HTA CG | MEMBER STATE COORDINATION GROUP O
HEALTH TECHNOLOGY ASSESSMENT

Joint Clinical Assessment and PICO

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SME infoday, 18 October 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: oncology and ATMPs
- From Jan. 2028: orphan drugs
- From Jan. 2030: full scope
- 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

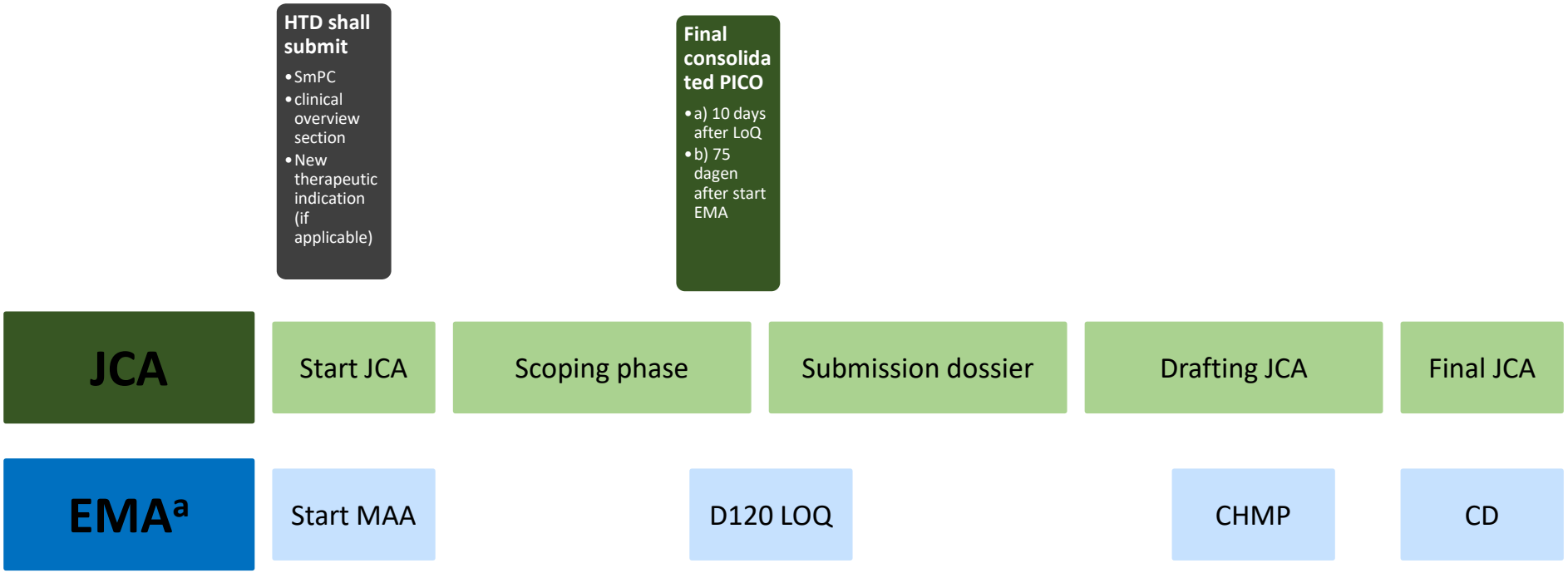
Adopted Methodological Guidance by the HTACG

Methodological Guidance	Adoption by CG
Methodological Guideline for Quantitative Evidence Synthesis: Direct and Indirect Comparisons	8 March 2024
Practical Guideline for Quantitative Evidence Synthesis: Direct and Indirect Comparisons	8 March 2024
Guidance on outcomes for joint clinical assessments	13 June 2024
Guidance on reporting requirements for multiplicity issues and subgroup, sensitivity and post hoc analyses in joint clinical assessments	13 June 2024
Scientific specifications of medicinal products subject to joint clinical assessments	13 June 2024
Guidance on the validity of clinical studies for joint clinical assessments	19 September 2024

Key documents - European Commission (europa.eu)

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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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

