IVDR Breakout
IVDR Classification and conformity assessment
Classification-
IVDR
Classification of IVDs

Re-classification of IVDs will mean 80-90% will no longer be able to ‘self certify’ conformity

Review of technical documentation will be at the same depth for all devices, but there will be sampling proportionate to risk

More scrutiny on risk, clinical evidence and post-market surveillance

D: High Population, High Patient risk

C: Low Population, High Patient risk

B: Medium-low patient

A: Low patient risk
Classification rules – Annex VIII

Rule 1
Blood screening
High risk disease

Rule 2
Blood or tissue compatibility

Rule 3
Infectious disease
Cancer testing
Companion diagnostics
Genetic testing
Congenital screening

Rule 4
Self testing
High risk near-patient tests

Rule 5
Specific IVD reagents
Instruments
Specimen receptacles

Rule 6
None of the other rules

Rule 7
Controls no assigned values

Blood screening

High risk disease

Blood or tissue compatibility

Infectious disease
Cancer testing
Companion diagnostics
Genetic testing
Congenital screening

Self testing
High risk near-patient tests

Specific IVD reagents
Instruments
Specimen receptacles

None of the other rules

Controls no assigned values

High risk blood groups

Self test: Exempted List

A

B

C

D

C

D

B
## New classes of IVD devices

### Class D

**High public health risk, high personal risk**

- HIV 1/2,
- Hepatitis C virus
- Hepatitis B virus
- HTLV I/II
- Blood grouping ABO, Rhesus (including RHW1), Kell, Kidd and Duffy systems
- CHAGAS
- Syphilis (used to screen blood donations)

### Class C

**High personal risk, moderate to low public health risk**

- Syphilis (diagnosis only)
- Neonatal screening for metabolic disorders e.g. PKU
- Rubella
- Cancer markers
- Genetic tests
- Companion diagnostics
- Blood glucose meters/strips
- Blood gas analysers
- Self tests

### Class B

**Moderate to low personal risk, low public health risk**

- Thyroid function
- Infertility assays
- Clinical chemistry
- Self-test devices that are not Class C: pregnancy, fertility, cholesterol and urine tests for glucose, erythrocytes, leucocytes and bacteria

### Class A

**Low personal risk, low public health risk**

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

*‘Near patient tests’ are classified in their own right*
Your device is ready to be placed on the market…

1. Routes to Conformity
   - What are your options?
   - Role of a Notified Body

2. Annex VIII – QMS Assurance
   - QMS Audit
   - Technical Documentation assessments
   - Class Ds & EU Reference Laboratories
   - Certificates issued

3. Annex IX & X - Type examination & Production Quality Assurance

   So you have your CE certification…

4. Maintaining your certification
Routes to Conformity
What are your options...

Conformity assessment routes are based on classification of the device/group of devices

- Manufacturer’s choice of conformity route, in line with classification
- Device/group of devices
  - Analyte, intended use, technology...
- Plan for the scope of your certification
What is the NB role?

The role of a Notified Body in the conformity assessment process

• A Notified Body is designated by an EU Competent Authority to **perform conformity assessments**

• Assessment based on the evidence & conclusions provided, that the device conforms to the relevant requirements (General Safety and Performance requirements)

• A Notified Body must demonstrate that it is competent to perform these reviews (based on NBOG codes)

• Annex VI

•  *shall carry out the conformity assessment activities with the highest degree of professional integrity and the requisite technical and scientific competence in the specific fields.*
To start the conformity assessment process...

**Quotation and Application**
- Formal application by manufacturer to a NB
- Contract between both parties

  *Terms to include:*
  - Application to single NB; information about previous applications for the same device
  - Manufacturer to inform NB of vigilance reports
  - Right of NB to suspend, restrict, or withdraw certificates
  - NB must be able to fulfil their information obligations

- Contract review by NB
  - Scope of designation
  - Competency for assessment
Annex IX – QMS Assurance
Conformity assessment

A
- EU Declaration of Conformity Annex III
  - Quality Management System Assurance Annex IX
    - Assessment of Technical Documentation per category device Annex IX 4.4-4.8
  - For Companion Diagnostics CA consultation Annex IX 5.2

