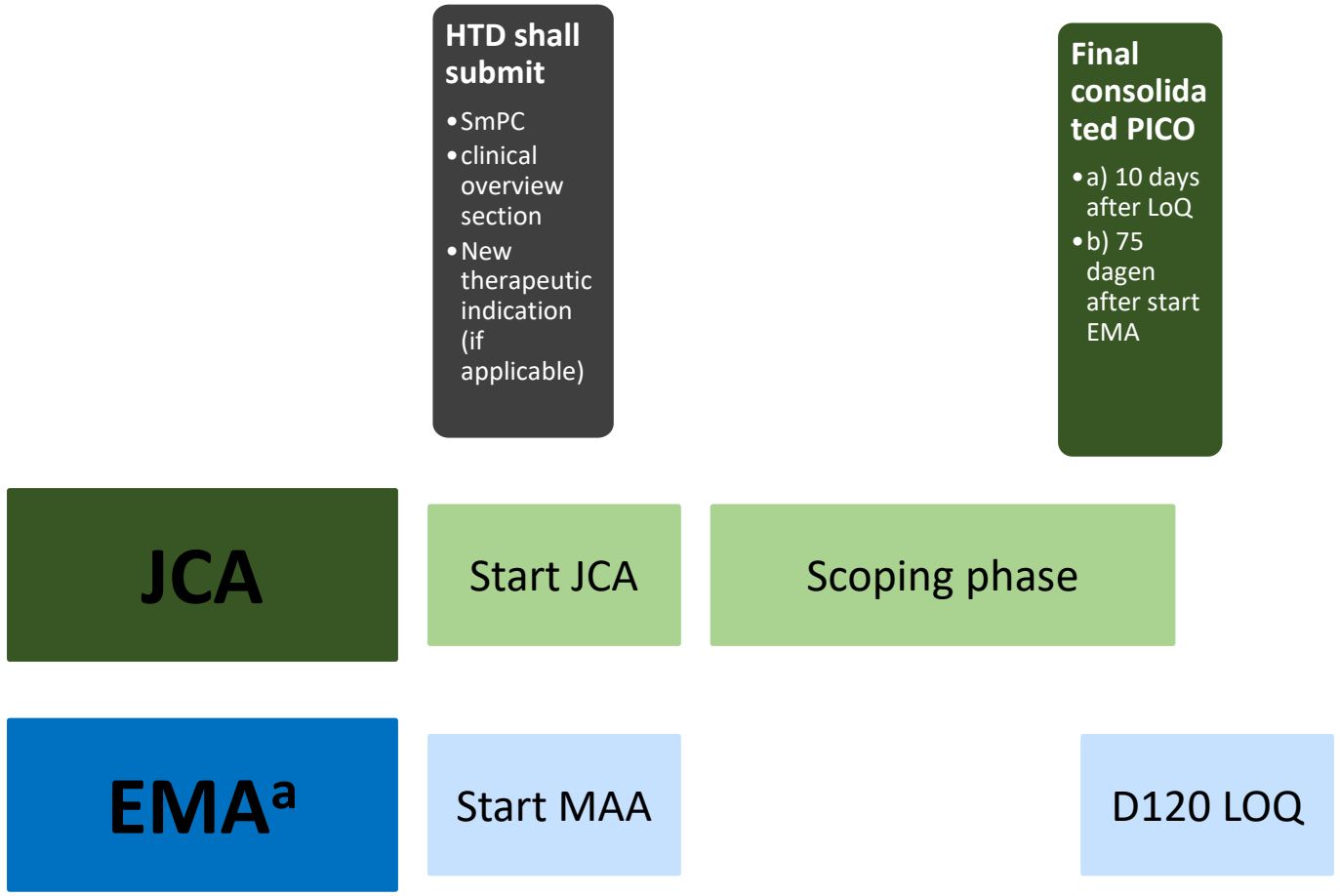

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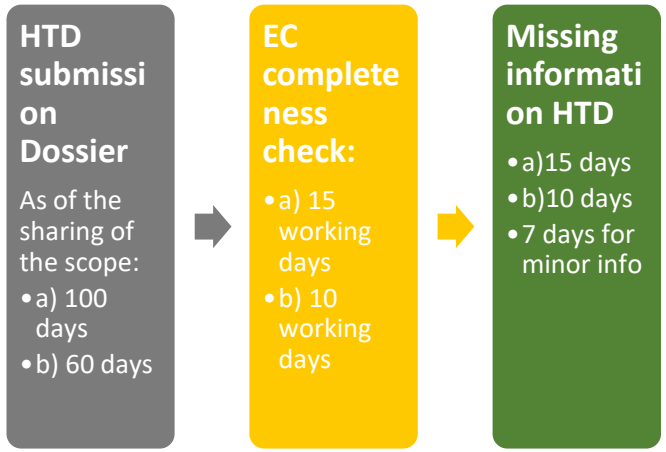

