CORE-MD

Coordinating Research and Evidence for Medical Devices

25 March 2024

CORE–MD Webinar #13

The notified body role and the conformity assessment process

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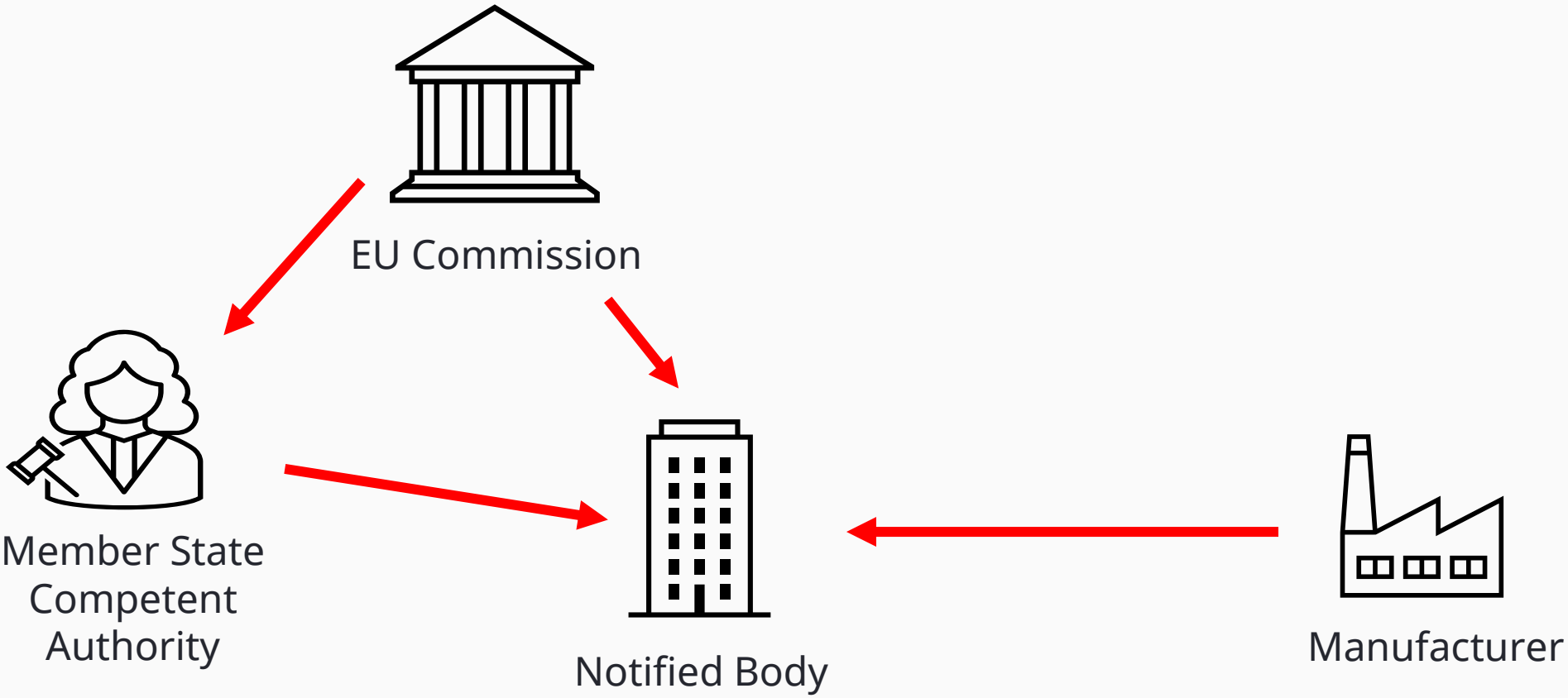
What is a Notified Body?

