Ready or Not: The New Medical Device Regulations Are Here!

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Objectives

By the end of this session attendees will be aware of…

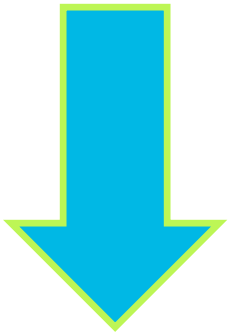
- The regulatory pathway to market authorization
  - Geography
  - Notified Bodies and Competent Authorities
  - CE Mark
  - Comparison *versus* US
- The regulatory framework involving MDRs
  - Device definitions
  - "Directives" *versus* "Regulations"
  - Timelines
- Examples of key changes imposed by MDRs
- Resources concerning MDRs

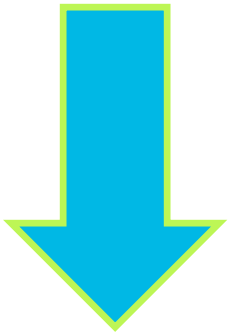
The Stage Is Set....

Directive (MDD) 93/42/EEC

Directive (AIMD) 90/385/EEC

Directive (IVDD) 98/79/EC





Regulation (EU) 2017/45

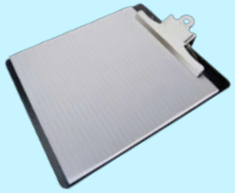
Regulation (EU) 2017/46

- MDR and IVDR strengthen the existing regulatory system by repealing the original Directives in place for ~ 25 years

Who Are the Players?

EU Commission, Parliament, Council

Member States, EFTA, EEC, Competent Authorities



Notified Bodies

Manufacturers, Sub-Contractors, Suppliers, Importers
EU Authorized Rep

New Regulatory Framework

European Union = 27 Member States

EU + [Iceland, Liechtenstein, Norway, Switzerland*] = **EEA**

European Economic Area

*Switzerland has bilateral agreements with EU

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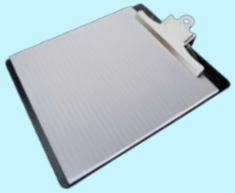

Notified Bodies

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New Regulatory Framework

What is a Notified Body (NB)?

- NBs exert regulatory control over market authorization and quality systems for medical devices
  - NBs perform technical and medical reviews of marketing applications / renewals
    - NBs critically review device safety and performance as part the regulatory package (Technical File or Design Dossier) submitted to obtain or maintain CE Marking
- NBs are independent, for-profit organizations – not manufacturers
- Not all NBs are designated for all medical devices
  - Per MDR, scope of NBs will be specified by 26 Nov 2017
- NBs are authorized / monitored by Competent Authorities

Find a Notified Body

EXAMPLE: Search for Notified Body accredited under 90/385/EEC (AIMD)

European Commission > Growth > Tools and Databases > ***Notified Bodies***

http://ec.europa.eu/growth/tools-databases/nando/index.cfm?fuseaction=directive.notifiedbody&dir_id=8

Notified bodies Nando

- Country
- **Legislation**
- Body
- Construction products
- Free search
- Mutual Recognition Agreements
- Notifying Authority - Notification procedures
- Accreditation Body

Name ▲	Country ▲
TÜV NORD CERT GmbH	Germany
National Standards Authority of Ireland (NSAI)	Ireland
BSI	United Kingdom
TÜV SÜD Product Service GmbH Zertifizierstellen	Germany
TÜV Rheinland LGA Products GmbH	Germany
AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS	Spain
DEKRA Certification B.V.	Netherlands
ISTITUTO SUPERIORE DI SANITA'	Italy
Laboratoire national d'essais / G-MED	France
MEDCERT ZERTIFIZIERUNGS- UND PRÜFUNGSGESELLSCHAFT FÜR DIE MEDIZIN GMBH	Germany
BSI Group Deutschland GmbH	Germany
PRÜFSTELLE FÜR MEDIZINPRODUKTE GRAZ	Austria
ELEKTROTECHNICKÝ ZKUŠEBNÍ ÚSTAV, s.p.	Czech Republic
INSTITUT PRO TESTOVÁNI A CERTIFIKACI, a. s.	Czech Republic
LGA INTERCERT ZERTIFIZIERUNGSGESELLSCHAFT MBH	Germany
POLSKIE CENTRUM BADAN I CERTYFIKACJI S.A.	Poland

Note: Manufacturers can use any Notified Body authorized to evaluate the specific device class

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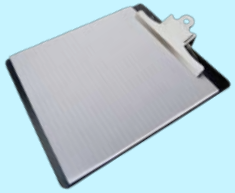

Notified Bodies

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New Regulatory Framework

What are Competent Authorities ?

