KEMA Quality

GHTF Proposed General Classification system for IVD Medical Devices

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Focus

- General Classification System for IVD Medical Devices by the GHTF Study Group 1 finalized in September 2008 (GHTF/SG1/N045:2008)

- Impact on current **global** IVD Regulations and specifically CE Marked devices

Summary

- What is the current IVD Directive 98/79/EC classification scheme?
- Other regulatory schemes?
- Who are the GHTF and why a different classification scheme?
- How will it affect us?

IVD Regulatory Pathway for Europe

IVD DIRECTIVE 98/79/EC - 27 October 1998

Classification is based on risks

- List A Highest Risk
- List B
- Self-Test
- Non A, Non B, Non Self Test - Lowest Risk

IVD Directive 98/79/EC classification *continued*

Annex II - List A

Reagents & reagent products, including related calibrators and control materials

- Determination of blood groups: ABO system, **rhesus (C, c, D, E, e) anti-Kell**
- 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**.

IVDD List A requirements

- Full Notified Body Involvement

- List A Highest Risk
  - Dossier Review and Approval for CE Marking
  - Batch Release by 3rd Party Reference Laboratory
  - Surveillance Audits

IVD Directive 98/79/EC classification *continued*

Annex II - List B

Reagents & reagent products, including related calibrators and control materials Determination of:

- blood groups **anti-Duffy** and **anti-Kidd**
- irregular **anti-erythrocytic antibodies**
- detection and quantification in human samples of congenital infections: **rubella** and **toxoplasmosis**
- diagnosing the hereditary disease **phenylketonuria**
- determining human infections: **cytomegalovirus** and **chlamydia**
- determining HLA tissue groups: **DR, A, B**
- determining tumoral marker: **PSA**
- product and software, designed specifically for evaluating the risk of **trisomy 21**
- **self-diagnosis**, measurement of **blood sugar**

IVDD List B requirements

- Notified Body Involvement

- List B Next level Risk
  - Dossier Review
  - Surveillance Audits

IVD Directive 98/79/EC classification *continued*

Self Test Devices

Reagents & reagent products, including related calibrators and control materials

Examples:

Pregnancy Test

Ovulation Test

IVDD Self test requirements

- Partial Notified Body Involvement

- Self Tests
  - Dossier Review only

IVD Regulatory Pathway for Europe

- Non A list, Non B list and not a Self Test
  - Declaration of Conformity by the manufacturer

- No Notified Body Involvement
  - Examples: ANA, EBV-VCA

Company's responsibility to develop, maintain and evaluate technical dossiers to state of the art compliance!

US Regulatory Pathway

FDA Classification of IVD Devices is **Risk Based**

- Class I, II or III
- Class is according to the level of Regulatory Control Required to assure safety and effectiveness
- Classification determines the Premarket process
  - 510k, PMA, De Novo etc..

Who are the GHTF?

- The Global Harmonization Task Force was conceived in 1992
- Partnership between regulatory **authorities** and regulated **industry**
- 5 Founding Members:
  - European Union,
  - United States,
  - Canada,
  - Australia
  - Japan
- Chairmanship is rotated among the Founding Members
- The GHTF has NO DIRECT REGULATORY AUTHORITY

GHTF goals and operation

- The objective of the Global Harmonization Task Force (GHTF) is to encourage convergence at the global level in the evolution of regulatory systems for medical devices in order to facilitate trade whilst preserving the right of participating members to address the protection of public health by regulatory means considered to be most suitable.

- The primary way in which the GHTF achieves its goals is through the production of a series of guidance documents that together describe a global regulatory model for medical devices (such as Study Group 1 for IVD).

Why a different Classification System?

What is the intent of the GHTF classification system?

- Assist a manufacturer to allocate its In Vitro Diagnostic (IVD) medical device to an appropriate risk class using a set of harmonized principles.
- Classification based on the intended use and indications for use as specified by the manufacturer
- Conformity assessment requirements appropriate to each of the four risk classes proposed *(GHTF document GHTF/SG1/N046:2008 Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices)*
- Regulatory Authorities have the responsibility of ruling upon matters of interpretation for a particular medical device.

