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Laboratory medicine:
Preparing for the 2020's
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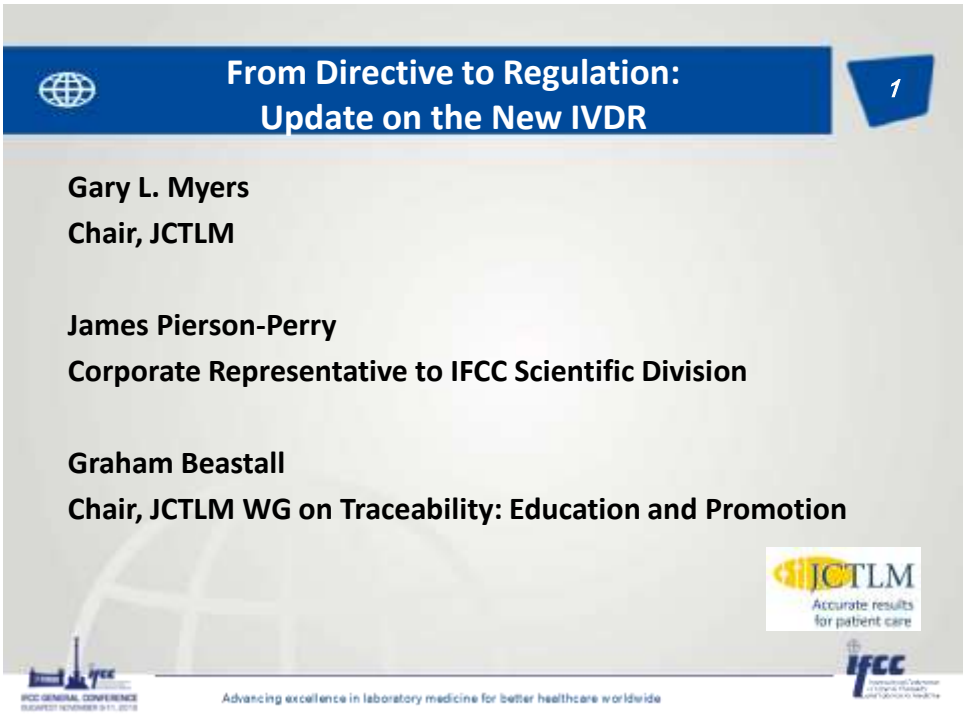
Advancing excellence in laboratory medicine for better healthcare worldwide
IFCC
International Federation of Clinical Chemistry and Laboratory Medicine


From Directive to Regulation:
Update on the New IVDR
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European Community IVD Directive

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.. "

Joint Committee for Traceability in Laboratory Medicine

In 2002, the JCTLM was formed bringing together the sciences of metrology, laboratory medicine and laboratory quality management to help the IVD industry meet traceability requirements of the EC IVD Directive

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JCTLM Database

- **JCTLM** through **BIPM** developed and maintains a database of **Reference Measurement Systems** @ http://www.bipm.org/jctlm/
- **JCTLM** coordinates the nomination and review process for database entries for compliance with appropriate ISO Standards

How is the IVDD changing ?

In-Vitro Diagnostic **Directive 98/79/EC** is repealed

In-Vitro Diagnostic **Regulation 2017/746/EU**

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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).

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L 117

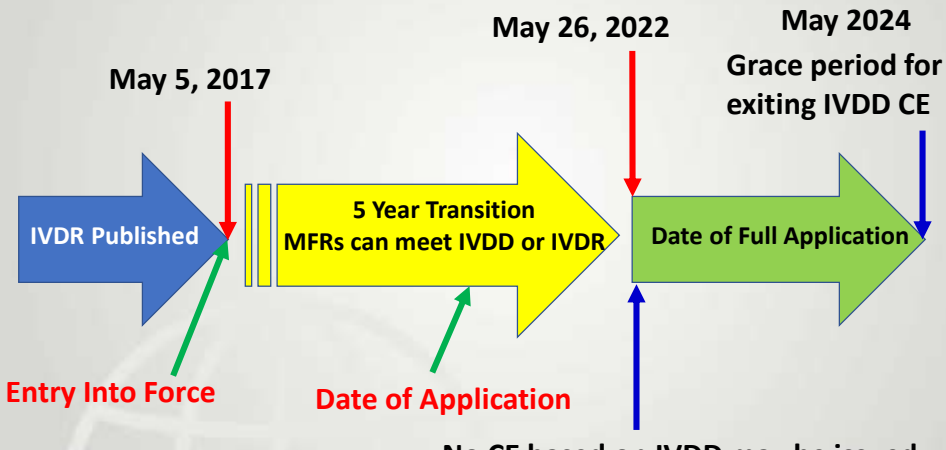
English edition — Legislation — Volume 60 — 5 May 2017

