Bristows

Software Medical Devices under the MDR & IVDR

DHAC Webinar Series #2

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Agenda

1. The Medical Devices Regulation & IVD Regulation
2. Scope
3. Classification
4. Obligations under the MDR – software focus
5. Obstacles

How did we get here?

- Medical Device Directive
- Response to scandals
- Repealed and replaced by MDR on 5 April
- MDR comes into force on 26 May 2020
- IVDR in parallel…

Medical Devices Regulation to apply from May 2020 (“MDR”)

In Vitro Diagnostic Medical Devices Regulation to apply from May 2022 (“IVDR”)

Biggest EU regulatory changes in decades

- New European regulatory framework
  - MDRs: No grandfathering!
    - All existing devices need to be re-evaluated and certified
    - Significant number of SKUs will be abandoned
  - IVDR: Fundamental restructuring

- In parallel - “bonfire of the notified bodies”
  - All Notified Bodies must apply to be certified under MDR
  - Industry considers the Notified Body limitations to be the greatest threat
  - One significant casualty already (Intertek)

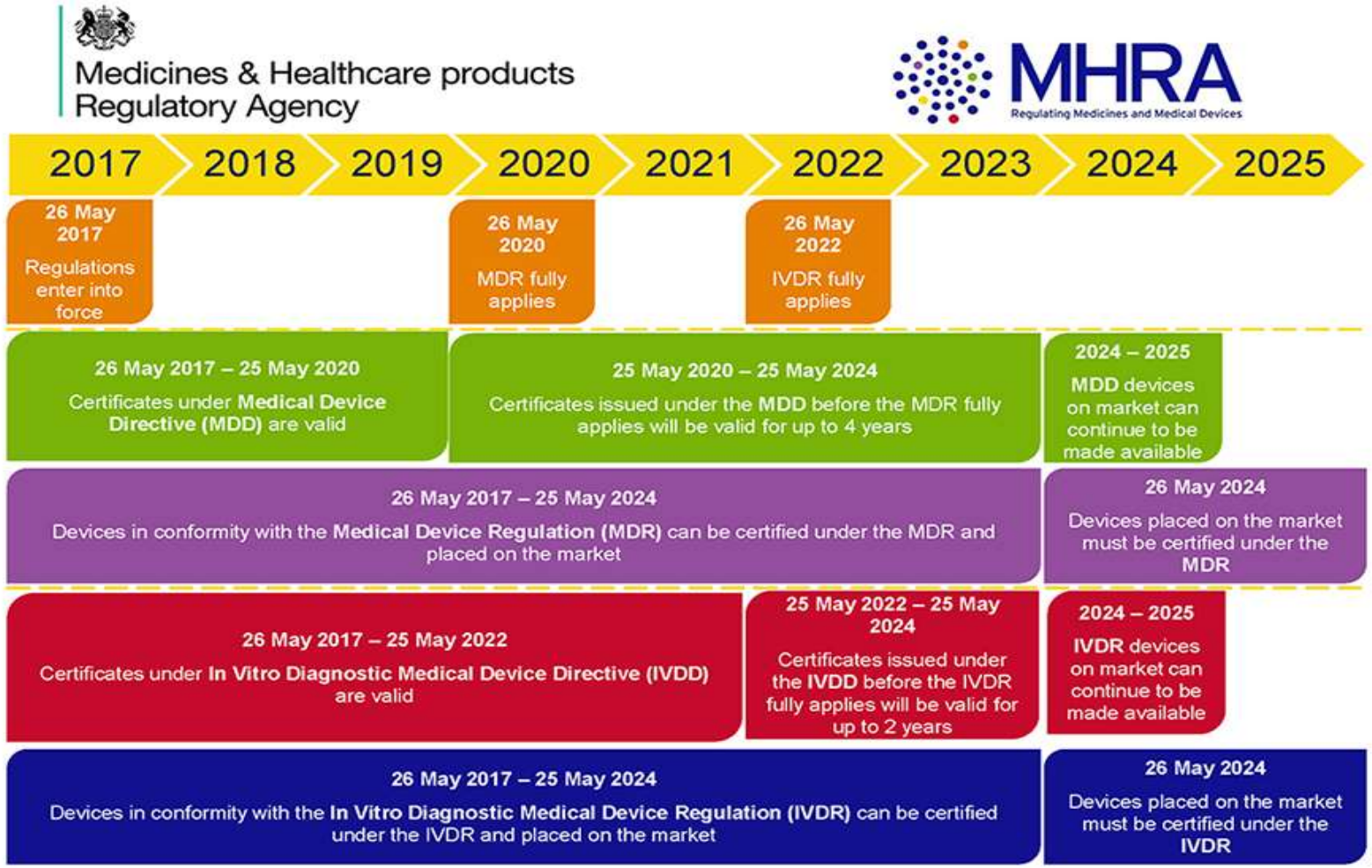
“Medical problems wipe £500m off Smiths Group's value” (18 July 2018)