Rationale, Purpose and Scope

- Promote Global regulatory model
- Inter-relationship between device class and conformity assessment is **critical**
- To establish a consistent approach to premarket approval across all countries/regions

Rationale, Purpose and Scope

- Applying an appropriate risk class using a set of **harmonized** classification principles
- Based on the IVD device's **intended use**
- To allow the development of a forum for consideration of **interpretation**, when appropriate
- Classification determines the conformity assessment route as described in the GHTF document on "*Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices*" N046

Rationale, Purpose and Scope

- All products that fall within the definition of an IVD medical device:
- "*A device ... for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes*"
- Reagents, Calibrators, Control materials
- Specimen receptacles
- Software, and related instruments, apparatus or other articles

Important Classification Criteria

What	■ **Intended use and indications for use as specified by the manufacturer**
Who	■ **Technical/scientific/medical expertise of the intended user**
How	■ **Contribution of the information to the diagnosis**
Risk	■ **Impact of the result to the individual and/or to public health**

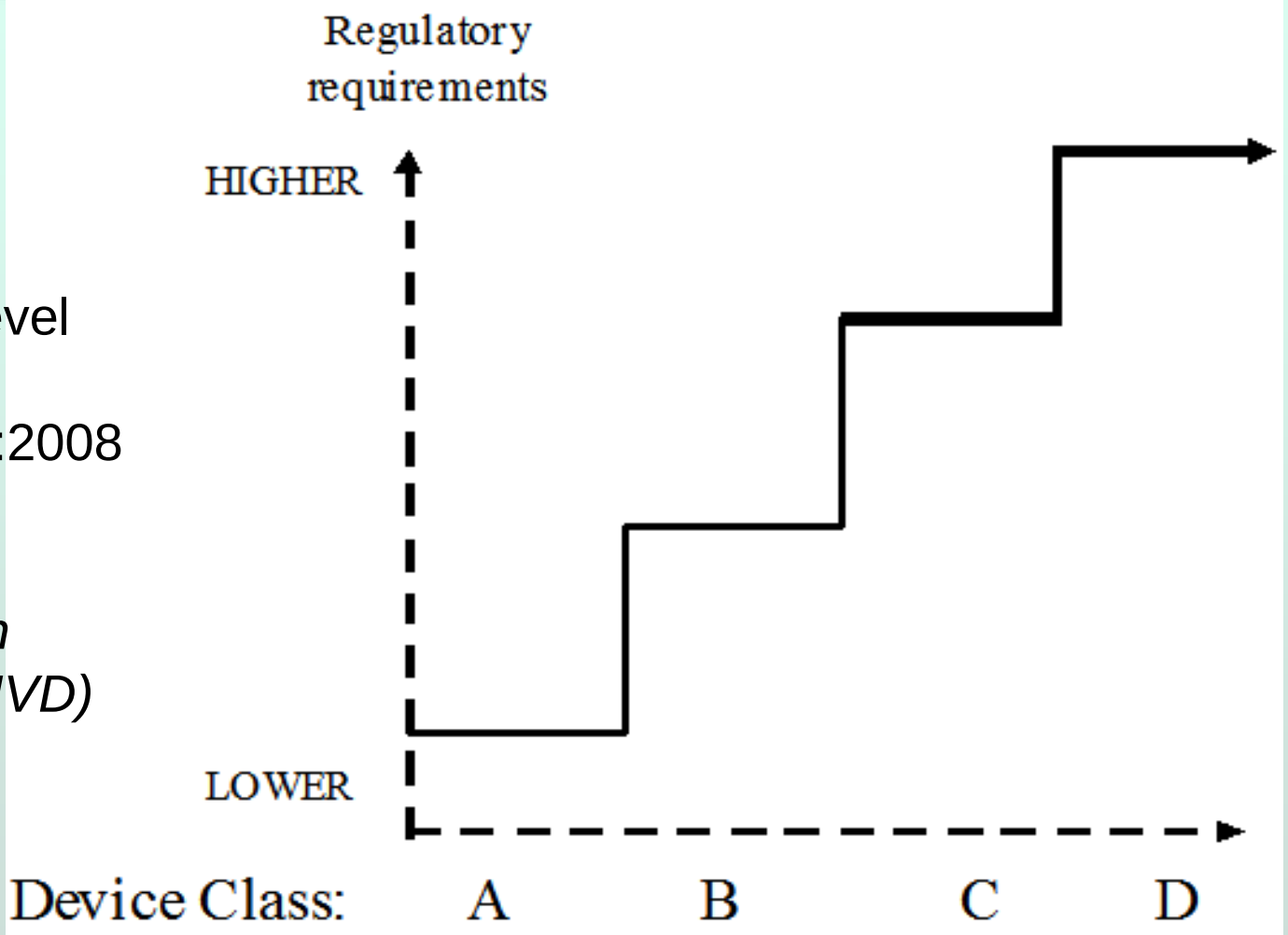
Classification Rules

4 Risk Classes: lowest Class A to highest Class D

CLASS	RISK LEVEL	EXAMPLES
A	• Low Individual Risk **and** • Low Public Health Risk	Clinical Chemistry Analyser , prepared selective culture media
B	• Moderate Individual Risk **and / or** • Low Public Health Risk	Vitamin B12, Pregnancy self testing, Anti-Nuclear Antibody, Urine test strips
C	• **High** Individual Risk **and / or** • Moderate Public Health Risk	Blood glucose self testing, HLA typing, PSA screening, Rubella
D	• **High** Individual Risk **and / or** • **High** Public Health Risk	HIV Blood donor screening, HIV Blood diagnostic