'Notified Body' means a conformity assessment body designated in accordance with this Regulation;

Medical Device Regulation EU 2017/745 (Article 2 (42))



Notified Body Role

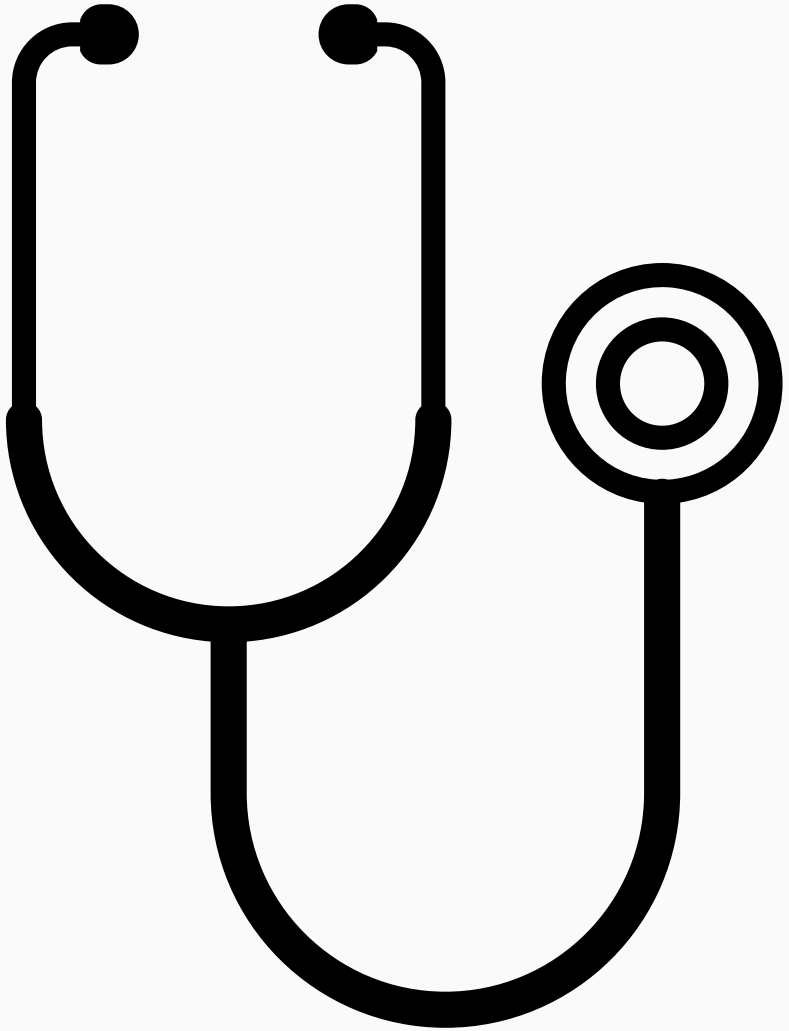
Notified bodies are looking for compliance not non-conformities.

Notified bodies are not permitted to consult.

Notified bodies must base its evidence on conclusions presented by the manufacturer.

Notified bodies cannot provide the answer for manufacturers.

What activities does the notified body get involved with through the life cycle of a device ?



Notified Body Activities

Technical File Surveillance for low-risk devices

Certificate Renewal

Assessment of the Technical Documentation

Post Market Surveillance – PSURs, Vigilance reporting, SSCP Updates

Quality Management System Audits

Unannounced Audits

Change Requests

Pre-market

Post Market

Maintaining Competency

Competent Authority Audits

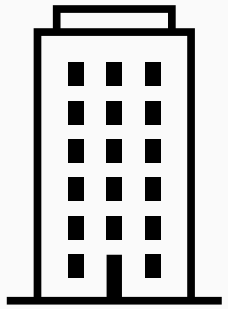
Maintaining State of the Art Knowledge and Competency

Designation Audits

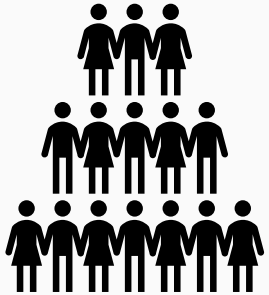
Competent Authority Information Requests

Transfer Requests

How does a notified body become designated?