- Competent Authorities, in each Member State, conduct market surveillance and enforcement
  - Monitor compliance at the national level
  - Approve clinical investigations
  - Protect public health and safety
  - Authorize, monitor, and audit NBs

EXAMPLES:

Federal Institute for Drugs and Medical Devices (Germany)

The Health Products Regulatory Authority (Ireland)

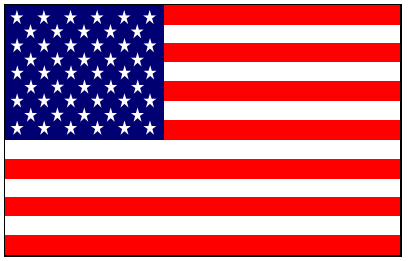
Danish Health and Medicines Authority (Denmark)

French National Agency of Medicine and Health Products Safety (France)

Regulatory Pathway to Market Authorization

- CE Mark…..
  - Symbolizes conformity with the relevant Essential Requirements for device safety and performance
  - Designates product registration and marketing approval in one country, followed by free trade across borders
    - Reimbursement varies by Member State
  - Is generally recognized across the globe
    - Australia and New Zealand
    - India

Comparison of Market Authorization for Medical Devices



- To achieve CE Mark, manufacturers submit to a Notified Body:
  - Technical File required for Class I, IIa, IIb devices
  - Design Dossier required for class III medical devices
  - Notified Body verifies whether medical device satisfies safety and performance requirements

- To achieve *clearance for* a "substantially equivalent device", manufacturers submit 510k application to FDA
- To achieve *approval* for a new medical device, manufacturers submit PMA package to US FDA

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NEW Regulatory Framework

Official Journal of the European Union

L 117

English edition

Legislation

Volume 60

5 May 2017

Contents

NEW Regulatory Framework: MDR

- **Known as Regulation (EU) 2017/745**
  - 175 pages
  - 101 “Whereas” = WHY
  - 10 Chapters of 123 Articles = WHAT
    - I: Scope and Definitions
    - II: CE Marking
    - III: Identification and Traceability
    - IV: Notified Bodies
    - V: Device Classification
    - VI: Clinical Evaluation
    - VII: Vigilance and Market Surveillance
    - VIII: Cooperation Among Member States
    - IX: Confidentiality, Data Protection, Penalties
    - X: Final Provisions
  - 17 Annexes = HOW

NEW Regulatory Framework

- Consolidates three prior Directives
  - Council Directive 93/42/EEC on Medical Devices (MDD)
  - Council Directive 90/385/EEC on Active Implantable Devices (AIMD)
  - Council Directive on In Vitro Diagnostics 98/79/EC

- Directives versus Regulations
  - ***Directives*** = Legislation ratified by the EU Parliament and transposed into national law by each Member State
  - ***MDR*** = "Direct entry into force" with clear and defined rules that are *binding* across all Member States

NEW Regulatory Framework: MDR

- **EU Definition of Medical Device (2017)**:
  - Any instrument, apparatus, appliance, material or other article, used alone or in combination with accessories or software, intended for:
    - Diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease ..... or injury
      - NEW - Does NOT necessarily have to be therapeutic
        EXAMPLE: Tinted contact lenses
    - Control or support of conception
    - Cleaning, disinfection, or sterilization of medical devices

  - Does not achieve its intended action by pharmacological, immunological or metabolic means, but may be assisted in its function by such means