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

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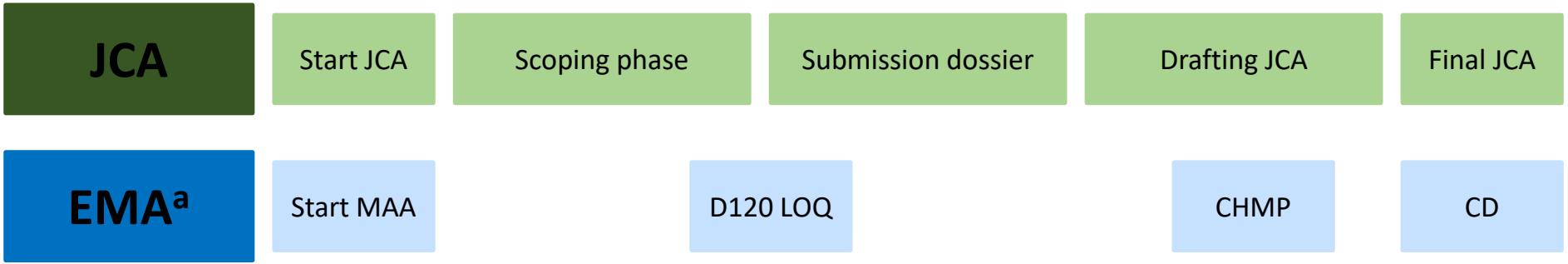
Clarifiying/additional info (by ASR/Co-ASR)
- 7 to 30 days

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

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



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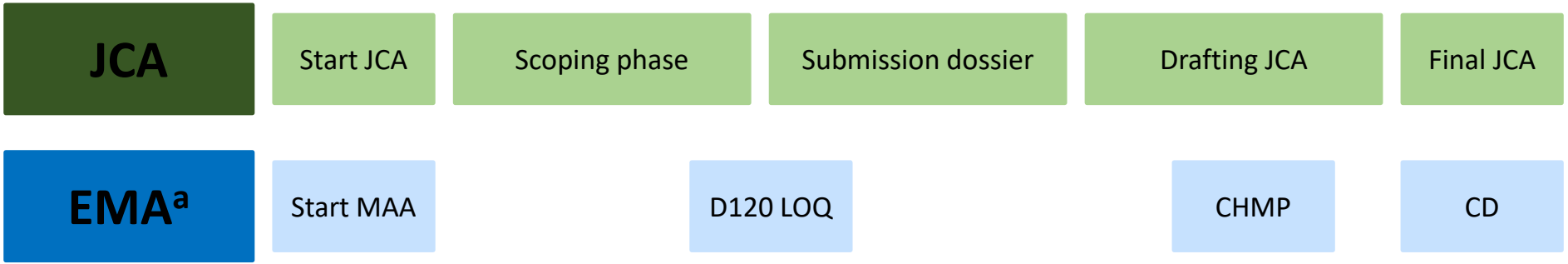
Finalize JCA

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



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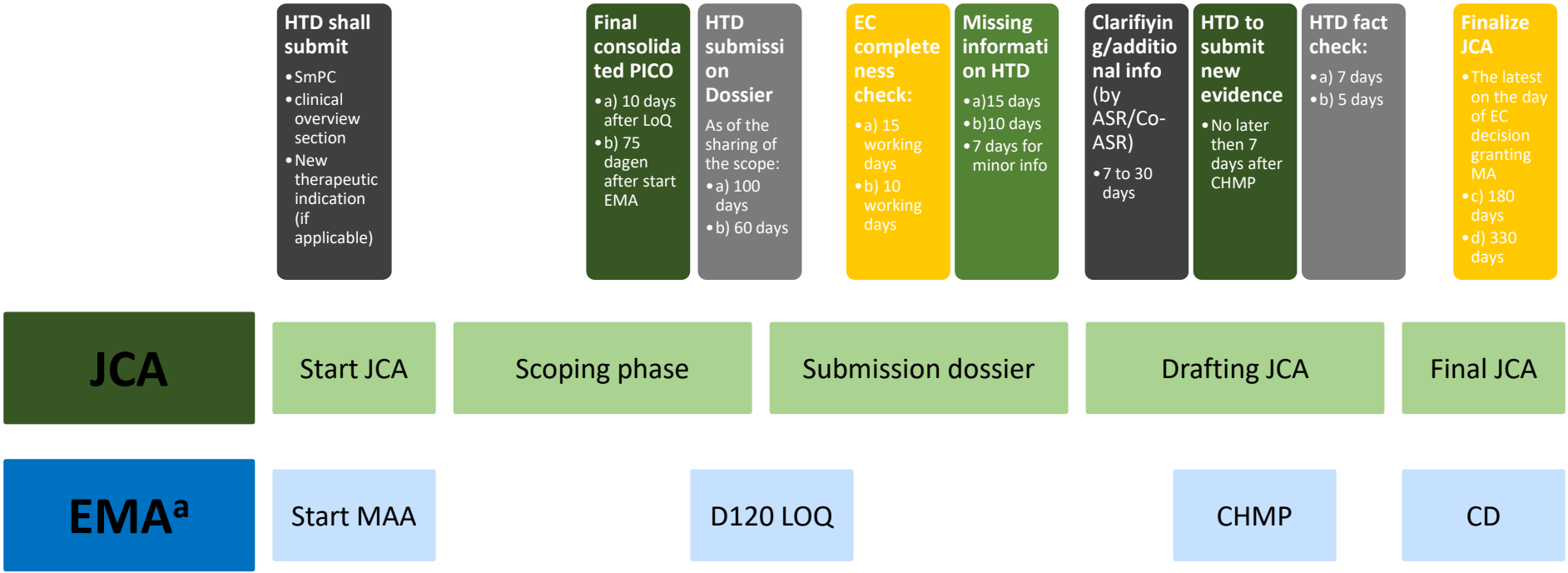