A notified body is designated by a Joint Assessment Team (JAT) -Usually the EU Commission and 2-3 Member states.



The designation of a notified body is based upon the competency within the notified body. The JAT assess the competency and decide which devices the notified body can be designated to.

There are strict requirements in the regulation on competency of notified body personnel, and this is based upon education, working experience and knowledge of Regulations.

Competent Authority audits focus heavily on the competence of the notified body and also how these individuals are maintaining their competence.

The notified body to demonstrate competency to device codes **AND** horizontal codes

I. CODES REFLECTING THE DESIGN AND INTENDED PURPOSE OF THE DEVICE

A. **Active devices**

1. *Active implantable devices*

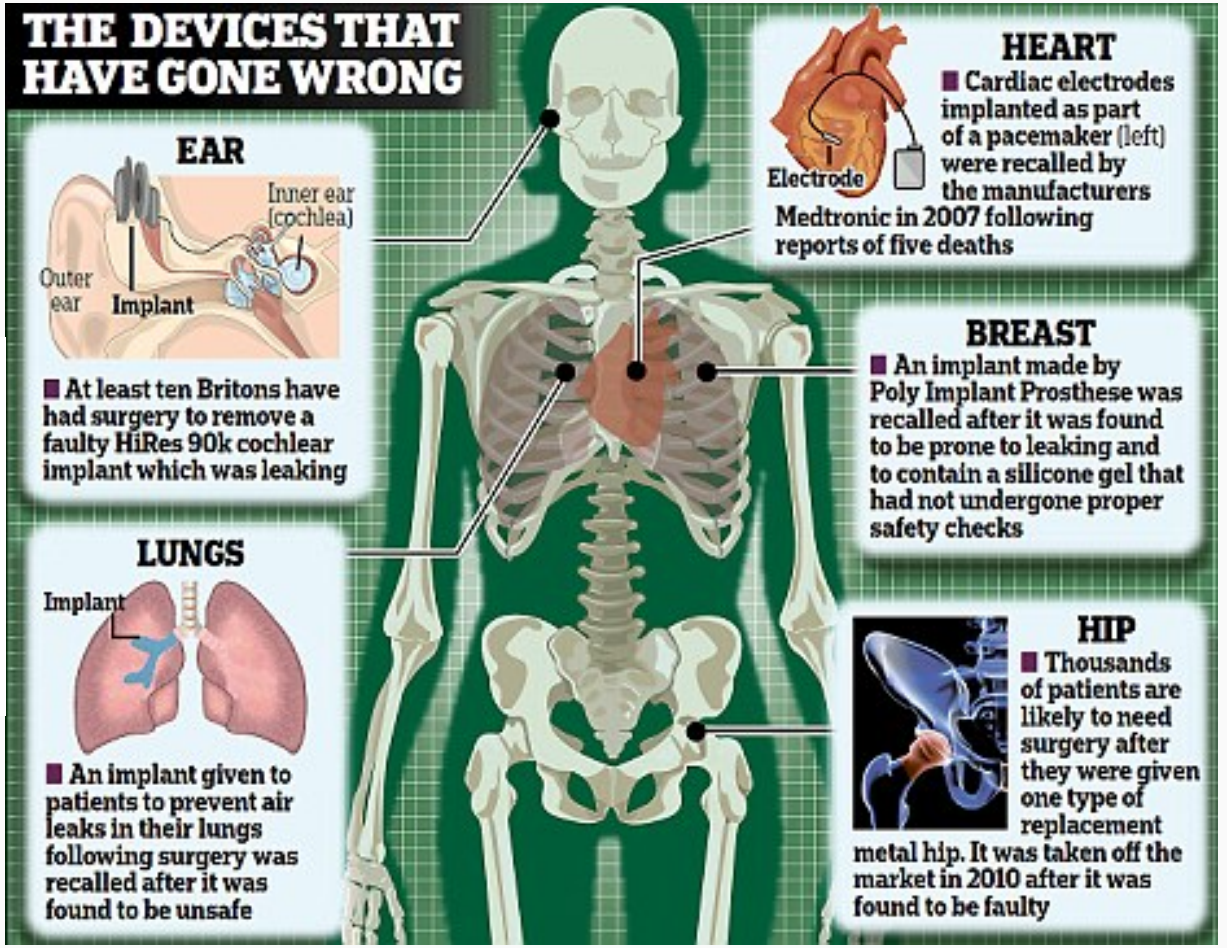
MDA CODE	Active implantable devices
MDA 0101	Active implantable devices for stimulation/inhibition/monitoring
MDA 0102	Active implantable devices delivering drugs or other substances
MDA 0103	Active implantable devices supporting or replacing organ functions
MDA 0104	Active implantable devices utilising radiation and other active implantable devices

