The PICO definition: the EUnetHTA 21 case study

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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/

- Key principles:
  - Inclusiveness
  - Independence

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

- Should reflect all Member States’ needs (HTAR Art. 8)
  - 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.
    - However, the JCA PICO should be generated under the conditions existing at the time of the survey.
PICO development process

**Survey**
- Online PICO survey
- Including information on intervention and claimed indication/intended use
- 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) that specify the scope of the JCA and data requirements to the HTD
- Ensure the MS needs are translated 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.
**P**
- **Full patient population** applied for

**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

**O**
- MS should define their needs by listing the outcomes required
- Listing of outcomes should be **free of any judgement or ranking**
  - MS to indicate if:
    - Any of these can be used (OR)
    - All are required (AND)
    - Individualized treatment
Comparators – different scenario’s

➢ AND scenario
  ▪ All the listed comparators are required for the comparison
  ▪ Separate PICO required for each of the comparators, so only 1 C per PICO

➢ OR scenario
  ▪ All comparators are equally suitable for the population
  ▪ The comparator(s) meeting most MS requirements can be selected/combined in consolidation

➢ Individualized treatment scenario
  ▪ If comparator does not apply to all patients in the population
  ▪ Treatment is chosen for an individual patient by the physician, from multiple available options
    • All are considered standard of care depending on patient characteristics
    • Choice is based on individual patient characteristics for treatment decision
    • e.g. pre-treatment, localisation of tumor
Learnings from EUnetHTA 21 PICO exercises

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<tr>
<th>EUnetHTA 21 PICO exercises</th>
<th>Pluvicto®</th>
<th>Ebvallo®</th>
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<tr>
<td><strong>CHMP opinion</strong></td>
<td>13 Oct 2022</td>
<td>16 Dec 2022</td>
<td>15 Dec 2022</td>
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<td><strong>Therapeutic area</strong></td>
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<td>ATMP; orphan</td>
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<td><strong>Indication</strong></td>
<td>Metastatic castration resistant prostate cancer</td>
<td>Epstein-Barr virus positive post-transplant lymphoproliferative disease</td>
<td>Late-onset Pompe disease</td>
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<td><strong>MS (associated HTAb participation)</strong></td>
<td>8 (n/a)</td>
<td>10 (3)</td>
<td>10 (4)</td>
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<td><strong># Populations</strong></td>
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<tr>
<td><strong># Comparators</strong></td>
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<td><strong># Outcomes</strong></td>
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**Key take-aways**

- Based on products with positive CHMP opinion
- In the first therapeutic areas in scope under the HTAR
- Through consolidation the number of PICOs were reduced significantly
  - The number of PICOs ranged from 5 to 9; these PICOs were consolidated across 8-10 MS only
  - All case studies included full population as per EMA label, with PICOs for up to 4 subpopulations
  - Comparators: included physician’s choice and individualised therapy
- Only the consolidated PICO at EU level will be published (not the individual MS level PICOs)
- Learnings and revisions made
  - Two weeks is short for MS to return the survey
  - PICO survey 2 and 3 based on proposal by assessor
  - Incorporation of glossary to standardize terminology used
  - Recommendations for a PICO Working Group to standardize consolidation process


*The first survey was only sent to EUnetHTA 21 members, the other two were sent to more organisations. MS were asked to give one answer per country.
**When different outcomes were mentioned in one line these were counted separately (e.g., radiological tumour assessment, including ORR and DoR was counted as 2 outcomes).
***Outcomes were not consolidated.