IVD Regulation Update

Status of 2013-09-26

Presented at
TÜV SÜD – USA NB-Training 2013
Reasons for Revision of IVD Regulation

- Review of IVD Directive already foreseen in the regulation
- Development in IVD regulations worldwide (GHTF -> Other countries)
- Upcoming importance of new diagnostic products (companion diagnostics, genetic testing, diagnostic services)
- Unflexibility of the classification system for IVDs
- Divergence in interpretation and application within the EU market, e.g. with regard to classification/regulatory status, designation of Notified Bodies
- General inflexibility of the system e.g. due to splitted up responsibilities
- (Development of MDD by amendments of generic nature)
Recast of the European Regulatory System for IVD MDs - History

- Public Consultation on the Revision of the Directive for IVD of June 29, 2010
  19 Questions on hot topics of the regulation of IVD in summer 2010

- Summary of responses to the Public Consultation was published Feb 23, 2011

- First incomplete Draft of the IVD Regulation was available 08 Feb 2012 for Discussion in MDEG


- Currently: Evaluation of the proposal by Committee on the Environmental, Public Health and Food Safety (ENVI) of EU Parliament
  - Draft Report of the Reporter April 2013
  - Elaboration of amendments by different members / groups within parliament
  - Voting of ENVI on Amendments on Sep 25, 2013
  - Voting of plenum pending
Expected time course for implementation of revised IVD regulation

- 2012-09-26 Publication of the proposal for the new IVD Regulation in EU

- Review (analysis and discussion) of the proposal by parliament and council – currently ongoing
- Up to 3 readings in Parliament until approval
- Publication in the Official Journal of the EU and entry into force (2014 ? - 2016)
- 5 years transition time post publication (2019 ? - 2021)
  => ENVI: only 3 years transition

- It is expected that qualification of Notified Bodies will be verified within the next 2 years, latest by 2015, to have operative Notified Bodies from the beginning of the transition period
  => See Implementing Act from Sept 2013
Notified Bodies and Certificates issued by them

Designation of NBs according to IVDD will become obsolete 5 \textbf{(ENVI: 3) years} after entry into force of the IVD Regulation

Certificates issued by NBs according to IVDD will become obsolete 2 \textbf{years} later

Application to become NB under IVD Regulation may be filed 6 \textbf{month} after entry into force

Assessment of application by designating authorities

Certificates under IVD Regulation can be issued after Notification as Notified Body under IVD Regulation
Structure of the proposed IVD Regulation

**Structure of the Regulation: 10 Chapters + 14 Annexes**

Chapter I  **Scope and definitions**

Chapter II  Making available of devices, obligations of economic operators, CE marking, free movement

Chapter III  Identification and traceability of devices, registration of devices and of economic operators, summary of safety and performance, Eudamed

Chapter IV  Notified bodies

Chapter V  **Classification and conformity assessment**

Chapter VI  Clinical evidence

Chapter VII  Vigilance and market surveillance

Chapter VIII  Cooperation between Member States, Medical Device Coordination Group, **EU reference laboratories**, device registers

Chapter IX  Confidentiality, data protection, funding, penalties

Chapter X  Final provisions

ENVI requested change of order
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Major Changes

- Scope Expansion / clarification that some specific products fall under IVD R, e.g. Companion Diagnostics, Products for Genetic Testing
- Classification System will change fundamentally (class A, B, C, D)
- Tighter regulations for clinical evidence and overall more tight requirements
- Unannounced surveillance audits (ENVI: once per year at each manufacturing site by NBs and annually by National Competent Authorities at respective NBs)
- Testing of product samples taken from the market or during audits
- Implementation of a “Scrutiny” process (ENVI: to be deleted)
- ENVI: Special Notified Bodies for Class D
- Nomination of Reference Labs
- Changes to the Notification Process of Notified Bodies (ENVI: EMA for Special NBs)
- Option for “Implementing Acts” by the Commission to adopt the requirements on a short term base
- Installation of MDCG – Medical Device Coordination Group
- ENVI: Installation of MDAC (scientific Advice) and ACMD (Assessment Committee)
Classification of IVD products is based on **positive listing** (IVDD Annex II List A and B) and use for **self testing**

- Annex II List A Devices
- Annex II List B Devices
- Self Testing Devices
- General IVD Devices

All devices listed in Annex II or intended for self-testing (use by lay-person) require participation of a Notified Body in Conformity Assessment
Classification of IVDs according to Art.39 IVD R

**Article 39:**

*Classification of in vitro diagnostic medical devices*

1. Devices shall be divided into **class A, B, C and D**, taking into account their intended purpose and inherent risks …  → Annex VII

2. Dispute between MAN and NB – Competent Authority of Member State where MAN / EU-R has his registered place of business – MDCG and COM to be notified on envisaged decision prior to decision

3. Implementing Acts by Commission on application of the classification criteria to a given device / category / group (Art. 83(4))

4. Commission shall be empowered to adopt **delegated acts** (Art 85) in the light of technical progress or vigilance information → reclassification of a device /category / group by derogation from classification criteria or amending / supplementing classification criteria
Risk – Classification – Requirement for Participation of NB in CA

