

# MIDLANDS ACADEMICS: IP & COMMERCIALISATION WORKSHOP

## Regulatory Considerations

16<sup>th</sup> September 2019







# EXAMINING THE IMPACT OF EU MDR AND IVDR ON SUPPLIER MANAGEMENT OPERATIONS

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# EXAMINING THE IMPACT OF EU MDR AND IVDR ON SUPPLIER MANAGEMENT OPERATIONS

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A photograph of two hikers with large backpacks and trekking poles, seen from behind as they ascend a vast, snow-covered mountain slope. The sky is filled with dramatic, dark clouds. The hikers are positioned on the left side of the frame, leaving a trail in the snow. Their shadows are cast long and dark on the white snow.

# A Brief History of Time

...with apologies to Stephen Hawking

# The Past

National registration developments started mid 70s

- Focussed on product registration
- No attention to manufacturing process or clinical benefit
- Heavily based on pharma world of regulations
- High approval times and high degree of divergence
- Needed separate legislation to stop barrier to trade

Adoption of New Approach to Technical Harmonization and Standards by EU Council in 1985

- New Approach legislation – intended to harmonise product safety requirements across EU
- Blue Guide (current version 2016/c 272/01)
- 3 Medical device directives developed late 80s and through the 90s
- Amendments in 2007 and further recast initiated in 2008

**Active Implantable Medical Device Directive (AIMDD) – 90/385/EEC .**

Introduced July 1990

**Medical Device Directive (MDD) – 93/42/EEC.**

Introduced June 1993 (mandatory 1998)

**In-Vitro Diagnostic Medical Device Directive (IVDMD) – 98/79/EC.**

Introduced October 1998

**Latest amendment to all 3 above directives March 2007 (2007/47/EC)**

# A Shift in the EU Regulatory Landscape

Heightened public awareness from high profile device issues

- PIP, 2010
- Metal on Metal, 2010
- Notified Body, 2012
- Vaginal Mesh 2017

Political pressure to make changes to address public concern

- Media targeted 'weak' regulatory framework as not fit for purpose

Spotlight on inconsistent Notified Body services

Un-level playing field throughout EU

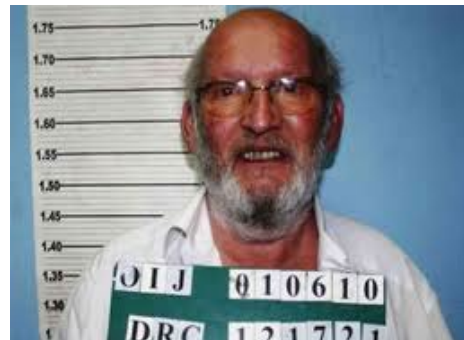
Technology evolved since 1990s



21 May 2011



10 December 2011





# The Present

Existing Directives remain valid but with enhanced requirements in certain areas:

