Review successes and challenges of past and current initiatives at harmonization of regulatory approval for IVDs

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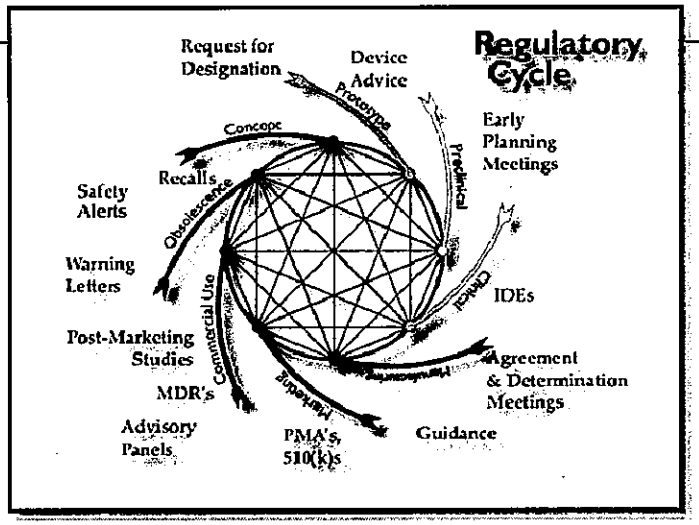

Source: CDRH/FDA

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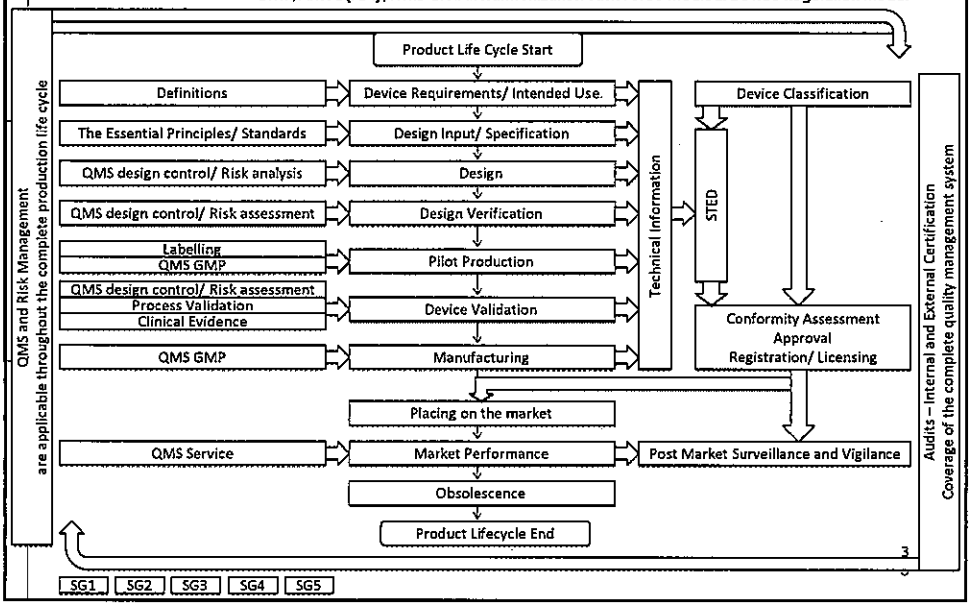
Global Model
Medical Device Regulation Application

**GHTF/AHWG(PD1)/N1R5 Global Harmonization Task Force Medical Device Regulation Model*



IVD Medical Devices Regulatory Elements and Related GHTF Guidance

Regulatory Element	Status
Definition and Classification	SG1-N45:2008 (Final Document)
Conformity Assessment	SG1-N46:2008 (Final Document)
Technical Documentation (STED)	SG1-N63:2011 (Final Document)
Clinical Evidence for IVD Medical Devices - Key Definitions and Concepts	SG5(PD)/N6R3 (Proposed Document) Public Consultation until Mar 21, 2012
Clinical Evidence for IVD Medical Devices - Scientific Validity Determination and Performance Evaluation	SG5(PD)/N7R4 (Proposed Document) Public Consultation until Mar 21, 2012
Clinical Performance Studies for In Vitro Diagnostic Medical Devices	SG5(PD)/N8R3 (Proposed Document) Public Consultation until Jun 2, 2012

The development of IVD medical devices regulations by GHTF countries is still progressing.

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Definition

IVD medical device: a device, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. This includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles.

Note: In some jurisdictions, some IVD medical devices may be covered by separate regulations.