NEW Regulatory Framework: MDR

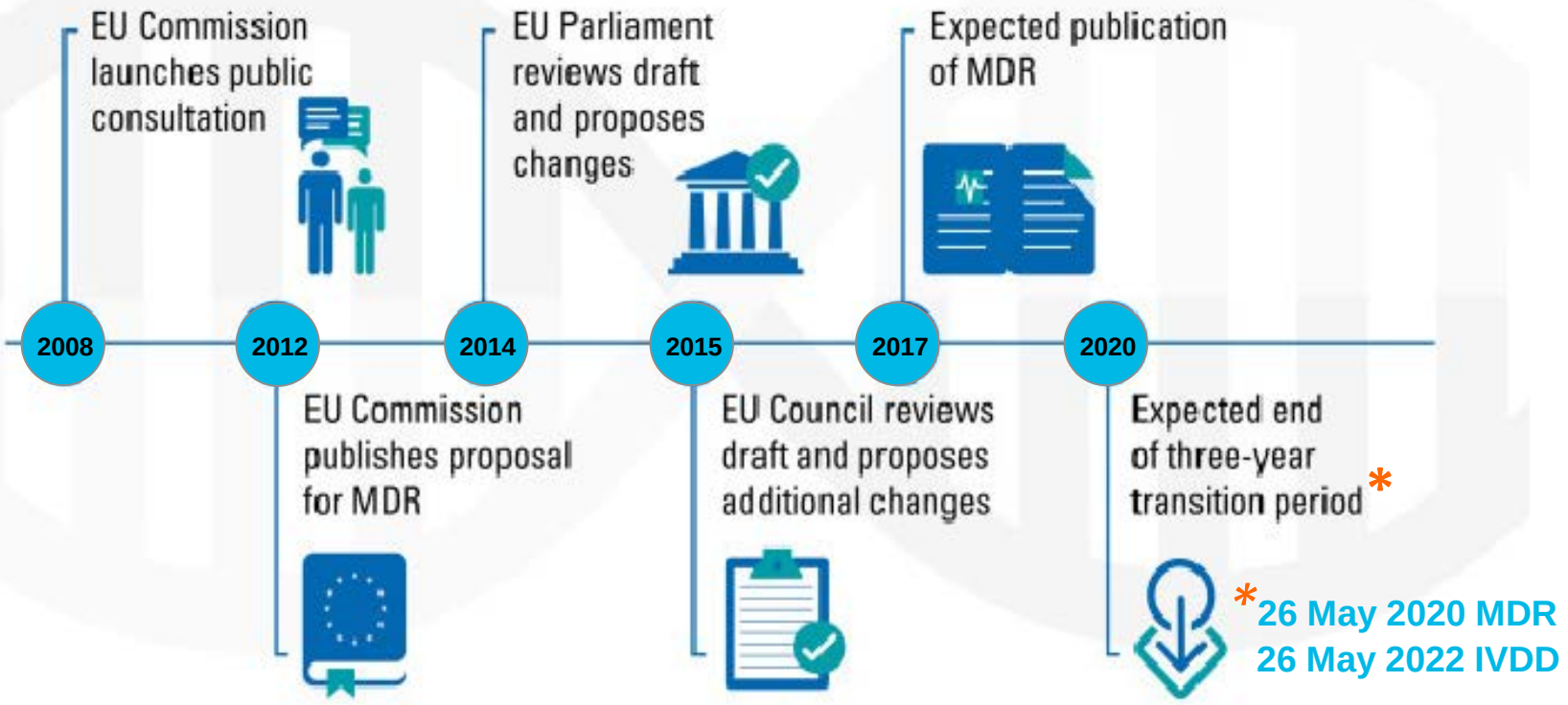
- **Implantable Medical Device EU Definition (2017)**:
  - Any device, including those that are partially or wholly absorbed, intended:
    - To be totally introduced into the human body, or
    - To replace an epithelial surface or the surface of the eye
    - AND remains in place after clinical intervention for at least 30 days

- **Active Medical Device EU Definition (2017)**:
  - Any device, the operation of which depends on a source of energy other than that generated by the human body, or by gravity, and which acts by converting that into energy

NEW Regulatory Framework: IVDR

- **EU Definition of IVD (2017):**
  - In vitro diagnostic medical device 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 for in vitro 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 more the following:
      - ✓ Physiological or pathological process or state
      - ✓ Congenital physical or mental impairments
      - ✓ Predisposition to medical condition or disease
      - ✓ Safety and compatibility with potential recipients
      - ✓ Treatment response or reactions
      - ✓ Monitoring or therapeutic measures

NEW Regulatory Framework: Timeline



Updated from www.tuv-sud.com/mdr

True or False?

- Existing medical devices will be “grandfathered” automatically into the MDR without need for (new? additional?) clinical investigation or further documentation

FALSE !

