SESSION 3

Coordinating expert panels on high-risk medical devices and *in vitro* diagnostics

Introduction by topic lead

Silvy da Rocha Dias
EMA Committees and Quality Assurance
Outline

1. Medical Device Regulation
2. The Expert Panels in the framework of Medical Devices Regulation
3. Expert Panels – 1 year review
4. EMA’s new mandate on coordination of the Expert Panels
5. Conclusion
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New Medical Device Regulation

More than 500,000 types of medical devices and in-vitro diagnostic medical devices on the EU market.

The previous regulatory framework of three Directives was replaced by the regulations on medical devices and in-vitro diagnostics:

With effect from:

26 May 2021

1 March 2022

26 May 2022
MEDICAL DEVICES

Overview of the types of medical devices

Medical device classification rules adopt a risk-based approach taking into account the risks associated with the use, technical and manufacture characteristics of the device.

The MDR (EC) 2017/745 divides the devices into 4 risk classes and 22 rules on classification of medical devices.

### Class I
- All non-invasive devices:
  - Stethoscopes
  - Eye occlusion plasters
  - Wheelchairs pushed by hand
  - Corrective spectacle frames (i.e. glasses) and lenses in frames

- **Self certification**

### Class IIa
- Syringes with needles
- Dental fillings
- Tracheotomy tubes
- Surgical gloves
- Clamps
- Suction pumps

- **Notified Body Conformity Assessment**

### Class IIb
- Rule 12: administer and remove medicinal products:
  - Ventilators
  - Infusion pumps
  - Anaesthesia machines

### Class III
- Breast implants
- Surgical meshes
- Total or partial joint replacements
- Spinal disc replacement
- Prosthetic heart valve

### Scope of the expert panels

LOW RISK

Notified Body Conformity Assessment

HIGH RISK

Self certification
Recent safety issues with medical devices

Metal-on-Metal (MoM) hip replacement implant

2010

Recall of MoM hip replacements due to device failure of metal wearing and release of metal particles into the bloodstream and soft tissues.

Poly Implant Prothese (PIP)

2012

Breast implants from the manufacturer PIP used low-grade industrial silicone that had not been approved by health authorities. Many of these implants ruptured, with no traceability.
New tools of the Medical Device Regulation

**Regulation (EU) 2017/745 and Regulation (EU) 2017/746** introduce stricter monitoring and certification procedures to ensure full compliance and traceability of medical devices, such as breast or hip implants.

Some new tools introduced with the new regulation:

- Pre-market obligation for consultation on **clinical evaluation** for certain high-risk devices – Expert panels
- EUDAMED - **Life cycle monitoring** with post-market clinical follow up (PMCF) data
- More **transparency, visibility and traceability** to patient and healthcare professionals

<table>
<thead>
<tr>
<th>Pre-market control</th>
<th>EUDAMED</th>
<th>Traceability</th>
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<tbody>
<tr>
<td>• Stricter pre-market control with the introduction of Expert panels</td>
<td>• Improved market surveillance with the EU DAtabase on MEDical Devices</td>
<td>• Unique Device Identification (UDI) system</td>
</tr>
<tr>
<td>• Provides mechanism of scrutiny for assessment of certain class III and class IIb devices</td>
<td>• Lifecycle of all products on the EU market</td>
<td>• Implant card for patients</td>
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Approval pathway for medical devices

Competent Authority (MS)
- Marketing
- Vigilance
- Enforcement

Authorities responsible for notified bodies
- Scrutiny
- Surveillance
- Inspections

Manufacturer
- Technical/dossier review
- Conformity assessment
- CE marking certification

European Commission (EC)

Notified body

EUDAMED
- Certificates
- Market incidents reporting
- Safety corrective actions
- Periodic summary reports
- Periodic safety update reports (PSUR)
NEW STRUCTURE
Expert Panels for medical devices

CONFORMITY ASSESSMENT

Manufacturer → Notified body → EMA → Expert Panels

Submission of:
- Clinical dossier (MD)
- Performance evaluation report (PER) (IVD)

Submission of:
- Clinical Evaluation Assessment Report (CEAR)
- Performance Evaluation Report (PER)

Coordination of:
- Clinical Evaluation Consultation Procedure (CECP)
- Performance Evaluation Consultation Procedure (PECP)

