Recent and Upcoming Changes and Challenges in the EU

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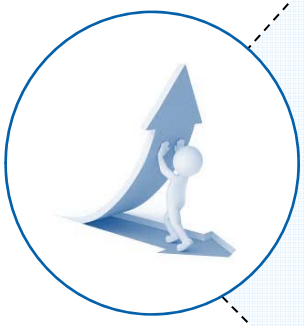
Agenda

Background

US expectation

Upcoming MDR requirements

Why do more and more drugs need medical devices?



- Medical innovation continues to move forward fast
- Empowered patients & consumers are demanding new ways to augment benefit of products leading to more drug **products being combined with a device**
- **Advances in digital technology** are supporting trend towards measuring & improving cost-effectiveness
- Non-traditional healthcare companies like Google, Apple, IBM... are entering healthcare field in search of opportunities

The term Combination Product results from three designations

"single entity" combination products comprised of two or more regulated components

"co-packed" combination products

"cross-labeled"[1] combination products

Product designation based on Primary Mode of Action

1. Including "any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect."

Source: FDA, 21CFR3.2 (e)

Current regulatory landscape for...

...drug products combined with a device (fixed combination or co-package)

FDA combination product legislation **21 CFR Part 4**

Combination Product (term. US)

Medical Device Directive (**MDD**) & Pharmaceutical legislation

Either medical device or medicinal product

Heterogeneous global Combination Product regulatory landscape

	Formal Definition in Regulation	Formal Status Determination Mechanism	Evaluation Process	Manu-facturing Controls	Labelling	Postmarket Reporting
USA	✓	✓		PMOA CP S	S ■	PMOA CP
European Commission	✗	✓		S	S ■	PMOA CP
Australia	✗	✓	S	PMOA CP S	PMOA CP ■	PMOA CP
Japan	✗	✗	PMOA CP	PMOA CP	S ■	PMOA CP
Canada	✓	✓	PMOA CP	PMOA CP S	PMOA CP S	PMOA CP
China	✓	✓	PMOA CP	S	S	✓
Singapore	✓	✓	PMOA CP	PMOA CP	PMOA CP	PMOA CP
India	✓	✓	PMOA CP	PMOA CP	?	?
South Korea	✓	✓	S	PMOA CP S	PMOA CP ■	PMOA CP ■
Hong Kong	✗	✗	PMOA CP	PMOA CP	PMOA CP	PMOA CP
Taiwan	✓ [1]	✓ [1]	PMOA CP	S	S ■	PMOA CP
Thailand	✗	✓	PMOA CP	?	PMOA CP	PMOA CP
Malaysia	✗	✓		PMOA CP	?	PMOA CP
Saudi Arabia	✓	✓	PMOA CP	PMOA CP	PMOA CP	PMOA CP

Legend: Yes: ✓ No: ✗ Regulations or practice applicable to PMOA applied: PMOA CP Cross labelling requirements for co-dependent products: ■ Regulations for all components applied: S Undefined – no regulation or guidance established: ? Regulations under development:

Source: Asian Harmonization Working Party N.B.: Data from 2015 2. Guidance in preparation

