MEDICAL DEVICE REGULATION
PRE-MARKET APPROVAL

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Roles and Responsibilities of regulatory authorities

To protect consumer health, especially, to ensure safety, quality and effectiveness of medical device products life cycle through

Pre-marketing control, Post-marketing control, Surveillance and Vigilance program for consumers' safety, Advertisement control and Consumer Education
Premarket Evaluation and Approval

- Definitions of Medical Devices (+Manufacturers)
- Classification
- Essential Principles of Safety and Performance of medical devices (STED-GHTF, CSDT-AHWP, CSDT-ASEN)
- Principles of Conformity Assessment
- Labelling (GHTF/SG1(PD)/N070)
- Use of Standards (GHTF/SG1/N044:2008)
GHTF Global model - Premarket Evaluation
“Medical Device“ means any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article:

a) Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:
Definition of “medical device” (2)

- Diagnosis, prevention, monitoring, treatment or alleviation of disease,
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- Investigation, replacement, modification, or support of the anatomy or of a physiological process,
- Supporting or sustaining life,
GHTF – Definition of “medical device” (3)

- Control of conception
- Disinfection of medical devices,
- Providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body;
and

• b) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means
## Classification of medical devices (non IVD)

GHTF/SG1/N15:2006 Principles of Medical Devices Classification

### 16 Rules – Risk-based Classification

<table>
<thead>
<tr>
<th>CLASS</th>
<th>RISK LEVEL</th>
<th>DEVICE EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk</td>
<td>Surgical retractors, tongue depressors</td>
</tr>
<tr>
<td>B</td>
<td>Low-moderate Risk</td>
<td>Hypodermic needles, suction equipment</td>
</tr>
<tr>
<td>C</td>
<td>Moderate-high Risk</td>
<td>Lung ventilator, bone fixation plate</td>
</tr>
<tr>
<td>D</td>
<td>High Risk</td>
<td>Heart valves, implantable defibrillator</td>
</tr>
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# Classification of IVD medical devices

GHTF/SG1/N045:2008 Principles of In Vitro Diagnostics (IVD) Medical Devices Classification

## 7 Rules – Individual and Public Health Risk-based Classification

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<th>CLASS</th>
<th>RISK LEVEL</th>
<th>DEVICE EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Individual Risk and Low Public Health Risk</td>
<td>Clinical chemistry analyser, Selective culture media</td>
</tr>
<tr>
<td>B</td>
<td>Moderate Individual Risk and/or Low Public Health Risk</td>
<td>Vitamin B12, Pregnancy self testing, Anti-Nuclear Antibody, Urine test strip</td>
</tr>
<tr>
<td>C</td>
<td>High Individual Risk and/or Moderate Public Health Risk</td>
<td>Blood glucose self testing, HLA typing, PSA screening, Rubella</td>
</tr>
<tr>
<td>D</td>
<td>High Individual Risk and/or High Public Health Risk</td>
<td>HIV Blood donor screening, HIV Blood</td>
</tr>
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</table>
Factors that may affect Risk

- Design
- Manufacture
- Intended Use
- User experience, education and training

More Risk, More Control Level
# Examples of Regulations

<table>
<thead>
<tr>
<th>EU</th>
<th>US</th>
<th>JAPAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 90/385/EEC Active Implantable Medical Devices Directive (AMDD)</td>
<td>• 1976 Medical Device Amendment MDA</td>
<td></td>
</tr>
<tr>
<td>• 98/79/EEC In Vitro Diagnostic Medical Devices Directive (IVDD)</td>
<td>• 1990 Safe Medical Device Act</td>
<td></td>
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</table>
## Classification of Medical Devices

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</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Class I</strong> – Annex 7</td>
<td>• <strong>Class I</strong> – General Control</td>
<td>• <strong>Class I</strong> – General Medical Device</td>
</tr>
<tr>
<td>• <strong>Class IIa</strong> – Annex 7 + Annex 2 or (Annex 4 or 5 or 6)</td>
<td>• <strong>Class II</strong> – General Control and Special Control</td>
<td>• <strong>Class II</strong> – Controlled Medical Device</td>
</tr>
<tr>
<td>• <strong>Class IIb</strong> - Annex 7 + Annex 2 or (Annex 3 + 4 or 5 or 6)</td>
<td>• <strong>Class III</strong> – General Control and Premarket approval</td>
<td>• <strong>Class III</strong> - Highly Controlled Medical Device</td>
</tr>
<tr>
<td>• <strong>Class III</strong> – Annex 2 including Sec. 4 or (Annex 3 + Annex 4 or 5)</td>
<td></td>
<td>• <strong>Class IV</strong> - Highly Controlled Medical Device: Invasive device of which malfunction may cause life threatening effects</td>
</tr>
</tbody>
</table>
Principles of Conformity Assessment