Regulatory Requirements Increase with Increasing Risk

Regulatory Requirements Increase with Increasing Risk level of the Device per GHTF/SG1/N046:2008 *Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices*



GHTF/SG1/N045:2008

Rule 1: Class D

High Individual Risk and/or **High** Public Health Risk

- Devices intended to be used to detect the presence of, or exposure to, a transmissible agent in blood, blood derivatives, cells, tissues or organs in order to assess their suitability for transfusion or transplantation. **Or**...
- .....that causes a life-threatening, often incurable, disease with a high risk of propagation

- Principally as a decision tree for transplantation / transfusion

- Examples: HIV, HCV, HBV, HTLV. This Rule applies to first-line assays, confirmatory assays and supplemental assays.

Rule 2 Class C and D:

High Individual Risk and/or **Moderate** Public Health Risk

- IVD medical devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation, are classified as **Class C, except for ABO and Duffy systems, which are Class D**

- The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: A high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation places the device into Class D. **The rule divides blood grouping devices into two subsets, Class C or D, depending on the nature of the blood group antigen** the IVD medical device is designed to detect, and its importance in a transfusion setting.

Rule 3: Class C

High Individual Risk and/or **Moderate** Public Health Risk

- in detecting the presence of; exposure to; presence in ;screening of immune status; human genetic testing; to monitor levels of pharmaceuticals / biologics; management of patients suffering life threatening; screening foetal congenital defects:

  •STD - ie *Chlamydia*

  •Infectious agents in blood, CSF- *N. meningitidis*

  •Prenatal - Rubella

  •Immune status - CMV

  •.....etc

Rule 4: Class C

High Individual Risk and/or **Moderate** Public Health Risk

- Self-testing, except for those devices from which the result is not determining to be of medically critical status, or is preliminary and requires follow-up with the appropriate laboratory test in which case they are Class B.

- Example for self-testing class C: Blood glucose monitoring,
- Example for self-testing class B: Pregnancy self test, Fertility testing, Urine test-strips.

Rule 5: Class A

Low Individual Risk and **Low** Public Health Risk

- Reagents or other articles with *specific characteristics* intended make them suitable for in vitro diagnostic procedures related to a *specific* examination.
- Instruments *specifically* to be used for in vitro diagnostic procedures
- Specimen receptacles
- Examples: Selective/differential microbiological media (excluding the dehydrated powders which are considered not to be a finished IVD medical device), identification kits for cultured microorganisms, wash solutions, instruments and plain urine cup.

Rule 6 & 7: Class B if not covered in Rules 1 through 5

Moderate Individual Risk and/or **Low** Public Health Risk

- Rule 6: Examples:

  Blood gases, *H. pylori* and physiological markers such as hormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers.

- Rule 7: Controls without a quantitative or qualitative value assignment

Determining the Class of your IVD Device

- *Is it an IVD medical device?*
- *What is the intended use?*
- *If multiple intended uses…highest classification applies*
- *If more than one of the rules applies to the IVD medical device, it should be allocated to the highest class indicated, as an example:*

  e.g. a self-testing for HIV would be a class D under rule 1 and not a class C under rule 4 - despite self tests being a class C