Challenges for global development

URS

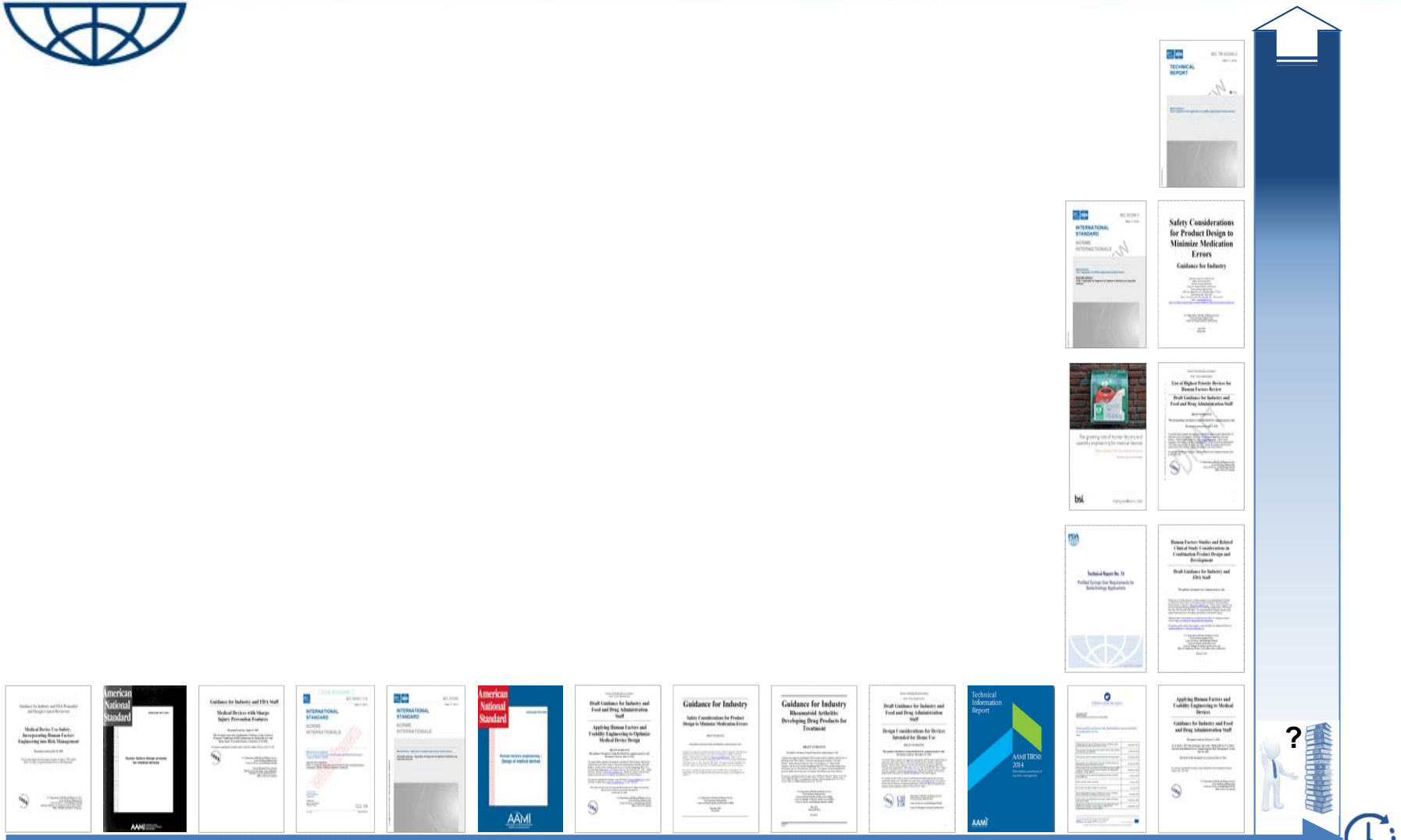
Countries / Regions defined

Rapidly changing landscape for

- Human Factors
- Risk management
- Shipping Studies
- Post Market Surveillance

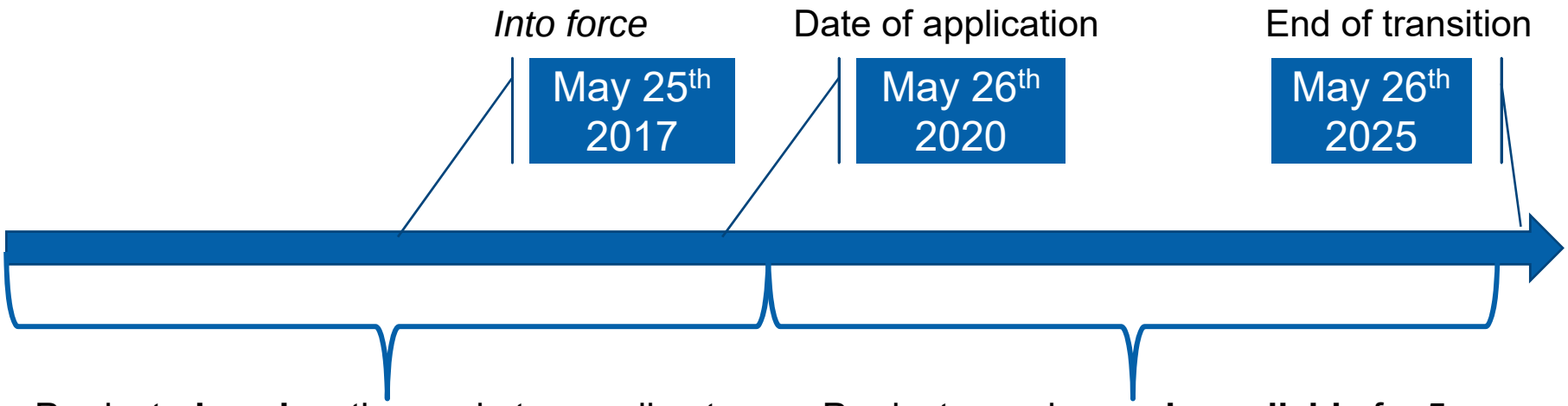
Expectations on defect notification (recalls)

HFE & HFE related “guidelines”



Future situation for EU

The following timeline is to be considered for products (article 120):



