Study Group 1

In- Vitro-Diagnostics and Global Harmonization

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Definition of an In-Vitro-Diagnostic Product

- Reagents, instruments and systems intended for use in the diagnosis of a disease or other condition affecting the state of health, in order to cure, mitigate, treat, or prevent disease.

- **No direct risk** for patients or the person examined, since the devices are not used on the human body However, hazards that are associated with the device give rise to **indirect risks** that lead or contribute to erroneous decisions. Extent of reliance on the analytical result (contribution to the medical decision)

IVD Definitions from ISO 18113-1 modified

- **In Vitro Diagnostic Reagent:** chemical, biological or immunological component of an in vitro diagnostic examination procedure that produces a detectable signal for the purpose of detecting or measuring a quantity in a sample. (Source :ISO 18113-1 modified)

- In Vitro Diagnostic Instrument : equipment or apparatus component of an in vitro diagnostic examination procedure that is used for detecting, measuring, or computing a quantity in a sample. (Source :ISO 18113-1 modified)

Classification

- IVDs are classified differently in worldwide regulations: Medical devices or drugs
- GHTF classifies them as Medical Devices, but admits the different nature and risk of IVDs
- Several GHTF papers for medical devices will include guidelines for IVDs, but others will reflect and describe IVDs separately (e.g. Draft N045- Principles of IVD Medical Devices Classification; conformity assessments and STED for IVDs to come)

GHTF Risk Classes

- Class A:

Low Individual Risk- No Public Health Risk

- Class B:

Moderate Individual Risk- Low Public Health Risk

- Class C:

High Individual Risk- Moderate Public Health Risk

- Class D:

High Public Health Risk

Case Study: Classification

- Case 1:

  HIV Test for screening blood donors or for diagnostic purposes

  A false negative result in a blood bank may result in high public health risk due to HIV transmission via blood products.

  EU Classification: Annex II List A (high-risk)

  GHTF Class: D

Case Study: Classification

- Case 2:

  Test kit for quanitative determination of ferritin in human serum and plasma

  Assay used in combination with : symptoms of anaemia, low hemoglobin levels or mean corpuscular volume (MCV)

  Low individual risk, no public health risk

  EU Classification: self-declared

  GHTF Class: B (A)

Case Study: Classification

- Case 3

  Assay for quantitative determination CA 15-3 concentrations as an aid in combination with other clinical methods for monitoring mamma carcinoma.

  Low Individual Risk- No Public Health Risk

  EU Classification: self-declared

  GHTF Class: B (A)

EU Classification

- Annex II List A Products (High- Risk):

  Reagents and reagent products, including related calibrators and control materials, for determining the following blood groups: ABO system, rhesus (C, c, D, E, e) anti-Kell,

  Reagents and reagent products, including related calibrators and control materials, for the detection, confirmation and quantification in human specimens of markers of HIV infection (HIV 1 and 2), HTLV I and II, and hepatitis B, C and D.

EU Classification – cont'd

- Annex II List B Products:

  CMV, Toxoplasmosis, Rubella, Chlamydia, HLA tissue groups: DR, A, B, Phenylketonuria, PSA, determination of risk for Trisomy 21, self-testing devices for blood sugar et al.

- Several different parameters - political compromise

EU Classification – cont'd

- All other self-testing devices (e.g. pregnancy tests)
- New parameters (under special governmental control, if required)
- All other IVDs

Benefits of the EU System

- Easy to classify (if not covered by Annex II or self test device, product has to be self-declared by the manufacturer)

- New products/ parameters with impact to public health can be covered by special governmental controls (flexibility for authorities)

Different Classes- Same Principles

- Common technical specifications for Annex II List A products (high risk)
- Third party assessments for Annex II List A, B and self- testing devices
- Quality system principles for all products to follow
- Essential requirements same for all products in dependant from risk

CE Mark for In-Vitro-Diagnostic Devices

- Any product which carries the CE mark has to be in compliance with the EU IVDD 98/79/EC, even it is sold outside the EU!

- Note: Annex II List A products must be batch verified by a Notified Body before it is sent (with CE mark on the box) to any country.

Outlook

- GHTF will adress IVD specific topics in more detail to differentiate to Medical Devices as needed (classification, conformity assessments, STED)
- Harmonization of regulations, but also duplications of regulations are moving forward in many worldwide countries
- Considerations: Regulators may spend more time to watch products in the market (surveillance and vigilance) than performing administration tasks to approve products: Emphazise on Post-Market versus Pre-Market