Conformity assessment of QMS
1. QMS (SG3)
2. System for post-market surveillance (SG2)

Registration and Listing (SG1)
- Registration of Manufacturers (Importers/Distributors/ Authorized representatives)
- Listing of Medical Devices

Conformity assessment of device safety and performance (SG1)
- Summary technical documentation
- Declaration of conformity
STED guidance overview (GHTF/SG1/N011:2008)

- 1.0 Introduction
- 2.0 Rationale, Purpose and Scope
- 3.0 References
- 4.0 Definitions
- PART 1 - PURPOSE OF THE STED
- 5.0 Preparation and Use of the STED
- PART 2 - Contents of the STED
- 6.0 Device Description and Product Specification, including Variants and Accessories
- 7.0 Labelling
- 8.0 Design and Manufacturing Information
- 10.0 Risk Analysis and Control Summary
STED guidance overview(2)

- 11.0 Product Verification and validation
- 11.1 General
- 11.2 Biocompatibility
- 11.3 Medicinal Substances
- 11.4 Biological Safety
- 11.5 Sterilisation
- 11.6 Software Verification and Validation
- 11.7 Animal Studies
- 11.8 Clinical Evidence
- 12.0 Format of the STED
- 13.0 Declaration of Conformity
- Appendix A (Table of and how to fill the Essential Principles Checklist)
PART 2- Contents of the STED

6.0 Device Description including Variants (Configurations) and Accessories
6.1 Device description
6.2 reference to Previous Device Generation(s) and/or Similar Devices or Device History

7.0 Essential Principles (EP) Checklist
8.0 Risk Analysis and Control Summary
9.0 Design and Manufacturing Information
10.0 Product Validation and Verification
STED for IVD (2)

10.1 Product Verification and validation
- 10.1.1 Specimen type
- 10.1.2 Accuracy
  - 10.1.2.1 Trueness
  - 10.1.2.2 Precision (Reproducibility + Repeatability)
- 10.1.3 Traceability of calibrators and control materials
- 10.1.4 Analytical Sensitivity
- 10.1.5 Analytical Specificity
- 10.1.6 Measuring range of the assay
- 10.1.7 Validation of assay Cut-off

10.2 Stability (excluding specimen stability)
- 10.2.1 Claimed Shelf life
- 10.2.2 In use stability
- 10.2.3 Shipping stability

10.3 Software Verification and Validation

10.4 Clinical Evidence

11.0 Labelling

12.0 Format of the STED

13.0 Declaration of Conformity

Appendix A
GHTF Clinical Safety / Performance Principles

SG5(PD)N3R7 Clinical Investigations

SG5/N2:2007 Clinical Evaluation and ISO 14155

Clinical Data
- Literature
- Clinical experience
- Clinical investigation

Clinical Investigation
- considering the need
- ethical consideration
- design for clinical relevance and scientific validity

Clinical evaluation report

Clinical Evidence for safety and performance of medical devices

Design verification and validation documentation, device description, Labelling, risk analysis, manufacturing information, etc to demonstrate conformity with essential principles
General Principles when considering the Need for a Clinical Investigation (CI)

- When should a CI be undertaken?
- What are the crucial steps in clarifying the need for CI?
  - identifying relevant clinical essential principles
  - performing risk management (ISO 14971)
  - conducting a proper clinical evaluation
- What is the role of risk analysis?
Depth and Detail of Information (preclinical and clinical data) depend on

- Classification and risk of subject device
- Complexity of subject device
- Characteristics:
  - Novel technology/relevant previous experience
  - Intended use/Indication
  - Adverse events or use errors
  - New to manufacturer
  - Novel or potentially hazardous materials
  - Specific public health concerns
  - etc
Implementation of Control

- Law and Regulation are required
- Select the best model to the public health concern of your country
- Try to harmonize
- Good Regulatory Practice
- Ethic concern of private partnership