REGULATION AND HTA OF MEDICAL DEVICES IN EU: WHAT CAN WE LEARN?

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Premise

2. Health technology assessment (HTA) aims at assessing medical devices’ effectiveness and to compare its added value against its incremental cost
3. Both processes have been developing fast in terms of requirements, revisions and diffusion, but little convergence has been achieved between the two
4. Manufacturers often need to develop clinical evidence for HTA bodies instead of regulators (i.e. in some European countries) or conversely for regulators and not for HTA bodies (i.e. USA)
Regulatory requirements in different jurisdictions

- All jurisdictions relate evidential requirements to the level of patient risk associated with the use of different categories of device:

The European risk-based classification system for MD
The risk-based classification system for MDs in other jurisdictions

<table>
<thead>
<tr>
<th>Jurisdiction</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>Low risk</td>
<td>Moderate risk</td>
<td>High risk</td>
<td>Very high risk</td>
</tr>
<tr>
<td>Canada</td>
<td>Low risk</td>
<td>Moderate risk</td>
<td>High risk</td>
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<tr>
<td>Australia</td>
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<td>Japan</td>
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<tr>
<td>Brazil</td>
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<td>China</td>
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<td>High risk</td>
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</tbody>
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Regulatory requirements in different jurisdictions

All jurisdictions relate evidential requirements to the level of patient risk associated with the use of different categories of device:

- There are differences in the requirements as to the balance between pre-market and post-market controls.
- Existing regulatory processes for MDs generate less clinical evidence than the corresponding processes for pharmaceuticals:
  - Insufficient clinical evidence relating to the safety and performance of a device before it is placed on the market.
- A challenge in all jurisdictions is in finding the appropriate balance between assessments of efficacy and safety on the one hand and allowing rapid access to patients on the other (e.g. early dialogues such as "EXCITE" in Canada or "SEEED" in EU).
Evidence requirements for pre-market approval

For CE marking for devices in Class III, the manufacturer must conduct some human clinical investigations, but it is not compulsory that these are randomized clinical trials:

- MDs’ features often make RCTs unethical, inapplicable or very difficult and too costly (e.g. proven effectiveness, learning curve, incremental innovation)
EU New Regulation on MDs

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 5 April 2017


(Text with EEA relevance)

Stricter requirements for clinical evidence to support assessments of high risk and implantable medical devices

EU (proposed) new Regulation on HTA

➢ the European Commission has proposed a regulation aimed at centralizing HTA of health technologies through Joint Clinical Assessments
### EC Regulation on HTA: scope

<table>
<thead>
<tr>
<th>HTA domains</th>
<th>Clinical domains</th>
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<tbody>
<tr>
<td>Health problem and currently used technologies</td>
<td></td>
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<tr>
<td>Description of technology under assessment</td>
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<td>Relative clinical effectiveness</td>
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<td>Relative safety</td>
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<td>Economic evaluation</td>
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<td>Ethical aspects</td>
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<td>Organisational aspects</td>
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<td>Social aspects</td>
<td></td>
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<tr>
<td>Legal aspects</td>
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</tbody>
</table>

| Non-clinical domains                             |

### EC HTA Regulation: activities

**Article 3**

#### HTA Coordination Group

**Joint work carried out by MS experts**

<table>
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<th>Sub-groups</th>
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<td>Joint clinical assessments - Medicines - Medical devices</td>
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<td>Joint scientific consultations - Medicines - Medical devices</td>
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<tr>
<td>Identification of emerging health technologies (input to work programme)</td>
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<tr>
<td>Voluntary cooperation - Other health technologies - Non-clinical HTA aspects</td>
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</tbody>
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**Preparation of annual work programme/reports, Common guidance documents**
Joint Clinical Assessments: products

- Medicinal products: centrally authorised new active substances and new therapeutic indications
- Medical devices:
  - Medical devices classified as class IIb and III pursuant to Article 51 of Regulation (EU) 2017/745 for which the relevant expert panels have provided a scientific opinion in the framework of the clinical evaluation consultation procedure pursuant to Article 54 of that Regulation
  - In vitro diagnostic medical devices classified as class D pursuant to Article 47 of Regulation (EU) 2017/746 for which the relevant expert panels have provided their views in the framework of the procedure pursuant to Article 48(6) of that Regulation
  - Additional selection by HTA Coordination Group based on criteria: Unmet medical needs; potential impact on patients, public health and healthcare systems; significant cross-border dimension; major Union-wide added value

Use of Joint Clinical Assessments

Joint clinical assessment – conclusions limited to:

- an analysis of the relative effects of the health technology being assessed on the patient-relevant health outcomes chosen for the assessment
- the degree of certainty on the relative effects based on the available evidence.

NATIONAL APPRAISAL

of joint clinical assessment and additional context-specific considerations (e.g. number of patients affected in Member State, how patients are currently treated in the healthcare system, costs)

Conclusions on added value
(e.g. added therapeutic value, cost-effectiveness...)
The International Medical Device Regulators Forum (IMDRF) was conceived in February 2011 as a forum to discuss future directions in medical device regulatory harmonization.

It is a voluntary group of medical device regulators from around the world who have come together to accelerate international medical device regulatory harmonization and convergence.

The current members are:

1. Australia
2. Brazil
3. Canada
4. China
5. Europe
6. Japan
7. Russia
8. Singapore
9. South Korea
10. United States of America

Scope for further harmonisation of standards beyond EU?

- Medical Devices have traditionally been placed in therapy with weaker clinical evidence if compared to drugs
- EU has made great efforts to fill the evidentiary gap of MDs and to harmonise the regulation and the HTA requirements but some issues are still to be solved:
  - Clinical evidence is key:
    - Pre-market (e.g. early dialogues)
    - Post-launch (e.g. RWE, see also FDA guidance)
  - Choice of the comparator (e.g. is «standard of care» the same across jurisdictions?)
  - Stakeholders’ engagement (e.g. clinicians, managers, patients, industry) is fundamental to develop the relevant data to inform the regulation processes but is still unclear how
  - How these issues relate to the Asian context?
Panel Issue Speakers

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