The role of the Notified Bodies in the assessment of clinical performance aspects

Dr. Marta Carnielli
11 February 2022
REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 5 April 2017


(Text with EEA relevance)

REGULATION (EU) 2022/112 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 25 January 2022

amending Regulation (EU) 2017/746 as regards transitional provisions for certain in vitro diagnostic medical devices and the deferred application of conditions for in-house devices

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 169(4), point (c), thereof.

Agenda

The role of the Notified Body

The IVDR Conformity assessment process

The qualification requirements of NB Clinical reviewers

TUVSud approach

Regulation 2022/112: NB perspective
The role of Notified Body

A Notified Body is an organization:

- that performs **third party** assessment of the conformity of the manufacturer’s quality system and products to the essential requirements as required by the respective directive

- notified by the European Commission based on **designation requirements**, such as knowledge, experience, independence and resources to conduct the conformity assessments, verified by the domestic competent authority, respectively by a joint audit team (domestic competent authority / other member state authorities / COM)

- which has established and maintains a **quality system**

- which has to follow **standards** and **rules** e.g. of designating authority

- which is regularly (annually) **surveyed** by the respective Designating Authority and Joint Audit Team and subject to **scrutiny** activities

- notified by the European Commission by **publication of name and scope** of the NB in the Official Journal and COM website (currently 19 IVD Notified Bodies under IVDD, 6 under the IVDR)

Collaboration between Notified Bodies: Team NB and NBCG-Med

- Group of EU NBs established by the EU Commission as per article 49 of the MDR and article 45 of the IVDR.
- Members are NB designated for above EU legislations
- Include two Technical Group (NBTG) that include:
  - a sub-group for medical devices and
  - a subgroup for in vitro diagnostics

- The European Association Medical devices of Notified Bodies
- 28 members represent 17 different countries.
- Communication with:
  - European Commission
  - Competent Authorities
  - Industry

Objectives:
Harmonization, draft technical recommendations/reach consensus on conformity assessment related topics (position papers, trainings for notified bodies, etc)
Provide input to the Commission, at its request, on medical device legislation
Drafts reports on ethical aspects of the activities of notified bodies
IVD Regulation: Conformity assessment procedures
Conformity Assessment Procedures

Article 48, Parts 1 & 2

- Must occur prior to placing a device on the market / putting into service,
- Follow conformity assessment procedures set out in Annexes IX to XI

### Annex IX
- Conformity Assessment based on a **Quality Management System** and **Technical Documentation Assessment**
  - EU quality management certificate
  - EU TD Assessment certificate

### Annex X
- Conformity Assessment based on **Type Examination**
  - EU type-examination certificate

### Annex XI
- Conformity Assessment based on **Production Quality Assurance**
  - EU production quality assurance certificate

### Article 48 (10)
- **Self declaration by manufacturer**
  - Class A devices
- Participation of Notified Body for devices of
  - Class D
  - Class C
  - Class B
  - Class A sterile

28.02.22
Assessment of technical documentation under Annex IX

- **Class D**
- **CDx**
- **Class C**
- **ST / NPT***
- **Class B**

Each device

Representative sample from each **generic device group** (audit)

Representative sample from each device **category** (audit)

EMDN 3\textsuperscript{rd} level + IVP code

IVR code

ST/NPT: self-testing/Near Patient Testing


28.02.22
IVDR: Expert Panel consultation

EUROPEAN COMMISSION

View in the context of the Performance Evaluation Consultation Procedure (PECP)
Expert panels on medical devices and in vitro diagnostic devices (ExPamed)

Contents

1 ADMINISTRATIVE INFORMATION ........................................................................................................... 2
2 INFORMATION PROVIDED BY THE NOTIFIED BODY ............................................................................. 2
3 VIEWS OF THE EXPERT PANEL ........................................................................................................... 3
   3.1 INFORMATION ON PANEL AND SUB-GROUP .............................................................................. 3
   3.2 SUMMARY OF EXPERT PANEL VIEWS ......................................................................................... 3
   3.3 VIEWS ON THE SPECIFIC REPORTS INCLUDED IN THE PERFORMANCE EVALUATION REPORT (PER) ......................................................................................................................... 5
   3.4 VIEWS ON SPECIFIC ASSESSMENT ASPECTS OF THE PERFORMANCE EVALUATION REPORT (PER) ......................................................................................................................... 8
   3.5 OVERALL CONCLUSIONS AND RECOMMENDATIONS ................................................................... 9
   3.6 STAKEHOLDER INFORMATION, WHERE AVAILABLE .................................................................... 9
   3.7 DIVERGENT POSITIONS IN CASE NO CONSENSUS CAN BE REACHED ........................................ 10
Expert Panel for IVD

Manufacturer submits IVD device Performance Evaluation Report

NB decides if expert panel consultation is needed based on art. 48 (6)

For class D devices
- where no CS are available and
- where it is also the first certification for that type of device

5 days

IVD Expert Panel

60 days

• Review should address:
  - Justification for the approach taken to gather the clinical evidence
  - Literature review (methodology, protocol, report)
  - Technology used, intended purpose
  - Scientific validity
  - Clinical evidence for acceptable performance compared to the state of the art

5 days
The qualification requirements of NB Clinical reviewers
Relevant regulatory requirements

- Regulation EU 2017/746 Annex VII Requirements to be met by Notified Bodies - Resource requirements § 3.2.4
  - Personnel with relevant clinical expertise should be:
    i. permanently available and employed by the notified body itself if possible
    ii. integrated throughout the notified body’s assessment and decision-making to review/evaluate clinical data; determine when an external expert is needed, identify and train them and evaluate their opinion