II. HORIZONTAL CODES

1. *Devices with specific characteristics*

MDS CODE	Devices with specific characteristics
MDS 1001	Devices incorporating medicinal substances
MDS 1002	Devices manufactured utilising tissues or cells of human origin, or their derivatives
MDS 1003	Devices manufactured utilising tissues or cells of animal origin, or their derivatives
MDS 1004	Devices which are also machinery as defined in point (a) of the second paragraph of Article Directive 2006/42/EC of the European Parliament and of the Council (1)
MDS 1005	Devices in sterile condition

The ‘BIG’ Change – EU 2017/745



What has changed for notified bodies from MDD to MDR?

(4) Key elements of the existing regulatory approach, such as the supervision of notified bodies, conformity assessment procedures, clinical investigations and clinical evaluation, vigilance and market surveillance should be significantly reinforced, whilst provisions ensuring transparency and traceability regarding medical devices should be introduced, to improve health and safety.

(50) The proper functioning of notified bodies is crucial for ensuring a high level of health and safety protection and citizens' confidence in the system. Designation and monitoring of notified bodies by the Member States, in accordance with detailed and strict criteria, should therefore be subject to controls at Union level.

(51) Notified bodies' assessments of manufacturers' technical documentation, in particular documentation on clinical evaluation, should be critically evaluated by the authority responsible for notified bodies. That evaluation should be part of the risk-based approach to the oversight and monitoring activities of notified bodies and should be based on sampling of the relevant documentation.

(54) The Member State in which a notified body is established should be responsible for enforcing the requirements of this Regulation with regard to that notified body.

EU MDR 2017/745

A classic example…

Pacemaker Lead – A High Risk (Class III) Medical device been on the market for 30+ years…

The Technical Dossier Assessment & Quality Management System Audit

The manufacturer submits an application to the notified body alongside the technical dossier this often contains 1000’s of pages of technical descriptions, designs and test reports, biocompatibility reports, clinical evaluation reports, labelling templates and post market surveillance reports.

Alongside the examination of the technical dossier the manufacturer is subject to an on-site audit of their quality management system ranging from witnessed testing at the production line, how they handle complaints and report vigilance to competent authorities.

Who is involved in the assessment of the technical dossier?

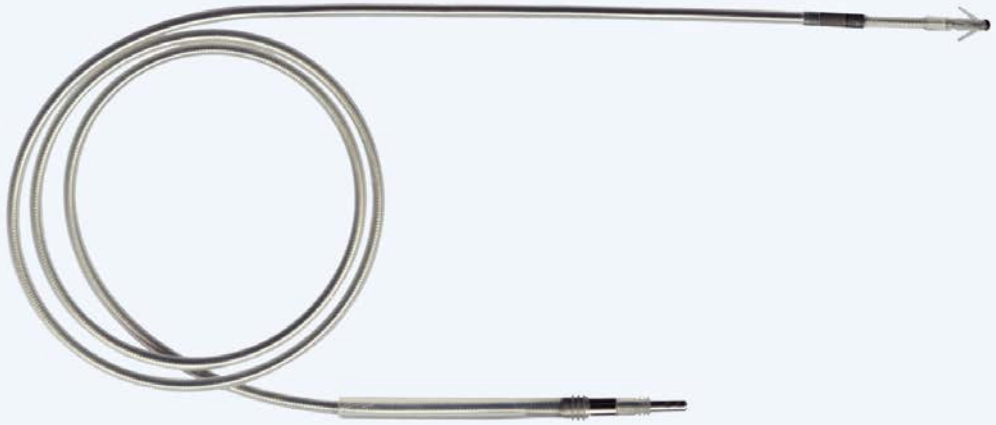
A clinician is employed to employed to evaluate the clinical data held on the device and benefit-risk assessment.

