The EU In-vitro Diagnostic Device Regulation (IVDR)

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Requirements for Traceability in Laboratory Medicine

In 1998 the European Community implemented the European Community Directive 98/79/EC on *in vitro* medical devices.

Essential Requirement of the IVD Directive

"The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.. "

The IVD Directive has changed

- European Community IVD **Directive 98/79/EC** has been repealed

replaced by

- European Union IVD **Regulation 2017/746/EU**

- Constant scientific and technological progress,
- Substantial deviations in the interpretation and application of the rules,
- A perceived lack of transparency

these issues led to the existing directive coming under criticism in recent years.

Official Journal of the European Union

L 117

English edition

Legislation

Volume 60

5 May 2017

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In this context what is the difference between a Directive and a Regulation ?

EU Directive:

- Applicable to all Member States
- Sets certain aims, requirements and concrete results that must be achieved in every Member State
- Member States have to adapt their laws to meet these goals but are free to decide how to do so.

EU Regulation:

- The most direct form of **EU law**
- Immediately applicable and enforceable in all Member States
- Member States ensure their national law does not define the subject matter any further (no room for different interpretations by member states).

Traceability remains an essential requirement

Annex I

General Safety & Performance Requirements

Chapter II

Requirements Regarding Performance, Design and Manufacture

9. Performance Characteristics

9.3 “Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order”

The new regulation clarifies and expands the scope of regulated IVDs to include:

- Tests providing information about the pre-disposition of a medical condition or disease, for ex. genetic tests
- Tests providing information to predict treatment response to medicines, for ex. companion diagnostics
- Medical software, which is explicitly mentioned in the definition of IVDs
- Lab developed tests (LDTs) used within health institutions are also required to meet safety and performance requirements

Key change:

- Risk Categories
  - Moved from list-based approach to risk-based approach (follows the Global Harmonization Task Force rules for classification)
  - Four risk categories – A (low risk) to D (high risk)
  - New Notified Body Organizational Group (NBOG) codes for notified bodies

Key change: New risk categories for IVD devices

A (low risk) to D (high risk)

Class A
Low personal risk
Low public health risk

- Accessories
- Wash buffers
- Specimen receptacles
- Instruments
- Culture media

Class B
Moderate to low personal risk, low public health risk

- Thyroid function
- Clinical chemistry
- Self-test devices listed as not Class C - Pregnancy, Fertility, cholesterol tests

Class C
High personal risk, moderate to low public health risk

- Syphilis (diagnosis only)
- Neonatal screening for metabolic disorders (PKU)
- Rubella,
- Cancer markers
- Genetic tests

Class D
High personal risk, high public health risk

- Hep C virus
- Hep B virus
- HTLV I/II
- Blood Grouping ABO
- CHAGAS
- Syphilis (used to screen blood donations)

Source: BSI

Key change: New risk categories for IVD devices

A (low risk) to D (high risk)

Class A
Low personal risk
Low public health risk

- Accessories
- Wash buffers
- Specimen receptacles
- Instruments
- Culture media

Class A devices will not require Notified Body involvement and will become the sole responsibility of the manufacturer to declare conformity with the regulation.

Source: BSI

Key change: New risk categories for IVD devices

A (low risk) to D (high risk)

Class B, C, and D devices will all require an assessment by a Notified Body.

The technical documentation must include performance evaluation, such as scientific validity, analytical performance and clinical performance.

The majority of JCTLM listed parameters are related to Class B list devices.

Class B
Moderate to low personal risk, low public health risk

- Thyroid function
- Clinical chemistry
- Self-test devices listed as not Class C - Pregnancy, Fertility, cholesterol tests

Class C
High personal risk, moderate to low public health risk

- Syphilis (diagnosis only)
- Neonatal screening for metabolic disorders (PKU)
- Rubella,
- Cancer markers
- Genetic tests

Class D
High personal risk, high public health risk

- Hep C virus
- Hep B virus
- HTLV I/II
- Blood Grouping ABO
- CHAGAS
- Syphilis (used to screen blood donations)

Source: BSI

Key change:

- Conformity Assessment Routes
  - Amended to reflect new classification rules
  - More manufacturers will need to use a Notified Body
    - ✓ Approximately 20% of IVDs are currently subject to Notified Body approval
    - ✓ The number of IVDs is estimated to increase 4-fold under new IVDR

Notified Bodies designated under the IVDR

DEKRA Certification GmbH
Handwerkstraße 15
70565 STUTTGART
Country : Germany
Website : www.dekra-certification.de
Notified Body number : 0124