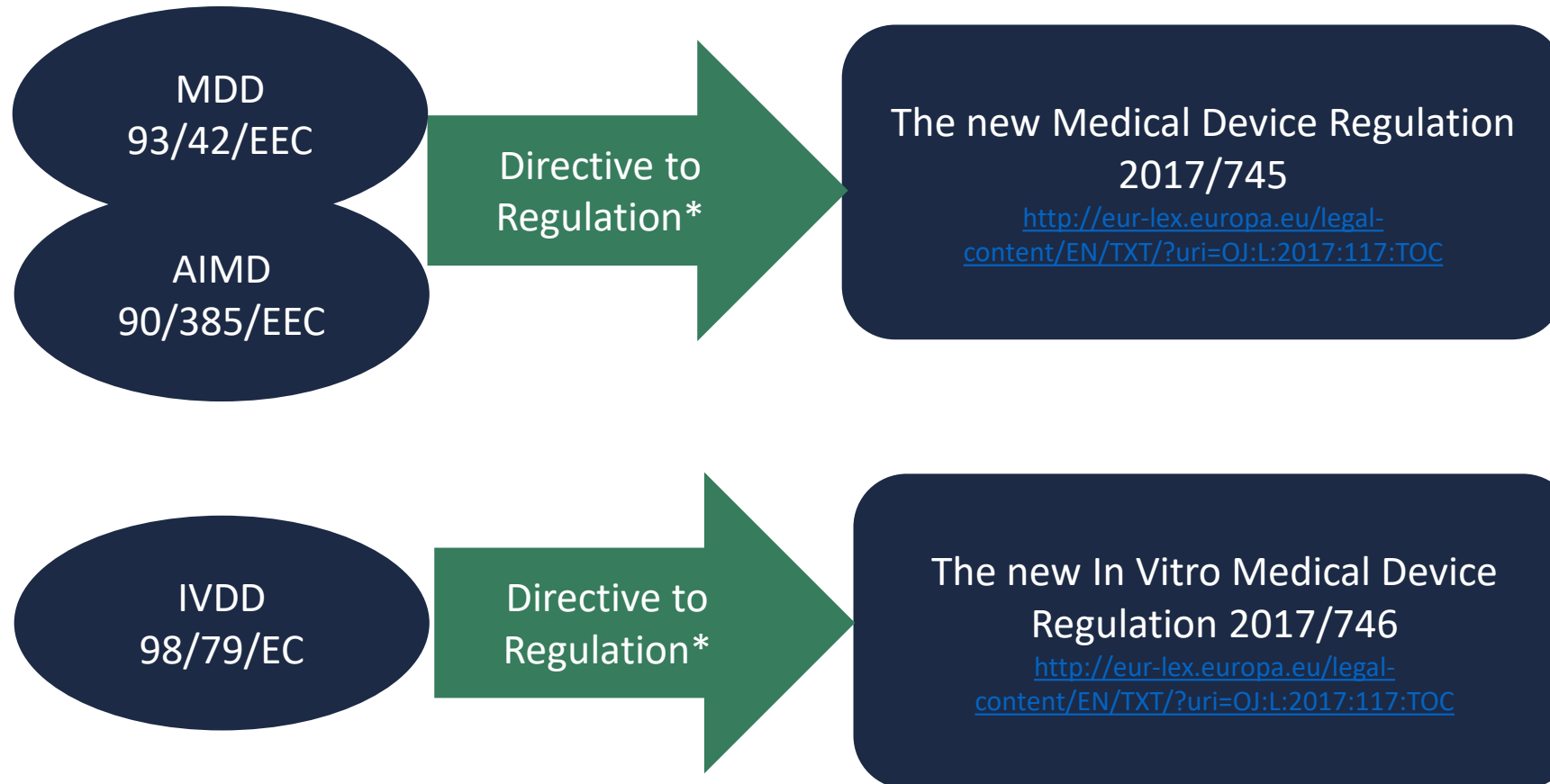
- John Dalli Joint Action Plan, 2012
- Unannounced Audits, 2012
- Improved oversight by Competent Authorities
  - Notified Bodies (joint audits)
  - PMS (EU wide discussions)
- Increased scrutiny on clinical evidence
- Increased scrutiny on PMS and PMCF
- Reduction in Notified Bodies
- Redefined responsibilities for Own Brand Labelling

New ISO 13485: 2016 standard published March 2016:

- Closer aligns with global regulatory requirements
- More focus on risk management throughout QMS
- Expands scope to all stakeholders in device lifecycle
- More focus on software validation