B
- Quality Management System Assurance Annex IX
  - Assessment of Technical Documentation per generic device Annex IX 4.4-4.8
  - For Companion Diagnostics CA consultation Annex IX 5.2

C
- Quality Management System Assurance Annex IX
  - Type Examination Annex X (includes Technical Documentation)
  - Production Quality Assurance Annex XI
  - For Companion Diagnostics CA consultation Annex X 3

D
- Quality Management System Assurance Annex IX
  - Type Examination Annex X (includes Technical Documentation)
  - Assessment of Technical Documentation Annex IX Ch II
  - Production Quality Assurance Annex XI
  - Verification by EU Reference Laboratory
  - Verification by EU Reference Laboratory
1. QMS Audit

• Quality Objectives
• Organisation and monitoring
  • Mandate with an Authorised Representative if applicable
• Procedures (data and records) for monitoring, verifying, validating and controlling device design
  • Regulatory compliance
  • Identification of requirements
  • Risk management
  • Performance evaluation and PMPF
  • Labelling
  • Management of changes

Where a harmonised QMS standard is used, the NB shall audit to that standard
Quality Management System Assurance

1. **QMS Audit**

- Assessment of QMS of manufacturer and any additional sites
  - Appropriate scope
- Device/s to be covered by QMS
- Procedures necessary to fulfil IVDR requirements
  - Post-market surveillance
  - Post-market performance follow up plan
  - Vigilance procedures
  - Performance evaluation plan and procedures
- On-site audit
- *Implementation of the QMS to ensure compliance*
Quality Management System Assurance

1. QMS Audit

• QMS obligations for the Manufacturer of the IVDR map to ISO 13485:2016

• Except for:

  a) a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system;

• Transition to certification to ISO 13485:2016 will help on your road to CE marking under the IVDR!
Quality Management System Assurance

2. **Assessment of Technical Documentation on a sampling basis** (Class C & B)

- Annex IX (I & III); *Chapter II, Sec 4.4-4.8 only*
- *Technical sampling:* Based on novelty of technology, risk of device and standard medical practice, similarities of design, technology and manufacturing
  - Generic devices (C) or Device subcategories (B)
- Performance Evaluation Report
  - Clinical evidence based on equivalence, NB will need to assess claimed equivalency, relevance and adequacy of data
- Adequacy of performance evaluation, risk-benefit, IFU, post-market surveillance, and any Post-Market Performance Follow-up
- Possible post-market NB follow up
- Performance Evaluation Assessment Report will be issued by NB

Content dependent on device
Quality Management System Assurance

3. **Assessment of Technical Documentation**
   - Class D & Self-Tests / Near Patient Tests
   - Annex IX (I & III) + **Chapter II**
   - Technical documentation – Annex II
   - Performance Evaluation Report
     - Clinical evidence based on equivalence, NB will need to assess claimed equivalency, relevance and adequacy of data
   - Adequacy of performance evaluation, risk-benefit, IFU, post-market surveillance, and any Post-Market Performance Follow-up
   - Possible post-market NB follow up
   - Performance Evaluation Assessment Report
   - **EU Technical Documentation certificate will be issued (Product specific)**
Quality Management System Assurance

3. Assessment of Technical Documentation

- Class D & Self-Tests / Near Patient Tests
- Annex IX (I & III) + Chapter II
- Technical documentation – Annex II
- Performance Evaluation Report
  - Clinical evidence based on equivalence, NB will need to assess claimed equivalency, relevance and adequacy of data
- Adequacy of performance evaluation, risk-benefit, IFU, post-market surveillance, and any Post-Market Performance Follow-up
- Possible post-market NB follow up
- Performance Evaluation Assessment Report
- EU Technical Documentation certificate will be issued (Product specific)

✓ Draft declaration of conformity
  ➢ Annex III
✓ Labelling (CE_{xxx})
EU Reference Laboratories & Class D devices

In addition to QMS and Technical Documentation audit - part of conformity assessment:

• Compliance with the Common Specification
  • Query on transition arrangements to current Common Technical Specification

• Consultation with MDCG where no Common Specification

• EU Reference laboratory will verify claimed performance of the device and compliance with Common Specification or other solutions
  • Scientific opinion within 60 days
  • Ref Lab will also be involved in review of device changes post-market