Reference: SG1/N045:2008 Principles of In Vitro Diagnostic (IVD) Medical Devices Classification

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Classification

Risk-based Classification and 7 classification rules

CLASS	RISK LEVEL	DEVICE EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Clinical Chemistry Analyzer, 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 High Public Health Risk	HIV blood donor screening, HIV blood diagnostic

Reference: SG1/N045:2008 Principles of In Vitro Diagnostic (IVD) Medical Devices Classification

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Principles of IVD Classification

- Intended use and indications for use as specified by the manufacturer
- Technical/scientific/medical expertise of the intended user
- The importance of the information to the diagnosis, taking into consideration the natural history of the disease or disorder including presenting signs and symptoms which may guide a physician
- Impact of the result (true or false) to the individual and/or to public health

Reference: SG1/N045:2008 Principles of In Vitro Diagnostic (IVD) Medical Devices Classification

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Conformity Assessment

Elements of Conformity Assessment	Proposed Practice
Quality Management System	A QMS based on risk management
Post-Market Surveillance System	Integrated as part of the QMS
Declaration of Conformity	*Utilizing the Essential Principles and Recognized Standards*
Registration of Manufacturers and Their Devices	Different practice in each country
Technical Documentation	*IVD STED*

Reference: SG1/N046 : 2008 Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices

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Conformity Assessment for Class A Devices

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS or a QMS without design and development controls	Premarket regulatory audit not required.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to GHTF SG2 guidance.	May audit post-market to investigate specific safety or regulatory concerns.	5.2
Technical Documentation	Upon request prepare STED .	Premarket submission of STED not required. May be requested to investigate specific safety or regulatory concerns	5.3
Declaration of Conformity	Prepare, sign and maintain	On file with the manufacturer; available upon request	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements	Maintain and verify as appropriate.	5.5

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Conformity Assessment for Class B Devices

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS or a QMS without design and development controls	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to GHTF SG2 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.	5.2
Technical Documentation	Upon request prepare STED.	Premarket submission normally not required but if requested, receive and conduct a review of the STED to determine conformity to Essential Principles.	5.3
Declaration of Conformity	Prepare, sign and submit	Review and verify compliance with requirements.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements	Maintain and verify as appropriate.	5.5

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Conformity Assessment for Class C Devices

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS.	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to GHTF SG2 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.	5.2
Technical Documentation	Prepare and submit STED for review.	Receive and conduct a premarket review of the STED to determine conformity to Essential Principles.	5.3
Declaration of Conformity	Prepare, sign and submit.	Review and verify compliance with requirements.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.	5.5

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Conformity Assessment for Class D Devices

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility	Section
Quality Management System (QMS)	Establish and maintain a full QMS	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	5.1
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to GHTF SG2 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.	5.2
Technical Documentation	Prepare and submit STED for review. A STED for this class should contain more extended information such as full performance evaluation reports	Receive and conduct a premarket review of the STED to determine conformity to Essential Principles.	5.3
Declaration of Conformity	Prepare, sign and submit.	Review and verify compliance with requirements.	5.4
Registration of manufacturers and their devices	Perform according to regulatory requirements	Maintain and verify as appropriate.	5.5

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IVD Classification in Various Countries

USA	EU	Australia	Canada	Singapore	Japan	Chinese Taipei
Class III/BLA HIV, HBV, HCV, HTLV, ABO blood typing	List A HIV, HBV, HCV, HDV, HTLV, ABO blood typing, rhesus (C, c, D, E, e) anti-Kell, etc.	Class IV HIV, HCV, HBV, HTLV test; and any confirmatory assays used to screen blood and tissue in selected populations, include CMV, dengue, malaria, etc.	Class D HIV, HBV, HCV, HTLV, ABO blood typing	Class D HIV, HBV, HCV, HTLV, ABO blood typing	Class III HIV, HCV, Tumor markers, Microbiology	Class III HIV, HBV, HCV, HTLV, ABO blood typing
Class II Syphilis, PSA (Prostate specific antigen), etc.	List B PSA, rubella, blood sugar self-test, etc.	Class III syphilis (RPR), Typhoid, Q Fever, Chlamydia trachomatis, etc.	Class C Self-test of blood glucose	Class C HSV, HLA typing	Class II Blood cell morphology, Autoimmune	Class II Syphilis, tumor marker
	Others	Class II sodium, ALT, LDH, ferritin, or folate	Class B Ferritin test	Class B Pregnancy test, urine test strip		
Class I microbiological culture media, General purpose reagent		Class I general laboratory equipment, reagents, specimen receptacles and microbiological culture media	Class A microbiological culture media	Class A Culture medium	Class I Liver function (GOT, GPT), LDH, Estradiol	Class I General purpose reagent

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IVD Classification and Conformity Assessment