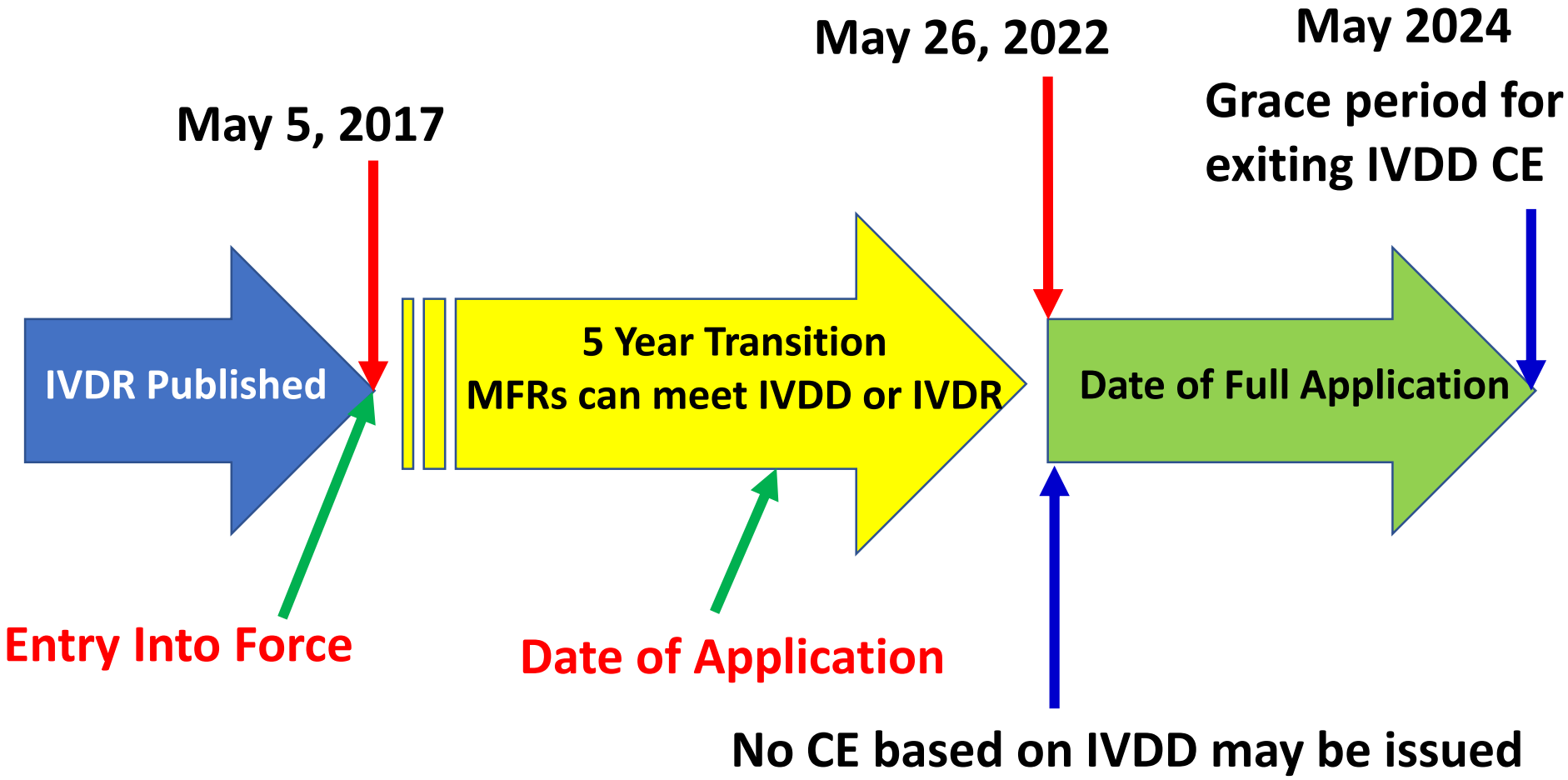
BSI Assurance UK Ltd
Kitemark Court Davy Avenue Knowlhill
Milton Keynes MK5 8PP
Country : United Kingdom
Website : www.bsigroup.com
Notified Body number : 0086

NANDO Database (New Approach Notified and Designated Organization Information System)

Key change:

- Post-market Reporting and Transparency
  - Post-market performance follow-up (PMPF) new requirement
  - An electronic portal (Eudamed) will be introduced where manufacturers can report:
    - ✓ serious incidents and safety corrective actions
    - ✓ field safety notices and summary reports
    - ✓ Scheduled for March 2020; delayed until 2022
  - Devices must be fit with a unique device identification (UDI)