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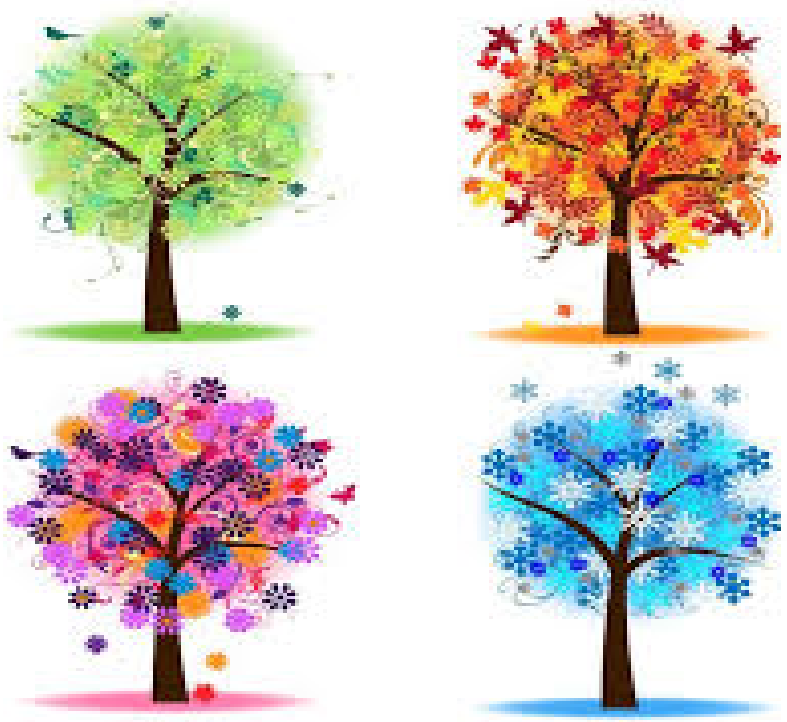
Examples of Key Changes Imposed by MDRs

- Strengthened device class designation
- More stringent and transparent clinical data will be required to demonstrate safety, performance, and clinical benefit
  - High-risk devices must be evaluated in clinical investigations
  - Mandatory unannounced audits conducted by Notified Body
- Most IVDs (~80-90%) will require involvement of Notified Body
- Unique Device Identifier ("UDI" = series of unique numeric or alpha numeric characters) will be required for unambiguous identification of specific devices on the market
- Recommendation for CE Mark can be reviewed by EC "Expert Panel"
- Post-market follow-up should be "proportionate to the device (risk) class and appropriate for the type of device
- More frequent device re-certification will be required

Example of Key Change: Device Equivalence

- "Equivalence" can only be established using a *single*, *CE-marked device* that satisfies all clinical, technical, and biological requirements



Example of Key Change: Device Equivalence

- Manufacturer must confirm that any differences between the device under evaluation and the designated equivalent device does not affect safety, performance, and clinical benefit

Difficulties with Device Equivalence Approach

- This approach may be limited by a lack of available, relevant clinical data pertaining to the designated equivalent device
  - The Notified Body shall have access to relevant pre-clinical data, drawings, diagrams, properties, and specifications, for the designated equivalent device
  - The only clinical data considered relevant are data obtained from CE-marked medical device(s) used in accordance with the approved labelling