Opinion on the CEAR or views on PER

CE certification → Access to EU market

Manufacturer Notified body EMA Expert Panels

Notified body

CEAR or PER

CE certification

Access to EU market
How are the Expert Panels organised

Medical devices regulation

1. Screening panel

Thematic expert panels and possible sub-groups:
2. Orthopaedics, traumatology, rehabilitation, rheumatology (sub-groups)
3. Circulatory system (sub-groups)
4. Neurology (sub-groups)
5. Respiratory system, anaesthesiology, intensive care
6. Endocrinology and diabetes
7. General and plastic surgery and dentistry (sub-groups)
8. Obstetrics and gynaecology, incl. reproductive medicine
9. Gastroenterology and hepatology
10. Nephrology and urology
11. Ophthalmology

In vitro diagnostics regulation

12. In vitro diagnostics devices panel
Role of the Expert Panels

**Focus:** Provide opinion on notified bodies’ assessment of clinical evaluation of certain high-risk medical devices and views on the performance evaluation of certain *in vitro* diagnostics

**To further implement:**
- Advisory role on technical, scientific and clinical matters
- Contribution to the development of common specifications for clinical evaluation of device categories, guidance documents or international standards
- Contribute to the identification of concerns and emerging issues on safety and performance of medical devices
- Play a relevant role in preparedness and management of public health emergencies with the ETF
NEW: CLINICAL EVALUATION CONSULTATION PROCEDURE (CECP)

Provide opinion on notified bodies’ assessment of clinical evaluation of certain high-risk medical devices

Consider the legal requirements
Type of device
• For class III implantable eg. Pacemakers, joint replacement devices, breast implants
• For class Iib administer/ remove medicinal product eg. Infusion pumps, ventilators

Consider exemptions
No Expert Panel if:
• Re-certification of MDR product
• Modification does not affect B/R
• Common Specification available for the type of device

Phase I: Screening Panel
Decide on 3 criteria:
• Novel AND major clinical / health impact
• Adversely changed benefit-risk profile in regard to valid health concerns
• Significant increase of serious incidents

Phase II: Thematic Panel
Provide an Opinion
• Non-binding opinion which is publicly available on EC website
• The Competent Authorities will be notified of the opinion

Notified body

Expert Panel
Overview of output of Expert Panels for medical devices

The EC started receiving applications for the CECP on 1 April 2021

During their first year of operation:

• 25 dossiers on high-risk devices and in vitro diagnostics were submitted
• 3 scientific opinions for CECP
• 15 scientific views for PECP

The EMA is coordinating the expert panels since 1 March 2022

Currently:

• 3 applications ongoing
• 2 recently submitted
Example of the work of the Expert Panel

<table>
<thead>
<tr>
<th>CECP#</th>
<th>Medical Device</th>
<th>Intended purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-000201</td>
<td><strong>An implantable device in contact with bone which is mainly resorbed.</strong> It consists of porous granules of hydroxyapatite derived from porcine teeth.</td>
<td>A medical device intended to be used as a bone graft material for the repair or augmentation of bone defects in dental procedures.</td>
</tr>
</tbody>
</table>

**The expert panel challenged** adequacy of clinical evidence assessment by the notified body and commented on:

- Length of study duration
- Endpoint of the study
- Possible immune adverse reaction from the source material
- Adequacy of the dataset to support the intended use of the medical device

**The expert panel recommended** additional measures to implement in the post-market clinical follow-up (PMCF) plan
**NEW: PERFORMANCE EVALUATION CONSULTATION PROCEDURE (PECP)**

Views on the performance evaluation of certain in vitro diagnostics

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**Consider the legal requirements**

**Type of device**
- For Class D: Intended for detection of presence/exposure to, a transmissible agent

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**Consider exemptions**

**No Expert Panel if:**
- Common Specification available for the type of device
- The type of device is already been certified

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**In vitro Diagnostic Panel**

**Provide a View**
- Non-binding view which is publicly available on EC website

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**Notified body**

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**Expert Panel**

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**60 days**

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Classified as public by the European Medicines Agency
Overview of the *in vitro* diagnostic Expert Panel work

The EC started receiving applications since 3 September 2021

**Views provided under PECP:** testing kits for detection/screening of Parvovirus B19, Hepatitis E, West Nile Virus, Babesia, Zika, chikungunya virus (CHIKV) and dengue virus, Epstein Barr Virus, Trypanosoma cruzi, Treponema pallidum and SARS-Cov-2