The Telegraph

Features of the MDR landscape

- Classification changes (including software)
- New definitions (e.g. economic operator)
- Introduction of PRRC (Person Responsible for Regulatory Compliance)
- Increased post-market surveillance (PMS) obligations
- Introduction of European Medical Devices Databases (EUDAMED)
- Introduction of Unique Device Identifiers (UDIs)
- More specificity for software

Transition from MDD to MDR



Scope

Old MDD Definition of Medical Device

- ‘any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used **specifically** for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings **for the purpose of**:
  - diagnosis, prevention, monitoring, treatment or alleviation of disease,
  - diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
  - investigation, replacement or modification of the anatomy or of a physiological process,
  - control of conception…

Article 1(2)(a) of Directive 93/42

“A product which is intended by the manufacturer to be applied for human beings for the purpose of investigation of a physiological process constitutes a medical device, within the terms of the third indent of Article 1(2)(a) of Directive 93/42/EEC, ***only where it is intended for a medical purpose****.”*

Brain Products GmbH, Case C-219/11

New MDR Definition of Medical Device

- “any instrument, apparatus, software […] 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 handicap,
  - investigation, replacement or modification of the anatomy or of a physiological **or** pathological process or state,
  - providing information by means of in vitro examination derived from the human body, including organ, blood and tissue donations […]”

MDR Art 2(1)

This declares that the listed items are medical purposes. A response to *Brain Products*?

Function – not just intended purpose – matters

- “[…] software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of a medical device, qualifies as a medical device, **while software for general purposes, even when used in a healthcare setting, or software intended for life-style and well-being purposes is not a medical device** [...]”

MDR Rec 19.

- “Examples of software which are not considered as being for the benefit of individual patients are those which aggregate population data, provide generic diagnostic or treatment pathways, scientific literature, medical atlases, models and templates as well as software for epidemiologic studies or registers [...]”

Decision steps 3&4, MEDEV 2.1/6.

Function – not just intended purpose – matters

- “If the software does not perform an action on data, or performs an action limited to storage, archival, communication, ‘simple search’ or lossless compression […] it is **not a medical device**.”

SNITEM (Case C-329/16)

- “It follows that software, of which at least one of the functions makes it possible to use patient-specific data for purposes, inter alia, of detecting contraindications, drug interactions and excessive doses, **is, in respect of that function, a medical device**.”

SNITEM (Case C-329/16

- Note CJEU’s lack of deference to “intended purpose”. Implies that function is more determinative.

Classification (Annex VIII)

Classification

- “Software, which drives a device or influences the use of a device, shall fall within the same class as the device.

  If the software is independent of any other device, it shall be classified in its own right”

  Annex VIII, s3.3

- “Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as **class IIa**, except if such decisions have an impact that may cause:
  - Death or an irreversible deterioration of a person’s state of health, in which case it **is class III**; or
  - A serious deterioration of a person’s state of health or a surgical intervention, in which case it is classified as **class IIb**.”

  “Rule 11”: Annex VIII, s6.3

Classification

- “Software intended to monitor physiological processes is classified as **class IIa**, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as **class IIb**.
- All other software is **class I**.”