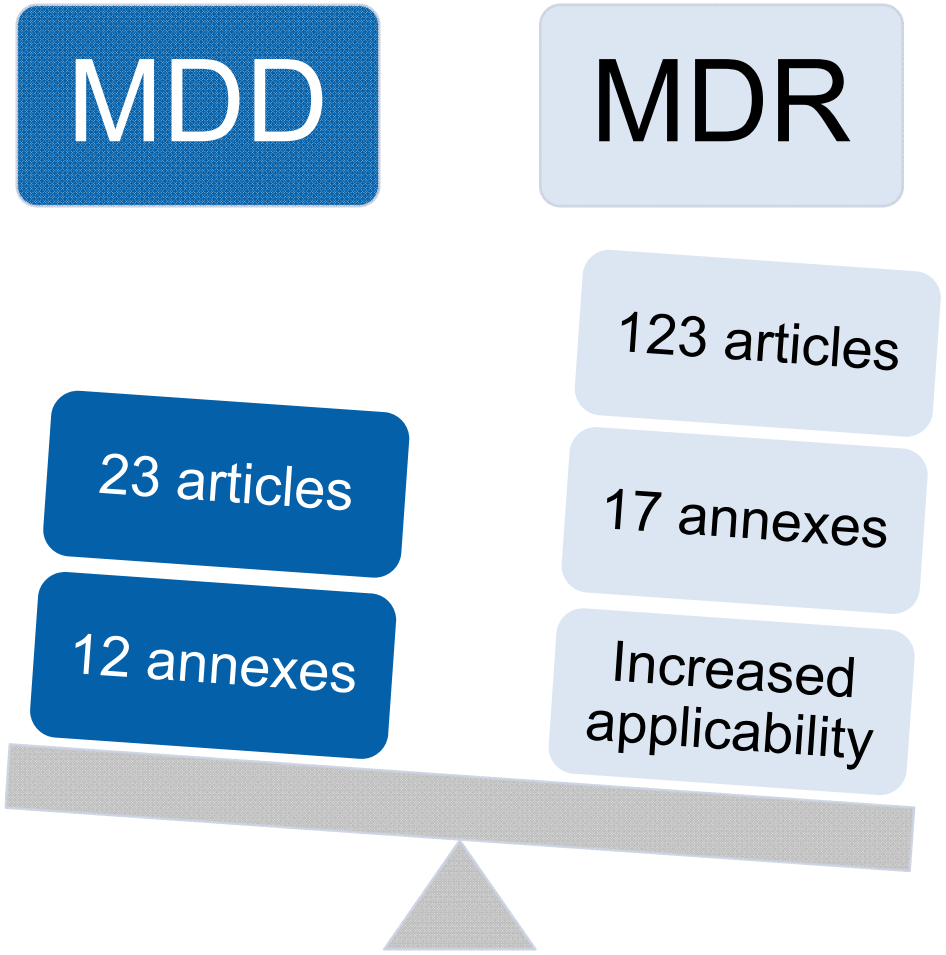
Product **placed** on the market according to MDD

Products can be **made available** for 5 more years

'placing on the market' means the **first making available** of a device, other than an investigational device, on the Union market

'making available on the market' means any **supply of a device... for distribution, consumption or use on the Union market** in the course of a commercial activity

Comparison MDD to MDR



Final version of MDR consists of ten chapters - Facts about the MDR

Chapter	Description	Articles
1	Scope and definitions	1 – 4
2	Making available on the market	5 – 24
3	Identification and traceability of devices	25 – 34
4	Notified bodies	35 – 50
5	Classification and conformity assessment	51 – 60
6	Clinical evaluation and clinical investigations	61 – 82
7	PMS, vigilance and market surveillance	83 - 100
8	Cooperation between Member States	101 – 108
9	Confidentiality	109 – 113
10	Final provisions	114 – 123

Key issues in the MDR – main chapters (I / IV)

2 Making available on the market

- General obligations of distributors
- "**Person responsible for regulatory compliance**
- CE marking identification number – also on promotional material

3 Identification and traceability of devices

- Unique Device Identification (UDI) System and respective database
- Registration on manufacturers – single registration number (SRN)

Key issues in the MDR – main chapters (II / IV)

4 Notified bodies

- New application for MDR; MDD notification is not automatically transferred
- Increased notification and monitoring requirements
- Coordination and cooperation of notified bodies

5 Classification and conformity assessment

- Conformity assessment reduced to three procedures
- Application in parallel with more than one notified body is explicitly interdicted

Key issues in the MDR – main chapters (III / IV)

6 Clinical evaluation & clinical investigations

Stricter requirements on clinical evaluation:

- Evaluation of relevant scientific literature AND
- Evaluation of the results of all available clinical investigations AND
- Consideration of available alternative treatment options
- Equivalence to an already marketed device by another manufacturer (in order to avoid a clinical investigation) requires „full access to the technical documentation on an ongoing basis“

Key issues in the MDR – main chapters (IV / IV)

7 PMS, vigilance and market surveillance

PMS: integral part of the QMS

Vigilance:

- Reporting of serious incidents and field safety corrective actions via the electronic system
- Concrete timelines are provided
- Trend reporting

Key issues also identified in the MDR Annex

7 **Requirements to be met by notified bodies**

- More strict requirements on audit criteria and assessment of technical documentation
- Strict requirements on handling of changes and modifications

9 **Conformity assessment based on a quality management system and assessment of the technical documentation**

- Criteria for documents to be submitted to the notified body (application for QMS assessment)
- At least once every five years an unannounced audit is to be performed

Q&A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Acknowledgements