JCA production process & relevant HTA Regulation Articles

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

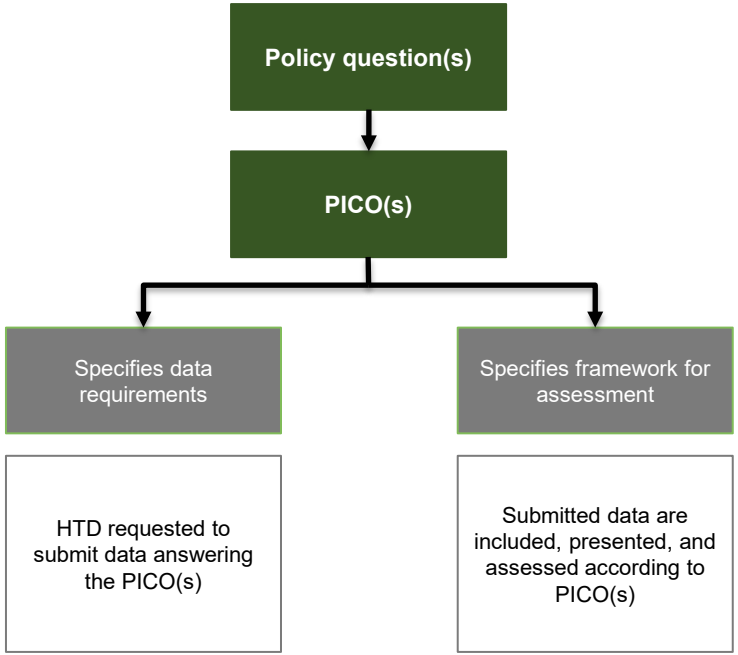
Art. 26 – format & templates of submission dossier & JCA report

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.

Annex I – Submission Dossier – Extract

Guidance on how to fill the dossier is coming Q4

Revision history

Unnecessary lines shall be deleted.

Version	Document	Legal reference	Submission date	Commission's check date
V0.1	Initial dossier	Article 10(2) HTAR		
V0.2	*(Updated dossier following Commission's second request)*	Article 10(5) HTAR		
V0.3	*(Updated dossier following assessors' request for further specifications, clarifications or additional information)*	Article 11(2) HTAR		N/A
V0.4	*(Updated dossier following changes to the therapeutic indication(s))*	Article 16(4) IR		N/A
V0.5	*(Updated dossier following re-initiation of a JCA)*	Article 10(8) HTAR		N/A
V0.6	*(Dossier with the HTD's indications and justification of confidential information)*	Article 11(5) HTAR		N/A

4.2.1. Information retrieval

The HTD shall conduct an information retrieval process with the objective of identifying the evidence to be used for the preparation of the dossier.