“Rule 11”: Annex VIII, s6.3

Reining in Rule 11

- “Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as **class IIa**, except if such decisions have an impact that may cause:
  - Death or an irreversible deterioration of a person’s state of health, in which case it **is class III**; or
  - A serious deterioration of a person’s state of health or a surgical intervention, in which case it is classified as **class IIb**.”

“Rule 11”: Annex VIII, s6.3

- Software could perform a relatively innocuous function, but if the resulting decision (such as a decision not to treat a patient) could result in death or irreversible deterioration, a device is class III.
- So, from Class I (MDD) to Class III (MDR)…..

MDCG Guidance on classification

- Not legally binding, but MDCG has an official role in advising Commission on classification
- “Rule 11 is “…intended to address the risks related to the information provided by an active device, such as [medical device software]”.
- In this regard, it notes that Rule 11 was introduced in line with guidance of IMDRF the International Medical Devices Regulators Forum (IMDRF).
- Rule 11 “…describes and categorises the significance of the information provided by the active device to the healthcare decision (patient management) in combination with the healthcare situation (patient condition)”.
  - Neither term is explicitly used in Rule 11.

MDCG Guidance on classification

- MDCG divides Rule 11 into three “sub-rules”
- ‘Sub-Rule 11a’ (the first three paragraphs of Rule 11). This sub-rule is ‘generally applicable’ to all software medical devices.
- ‘Sub-Rule 11b’ (the fourth paragraph of Rule 11). This is a specific rule intended to cover software medical devices that are for monitoring purposes only.
- ‘Sub-Rule 11c’ (the last paragraph of Rule 11). This covers ‘all other’ software medical devices.
    - (What, actually, would fall under this rule?)
- Sub-Rule 11a, the Guidance states that Rule 11 was introduced to ‘mirror’ IMDRF approach, which is based on the significance of the information the software provides to the healthcare decision in combination with the healthcare situation or patient condition.

MDCG Guidance on classification

- "Illustrative purposes only"
- Excludes Class I MDSW

State of Healthcare situation or patient condition	Significance of Information provided by the MDSW to a healthcare situation related to diagnosis/therapy		
	High Treat or diagnose ~ *IMDRF 5.1.1*	**Medium** Drives clinical management ~ *IMDRF 5.1.2*	**Low** Informs clinical management *(everything else)*
Critical situation or patient condition ~ *IMDRF 5.2.1*	**Class III** *Category IV.i*	**Class IIb** *Category III.i*	**Class IIa** *Category II.i*
Serious situation or patient condition ~ *IMDRF 5.2.2*	**Class IIb** *Category III.ii*	**Class IIa** *Category II.ii*	**Class IIa** *Category I.ii*
Non-serious situation or patient condition *(everything else)*	**Class IIa** *Category II.iii*	**Class IIa** *Category I.iii*	**Class IIa** *Category I.i*

Table 1: Classification Guidance on Rule 11

Conformity Assessment & PMS

- Before putting any device on the market or putting a device into service, manufacturers shall undertake an assessment of the conformity of that device.

[Art 52(1)&(2)]

- Manufacturers of **class I** devices must self-declare the conformity of their products after drawing up the prescribed technical documentation. However, **if they have a measuring function**, the manufacturer must follow prescribed procedures in which a **notified body** assesses conformity with metrological requirements.

[Art 52(7)]

Obligations

Why being a “device” matters

- “A device may be placed on the market or put into service only if it complies with this Regulation when duly supplied and properly installed, maintained and used in accordance with its intended purpose.”

Art. 5(1) MDR

- “A device shall **meet the general safety and performance requirements** … which apply to it, taking into account its intended purpose.”

Art. 5(2) MDR

- “Demonstration of **conformity with the general safety and performance requirements** shall include a **clinical** evaluation …”

Art. 5(3) MDR

Obligations with particular software relevance

1. General Safety & Performance Requirements (Annex I)
2. UDI system (Annex VI)
3. Clinical Evaluation & Post-Market Clinical Follow-up (Annex XIV)

General Safety & Performance Requirements (Annex I)

Risk management system

- “Manufacturers shall establish, implement, document and maintain a **risk management system**.”
- “a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating.”

