MedTech Europe
from diagnosis to cure

Overview of requirements under the IVD Regulation

Regulation 2017/746/EU on *In Vitro* Diagnostic Medical Devices

December 2017

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Design

Defines

Define Properties of the IVD

IVD Intended Purpose

- Article 2(12) Annex I Section 20.4.1(c): What is detected / measured; Function; Specific info to be provided
- Self-test
- Near-patient test → Intended User
- Instrument
- Companion Diagnostic
- Software

Classification (Article 47, Annex VIII)

Determines

Basis for Requirements Checklist

Define Applicable Requirements for the IVD (CE) Technical Documentation

Annex I

- Annex I Section 1: General Design and Safety requirements
- Annex I Section 3: Risk Management System
- Annex I Section 4: Risk Control Measures
- Annex I Section 8 / Article 9: Use of Harmonised Standards / CS

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Annex I

- Annex I Section 9: Performance Characteristics
- Annex I Section 10: Chemical, Physical & Biological Properties
- Annex I Section 11: Infection & Microbial Contamination
- Annex I Section 12: Material of Biological Origin
- Annex I Section 13: Interaction with the Environment
- Annex I Section 14: Measuring Function
- Annex I Section 15: Protection Against Radiation
- Annex I Section 16: Software
- Annex I Section 17: Energy Source
- Annex I Section 18: Mechanical and Thermal Risks
- Annex I Section 19: Devices for Self Testing and NPT
- Annex I Section 20: Information Supplied With the Device

Machinery Directive
WEEE
RoHS
REACH / CLP
Euratom
Biocides
Other Legislation

Obligations of Manufacturers

Manufacturer Obligations

Requirements for manufacturers

- Article 10 Para 2: Risk Management System
- Article 10 Para 3: Performance evaluation incl. PMPF
- Article 10 Para 4: Technical documentation
- Article 10 Para 5: Conformity assessment, DoC and CE marking
- Article 10 Para 6: UDI assignment
- Article 10 Para 7: Availability of Technical Doc, Cert. and DoC
- Article 10 Para 8: Quality Management System
- Article 10 Para 9,12: PMS, Vigilance
- Article 10 Para 11: Ensure implementation of corrective actions
- Article 11 Para 1: If outside the EU – designate authorised rep → Article 11 Para 2: Define a mandate for authorised rep.
- Article 10 Para 14: Registration original equipment manufacturer — EUDAMED
- Article 10 Para 15: Liability
- Article 15: Person Responsible for Regulatory Compliance
- Article 26,28: Registration, SRN — EUDAMED
- Article 48: If class B, C, D or A sterility – Notified Body

Evidence Collection

Clinical Evidence Article 56

- Annex XIII Section 1.2.1: Scientific Validity
- Annex XIII Section 1.2.2: Analytical Performance
- Annex XIII Section 1.2.3: Clinical Performance

Identify Evidence

Compile Performance Evaluation Plan (Annex XIII Section 1.1)

Sources of Evidence

Annex XIII Section 1.2

- Peer Reviewed Literature
- Consensus / Expert opinions
- Proof of concept studies
- Performance Studies
- Information on scientific validity from devices measuring the same analyte
- Published experience gained by routine testing

Other Evidence

- Annex I Section 10: Chemical Safety
- Annex I S. 10,11 & 12: Biological Safety
- Annex I Section 17: Electromagnetic Compatibility
- Annex I Section 18: Mechanical Safety

Appraise data for suitability to establish safety and performance

Sufficient Evidence? YES → *Compile Performance Evaluation Report including Clinical Evidence (Annex XIII Section 1.3)*

NO → Performance Studies (Annex XIII Section 2 and Section 3)

(Clinical) Performance Study Plan Annex XIII Section 2.3.2

Studies using prospective specimens

Simplified Annex XIII Procedure

Study using leftover/archived specimens

- Preamble 73: No notification needed
- Article 57 Article 58 Para 2-4, 7: General Requirements
- Annex XIII Sec 2.2: Ethical Considerations
- Annex XIII Sec 2.3: Simplified Methodology
- Annex XIII Sec 2.3.2: Designate a Sponsor

Complete Annex XIII Procedure

Study posing low or no risk to subjects

- Article 57 Article 58 Para 2-4, 7: General Requirements
- Annex XIII Sec 2.2: Ethical Considerations
- Annex XIII Sec 2.3: Complete Methodology
- Annex XIII Sec 2.3.2: Designate a Sponsor