<table>
<thead>
<tr>
<th>PECP#</th>
<th>In vitro diagnostic medical device</th>
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<tr>
<td>IVD-2021-000007</td>
<td>The device is a qualitative double-antigen sandwich assay for the detection of Antibodies to <em>SARS-CoV-2</em> in serum/plasma</td>
</tr>
<tr>
<td>IVD-2021-000008</td>
<td>The device is a qualitative real-time PCR test for the simultaneously detection and differentiation of <em>SARS-CoV-2, Influenza A, and Influenza B</em> in respiratory specimens (Nasopharyngeal swab/nasal swab)</td>
</tr>
<tr>
<td>IVD-2021-000010</td>
<td>This test is an in vitro nucleic acid amplification test intended for qualitative detection of <em>SARS-CoV-2</em> genomic RNA by real-time polymerase chain reaction (PCR) method.</td>
</tr>
<tr>
<td>IVD-2021-000012</td>
<td>Chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgM antibodies to <em>SARS-CoV-2</em> in human serum and plasma</td>
</tr>
<tr>
<td>IVD-2021-000013</td>
<td>Chemiluminescent microparticle immunoassay (CMIA) used for the qualitative and quantitative determination of IgG antibodies to <em>SARS-CoV-2</em> in human serum and plasma</td>
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Advisory role on technical, scientific and clinical matters

<table>
<thead>
<tr>
<th>Expert panels to provide scientific advice</th>
<th>Long term activity</th>
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<tr>
<td></td>
<td>• To Medical Device Coordination Group (MDCG) and EC concerning safety and performance of high-risk medical devices and in vitro diagnostics</td>
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<tr>
<td></td>
<td>• To manufacturers on their clinical development strategy and proposals for clinical investigations for certain high-risk medical devices</td>
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<tr>
<td></td>
<td>• To manufacturers, notified bodies and Member States on the criteria for appropriate data sets for clinical evaluation as part of conformity assessment of medical devices</td>
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Benefits of the Expert Panels

Benefit by improving public health and safety and supporting harmonization and standardization of device specifications:

• Provides **greater transparency** for patients and healthcare professionals on the clinical assessment done by the Notified Bodies

• Provides the **reinforcement of the supervisory** role of the Competent Authorities regarding the use of these medical devices

• Issues **critical opinion** on the clinical evidence provided at the time of certification and recommendations on future clinical data collection

• Help with **developing common specifications** which will support manufacturers to standardise the quality and performance of their devices and play a relevant role in crisis preparedness during public health emergencies eg SARS-Cov-2 IVDs (detection or quantification of SARS-CoV-2 nucleic acid and antibodies)

**KEY BENEFIT**

Increased transparency and public information on medical devices used across the EU
Handover Roadmap of the Expert Panels

Expert Panels’ have been set up, managed and coordinated by the Joint Research Center and DG-SANTE for the past year.

Q2 2021
Role of the Expamed secretariat
Expanded EMA mandate for the coordination and administration of CECP and PECP

Q3 2021
Expert database management
Review of the EC policy on the management of competing interests for MD

Q4 2021
Expert selection
Managing pool of applications of experts and assignment into thematic panels based on workload
End Q4 2021
Expert engagement and payments
Assignment of rapporteurships and assessment team

Q1 2022
Final transfer steps
Preparatory work for official handover 1st March 2022

Terms of references and Rules of procedure
Legal provisions that have led to the process design

Conflict of interest declaration (CoI)
CoI evaluation based on the EMA policy, however with some adaptation

Call for expression of interest
Open call for applications and appointment of experts by the EC

IT tools
Internal workflow for CECP and PECP, CIRCABC for dossier management with notified body

Handover activities
Training, knowledge transfer and expert onboarding
How will EMA support the Expert Panels?

WHAT IS THE ADDED VALUE OF THE EXTENDED MANDATE

- Bring considerable know-how in managing experts from all across the EU to ensure impartiality
- Offer excellence in the best available scientific knowledge in the EU for scientific opinions and advice for pre-market and post market clinical development plans
- Encourage innovation through support structures for SMEs and timely access for patients of innovative products
- Management of competing interests and providing independent opinions, views and scientific advices on products
- Increase transparency with the publication of scientific opinions to allow for public scrutiny
Conclusion

• Expert panels are one of the tools in the new MDR to **improve safety and performance** of MDs and IVDs as well as transparency for patients and healthcare professionals

• Under the new Extended Mandate, expert panels **activities are under the coordination** of the EMA and implementation is done on a step-wise approach

• **With its extensive experience in coordinating expert groups**, EMA will be able to meet its new role’s expectation which would complement EMA’s mission

• EMA’s new mandate **strengthens the preparedness for major public health crisis and provides further resilience** for the availability of medical devices through its advisory role on critical medical devices

• EMA’s coordination of the expert panels will lead to a **more integrated and synergistic approach** to the management of the scientific panels for medical devices that will help improve public health protection for the entire Union