Annex I, s3 MDR

Risk management system

- (a) establish + document a **risk management plan**
- (b) identify + analyse **known and foreseeable hazards** for each device
- (c) estimate + evaluate **risks of intended use and reasonably foreseeable misuse**
- (d) **eliminate or control risks** referred to in point (c)*
- (e) evaluate the **impact of information** from the production phase and, in particular, from the post-market surveillance system, **on hazards and the frequency of occurrence thereof**, **on estimates of their associated risks**, as well as on the **overall risk**, **benefit-risk ratio** and **risk acceptability**
- (f) **Amend control measures**, if indicated following the impact assessment referred to in point (e)*

Detailed considerations (e.g. ergonomics)

Annex I, s3 MDR

Performance, Design & Manufacture

- “Devices shall be designed and manufactured in such a way as to **remove or reduce as far as possible**…. (d) the **risks associated with the possible negative interaction between software and the IT environment** within which it operates and interacts”.

Annex I,s14.2 MDR

Performance, Design & Manufacture

- “Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, **shall be designed to ensure repeatability, reliability and performance in line with their intended use**. In the event of a single fault condition, **appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks** or impairment of performance.”

Annex I, s17.1 MDR

- “For devices that incorporate software or for software that are devices in themselves, the software shall be **developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation**.”

Annex I, s17.2. MDR

Performance, Design & Manufacture

- “**Software** referred to in this Section that is **intended to be used in combination with mobile computing platforms shall be designed and manufactured** taking into account the **specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise)**.”

Annex I, s17.3.

- “Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT **security measures, including protection against unauthorised access**, necessary to run the software as intended.”

Annex I, s17.3.

Label and instructions for use

- “The instructions for use shall contain **all** of the following particulars:

  […]

  - (f) where applicable, **information allowing the healthcare professional to verify if the device is suitable and select the corresponding software and accessories**

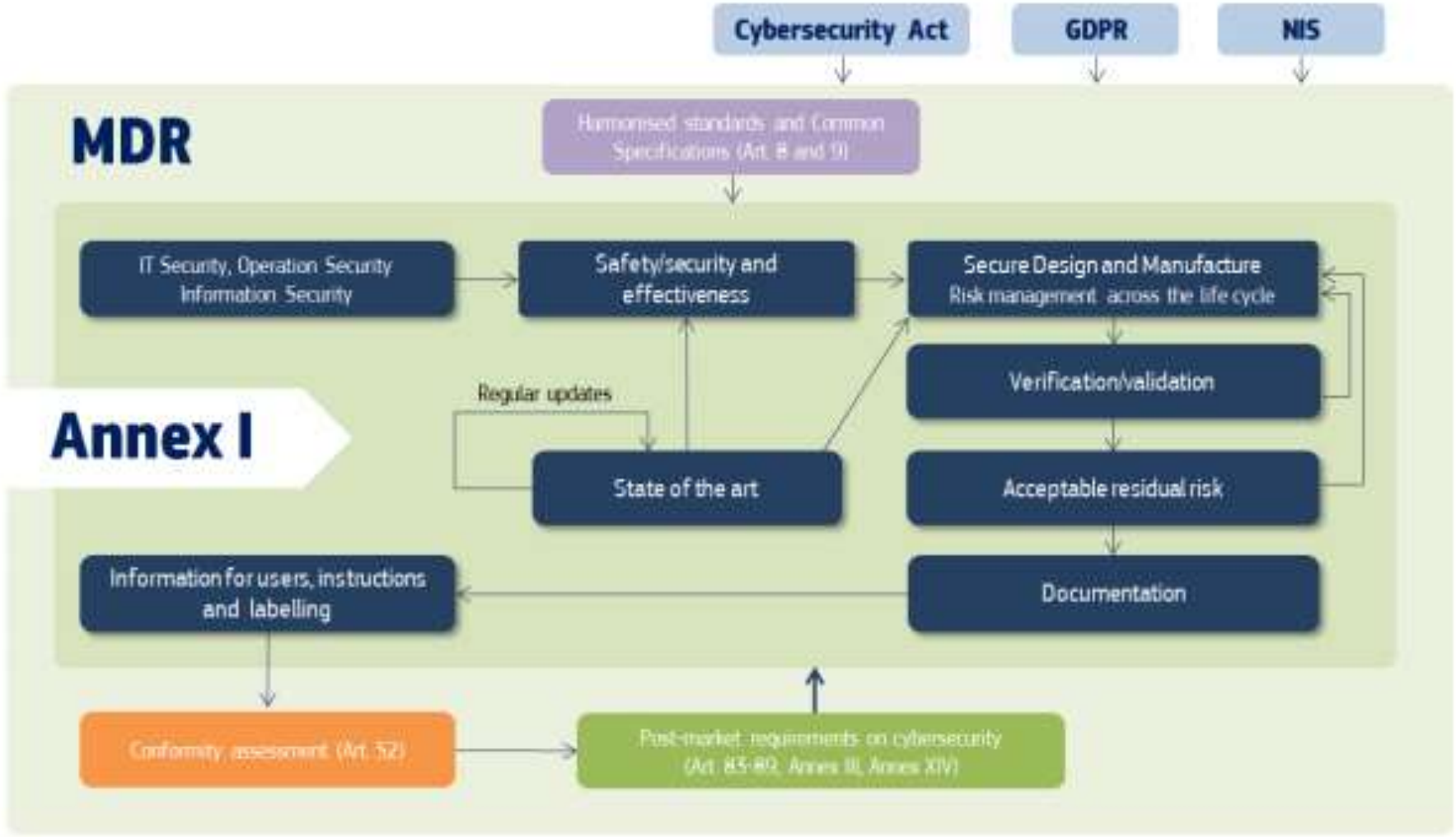
  […]