JCA	Start JCA	Scoping phase	Submission dossier
EMA[a]	Start MAA	D120 LOQ	

JCA timeline in parallel to EMA

a) Standard procedure for New Chemical Entities
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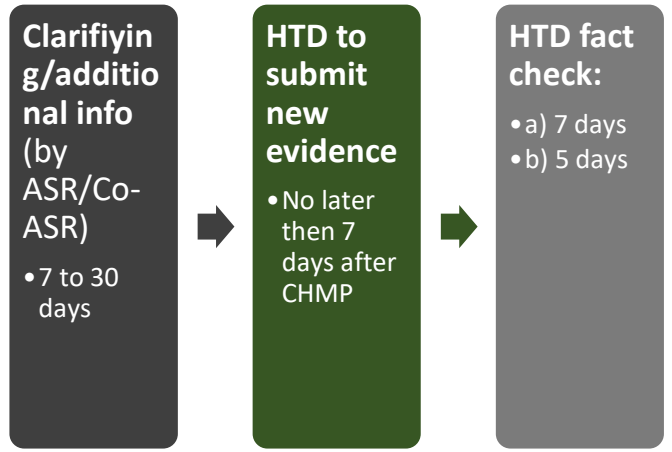


JCA	Start JCA	Scoping phase	Submission dossier	Drafting JCA	
EMA[a]	Start MAA		D120 LOQ		CHMP

JCA timeline in parallel to EMA

a) Standard procedure for New Chemical Entities
b) Type II variation (Extension of Indication) and accelerated procedure
c) re-initiation of JCA or update of JCA without a new scope
d) Update of JCA with a new scope

Finalize JCA

- The latest on the day of EC decision granting MA
- c) 180 days
- d) 330 days

JCA	Start JCA	Scoping phase	Submission dossier	Drafting JCA	Final JCA
EMA[a]	Start MAA	D120 LOQ		CHMP	CD

JCA timeline in parallel to EMA

a) Standard procedure for New Chemical Entities
b) Type II variation (Extension of Indication) and accelerated procedure
c) re-initiation of JCA or update of JCA without a new scope
d) Update of JCA with a new scope

HTD shall submit
- SmPC
- clinical overview section
- New therapeutic indication (if applicable)

Final consolidated PICO
- a) 10 days after LoQ
- b) 75 dagen after start EMA

HTD submission Dossier
As of the sharing of the scope:
- a) 100 days
- b) 60 days

EC completeness check:
- a) 15 working days
- b) 10 working days

Missing information HTD
- a)15 days
- b)10 days
- 7 days for minor info

Clarifiying/additional info (by ASR/Co-ASR)
- 7 to 30 days

HTD to submit new evidence
- No later then 7 days after CHMP

HTD fact check:
- a) 7 days
- b) 5 days

Finalize JCA
- The latest on the day of EC decision granting MA
- c) 180 days
- d) 330 days

JCA	Start JCA	Scoping phase	Submission dossier	Drafting JCA	Final JCA	
EMA[a]	Start MAA		D120 LOQ		CHMP	CD

JCA production process & relevant HTA Regulation Articles

Initiation Phase

Art. 6 – annual work plan

Art 7 – health technologies subject to JCA

Scoping Phase

Art. 8 – Initiation of JCA & PICO development

Art. 9 – Submission Dossier

Art. 10 – Obligations of HTD

Assessment phase

Art. 10 – Obligations of HTD

Art. 11 – Assessment process

Art. 12 – finalization of JCA

Art. 13 – MS obligations

Art. 14 – updates of JCA

Implementing Acts

Art. 15 –detailed procedural rules JCA

Art. 25 – rules involvement & selection external experts and stakeholder organisations