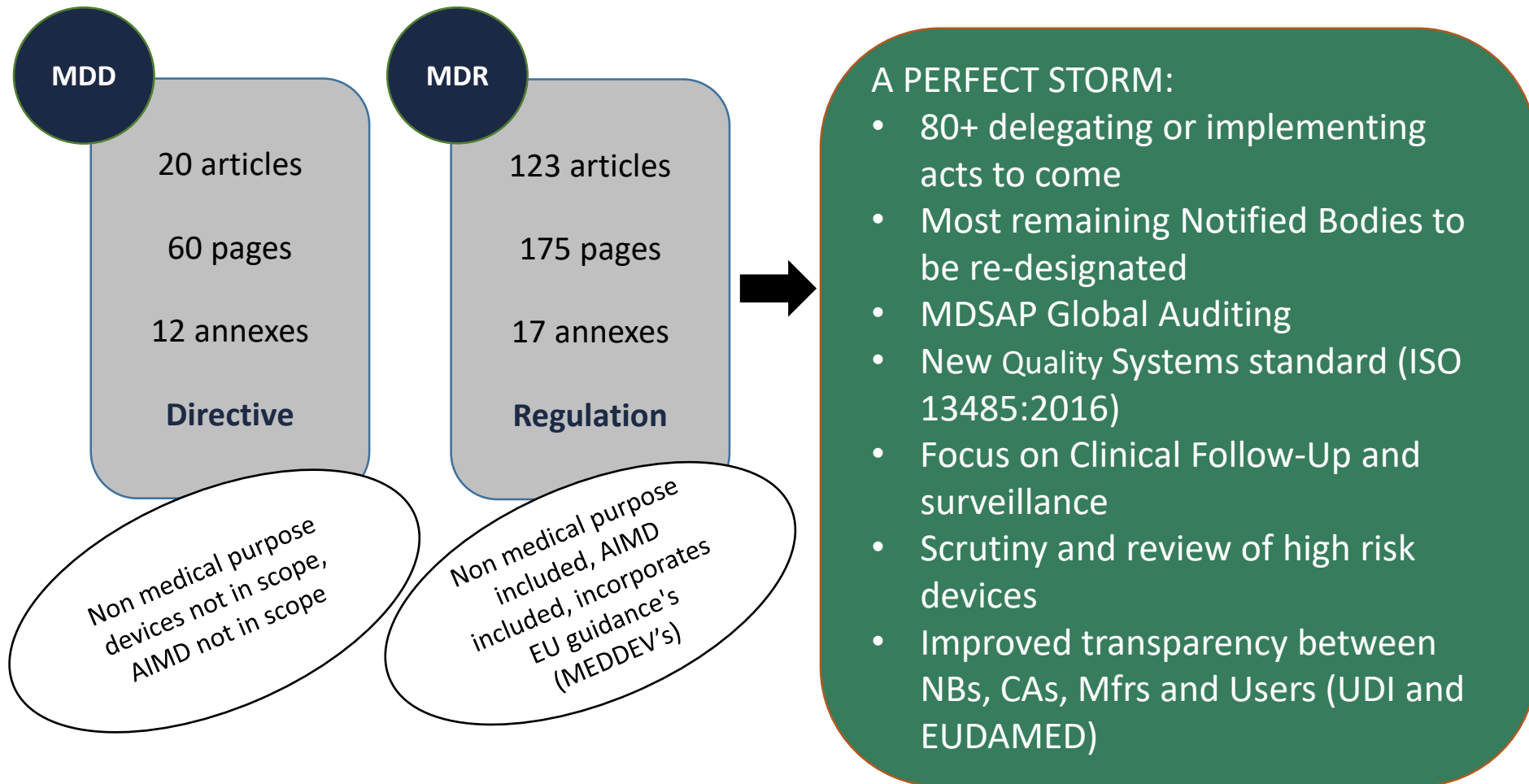
# The Future...is here



\*EU Regulation is immediately applicable and enforceable by law in all member states



# The Future...is here



Don't Assume that it's a  
Medical Device





## Definitions – Medical device

*'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:*

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,*

*and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.*

*The following products shall also be deemed to be medical devices:*

- devices for the control or support of conception;*
- products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.*

## Definitions - Accessory

*“**accessory for a medical device**” means an article which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s);*