Complete Annex XIII & Annex XIV Procedures

Interventional study or study posing risk to subjects

- Article 57 Article 58: General Requirements
- Article 66: Authorisation needed — EUDAMED
- Articles 59-76: Considerations to Ensure Patient Safety
- Annex XIII Sec 2.2: Ethical Considerations
- Annex XIII Sec 2.3: Complete Methodology
- Annex XIII Sec 2.3.2: Designate a Sponsor
- Annex XIV: Additional Sponsor Obligations

(Clinical) Performance Study Report Annex XIII Section 2.3.3

Define Applicable Requirements for the IVD/CE

Machinery Directive
WEEE
RoHS
REACH / CLP
Euratom
Biocides
Other Legislation

Conformity Assessment

Demonstration of Conformity

Presumption of Conformity

- Article 8: Conformity Through Harmonised Standards
- Article 9: Conformity through Common Specifications

Other Means of Conformity

- Annex II Section 4: Controlled Documents Demonstrating Conformity

Classification

- Article 47 Annex VIII: Classification of each device

Technical Documentation

Technical Documentation Annex II & Annex III: Documenting conformity includes all information on design, evidence and manufacturer's procedures; PMS plan

Summary of Safety & Performance Article 29: Class C & D Summary of device information

EU Technical Documentation Assessment Certificate: Annex IX – Class D, Companion Diagnostics, Self Tests, Near-patient Tests

EU Quality Management System Certificate: Annex IX – Class B, C & D Class A sterile devices

EU Type Examination Certificate: Annex X – Class C & D

EU Production Quality Assurance Certificate: Annex XI – Class C & D Class A sterile devices

Certificates issued by Notified Bodies → EUDAMED

Class A

- Annex II & Annex III: Technical Documentation

Class A Sterile

- Annex IX or Annex XI: Quality Management System / Production Quality Assurance — Notified Body

Article 48 Para 10

Class B

- Annex IX: Quality Management System

Article 48 Para 9

Device Category

- Article 48 Para 9: If no certificate exists that covers the category – NB needs to be involved before placing on the market — Notified Body

Class C

- Annex IX or Annex X & Annex XI: Quality Management System / Type Examination & Production QMS — Notified Body

Article 48 Para 7, 8

Generic Device Groups

- Article 48 Para 7: If no certificate exists that covers the generic device group – NB needs to be involved before placing on the market — Notified Body

Class D

- Annex IX or Annex X & Annex XI: Quality Management System / Type Examination & Production QMS — Notified Body

Article 48 Para 1, 4

- Article 48: Reference Laboratory Common Specifications Testing, Batch Release Testing
- If no Common Specification → Article 50 Scrutiny Procedure

Declaration of Conformity, Article 17 & Annex IV

Notified Bodies Involved Irrespective of Class

Additional Conformity Requirements

- CoDx, Article 48: Consultation with European Medicines Agency or medicines competent authority — Notified Body
- Self Tests & NPT, Article 48: Technical Documentation Assesment — Notified Body

Placing on the market

- Article 18 & Annex V: Affix CE Mark

Placing on the market and putting into service

Registration

Registration Economic Operators

- Article 28 Para 1 & 2: SRN Registration: Manufacturer Authorised Rep. Importer — EUDAMED Annex VI Part A
- Article 27 Para 2: Distributor Registration — National Database

Registration Devices

- Article 26: Basic UDI-DI Basis of registration
- Annex VI Part A: Database Requirements
- Article 29: Summary of Safety and Performance

Unique Device Identification

- Article 24, Annex VI Part C

Electronic System for NB Certificates

- Article 49: Notified body involvement
- Article 51: Notified body Certificates
- Article 52: Notifications regarding Certificates

Notified Body

Electronic System for Studies

- Article 66 Article 69: Application for Performance Studies
- Article 73: Performance Study Report & Summary

Post-Market Surveillance and Vigilance

Post-Market Surveillance

System for updating Technical Documentation on Post-Market Surveillance

- Article 78: Post-Market Surveillance System
- Article 79: Post-Market Surveillance Plan (all classes)
- Article 80: Post-Market Surveillance Report (Class A & B)
- Article 81: Periodic Safety Update Report (Class C & D) — Notified Body Class D — EUDAMED

Update over device lifecycle

Continuous Process of Performance Evaluation

Performance Evaluation Report (Annex XIII section 1.3)

Update over device lifecycle

Post-Market Performance Follow-up

Annex XIII, Part B

- Preamble 63: Continuous Process
- Annex XIII Section 4: Principles of PMPF
- Annex XIII Section 8: Justification for no PMPF
- Annex XIII Section 5: PMPF Plan