Transition from the IVDD to the new IVDR



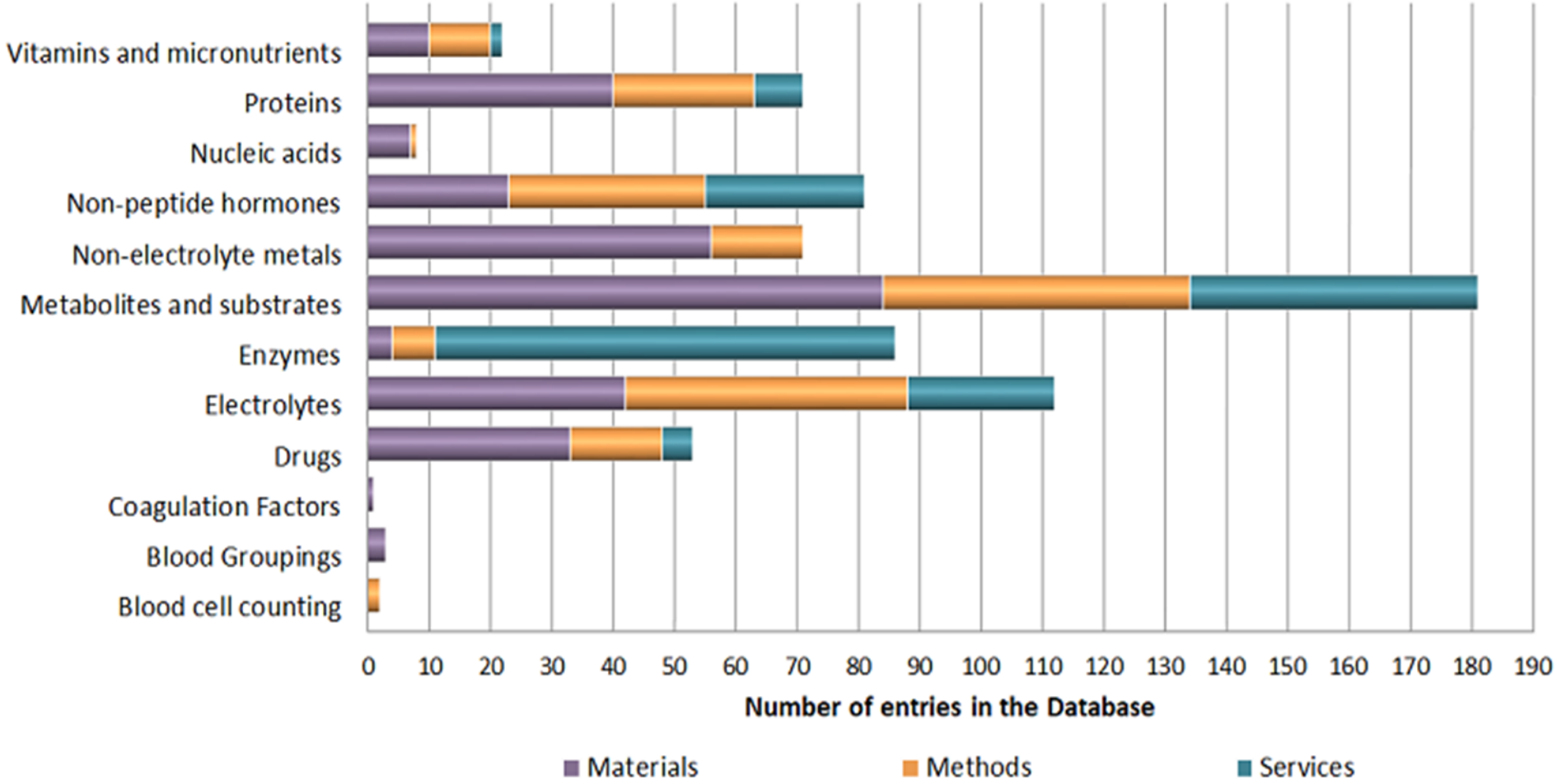
Source: BSI

Important Note:

- There is no “grandfathering “ for existing products.
- All manufacturers will need to review existing products against the requirements of the regulation.
- Current devices will need to be re-evaluated and re-certified when the existing IVD Directive certificates expire.

In 2002, the JCTLM was formed and created a database of reference resources to help the IVD industry meet traceability requirements of the EC IVD Directive

JCTLM Database: Entries as of April 2019



289 Certified Reference Materials
194 RMPs that represent 80 different analytes in 10 categories
176 reference measurement services delivered by 17 reference labs

Important ? for JCTLM

Will the Notified Bodies use the resources of the JCTLM Database to assess how manufacturers meet the traceability requirement?

It is difficult to predict how Notified Bodies will deal with the traceability requirement in the IVDR. The harmonized standards ISO 17511, ISO 15193, ISO 15194 and ISO DIS 21151 should give them guidance.

Thank You

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for patient care