  - (ab) for devices that incorporate electronic programmable systems, including software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and **IT security measures, including protection against unauthorised access, necessary to run the software as intended**.”

Annex I, s23.4.

Cybersecurity

Relevant Legislation



Cybersecurity Lifecycle

Pre-market activities	Post-market activities
Secure Design (Annex I)	
Risk management (Annex I)	Risk management (Annex I)
Establish Risk Control Measures (Annex I)	Modify Risk Control Measures /Corrective Actions/Patches (Annex I)
Validation, Verification, Risk Assessment, Benefit Risk Analysis (Annex I)	Validation, Verification, Risk Assessment, Benefit Risk Analysis (Annex I)
Technical Documentation (Annex II and III)	Maintain and update a Post-market Surveillance Plan and Post-market Surveillance System (Article 83 and 84)
Conformity Assessment (Article 52)	Trend Reporting (Article 88)
Establish a Post-market Surveillance Plan and Post-market Surveillance System (Article 83 and 84)	Analysis of Serious Incidents (Article 89)
Clinical evaluation process (Chapter VI)	Post-Market Surveillance Report (Article 85)
	Periodic Safety Update Report (Article 86)
	Update Technical Documentation (Annex II and III)
	Inform the Electronic System On Vigilance (Article 92)

Fundamentals

'Risk' means the combination of the probability of occurrence of harm and the severity of that harm.

3 types of security

IT Security

- **Protect computer systems from adverse effects**
- **Concerns confidentiality of information**
- **Data integrity**

Operation Security

- Protection against intended corruption (cyber security attacks)

Information Security

- Developing software in accordance with the state of the art

Security vs Safety

UDI system (Annex VI)

Unique Device Identifier (“UDI”)

- “UDI is a series of numeric or alphanumeric characters that is created through a globally accepted device identification and coding standard. It allows the unambiguous identification of **a specific device** on the market. The UDI is comprised of the UDI-DI and the UDI-PI.
- The word ‘**Unique**’ **does not imply serialisation of individual production units**.”
- “UDI-DI unique numeric or alphanumeric code **specific to a model of device** and that is also used as the ‘access key’ to information stored in a UDI database. [Software ID/expiry on label becomes part of UDI-DI]”
- “The UDI-PI is a numeric or alphanumeric code that **identifies the unit of device production**. The different types of UDI-PIs include serial number, lot number, software identification and manufacturing or expiry date or both types of date.”