## Example: Femoral Head & Cup

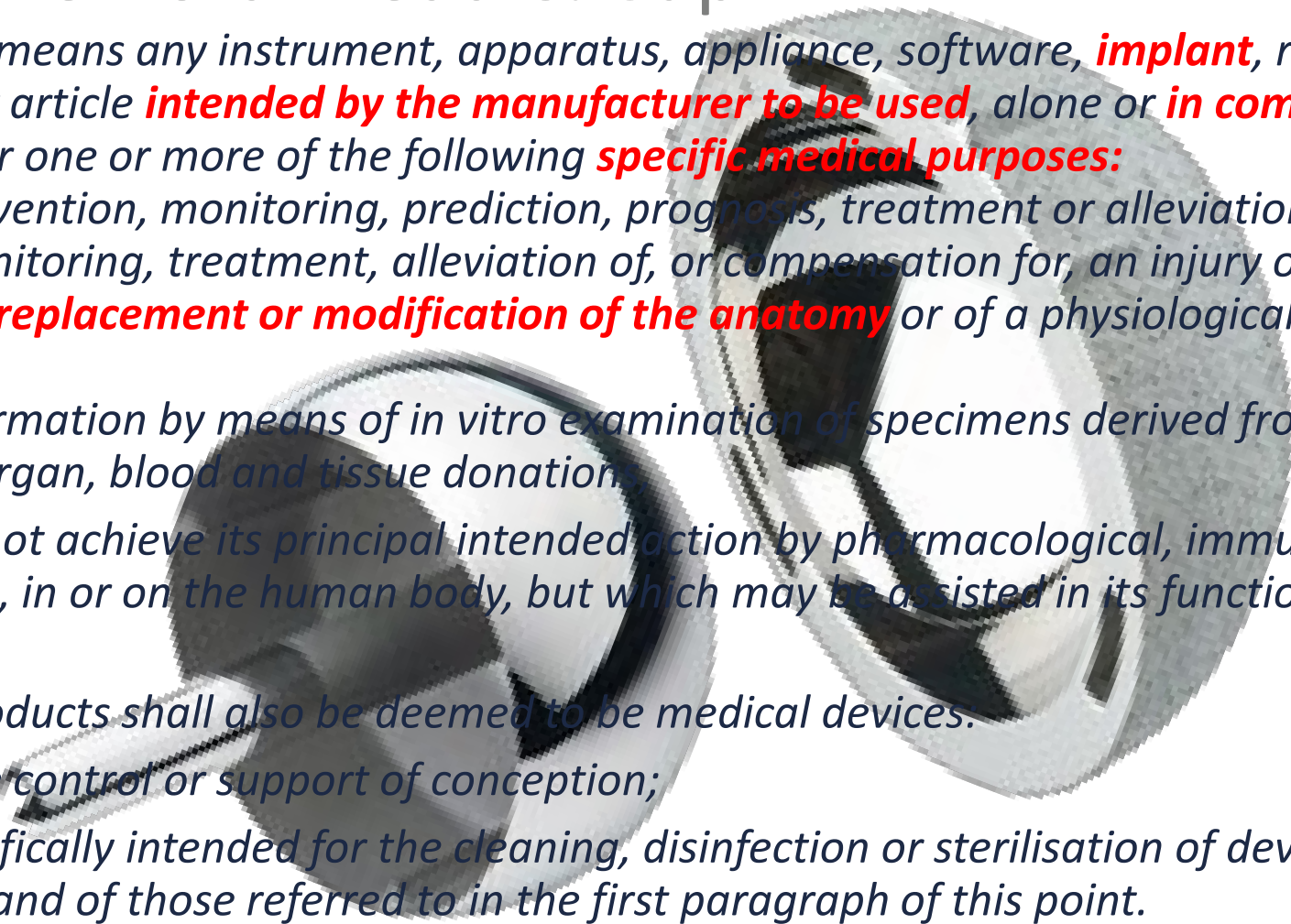
*'medical device' means any instrument, apparatus, appliance, software, **implant**, reagent, material or other article **intended by the manufacturer to be used**, alone or **in combination**, for **human beings** for one or more of the following **specific medical purposes**:*

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, **replacement or modification of the anatomy** or of a physiological or pathological process or state,
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

*and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.*

*The following products shall also be deemed to be medical devices:*

- devices for the control or support of conception;
- products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.