The following sources of information shall be systematically considered in the retrieval process:

(1) clinical efficacy and safety studies and where relevant, other applicable studies performed or sponsored by the HTD or by third parties in order to include all up-to-date published and unpublished information (data, analyses and any other evidence) from studies on the medicinal product for which the HTD was a sponsor and corresponding information about studies by third parties, if available;

(2) bibliographic databases. The search shall at least be conducted in the National Library of Medicine's bibliographic database (MEDLINE) and the Cochrane Central Register of Controlled Trials database;

(3) study registries and study results registries (clinical trial databases);

(4) HTA reports on the medicinal product subject to the JCA from EEA States in which the HTAR is applicable and from Australia, Canada, the United Kingdom and the United States of America;

(5) the clinical safety and efficacy data included in the submission file to the EMA;

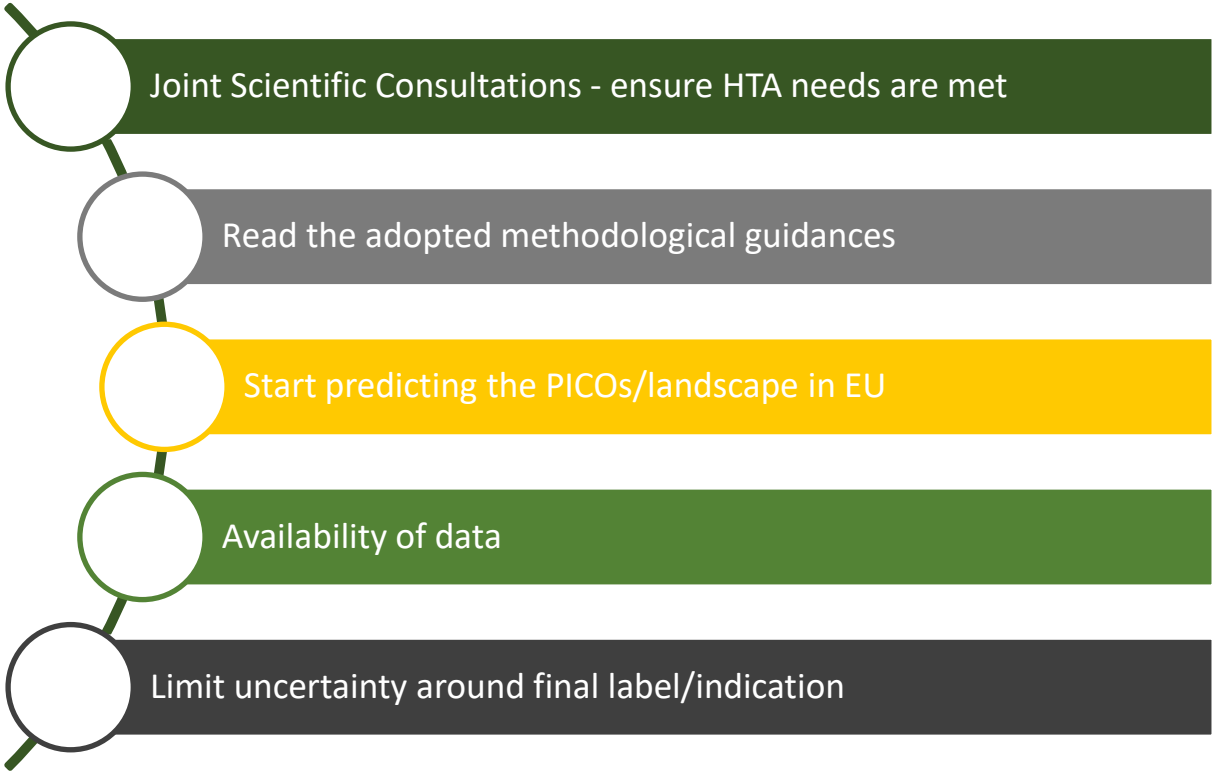
(6) patient registries.

This section shall:

- *provide a list of the sources that were systematically searched for studies that are relevant for the JCA according to the assessment scope and indicate the date of each search. The cut-off date for the searches shall be a maximum of 3 months before the submission of the dossier;*
- *report whether and when new data with relevance for the assessment scope might become available.*

All search strategies shall be fully documented in Appendix D.2.

Key take aways for January 2025



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Thank you

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ASR/Co-ASR: Assessor en Co-Assessor
CD: Commission Decision
CG: Coordination Group
EC: European Commission
EUnetHTA: European Network for HTA
HTAR: HTA Regulation
HTD: Health Technology Developer
IA: Implementing Act
JCA: Joint Clinical Assessment
JSC: Joint Scientific Consultation
LOQ: List of Questions
MD: Medical Devices
MP: Medicinal Products
MS: Member States
PICO: Patient, Intervention, Comparator(s), Outcomes
SOC: Standard of Care
SG: Subgroup