Annex VI C, s1.

UDI – Device Software

- UDI shall be assigned at the system level of software which is commercially available per se **and software which constitutes a device in itself.**
- The software identification shall be considered to be the manufacturing control mechanism and shall be displayed in the UDI-PI.
- A **new UDI-DI shall be required** whenever there is a modification that changes:
    (a) the original performance;
    (b) the safety or the intended use of the software;
    (c) interpretation of data.
- Such modifications include **new or modified algorithms, database structures, operating platform, architecture or new user interfaces or new channels for interoperability**.

Annex VI C, s6.5.1&2

UDI – Device Software

- “Minor software revisions” require a new UDI-PI and not a new UDI-DI
  - e.g. “bug fixes, usability enhancements that are not for safety purposes, security patches or operating efficiency”.
  - shall be identified by a manufacturer-specific form of identification.

Annex VI C, s6.5.3

- Placement criteria
  - e.g. “UDI shall be provided on a readily accessible screen for the user in an easily-readable plain-text format, such as an ‘about’ file, or included on the start-up screen”.

Annex VI C, s6.5.4

Clinical Evaluation & Post-Market Clinical Follow-Up (Annex XIV)

Clinical Evaluation

- "… manufacturers shall plan, conduct and document a clinical evaluation…"

MDR Art 61.

- "To plan, continuously conduct and document a clinical evaluation, manufacturers shall:
  - (a) **establish and update a clinical evaluation plan** [...];
  - (b) identify available clinical data relevant to the device and its intended purpose and any gaps in clinical evidence through a **systematic scientific literature review**;
  - (c) **appraise all relevant clinical data** by evaluating their suitability for establishing the safety and performance of the device;
  - (d) generate, through **properly designed clinical investigations** in accordance with the clinical development plan, any new or additional clinical data necessary **to address outstanding issues**; and
  - (e) **analyse all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device including its clinical benefits**."

Annex XIV A, s1.

Clinical Evaluation

- "A clinical evaluation **may be based on clinical data relating to a device for which equivalence to the device in question can be demonstrated**. The following technical, biological and clinical characteristics shall be taken into consideration for the **demonstration of equivalence**:
  - Technical: the device is of similar design; is used under similar conditions of use; has similar specifications and properties including … software algorithms; uses similar deployment methods, where relevant; has similar principles of operation and critical performance requirements;
  - Biological: […]
  - Clinical: device is used for the same clinical condition or purpose, including similar severity and stage of disease, … in a **similar population**, including as regards age, anatomy and physiology; has the same kind of user; has similar relevant critical performance in view of the expected clinical effect for a specific intended purpose.

Annex XIV A, s1.

Post-Market Clinical Follow-Up (“PMCF”)

“PMCF shall be understood to be a continuous process that updates the clinical evaluation […] and shall be addressed in the manufacturer's post-market surveillance plan. When conducting PMCF, the manufacturer shall **proactively collect and evaluate clinical data** from the use in or on humans of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, **with the aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence**”

IVDR (May 2022)

IVDR

- 7% fraction of IVDs needing notified body evaluation under the IVDD
- 85% fraction of IVDs needing notified body evaluation under the IVDR
- 78% fraction of IVDs now marketed that will need notified body evaluation that didn’t before
- Short transition period (2 years shorter than for the MDR