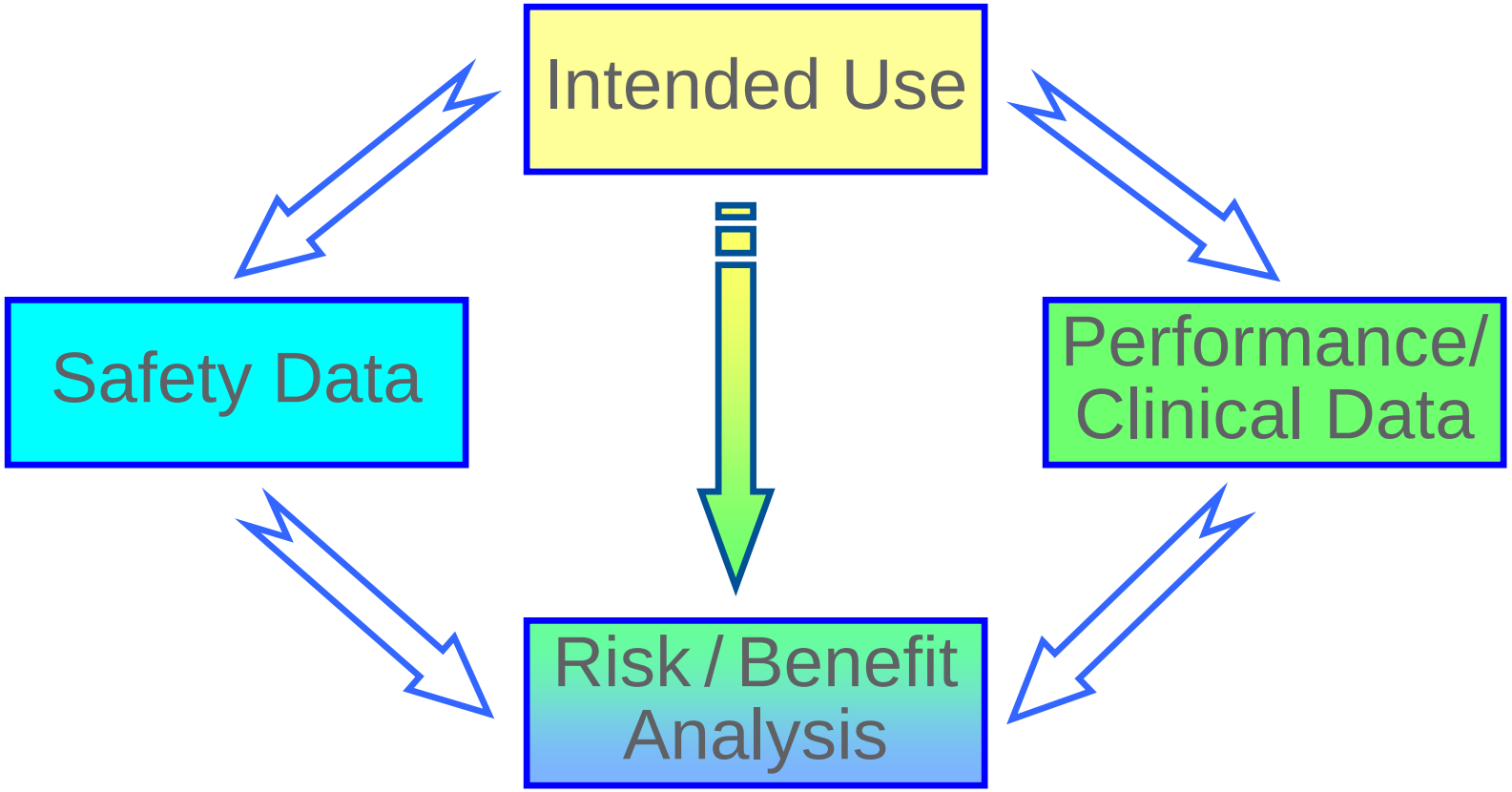
Example of Key Change: PMCF

- Manufacturers must implement post-market clinical follow-up investigations after CE Marking
  - Device is used in accordance with approved labelling
  - Objective is to answer specific questions relating to clinical safety, usability, and performance
  - These studies may identify risks not observed during pre-market testing
- Describe planned or ongoing post-market clinical follow-up studies in the clinical evaluation
- In the event that post-market clinical follow-up data will NOT be collected, discuss with Notified Body *a priori* and justify in the clinical evaluation

Example of Key Change: PMS

- Post-market surveillance is ***required*** for all CE-Marked devices sold in the EU
- Manufacturers must execute *pro-active* PMS plans that are fully described in the clinical evaluation
  - Confirm safety and performance during expected lifetime of device
  - Determine acceptability of known risks within a large patient population
  - Detect emerging risks based on factual evidence
- Eudamed (European Databank on Medical Devices) proposed under MDRs
- Periodic safety reports required for device Classes IIa, IIb, III