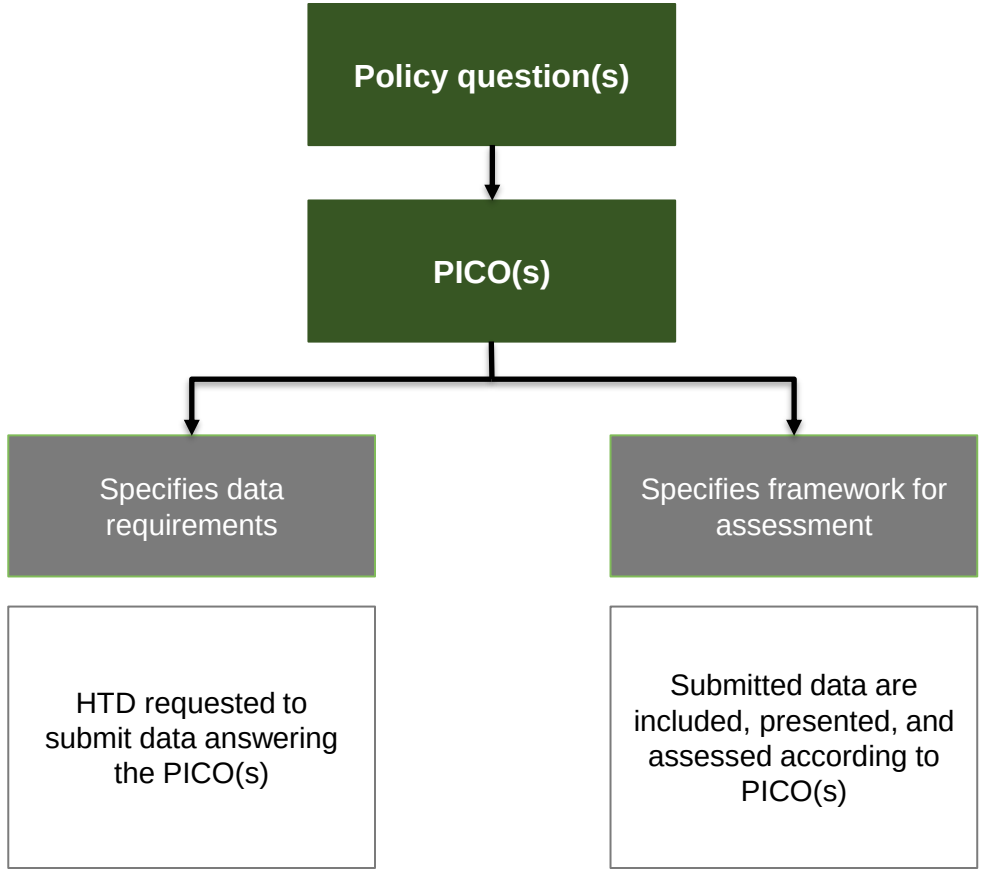
Art. 26 – format & templates of submission dossier & JCA report

Role of PICO into JCA

More information on: https://www.eunethta.eu/d4-2/

- PICO should **not be data** driven, but based on policy needs
  - **Inclusiveness & Independence**

- MS receive information on:
  - The intervention to be assessed and claimed indication/intended use in EU is provided
  - Any Joint Scientific Consultation that might have taken place.
  - The JCA PICO should be generated under the conditions existing at the time of the survey.



P

Full patient population applied for

subpopulations; defined as part of the full population

I

information about the intervention to be assessed

the **applied for indication/intended use**

Variations on the intervention, e.g. dose, **are potential effect modifiers**

- do not require a separate PICO.

C

Comparator(s) relevant for the MS HTA for each of the populations they request

- Defined by MS

Comparator(s) could be approved or not (off-label) in the EU

MS to indicate if:

- any of these can be used (OR)
- all are required (AND)
- Individualized treatment

O

MS should define their needs by listing the outcomes required

Listing of outcomes should **be free of any judgement or ranking**

PICO development process

Survey

- Based on scope proposal by asr/co-asr
- To be completed by all MS
- MS encouraged to seek national patient and clinical expert input*

Consolidate

- Converge the variety of needs into a set of PICO(s)
- Translate MS needs in the lowest number of PICO(s) possible
- Consolidation meeting to discuss the MS needs

Validate

- Consolidated PICO(s) to be validated by JCA Subgroup

Share

- Inform HTD of consolidated PICO(s)
- HTD is required to provide evidence for the PICO(s) in their submission dossier

**this process flow does not show the EU level patient and HCP input.*

Key take aways for January 2025

- Joint Scientific Consultations - ensure HTA needs are met
- Read the adopted methodological guidances
- Start predicting the PICOs/landscape in EU
- Availability of data
- Limit uncertainty around final label/indication

HTA CG

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HEALTH TECHNOLOGY ASSESSMENT