BUT…

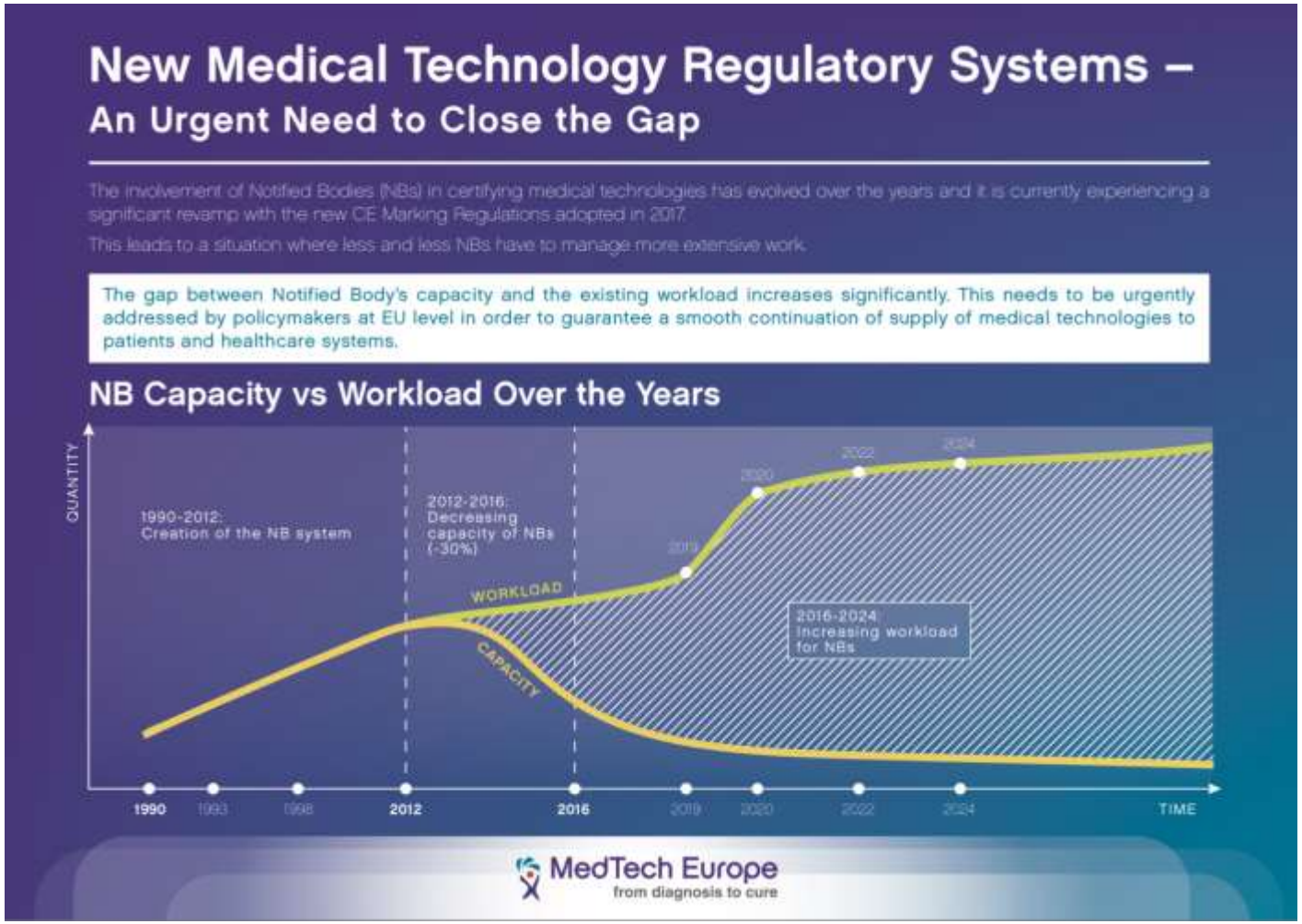
- Not enough notified bodies…

NO-tified Bodies

Notified Body Bottleneck

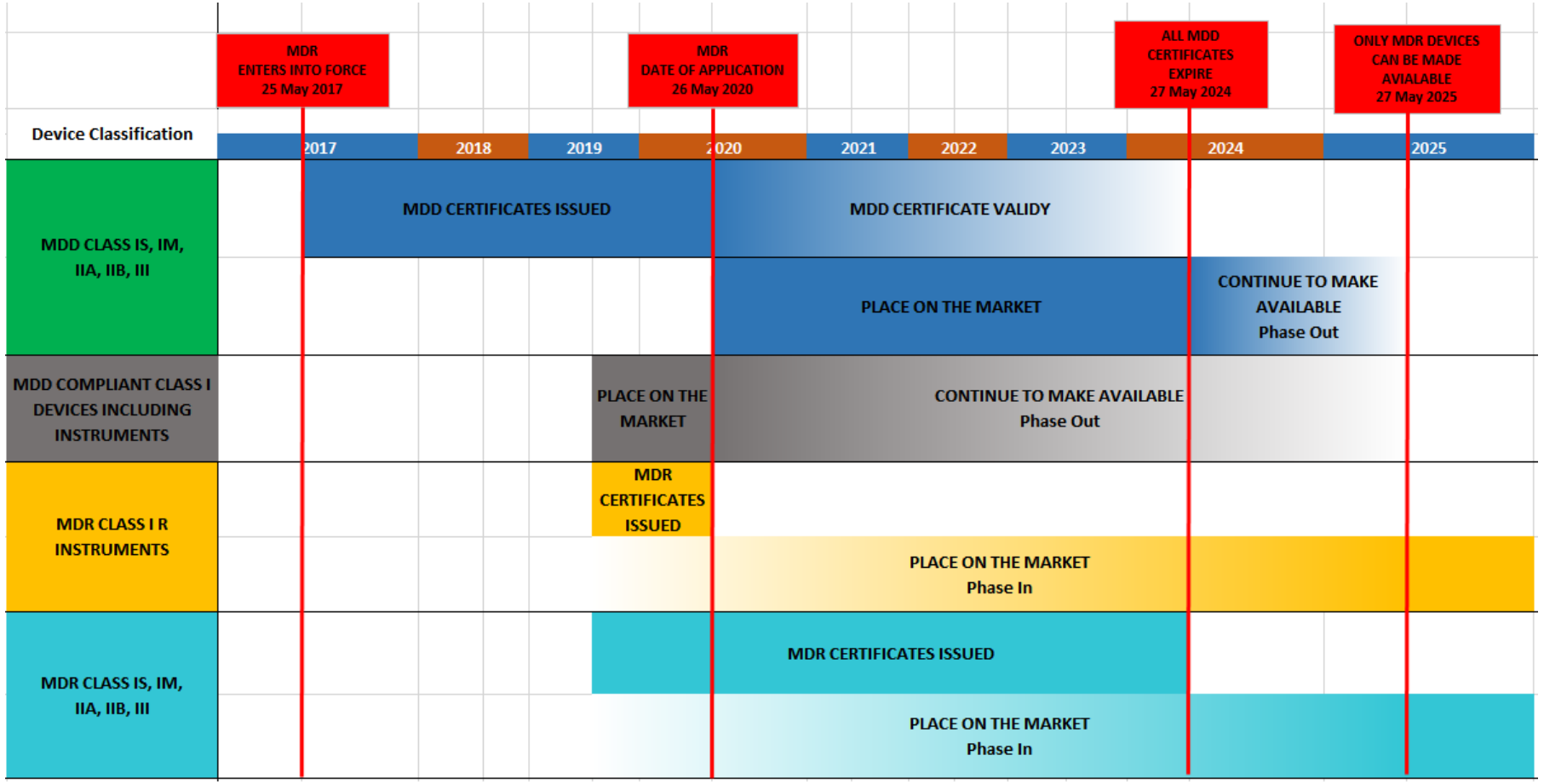
- From 58 notified Bodies in Europe to 2.
- Significant staffing concerns
- Significant experience concerns
- Absence of guidance documents and standards
- Some Med Dev innovators find it virtually impossible to find a Notified Body to take on their product
- We are contacted every week by clients with significant issues caused by Notified Body conduct

Notified Body Capacity Crisis



Thanks: MedTech Europe

Transitional Provisions: MDR



Commercial strategic options: M&A and others

- Target companies (especially “Me Too” products) that will struggle (difficulty obtaining clinical data; difficulty updating or enhancing QMS or just slow)
  - Acquire companies
  - Acquire IP
  - Acquire right to manufacture their products relying on your original clinical data
  - Licence-out access to your original clinical data to enable competitor to “bridge the gap”
  - Authorise others to manufacture and/or sell any products that you will abandon

Discussion

Thank you

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