• EU Reference laboratories will need to be designated
  • Time frame dependent on implementing provisions
Batch release - differences compared to IVD Directive:

• All batches will have to be tested
  • IVDR does not allow for reducing the level of testing after a certain number of batches

• All batches will have to be tested by an external laboratory
  • IVDD allows testing to take place in the manufacturer’s laboratory with a panel of samples supplied by the NB

• It is assumed that the Reference Lab for testing of the batches will be the same at the Reference Lab that reviews the performance data, however, this has not been confirmed by CAs
Definition

**Companion Diagnostic**

means a device which is essential for the safe and effective use of a corresponding medicinal product to:

- identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or
- identify, before and/or during treatment, patients likely to be at increased risk for serious adverse reactions as a result of treatment with the corresponding medicinal product;
IVDR, Annex VIII 6.2

Examination of the design of companion diagnostics

a) Manufacturer applies to Notified Body for examination of technical documentation

b) Documentation to enable assessment of conformity with the IVDD

c) Notified body consults with the European Medicines Agency (EMA) or country competent authority (CA)

d) EMA or CA gives opinion to the Notified Body within 60 days

e) Notified body gives due consideration to EMA/CA input

f) Manufacturer to notify the Notified Body of changes. Notified Body determines if a new assessment is needed. Notified Body seeks EMA/CA input
Certificates issued under Annex IX

Class B & C devices

1. **EU Quality Management System certificate** (Annex IX, I & III)
   - Accompanied by assessment of technical documentation on representative basis for each generic device group (C) or device category (B)
   - *Ref Article 48*
Certificates issued under Annex IX

Class B & C devices
1. EU Quality Management System certificate (Annex IX, I & III)
   • Accompanied by assessment of technical documentation on representative basis for each device group (C) or device category (B)
   • Ref Article 48

Class D & Others specified*
1. EU Quality Management System certificate (Annex IX, I & III)
2. EU Technical Documentation Assessment certificate (Annex IX, II exclu sec 5)
   • For each Class D device to be placed on the market
   • Reference laboratory will verify claimed performance and Common Specification requirements – needs to be positive outcome
   • MDCG consultation if no Common Specification
   • Verification of manufactured batches (Class D)

*Self-test and near patient tests, Classed B-D; Companion Diagnostics
Certificates issued under Annex IX

Class B & C devices

1. EU Quality Management System certificate (Annex IX, I & III)
   - Accompanied by assessment of technical documentation on representative basis for each generic device group (C) or device category (B)
   - Ref Article 48

Class D & Others specified*

1. EU Quality Management System certificate (Annex IX, I & III)
2. EU Technical Documentation Assessment certificate (Annex IX, II exclu sec 5)
   - For each Class D device to be placed on the market
   - Reference laboratory will verify claimed performance and Common Specification requirements – *needs to be positive outcome*
   - MDCG consultation if no Common Specification
   - Verification of manufactured batches (Class D)

   • OR EU Technical Documentation Assessment certificate (Annex IX, II sec 5)
     - For each device* to be placed on the market *(to be confirmed)*
     - Drug consultation for Companion Diagnostics

*Self-test and near patient tests, Classed B-D; Companion Diagnostics
QMS Assurance conformity assessment process

Quality Management System Assurance under the IVDR

*What will be needed...*

- Application to a NB
- QMS certification with a scope to cover the processes / technologies / devices
  - QMS assessment by a NB for the purposes of CE marking
  - ISO 13485 +
- Submission of technical documentation for review
  - Dependent on the device risk and scope
- Additional processes for Class D devices, Companion diagnostics
Annex X & XI
Type Examination &
Production QA
Annex X and Annex XI

**Type Examination**
- Certification that a device (incl technical documentation and sample) fulfils requirements
- Certificate issued for specific device; the ‘type’
- Tests to verify conformity of the Type
- All changes that affect conformity to general requirements must be assessed
- EU Reference Lab verification for Class D devices

**Production Quality Assurance**
- Audit of the QMS to manufacture the specified device ‘Type’
  - Cross reference to Annex IX
- Certificate issued for manufacture of specified device
- Changes to the QMS may need re-assessment (as per Annex IX)
- EU Reference Lab verification of manufactured batches for Class D devices