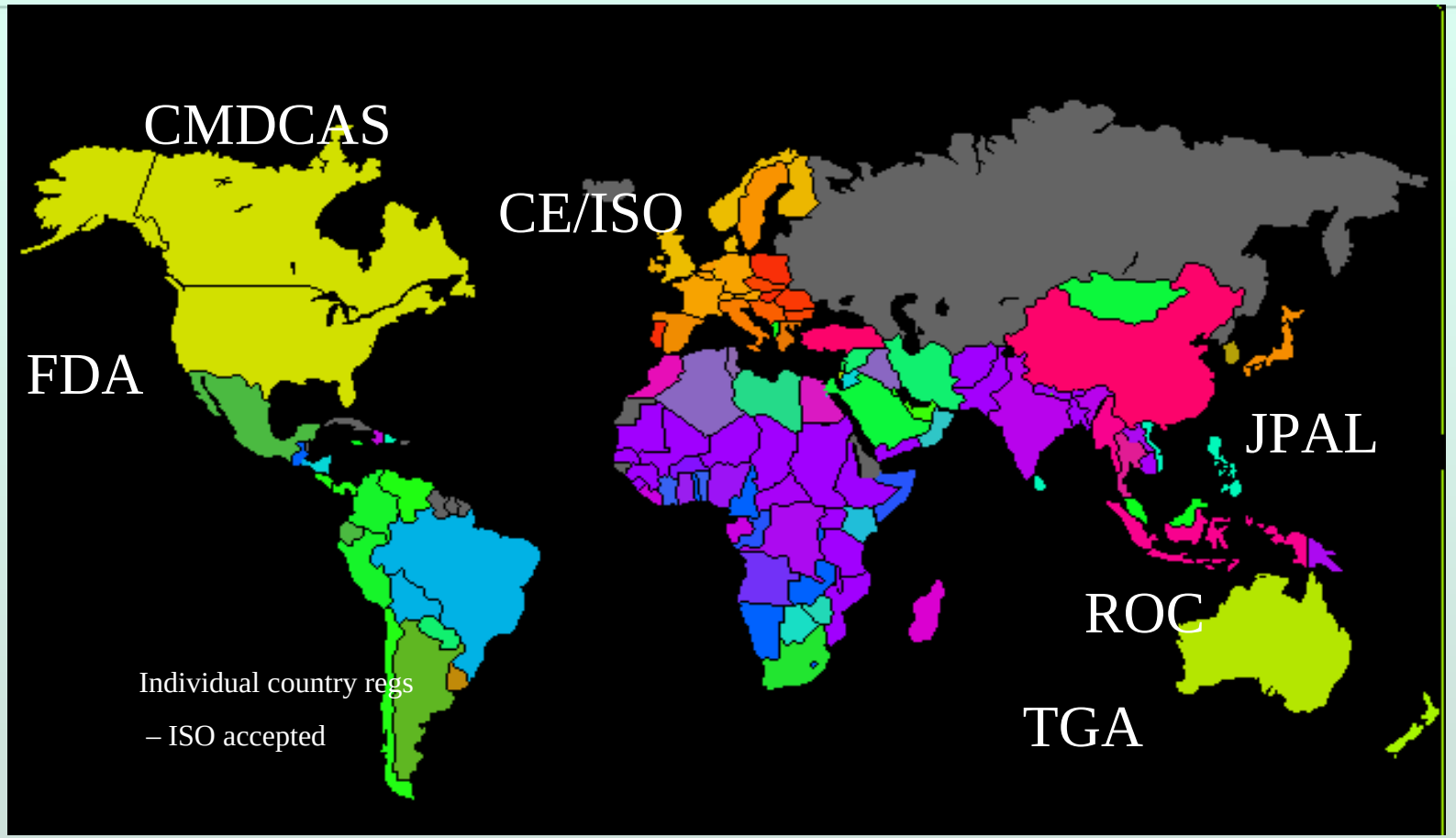
Determining the Class of your IVD Device *continued*

Consider your market…. if the device is subject to special national rules that apply within a particular jurisdiction and can be classified lower than these rules would apply

- if a lower classification of a particular IVD medical device is allowed and as a consequence, a less vigorous conformity assessment procedure is carried out, this may be unacceptable to other jurisdictions.

What is your Market!!

WHERE is your device to be marketed?



What are the requirements in this regions? Have you considered all areas?

So, how does all of this affect us?

- Where do you sell your device?
- Where do you intend to sell your device in five years?
- What is your current regulatory strategy?
- What resources do you need to reflect the above requirements?

Current Status:

What countries have adopted the GHTF Classification System?

- TGA (July 2010)
- Hong Kong (2009)
- EU / CE Classification, Requirements (not yet!)
- FDA – 510K, PMA, etc.? (not yet)
- JPAL (?)
- CMDCAS / Health Canada (not yet)

What's in your Technical Files?

- Design Requirements well documented?
- Self Declared mature products on the market before CE marking?
- Risk Analysis still applicable today?
- Have you maintained the files to your state of the art?

So that's all very nice, ... what do we do?

- Start early – review your technical documentation and perform a gap analysis
- Are risks sufficiently addressed and up to date?
- Consider ALL of the data required – consider consolidation of the necessary testing
- You know the state of your files, are they well organized, easy to follow?
- will your objective evidence

Thank You!

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References:

- GHTF/SG1/N045:2008 *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*
- GHTF/SG1/N046:2008 *Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices*
- GHTF/SG1/N029:2005 *Information Document Concerning the Definition of the Term 'Medical Device'.*
- GHTF/SG1/N041:2005 *Essential Principles of Safety and Performance of Medical Devices.*
- *In Vitro Diagnostic Directive 98/79/EC (IVDD)*


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