## Definitions - IVD

*“**in vitro diagnostic medical device**” means any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:*

- (a) concerning a physiological or pathological process or state;*
- (b) concerning congenital physical or mental impairments;*
- (c) concerning the predisposition to a medical condition or a disease;*
- (d) to determine the safety and compatibility with potential recipients;*
- (e) to predict treatment response or reactions;*
- (f) to define or monitoring therapeutic measures.*

*Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices;*



# Definitions – Specimen Receptacle

*“**specimen receptacle**” means a device, whether of a vacuum-type or not, specifically intended by its manufacturer for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination;*

## Example: - Blood Glucose Test

*“in vitro diagnostic medical device” means **any medical device which is a** reagent, reagent product, calibrator, control material, **kit**, instrument, **apparatus**, piece of equipment, software or system, **whether used** alone or **in combination**, **intended by the manufacturer to be used in vitro for the examination of specimens, including blood** and tissue donations, **derived from the human body**, solely or **principally for the purpose of providing information** on one or more of the following:*

- (a) **concerning a physiological** or pathological process or **state**;*
- (b) concerning congenital physical or mental impairments;*
- (c) concerning the predisposition to a medical condition or a disease;*
- (d) to determine the safety and compatibility with potential recipients;*
- (e) to predict treatment response or reactions;*
- (f) to define or monitoring therapeutic measures.*

*Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices;*



# Software

*'medical device' means any instrument, apparatus, appliance, **software**, implant, reagent, material or other article **intended by the manufacturer to be used, alone or in combination**, for human beings **for one or more of the following specific medical purposes**:*

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,*

*and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.*

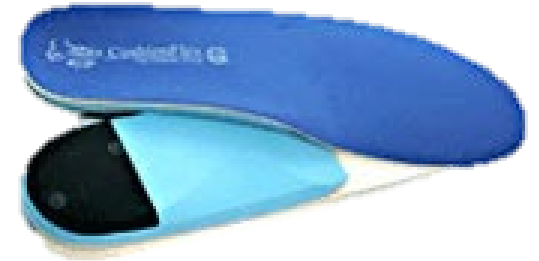
*The following products shall also be deemed to be medical devices:*

- devices for the control or support of conception;*
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# What is NOT a Medical Device

- 'Most (but not all) creams, lotions and potions
- Most (but not all) disinfectants
- Dental whitening products
- Aids for daily living
- Some products that incorporate a drug
- Peritoneal solutions for CAPD
- IUD with hormone action





# Device Classification



# Medical Device Classification

- Classified According to Risk
- Class I n/s, n/m, n/r
- Class I sterile
- Class I measuring
- Class I reusable
- Class IIa
- Class IIb
- Class III

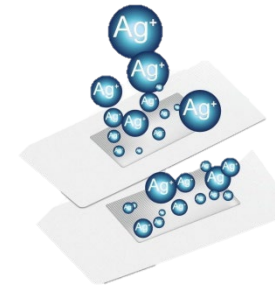
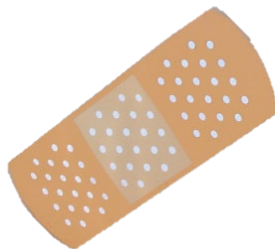


# Medical Device Classification

- Annex VIII of 2017/745 MDR
- 4 sections
  - Non-invasive devices
  - Invasive devices
  - Active devices
  - Special Rules
- 22 rules

## Example: Plasters & Wound Dressings

- Section 1 - Non invasive
- Rule 4
- All non-invasive devices which come into contact with injured skin:
- Normal plasters for superficial wounds. Class I
- Absorbent dressing for major trauma. Class IIb
- Antimicrobial Silver ion dressing. Class III



## Example: In Ear Thermometer

- Section 2 – Invasive
- Rule 5
- All invasive devices with respect to body orifices, other than surgically invasive devices and which are not intended for connection to an active medical device or which are intended for connection to an active medical device in Class I:
- Transient Use. Class I





# IVD Classification

- Classified According to Risk
- Class A
- Class B
- Class C
- Class D

# IVD Classification

- Annex VIII of 2017/746 IVDR
- 1 section
- 7 rules

# IVD Classification – Rule 1

Devices intended to be used for the following purposes are classified as class D:

- detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration;
- detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation;
- determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.