Risk

Class

A  B  C  D

No NB  Participation of NB
## Implementing Rules for the Classification Rules

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<th>Rule</th>
<th>Description</th>
<th>Value</th>
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<tr>
<td>Rule 1</td>
<td>Transmissible Agent / Blood Screening</td>
<td>D</td>
</tr>
<tr>
<td>Rule 2</td>
<td>Blood Grouping + Tissue Typing</td>
<td>C / D</td>
</tr>
<tr>
<td>Rule 3</td>
<td>Mixed Criteria</td>
<td>C</td>
</tr>
<tr>
<td>Rule 4</td>
<td>Self + Near Patient Testing</td>
<td>C / B or other</td>
</tr>
<tr>
<td>Rule 5</td>
<td>w Spec. Character., Instruments, S.Receptacles</td>
<td>A</td>
</tr>
<tr>
<td>Rule 6</td>
<td>All Devices not specifically covered</td>
<td>B</td>
</tr>
<tr>
<td>Rule 7</td>
<td>Controls w/o quant. or qualitat. assigned value</td>
<td>B</td>
</tr>
</tbody>
</table>
Exempt EC Verification
same type of conformity assessments as describes in IVDD
apply acc to IVD R:

- Full Quality Assurance and Design Examination (Annex VIII)
- Type Examination (Annex IX)
- Production Quality Assurance (Annex X)

For class D as well as C Annex VIII or Annex IX and X apply in addition
For class B also Annex VIII (full quality assurance) applies
For class A with measuring function and class A sterile Annex VIII or X applies
For class A POC Annex VIII 6.1 applies
Scrutiny Mechanism – Article 42 and special items of Art. 40

- Scrutiny process for initial design examination of Class D
  - Draft summary of safety and performance and draft IFU to be provided to Commission who will forward to MDCG
  - MDCG may request summary of the preliminary conformity assessment within 28 days
  - MDCG will submit comments on the summary of preliminary conformity assessment at the latest 60 days after submission of summary
  - MDCG may request the submission of additional documents within that period
- ENVI: to be deleted and replaced by special Notified Bodies for Class D and case-by-case assessment by Assessment Committee for MD (ACMD)

- Companion Diagnostics (Class C) will require a consultation process with a Agency for Medicinals (e.g. EMA)

- Unannounced surveillance audits (extent unclear yet – ENVI: at least once a year) (Art 40), also at supplier in justified cases

- Class C and D products: Testing of samples taken from the market or during audits – frequency not defined yet (Art 40)
EU Reference Labs will to be nominated to participate in
- Design Examination – to verify compliance with CTS,
- Testing for Verification of Manufactured Products (Batch Verification),
- Testing products from the market
- to determine state of the art
- to provide scientific and technical assistance to commission
- ...

Current Partner Labs
- IVD – Testing Laboratory at Paul-Ehrlich-Institute (PEI), Langen (will apply as EU Reference Lab)
- Institute National de la Transfusion Sanguine - Centre National de Référence pour les Groupes Sanguins, Paris (?)

- Other EU Reference Labs will be nominated
IVD R – Several other changes upcoming compared to IVDD, e.g.

- New Definitions
- In house testing – rules modified
- Additional requirements for specific products e.g. Point of Care products
- Distance sales now clearly covered
- Supplementary Conformity Assessment for Repackaging
- Traceability in the supply chain
- Qualified Person
- UDI on Labeling
- More tight regulations for clinical evidence of not yet established parameters
- Obligatory periodic change of auditors in the audit team (Annex VIII 4.6), Lead Auditor must not lead or attend the audit for more than 3 consecutive years
- More tight requirements for vigilance processes at manufacturer
- ...

- ENVI: Special NBs under surveillance of EMA and very strictly controlled by CAs
- ENVI: several requirements have been amended to become more strict, many information to be published which is now considered confidential
General benefits

- System becomes more flexible in general, especially with regard to classification
- More appropriate classification
- More clarity regarding several requirements – MEDDEV guidances integrated
- Harmonisation due to centralized decisions
- Batch Verification based on testing by Reference Laboratory will be required
- Attempt to have State of the Art defined by Reference Labs
- Discontinuation of CA procedures not used
- Requirements for Importers and Distributors to ensure traceability within Supply Chain for 5 years specified
Benefits for Notified Bodies

- Approximately 80% of all manufacturers in the IVD field will require conformity assessment of their QA system by a Notified Body
- Appr. 4 - 5x more different products to be covered by Notified Body assessment
- Reasonably higher number of technical files to be assessed
- Number of NBs for IVD will probably decrease – some „black sheeps“ eliminated

Estimate:
Duplication to triplication of workload for remaining Notified Bodies

Dynamic development expected after designation of first organizations as Notified Bodies under the IVD Regulation
## Challenges for Notified Bodies

- **Expansion of resources**
  - Investments in qualification / training

- **Higher complexity of CA**
  - During transition 2 systems in parallel

- **Very limited time to adapt**
  - (regulatory wise – market wise)

- **New notification process for NBs**
  - Surveillance probably more tight, too

- **Higher prices to be pushed through**
  - Increasing unplannable costs due to inquiries of Competent Authorities
Benefits and challenges for Industry (NB view)

- Evidence for assessment of Products by Notified Body may support market / regulatory acceptance in other markets.

- More balanced level of quality of documentation over all diagnostic manufacturers due to participation of Notified Bodies in conformity assessment of most manufacturers and more aligned processes of Notified Bodies.

- More resources required to prepare the Technical Files for Notified Body Assessment.

- Risk for delays through third party process (NB, Reference Lab, MDCG).

- Higher internal and external costs for CE marking of IVDs.
MDR and IVDR

• Requirements defined by rapporteur of MDR will be taken by the rapporteur of the IVDR
• That means:
  – More involvement by European agency and other organizations
  – More involvement means: more discussion, means more time, means higher costs
  – NB’s are facing tougher supervision, means more costs
  – Technical documentation will require more attention
  – Unannounced audits by NB’s
  – Tougher market surveillance, more communication between authorities and NB’s, NB’s and manufacturers
• Transition period might be shortened to 3 years
• Same as for MDR:
  – No audit by NB = no certificate = no declaration of conformity = no CE marking = no products on the market
Thank You for your attention!

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