Notified Bodies

What are they and what do they do?

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First steps in IVD Regulation – Define and classify your device

**Is it an IVD device?**
- Check the definition of an IVD Medical Device in IVDR
- What will you “place on the market”?
  - Sample prep / library prep / sequencing instrument / software / test report
- If it is an IVD, classify your device according to Annex VIII in IVDR

**Is it a testing service?**
If you are not manufacturing a “device” are you providing a testing service instead?
- UKAS Accreditation
  - ISO 15189:2012
  - ISO 17025:2017
- Your test method may still qualify as an IVD device
- Check to see if you qualify for Health Institution Exemption (*IVDR Whereas: indent (29)*)
Classification - IVDR
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

High risk blood groups

Self test: Exempted List

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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 – Annex I)

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

• Annex VII

• *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.*
Conformity assessment

A

EU Declaration of Conformity Annex III

B

Quality Management System Assurance Annex IX

Assessment of Technical Documentation per category device - Annex IX 4.4-4.8

C

Quality Management System Assurance Annex IX

Assessment of Technical Documentation per generic device - Annex IX 4.4-4.8

Type Examination Annex X (includes Technical Documentation)

Production Quality Assurance Annex XI

For Companion Diagnostics CA consultation Annex IX 5.2

D

Quality Management System Assurance Annex IX

Assessment of Technical Documentation Annex IX Ch II

Type Examination Annex X (includes Technical Documentation)

Production Quality Assurance Annex XI

Verification by EU Reference Laboratory

Verification by EU Reference Laboratory
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 13485:2016 +
- Submission of technical documentation for review
  - Dependent on the device risk and scope

Engage with an NB early and select one that will be designated to cover your specific device and conformity assessment route.
Quality Management System Assurance

Assessment of Technical Documentation

- Annex IX (I & III); Chapter II, Sec 4.4-4.8
- Technical sampling: Based on novelty, risk and technology
- Adequacy of performance evaluation, risk-benefit, IFU, post-market surveillance, and any Post-Market Performance Follow-up
- Sampling is not applicable for class D, self-test, near-patient tests and Companion Diagnostic devices (additional requirements in Annex IX Chapter II)
Quality Management System Assurance

Assessment of Technical Documentation

• Additional requirements for Companion Diagnostics

• ...the notified body shall consult a competent authority designated by the Member States...or the EMA...in accordance with the procedure set out in Section 5.2 of Annex IX.

• Suitability of the device in relation to the medicinal product concerned

• EMA shall provide its opinion within 60 days of receipt of documentation. May be extended once for a further 60 days on justified grounds.
IVDR – Clinical Evidence and Performance Evaluation
‘Clinical benefit’ consideration

Clinical benefit of an IVD = Accurate medical information ≠ Final clinical outcome
‘Clinical benefit’ consideration

Clinical benefit of a Companion Diagnostic IVD

Does it accurately detect the analyte(s) claimed?

Final clinical outcome

EMA consultation approves link with drug
Performance Evaluation

*Process* of obtaining clinical evidence = Performance Evaluation

- Done according to a **Performance Evaluation Plan**
- Collated as a **Performance Evaluation Report**
- Continuous during life-time of the device
**Clinical Performance**

Ability to yield results that relate to a particular clinical condition or physiological state for the intended use and in accordance with target population, and where applicable to the intended user.

Data to support diagnostic accuracy compared to reference test; information related to expected values.

**Scientific Validity**

Refers to the association of an analyte to a clinical condition or physiological state.

For established analytes, this may be from literature; but for novel analytes or companion diagnostics this would need to be established.

**Analytical Performance**

Refers to the ability of an IVD medical device to correctly detect and measure a particular analyte.

Performance requirements similar to IVD Directive essential requirements.

For CDx at clinical trial could this be less detailed if product Intended Use is limited?
Expectations for Performance

Annex XIII / XIV

Clear list of documents required:

- Scientific validity
- Analytical performance
- Clinical performance
- Performance Evaluation

- Evidence must support **CLAIMS** in IFU (Annex I & II)

- Process must be **PLANNED**

Link to Risk Management, PMPF and PMS

- Manage any outstanding risks - Risk Management process

- Does benefit of device still outweigh the risk?

- Post-Market Performance Follow-up studies
  - Monitor outstanding risks over a longer period

- Post Market Surveillance process
  - Gather more data to support/adjust claims
  - Feed into updated Performance Evaluation
So you have your CE certification...
Maintaining your certification

- **Vigilance** requirements
  - Incident Reporting
  - Trending

- **Post-market Surveillance Plan & Post-market Surveillance**
  - Reviewed as part of Surveillance visits
  - Post-market surveillance Report (Class A & B); or
  - Periodic Safety Update Reports (Class C & D)

- Maintaining **Clinical Evidence**
- **Post-market Performance Follow-up (PMPF)**

- For **Class C & D devices**, updates to the **Summary of Safety and Performance**, at least annually
  - Will be publicly available
Summary
Summary

**IVDR Conformity Assessment**
- Define and classify your device (including accessories)
- Prepare ISO 13485:2016 compliant QMS
- Identify appropriate harmonised standards
- Engage with a suitable Notified Body
- Plan and execute Annex XIII or XIV compliant performance studies
- Prepare Technical Documentation
  - Annex I, II, III, IV and XIII/XIV particularly important

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Quality standards

Already exist for:
- Medical device QMS (EN ISO 13485:2016)
- Risk management for medical devices (EN ISO 14971:2012)
- Labelling/IFUs of IVDs (EN ISO 18113-1 to 4:2009) and symbols (EN ISO 15223-1:2016)
- Stability testing of IVDs (ISO 23640:2011)

In the pipeline:
- Sample prep from FFPE for molecular IVDs
- Multiplex molecular testing
- Clinical performance studies
- Updates to Labelling & Symbols
- ....more

• Check European Commission Official Journal for full list of EU harmonised standards -
Where can I find full details of the changes?

bsigroup.com/MDR-revision
bsigroup.com/IVDR-revision

Webinars: bsigroup.com/webinars
Whitepapers: bsigroup.com/whitepapers

Please ask if you want any extra information from BSI.
Questions & Answers