## IVD Classification – Rule 2

Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C, except when intended to determine any of the following markers:

- ABO system [A (ABO1), B (ABO2), AB (ABO3)];
- Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)];
- Kell system [Kel1 (K)];
- Kidd system [JK1 (Jka), JK2 (Jkb)];
- Duffy system [FY1 (Fya), FY2 (Fyb)];

in which case they are classified as class D.

# Intended Use Statement



# Intended Use

- The Intended Use Statement is the manufacturers stated intentions for the device and all claims and regulations hinge on that
- Important to be consistent with the Intended Use Statement in marketing and literature including salespersons behaviour and website
- Validation and Verification of performance claims must be aligned to the Intended Use Statement



# Planning for Routine Production



# Typical Approaches

- Manufacture using own facilities
  - Document manufacturing methodology
  - Document Risk Analysis
    - dFMEA, pFMEA, uFMEA
  - Design History File
- Use sub-contract manufacturing facilities
  - Can delegate some responsibilities
- Licence / Sell IPR
  - Greater success if CE marked



# Technical Documentation





# Safety, Efficacy & Manufacture

- Legal requirement for legal manufacturer to hold technical documentation regarding the safety and efficacy of the device
- Applicable to all classifications of devices, irrespective of the Conformity Assessment route taken
- Must be available at all times for regulatory authorities
- Must be kept up to date
- Must be retained for the lifetime of the device, and at least 10 years from the date of the last production (implants 15 years)



# Typical Contents

- 2017/745 MDR Annex II

Section 1: Device Description & Specification, Including Variants & Accessories

Section 2: Information to be Supplied by the Manufacturer

Section 3: Design & Manufacturing Information

Section 4: General Safety & Performance Requirements

Section 5: Benefit-Risk Analysis & Risk Management

Section 6: Product Verification & Validation

# Section 1: Device Description & Specification...

- General description
- Product variants and configurations
- Accessories, other medical devices and other products that to be used with
- Intended use statement:
- Medical condition is to be treated
- Intended patient population
- Contraindications
- Description of how the device works including unique features and performance claims

## Section 1: Device Description & Specification...

- Product specification
- List of components and their materials
- Materials of Animal Origin statement
- Human cells/tissue products/derivatives statement
- Previous generations or similar competitor devices
- Device classification
- Conformity assessment route

## Section 2: Information to be Supplied by the Manuf.

- All labelling associated with the device
- labels on the device itself
- labels on the primary pack
- labels on the packaging, etc
- UDI
- IFU (Instructions for Use)
- Sales / Promotional Literature
- A list of countries where the device will be marketed, and corresponding translations into official languages