Contents

1 *Legislative acts*

- Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (1) 1
- Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on *in vitro* diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (1) 176

Transition from the IVDD to the new IVDR



Source: bsi

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
  - Move from list-based approach to risk-based approach (follows GHTF 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 of 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

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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

Key Change:

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

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.

Thank You

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IVDR: IVD Manufacturers Concerns

- Effort and Cost to update and maintain Technical Files
  - No grandfathering—~85% of manufacturers' products will require Notified Body (NB) involvement to put on market (formal submissions)
  - Many new standardized documents and requirements
  - May be difficult to find relevant data for old products—requiring new work to meet the IVDR requirements
  - Burdensome lifecycle management (some Tech Files need annual updates)
  - Estimates of £25-50K per product, then ongoing NB fees, post-commercial lifecycle management costs, etc.
  - Major drain on internal resources and competition for external consultant
- More rigorous clinical evidence is required
  - Must provide evidence of safety and performance according to a device's assigned risk class
  - If performance data are missing, Intended Purpose will need to be limited or additional studies will need to be performed

IVDR: IVD Manufacturers Concerns

- Many literature searches required to support claims
  - Clinical performance
  - Scientific validity
- New labeling requirements
  - Lot-to-lot variation not yet defined—may impact registrations worldwide
  - No agreement yet for UDI symbol
  - Requirement to submit labeliing in all lanugages to NBs where product is sold in EU
- Notified Bodies (NBs)
  - IVDR increases workload and scope to NBs
  - NBs must be designated before they can certify site or register products to IVDR
  - Many NBs not yet IVDR designated—not likely to do so until mid-2019 or later
  - No consulting services—NBs won't answer questions or give guidance due to fear of being considered "consultants"

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IVDR: IVD Manufacturers Concerns

- Agreement between Notified Bodies and EU Commission
  - Groupings not finalized for sampling of Class B and C devices
  - " Intended Purpose " has more requirements that need to be added (if not already in the IFU)—may impact registrations worldwide
- EUDAMED
  - Implementation date not yet communicated
  - Functionality of Post-Market Surveillance & Vigilance module of EUDAMED database not yet defined
- Impact of BREXIT
  - ~45% of medical devices CE marked in Europe utilize UK NBs
  - ~70% of Non-EU based manufacturers use UK NBs; e.g., Authorized Rep (AR)
  - UK-based AR will need to move or need new offices in EU country
  - Change in AR address will require updates to NB address on product labeling

IVDR: Implications for IFCC/Societies

- Education
  - Do professional organisations have a role in educating members about the IVDR?
  - If so, how should this be achieved?
- Monitoring
  - Do professional organisations have a role in monitoring and collating experience following IVDR roll out?
  - If so, how should this be achieved?
- Liaison with IVD manufacturers
  - Do professional organisations have a role in working with IVD manufacturers during IVDR roll out?
  - If so, how should this be achieved?

IVDR: Implications for IVD users

- Method status
  - Are the methods my lab uses IVDR compliant?
  - If not, when will they become IVDR compliant?
- Availability of methods
  - Will IVDR require global or just EU compliance?
  - Will IVDR limit availability of methods in EU countries?
  - Will new IVDs take longer to reach market?
- Cost
  - Will IVDR compliance increase cost of IVDs?
  - Will non-compliant IVDs be cheaper?
- Harmonisation of patient results
  - Will IVDR improve or worsen between-method agreement?