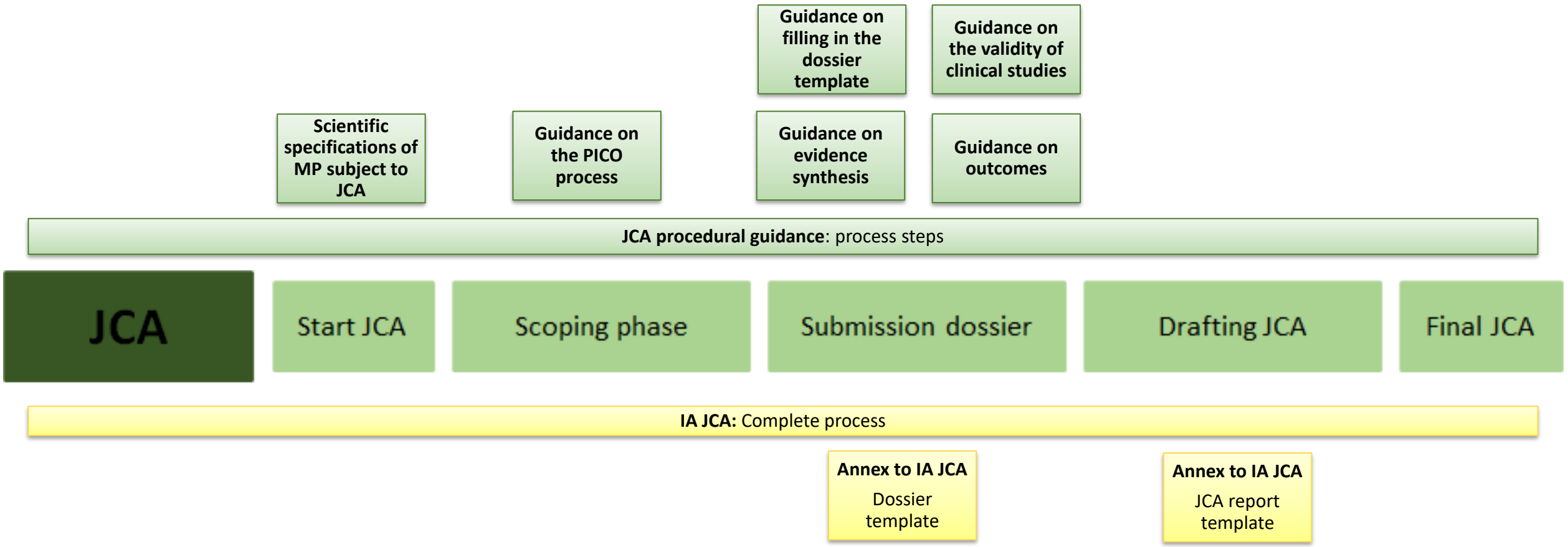
Methodologies and Procedures

Beate Wieseler
Chair of the MPG Subgroup
SME webinar, 15 November 2024

Guidance on the Joint Clinical Assessment (JCA)

HTA Regulation	https://health.ec.europa.eu/publications/regulation-eu-20212282-health-technology-assessment_en
Implementing Regulation	https://health.ec.europa.eu/health-technology-assessment/key-documents_en?f%5B0%5D=topic_topic%3A226
Guidance documents by the HTACG	https://health.ec.europa.eu/health-technology-assessment/key-documents_en?f%5B0%5D=topic_topic%3A227

Guidance for HTDs along the process



Scientific specifications of MP subject to JCA

- Gradual introduction of the JCA: from 12 January 2025 onwards medicinal products with a new active substance for which the therapeutic indication is the treatment of cancer and medicinal products which are regulated as advanced therapy medicinal products (ATMP) are included

- ATMPs are defined according to Regulation (EC) No 1394/2007

- ‘new active substance’ and ‘therapeutic indication of treatment of cancer’ are defined in these scientific specifications to support the identification of the products in scope of the HTA Regulation

The procedural guidance for JCA

- The guidance describes the process of conducting a JCA from the start (first submission of materials to the HTA secretariat) to the end (endorsement of the JCA report by the HTACG and procedural check by the EC)

- Gives HTDs an overview of when to expect
  - the assessment scope (and the corresponding information meeting)
  - the time slot for dossier preparation
  - requests for further information due to potential incompleteness of the dossier
  - the draft JCA report for the fact check
  - the final endorsed JCA report

The dossier guidance (1)

Guidance for filling in the JCA dossier template – Medicinal Products

Annex 1: table template collection

Annex 2: technical specifications for dossier submission

- Based on template from JCA IR
- More granular structure in some sections
- Additional guidance on required content
- Table template collection to support data presentation
- Technical specifications to support the organised submission of the many files that will comprise the dossier

The dossier guidance (2)

Guidance for filling in the JCA dossier template – Medicinal Products

Annex 1: table template collection

Annex 2: technical specifications for dossier submission

Word templates for the dossier and the table templates

Filled-in example tables

- Word templates for the main part of the dossier and for the tables to support preparation of documents
- Filled-in example tables to support preparation of data tables for the dossier