A medicinal expert (pharmacist) is employed to evaluate the impact of any substances. (E.g. dexamethasone.)

An MRI Technical expert is also employed to evaluate any potential issues associated with claims of MRI Conditionality.

Biocompatibility experts are employed to assess exposure and compatibility/degradation of materials in the human body.

IS-1 Pacemaker Lead



Technical expert is employed to assess the technical specifications to standards (ISO5841) and review pre-clinical data such as bench testing, ageing tests.

Microbiologists employed to assess sterility methods.

Packaging and transit tests are reviewed by a technical expert including labelling requirements.

Animal tissue experts assess impact of the use of animal by-products either in the device or used in the manufacturing process.

Scheme Manger (Legal Expert) to recommend certification and ensure process is organised/manufacturer is informed.

Minimum Years of experience required in this assessment

Role of Individual	NBOG 2017 -2* Guidance Requirements (Minimum)	Actual Experience used in the assessment
Clinical Expert	4 Years	>25 years
Technical Expert	4 Years	12 years
Biocompatibility Expert	2 Years	10 years
Medicinal Expert	Pharmacological background (4 years)	15 years
Animal Tissue Expert	No detail in guidance but typically 4 years	12 years
MRI Expert	No detail but typically 4 years	7 Years
Microbiologist	2 years per type of sterilisation	10 years
Packaging and Transit Expert	No detail but typically 4 years	4 years
Site Auditor	4 Years	10 years
Project Leader	No detail but typically 4 years	4 years
TOTAL YEARS	**30 years**	**109 Years**

**NBOG 2017-2 Guidance on the Information Required for Conformity assessment bodies' Personnel Involved in Conformity Assessment Activities*

Notified Body Post Market Surveillance under the MDR…

A CE Certificate will typically last 5 years before recertification is required

Review of Periodic Safety Update Reports

Monitoring of Post Market Clinical Follow Up

Technical File Surveillance

Competent Authority Information Requests

Design Change Requests

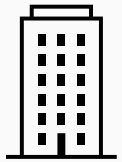
Validation of Summary of Safety Clinical Performance Reports

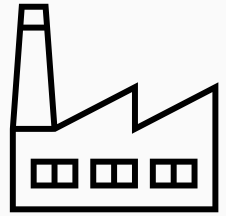
Review of Vigilance Events

Unannounced audits

Certificate Renewal

During the conformity assessment...





Questions to the Manufacturer

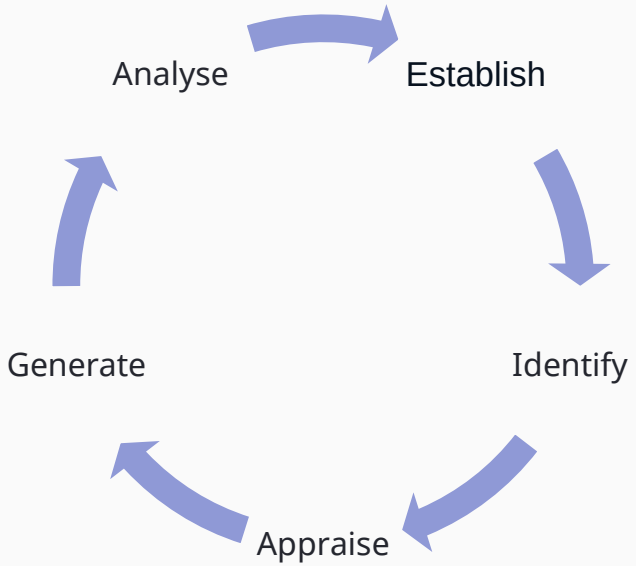
Responses from the manufacturer

During the assessment, the notified body will ask questions to the manufacturer on the technical documentation or may request further information for clarity.