- MDCG 2019-6 v3 Questions and answers: Requirements relating to notified bodies
  - Notified bodies should have at least one internal clinician; possibility to subcontract this role if justifiable;
  - If the internal clinician is a subcontractor, the Notified Body should ensure that she/he is fully integrated throughout the conformity assessment and the decision-making process
  - If a subcontractor, the clinician cannot be a final reviewer or decision maker
  - Internal clinicians are responsible to decide if the review of clinical evaluation is to be carried out by themselves or to be delegated to other qualified staff or if it necessitates the input of external clinical experts
  - In any case, internal clinicians are responsible to clinically judge the opinion provided by any external expert and to make a recommendation to the decision maker on the adequacy of the clinical evaluation.
Relevant regulatory requirements

- **NBOG 2017-2 Guidance on the information required for conformity assessment bodies’ personnel involved in conformity assessment activities**

  - Internal clinicians are responsible for the oversight of the clinical assessment of the technical documentation and fully integrated in the CAB’s assessment and decision-making process.
  - They can delegate the review of part or all the clinical aspects to:
    i. External experts (i.e. clinical specialists) for example for innovative products and/or of high risk (class C and D devices under the IVDR).
    ii. Other appropriately qualified experts including product reviewers
  - The internal clinician maintains responsibility for the final review of the clinical aspects in which case he/she will make a clinical judgment of the opinion provided by these experts.
  - NBOG 2017-2 provides guidance on the qualifications needed for the various roles included in the conformity assessment including internal clinicians, clinical specialists and product reviewers
TÜV SÜD Approach
TÜV SÜD as Notified Body under IVDD & IVDR

All product categories

All conformity assessment routes

NB under IVDD/IVDR since 2001/2020

Collaboration with
- Paul-Ehrlich-Institute
- Others...

100+ IVD experts worldwide
Clinical Review-TÜV SÜD Approach

- An assessment by an Internal Clinical Reviewer (ICR) is mandatory in following cases:
  - Performance evaluation of a class D device
  - Performance evaluation of a class C Companion Diagnostics device
  - Performance evaluation of an innovative class C devices

- Involvement of the ICR has to be considered in the following cases:
  - any assessment related to innovative device or innovative technology,
  - new indication for this type of medical device,
  - dubious indication or mechanism of action,
  - justification and rationale by the manufacturer for acceptance and compliance, which requires more specialized clinical knowledge,
  - unclear state-of-the-art related to the benefit/risk evaluation.
Clinical Review-TÜV SÜD Approach

- External Clinical Expert qualifications based on:
  - Educational background: Physician (currently registered) or adequate education with certified specialization in a medical field or laboratory medicine
  - Direct and current experience in a clinical or laboratory medicine field related to the IVD (laboratory and clinical discipline) code
  - Experience in using comparable in vitro diagnostic medical device, the pathology of the condition being diagnosed, the usual treatment and other medical and diagnostic alternatives.
  - Trainings on EU IVD devices legislation, relevant guidance documents and internal forms to ensure that E-ExC are able to draw up appropriate records and reports as necessary are provided by the ICR.

NB: External clinical Experts are authorized on a case by case basis
Certification fees

- Article 46 9 (List of standard fees) of the IVDR requires notified bodies to establish lists of their standard fees for the conformity assessment activities that they carry out and make those lists publicly available.
- The certification costs are based on hourly rates and complexity of the devices and procedures.
- TUV Sud fees are available on TUV Sud webpage:
Regulation 2022/112: NB perspective
Regulation 2022/112 IVDR Transitional provisions: Background

NB Designation process

<table>
<thead>
<tr>
<th>Body type</th>
<th>Name</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>NB 2797</td>
<td>BSI Group The Netherlands B.V.</td>
<td>Netherlands</td>
</tr>
<tr>
<td>NB 0344</td>
<td>DEKRA Certification B.V.</td>
<td>Netherlands</td>
</tr>
<tr>
<td>NB 0124</td>
<td>DEKRA Certification GmbH</td>
<td>Germany</td>
</tr>
<tr>
<td>NB 0459</td>
<td>QMED SAS</td>
<td>France</td>
</tr>
<tr>
<td>NB 0197</td>
<td>TÜV Rheinland LGA Products GmbH</td>
<td>Germany</td>
</tr>
<tr>
<td>NB 0123</td>
<td>TÜV SÜD Product Service GmbH Zertifizierstätten</td>
<td>Germany</td>
</tr>
</tbody>
</table>
Regulation 2022/112 IVDR Transitional provisions: Notified Body considerations

- **IVDR & Revised transitional provisions**
  - A welcomed approach, however several challenges remain

- **IVDR Readiness**
  - NB designation process
  - Availability of regulatory infrastructure

- **Shift in focus**
  - IVDD certificate extensions/modifications
  - Slowdown in IVDR applications
Resources

- Nando (New Approach Notified and Designated Organisations) Information System:

- MDCG endorsed documents and other guidance:

- Expert Panel website:

- List of views provided and ongoing consultations under the PECP
Resources

- TUV Sud IVDR Request for service registration page:

- TUV Sud IVDR application procedure with list of fees:
QUESTIONS?
Stay informed and updated

Check out our resource centre and Sign-up for TÜV SÜD’s complimentary newsletter about Healthcare and Medical Devices that delivers updates on the latest regulations and standards, at:

www.tuv sud.com/en/subscribe

Marta Carnielli, Pharm D
Technical Director IVD
TÜV SÜD Product Service GmbH, München

Marta.Carnielli@tuv sud.com