## Section 3: Design & Manufacturing Information

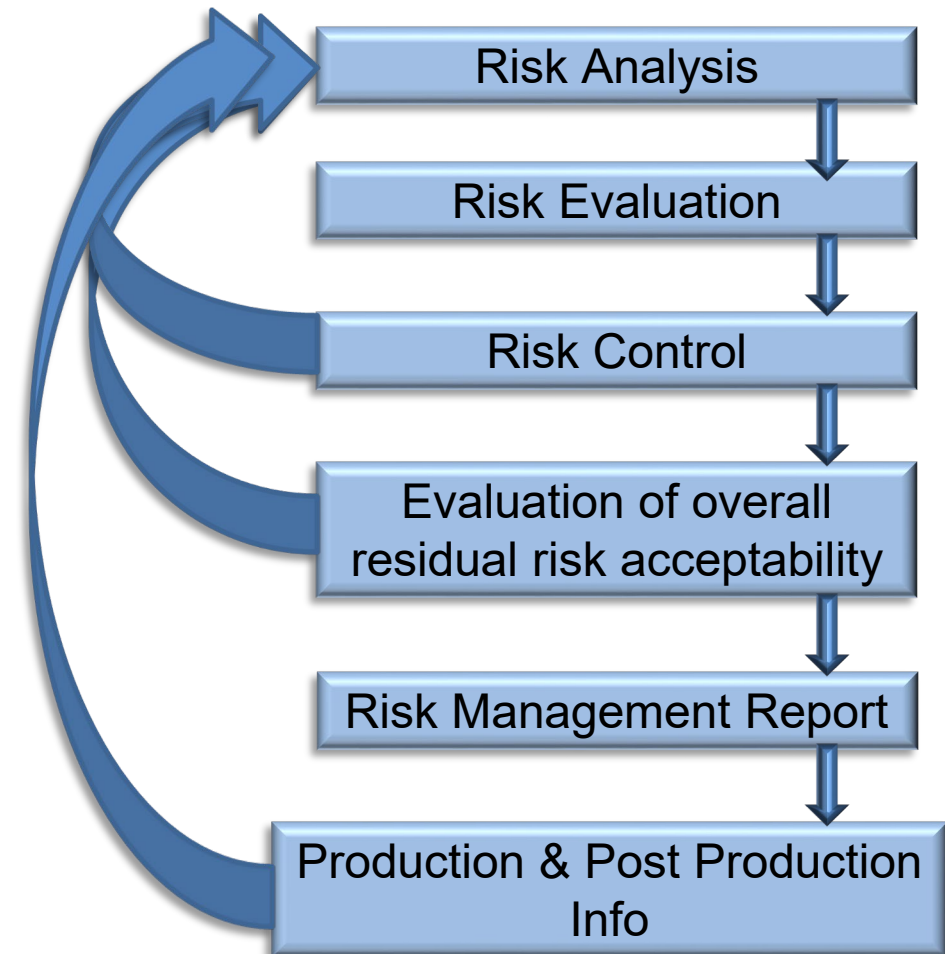
- Description of the design stages applied to the device
- Technical drawings
- Detail on product design
- General overview of the manufacturing process
- Manufacture, assembly, in process and final product testing, device packaging
- Documentation comprising the Device Master Record
- Critical suppliers including sub-contracted manufacturing processes
- Product Release process

## Section 4: GSPR

- EC Declaration of Conformity
- Full details for product classification
- Completed GSPR Checklist
- List of Applied Standards
- List of Applied Common Specifications

## Section 5: Benefit-Risk Analysis & Risk Management

- Risk Management according to EN ISO 14971:2019
- Risk Management Plan
- dFMEA
- pFMEA
- uFMEA



## Section 6: Product Verification & Validation

- Summary of the results of verification and validation activities typically:
  - Engineering tests
  - Laboratory tests
  - Clinical test data
  - Published literature inc. relevant competitor products
- Biocompatibility data
- Medicinal substances
- Animal or human cells, tissues or their derivatives
- Sterilization



## Section 6: Product Verification & Validation

- Software verification and validation
- Pre-clinical data related to clinical safety and performance of the device.
- Clinical Evaluation
- Shelf Life with supporting data
- Any and All other relevant data

A photograph of two hikers with large backpacks and trekking poles, seen from behind as they ascend a steep, snow-covered mountain slope. The sky is filled with dramatic, dark clouds. The scene conveys a sense of challenge and perseverance.

# Post Market Obligations

# Post Market Surveillance – Key Activities

## Inputs

- FSCA & CAPA
- Vigilance
- Complaint Trends
- Clinical Registries/ Studies
- Publications
- Significant Changes

Post-Market Surveillance System (SOPs & Infrastructure)

Product-Specific  
Post-Market Surveillance (PMS) & Post-Market Clinical Follow-Up (PMCF) Plans

EUDAMED  
EU Database  
(UDIs)



Risk Management  
File Update

Post-market Clinical  
Follow-up Report  
(PMCF-R)

Clinical Evaluation  
Plan/Report Update

IFU/Patient  
Brochure/Promo Material  
Alignment with RM/CER  
Updates

Class III, IIb, or Implantable Devices – Annual or Triggered Update. Class IIa, Class I – Every 2 years or Triggered Update

PMS Trend Report

Class I devices

Periodic Safety  
Update Report  
(PSUR)

NB/CA Accessible: Class IIa, IIb, III and  
Implantable devices

Summary of Safety &  
Clinical Performance  
(SSCP)

PUBLIC INFO: Class III and  
Implantable devices



# THANK YOU

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