Analyse Findings

PMPF Evaluation Report

Surveillance Assessment

Surveillance of Quality Management System and Devices

- Annex IX Section 3: Surveillance Assessment Class C & D — Notified Body → *Surveillance Assessment Report & Test Report*
- Annex IX Section 3: Unannounced audit Class C & D — Notified Body → *Surveillance Assessment Report & Test Report*

Vigilance

Reporting & Investigating Serious Incidents

EUDAMED

- Article 82 Para 1: Reporting Serious Incidents → *Manuf. Incident Report*
- Article 82 Para 3: Reporting time 15 days
- Article 82 Para 9: Periodic Reporting → *Periodic Summary Report*
- Article 83: Trend Reporting → *Trend Report*
- Article 84: Assessment of Serious Incidents
- Article 82 Para 1: Reporting Field Safety Corrective Actions → *Field Safety Corrective Action*
- Article 84 Para 8: Issue Field Safety Notice → *Field Safety Notice*
- Article 84: Assessment of Corrective Actions
- Article 90 Para 3: Application of corrective actions

Obligations of Authorised Representatives, Importers and Distributors

Importer Obligations

Requirements for Importers

- Article 13 Para 1,2: Verify device compliance
- Article 13 Para 3: Add contact details to device or packaging or accompanying document
- Article 13 Para 4: Verify device registration, add own details — EUDAMED
- Article 13 Para 5: Safeguard storage and transport conditions
- Article 13 Para 6: Keep register of complaints, non-conforming devices, etc.
- Article 13 Para 7: Inform of non-conformities and serious risk
- Article 13 Para 7: Ensure implementation of corrective actions
- Article 13 Para 8: Inform of complaints & suspected incidents
- Article 13 Para 9: Keep Declaration of Conformity and certificate(s)
- Article 13 Para 10: Cooperation with Competent Authorities
- Article 22: Identification within the supply chain
- Article 24 Para 8: Storage of UDI data
- Article 27 Para 3: Verify registration of manufacturer or authorised representative; add own details — EUDAMED — Within 2 weeks of placing on market
- Article 28: Registration of the importer — EUDAMED
- Article 90 Para 3: Application of corrective actions

Distributor Obligations

Requirements for Distributors

- Article 14 Para 2: Verify device compliance — Sampling method
- Article 14 Para 3: Safeguard storage and transport conditions
- Article 14 Para 4: Inform of non-conformities and serious risk
- Article 14 Para 4: Ensure implementation of corrective actions
- Article 14 Para 5: Inform of complaints & suspected incidents
- Article 14 Para 5: Keep register of complaints, non-conforming devices, etc.
- Article 14 Para 6: Cooperation with Competent Authorities
- Article 22: Identification within the supply chain
- Article 24 Para 8: Storage of UDI data
- Article 27 Para 2: Distributor Registration — National Database
- Article 90 para 3: Application of corrective actions

If device is modified before placing on the market

Device Modification

- Article 16 Para 1: Market device under own name, change intended purpose or modify in a way which may affect compliance
- Article 16 Para 2: Relabel or repackage device

Assume the obligations of the manufacturer

If device is modified before placing on the market

Requirements if Relabel or Repackage a Device

- Article 16 Para 3: Add modification activity and contact details to the device, packaging or accompanying document
- Article 16 Para 3: Quality Management System — Notified Body
- Article 16 Para 4: Inform manufacturer and competent authority

Authorised Representative Obligations

Authorised Representative

- Article 11 Para 2, 3 ,4: Mandate
- Article 11 Para 5: Liability
- Article 11 Para 6: Termination of mandate if manufacturer acts illegally: communication
- Article 12: Change of authorised representative
- Article 15 Para 6: Person responsible for regulatory compliance
- Article 24 Para 8: Storage of UDI data
- Article 28: Registration, SRN — EUDAMED
- Article 90 para 3: Application of corrective actions

Authorised Representative Mandate - Minimum Requirements

Authorised Representative - Mandate

Article 11 Para 3

- Verify declaration of conformity, technical doc., conformity assessment
- Keep available copy of technical doc., declaration of conformity, certificates
- Registration, verify device and UDI registration — EUDAMED
- Device information to competent authority upon request
- Samples and access to device
- Preventive or corrective actions
- Inform of complaints and suspected incidents
- Terminate mandate if manufacturer acts illegally

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