The guidance on evidence synthesis (1)

- The dossier and the JCA report shall present relative effects of the new medicinal product compared to the standard of care as defined by the Member States (laid down in the PICOs comprising the assessment scope)

- The guidance on evidence synthesis describes the methodological options and requirements given different study types available for the JCA

- The guidance describes assumptions and requirements for each analytical approach and how the certainty of the results should be assessed

- HTDs need to provide sufficient information in the dossier to enable the assessment of the submitted analyses

The guidance on evidence synthesis (2)

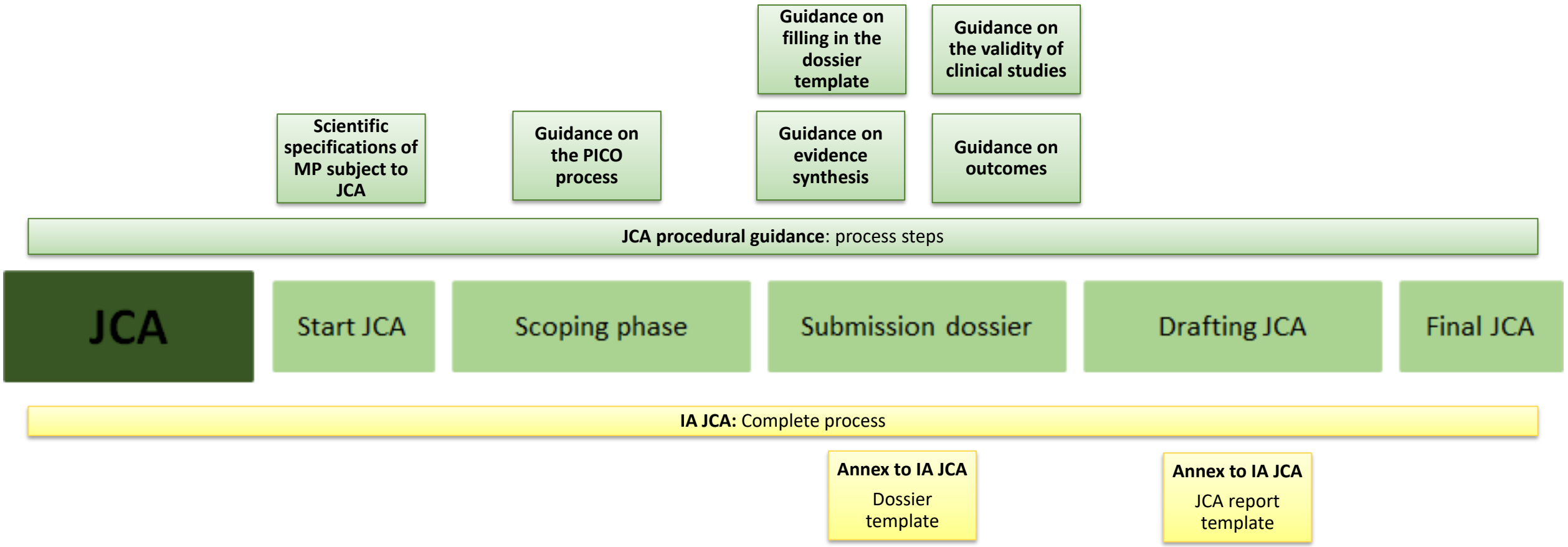
Available studies	Methodological option
RCTs comparing the new MP with the C from a PICO	Direct comparison (single study or meta-analysis)
Different RCTs with either the new MP or the C from a PICO	Anchored indirect comparison
Single arm trial with the new MP (or non-randomised comparison of the new MP with the C from a PICO)	Unanchored indirect comparison vs an external/non-randomised control

The guidance on outcomes

- Includes considerations for different types of health outcomes relevant for the JCA
  - classification of outcomes by type of source of information
  - considerations of clinical relevance of outcomes, incl. handling of surrogate outcomes and requirements for validation of surrogates
  - outcomes for specific therapeutic areas (incl. definitions of oncology outcomes)
  - specific requirements for safety outcomes
  - validity, reliability and interpretability of outcome measurement instruments

- Describes how outcomes will be defined in the PICO process
- Includes reporting requirements for assessors for the JCA => relevant for HTDs because these data need to be provided in the dossier

Guidance for HTDs along the process



HTA CG | MEMBER STATE COORDINATION GROUP ON HEALTH TECHNOLOGY ASSESSMENT

Thank you

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Any questions?

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