The manufacturer will ask internal personnel questions raised by the notified body .

The rounds of questions form part of the notified body's audit trail.

The Clinical Evaluation Assessment



The manufacturer is required to establish a plan and define the objectives of the device under evaluation.

They are then required to identify all favourable and unfavourable clinical evidence of the device under evaluation and appraise the data to support the general and safety performance requirements

They are then required to identify any gaps in the evidence and consider generation of clinical data (e.g. through a clinical investigation)

This is a continuous process as data feeds in from the post market surveillance space.

All these results and analysis along with benefit-risk assessments are documented in the clinical evaluation report.

The Clinical Evaluation Assessment

The Key Questions…

1. Is the manufacturers clinical evaluation plan appropriate?

2. Has the manufacturer considered all diagnostic or treatment options as part of the ‘state-of-the-art’ assessment? Has the manufacturer defined appropriate objectives from an assessment of ‘state-of-the-art’?

3. Is the manufacturer claiming equivalence? Is the claim of equivalence appropriate and legal?

The MDR Requirements of the Clinical Evaluation Plan

- The MDR is prescriptive on the requirements of the CEP. Annex XIV Part A (1) sets out 8 clauses related to the CEP:

GSPR

The CEP needs to identify the general safety and performance requirements that require clinical data

The intended purpose of the device

Intended target groups, clear indications and contra-indications

Intended clinical benefits to patients with relevant and specified clinical outcome parameters

Methods used for qualitative and quantitively aspects of clinical safety to determine residual risk/side effects

Parameters to be used to determine State of the Art and acceptability of benefit/risk for all indications

Benefit-risk issues relating to specific components such as use of pharmaceutical, non- viable animal or human tissues

A clinical development plan....

‘**state of the art**’: IMDRF/GRRP WG/N47 provides the following definition:

*Developed stage of **current technical capability** and/or **accepted clinical practice** in regard to products, processes and patient management, based on the relevant consolidated findings of science, technology and experience.*

*Note: The state-of-the-art embodies what is currently and generally accepted as **good practice in technology** and **medicine**. The state-of-the-art does not necessarily imply the most technologically advanced solution. The state-of-the-art described here is sometimes referred to as the “generally acknowledged state-of-the-art’*

Reproduced from MDCG 2020-6 (1. Definitions)

State of the Art & Defining Objectives

3 Stents identified from State-of-the-Art Search

Stent under Evaluation

State of the Art Results should drive the Safety and Performance objectives for the device under evaluation

Results of SoTA Search

Risk identified - Thrombosis at 12 months – 6-9%
Performance identified – Patency at 5 years – 82-86%

Objectives for Device under Evaluation

Safety Objective - Thrombosis at 12 months – < 9%
Performance Objective – Patency at 5 years – >82%

- Understanding the safety and performance profile of similar devices from State of the Art allows the manufacturer to develop an acceptable safety and performance profile for the device under evaluation. This allows the manufacturer to compare its data against those other technologies to confirm its safety and performance is equal or better than those available devices and ultimately its right to have a position on the market

The Clinical Evaluation Assessment

4

The Key Questions…

- What clinical data is held on the device? Have literature search protocols been conducted appropriately? What are the conclusions of these searches?

5

- Have Clinical Investigations been conducted? Are these compliant investigations? What are the conclusions of these investigations?

6

- What Post market data is held on the device – PMCF Study data? Complaints? Vigilance? Registry data?