GHTF	USA	Australia	Canada	Singapore	Japan	Chinese Taipei
Class A: Required QMS and Technical File, No-premarket approval audit Class B: Approved QMS, Technical File maybe sampled by Notified Body Class C: Approved QMS, pre-market audit of Technical File by Notified Body Class D: Approved QMS, pre-market audit of Technical File by Notified Body, design review-more extensive data required	Class I: General controls, Most exempt from premarket submission Class II: Special controls, Most require Premarket Notification [510(k)] Class III: All require Premarket Application [PMA]	New IVD regulatory framework published into law and came into force at 2010- with 4 years' transition period. Before changes, TGA only review for HIV and HCV tests. The new IVD regulations modeled on GHTF.	Class I: establishment license Class II, III, IV: Required QMS and medical device license	Class A: 1.Exempt from product registration 2.notification Class B,C,D: Dossier Submission (Common Submission Dossier Template,CSDT) -higher the risk class more the dossier requirements	Class I: self-declaration (market notification) Class II: Third party certification (marketing certification) Class III: MHLW Approval (marketing approval)	Class I: Premarket approval, most exempt QSD Class II, III: Premarket approval, all require QSD -the higher the risk class, the more the dossier requirements

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Survey on IVD Medical Devices Regulations (July, 2010)

Feedback was collected from 5 out of 20 member economies:

Country / GHTF	PRC	Chinese Taipei	Hong Kong SAR	India	KSA	Singapore
Definition	Yes	Yes	Yes	Yes*	Yes	Yes
Classification	Yes	Yes	Yes	Yes*	Yes	Yes
QMS	ISO13485: 2003	ISO13485: 2003	ISO13485: 2003	ISO13485: 2003*	ISO13485: 2003	ISO13485: 2003
Risk Management	Yes	Yes	Yes	Yes*	Yes	Yes
Performance Evaluation	Yes	Yes	Yes	Yes*	Yes	Yes
Use of Standards	Yes	Yes	Yes	Yes*	Yes	Yes
STED/CSDT	N/A	N/A	N/A	N/A	N/A	CSDT
Clinical Evidence	Yes	Yes	Yes	Yes*	Yes	Yes
PMS and vigilance	Yes	Yes	Yes	Yes*	Yes	Yes

* Prepare to adopt related practices

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Challenges

- The biggest challenge stands that most of the member economies do not have IVD regulations or are developing related regulations
- To the manufacturer, current regulatory challenges are to meet the differences on IVD classification and the submission requirements
- Regulatory frameworks have been slow to respond to advances in science and technology (Laboratory Development Tests, software algorithms and genetic testing etc.)
- Counterfeit devices elevate health concerns

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Future Initiatives

- Implementation of GHTF regulatory model
  - Classification and related conformity assessment requirements
  - Safety and performance evaluation based on state-of-the-art technology and regulatory consensus
  - Best practices for clinical evaluation and clinical investigation for IVD medical devices
- Capacity building and training for underdeveloped or developing countries
- Working towards a unified medical device nomenclature system

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Future Initiatives

- To promote Good Review Practice (GRevP) of medical products, including IVD medical devices
  - Good review practice (GRevP) for medical devices is the best practice for review process in assessing the registration of medical device and pharmaceuticals by regulatory authority.
  - In 2010, Chinese Taipei held APEC GRevP Workshops to address the fundamental elements of a well-designed regulatory review system.
  - To accelerate mutual recognition through enhancing mutual trust between member economies.

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Future Initiatives

- Collaboration with WHO to launch prequalification program for IVD medical devices
  - QMS audit/review
  - Technical review
  - Sampling and inspection program

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Thank You for Your Attention

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AAIVD WORK PLAN

Description of Task	Remark	Timeline	Officer in Charge
Meeting Report for Feb 6-7 Meeting in Hong Kong		20 Feb 2012	**Albert** coordinates inputs from team
Positioning statement/Paper	To AAIVD members	Early March	**Rosanna**
Identify **Best Practices**		Feb - March	**WG01a (Ms Liu)**
Collect **GHTF guidance document feedback** from AHWP Member Economies	3 documents for public consultation	14 March and 20 May	**WG01a (Ms Liu)** to respond to GHTF's call for comments 15 March and 24 May respectively
Circulate AAIVD **Position Paper and** review		mid March	**AAIVD**
Develop a **model for harmonization and plans for piloting model**		April	**Rosanna + AAIVD WG**
Invitation for **pilot and expert panel participation**	Circulate to AHWP members	April	WG01a Chair **(Ms Liu)**
Special follow up with member economies expressing interest		April	**Rosanna + WG01a + AAIVD WG**
Identify and consensus on **Pilot Member Economies**		Early May	**Rosanna + WG01a + AAIVD WG**
AAIVD Planning Meeting with interested parties and pilot economies		May	**Rosanna + WG01a + AAIVD Secretariat**
Develop Training material based on best practices		May - Sept 2012	**AAVID and Expert Panel for pilot**
AAIVD Project kick off and one-day training workshop		Sept in Taiwan	**AAVID and Expert Panel for pilot**
AHWP Annual Meeting	Invite heads of African and Latin American harmonization groups	3-7 Nov 2012 in Delhi	**Rosanna + WG01a + AAVID**