Risk/Benefit Assessment



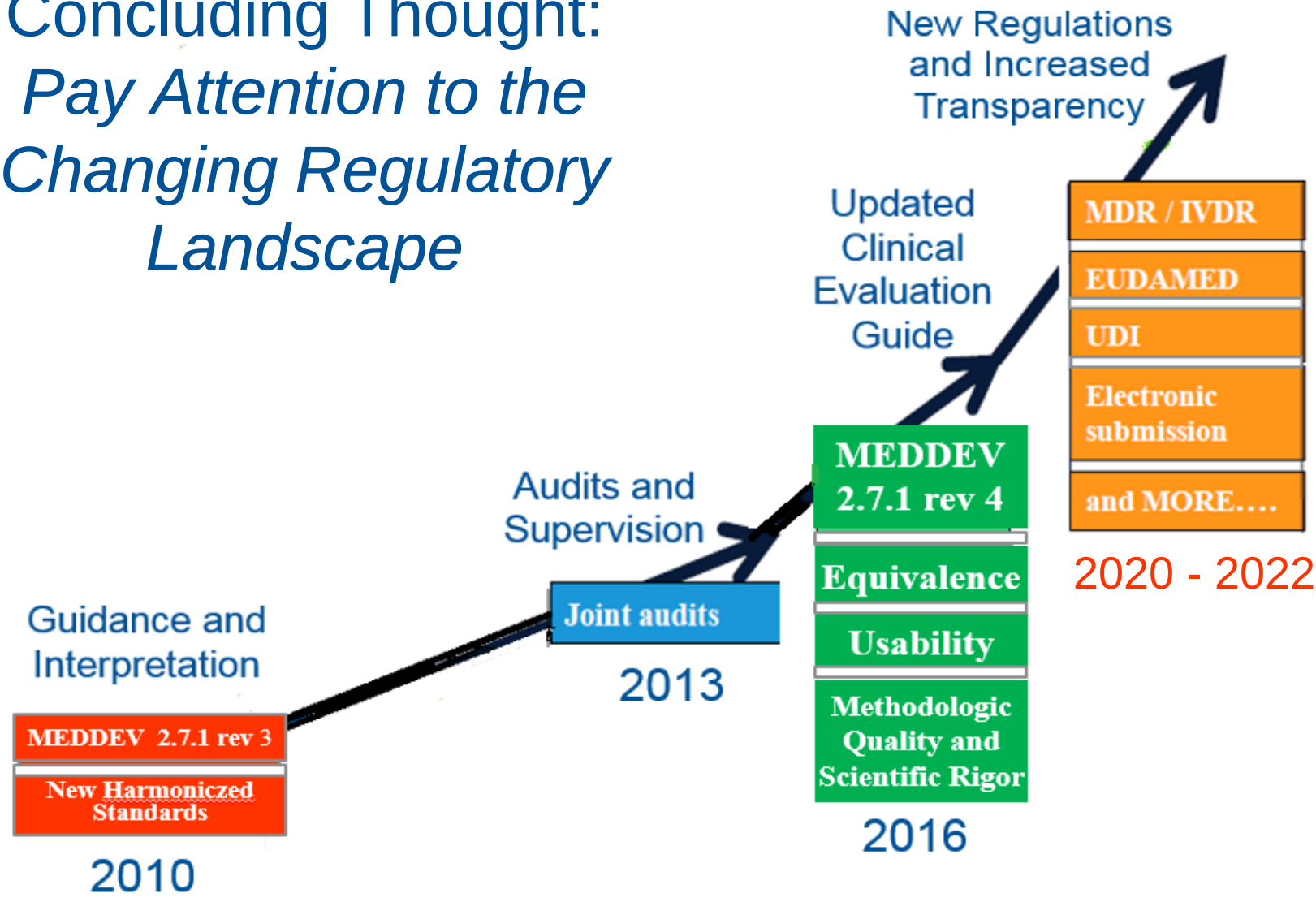
Risk / Benefit Assessment

- Risk / benefit
  - Known and foreseeable adverse health effects must constitute acceptable risk when weighed against intended clinical benefits
  - Evaluation of side-effects and risk / benefit profile must rely on clinical data

Resources to Help with CER Preparation

- Reg (EU) 2017/45 and Reg (EU) 2017/46
- MEDDEV Guidelines
  - 2.7.1/rev. 4 “Clinical Evaluation”
  - Other relevant MEDDEV guidelines
    - 2.7.4 “Clinical Investigations”
      See also ISO 14155 (under revision)
    - 2.12.2 / rev. 2 “Post-Market Clinical Follow-up”
- Notified Body guidance documents
  - Documents issued by the Notified Bodies themselves (NB-MED)
    - Bulletins from TÜV
    - CER checklist from TÜV

Concluding Thought: *Pay Attention to the Changing Regulatory Landscape*



Thank You!