Types of clinical evidence reviewed

Typically for high risk devices, clinical investigation data is presented.

Peer-reviewed literature data is also considered and is typically used to support lower risk devices.

Data from Post Market Clinical Follow Up is also considered such as PMCF Studies, registry data and to some extent complaints and vigilance episodes.

The clinical data needs to cover the device under evaluation for all intended purposes/indications along with any clinical claims made by the manufacturer. There is also an expectation that all variants of a device are covered with clinical data. Bench testing, animal study data, Insilco trial data is not considered clinical data under the Medical Device Regulation.

The Clinical Evaluation Assessment

The Key Questions…

7

- What are the benefit/risk conclusions? Is the data **‘sufficient’** ?

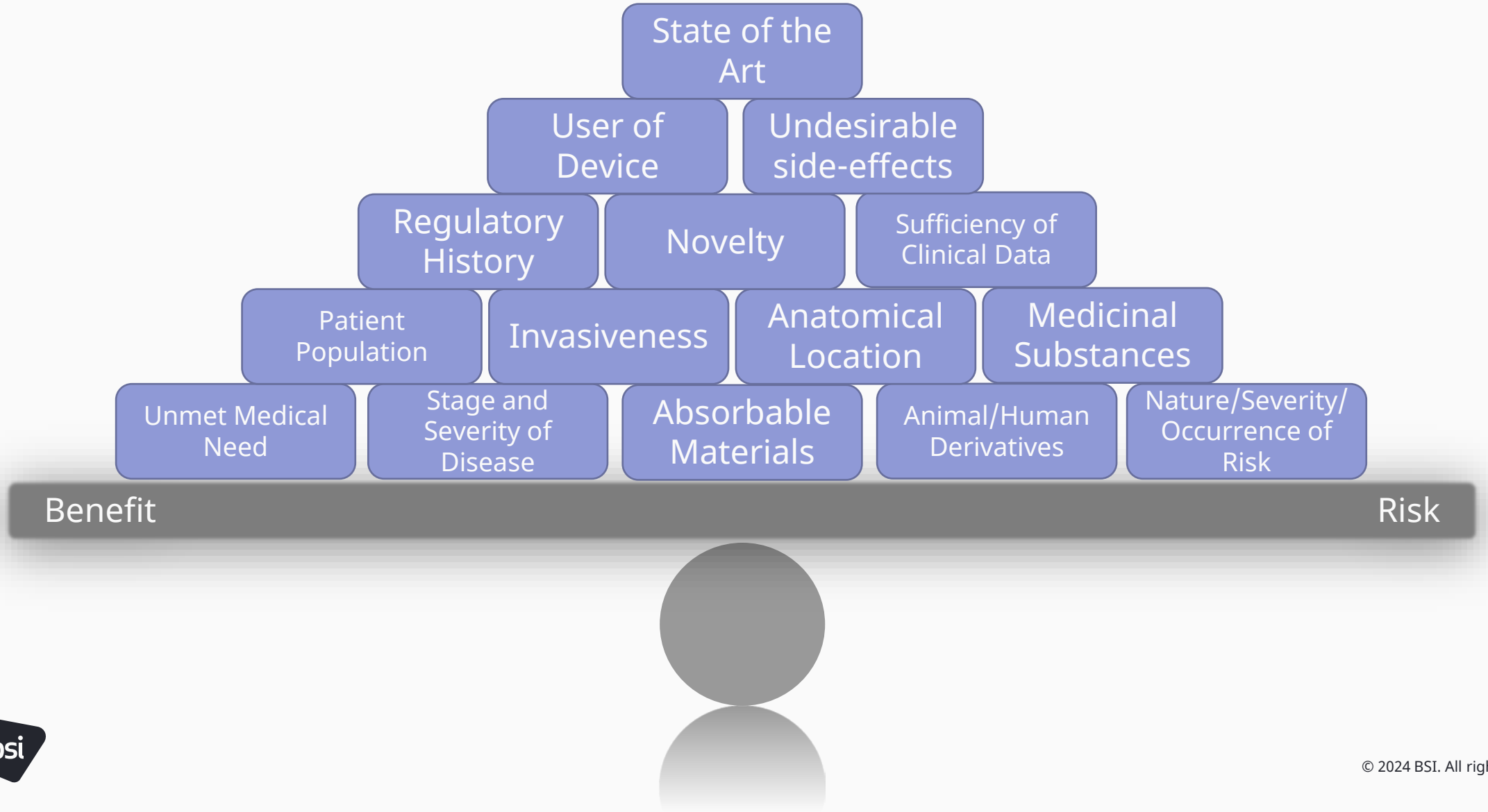
8

- Is there **sufficient** data covering all indications?

9

- What are the post market surveillance plans and what are the post market clinical follow up plans? Do these plans address any gaps in the data?

Benefit/Risk



Benefit/Risk

Benefit | Risk

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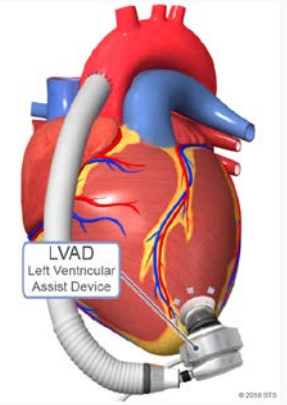
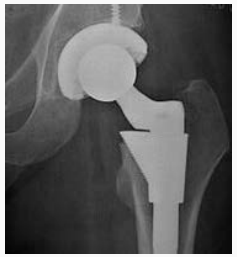
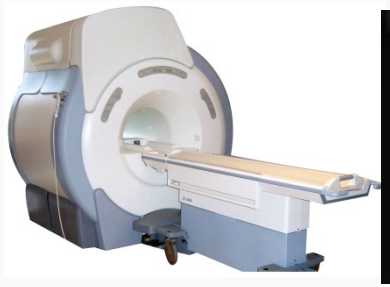
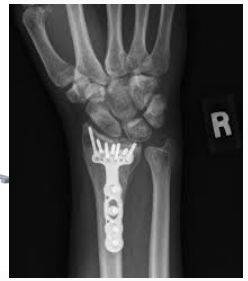


PMCF & Risk

Selected methods should be **justified,** surveys for example may only be appropriate for lower risk devices , or established technologies



RISK, DURATION, INVASIVENESS or UNKNOWNS

POST MARKET CLINICAL FOLLOW UP

SPECIFIC

- Prospective trials (e.g. Expansion of pre-market study, New prospective clinical trial)
- Device registries
- Retrospective studies

GENERAL

- Literature Review
- Complaints/vigilance
- Patient / surgeon questionnaires
- Field surveys

Conclusions

- The Notified bodies number one priority is **patient safety**.
- Notified bodies are resource intensive requiring a unique professional skill set within the regulatory space where there is a limited pool of resources to employ from.
- Notified bodies on instruction through the legislation and competent authorities are ensuring that the MDR is a timepoint that we ensure that only safe and effective medical devices move forward.
- Notified bodies have had to increase their assessment times and depth of assessment in line with the requirements of the regulation.
- It is important to remember that costs to manufacturers is coming from the regulation itself, the need to collect clinical data to drive evidence-based medicine, the cost of additional documentation, the cost of additional audits throughout the certificate cycle such as PSUR, SSCP updates.
- The MDR **is improving patient safety** and transparency in Europe and driving an ‘evidence-based medicine’ culture.

CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945260

For more information, visit: www.core-md.eu

ESC

Biomedical Alliance in Europe

European Academy of Paediatrics
Paediatric Section of U.E.M.S

EPF European Patients Forum

Leiden University Medical Center

University of Oxford

Region Uppsala

RCSI University of Medicine and Health Sciences

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Universitätsspital Bern
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The Tyrolean Private University

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