Overview of the Global Harmonization Task Force for Medical Device Regulation and Related Initiatives

Strengthening Regulatory Systems in Developing Countries

Institute of Medicine

M. Gropp; Medtronic, Inc., Minneapolis, USA
Introduction

• Overview
  • Policy objectives
  • Objectives of the Global Harmonization Task Force
  • Historical background of GHTF
  • GHTF guidance
  • International regulatory harmonization initiatives
  • GHTF regulatory model

• Speaking in personal capacity
Policy objectives – medical device regulation

- Protect patients, users, and consumers
  - Safety, quality, and performance of medical devices over device life cycle
  - Provide information
Policy objectives – medical device regulation

Regulator
evaluates benefits/risks for the population

Provider
evaluates benefits/risks for a patient

Patient
evaluates benefits/risks in terms of personal values

Source: Managing the risks from medical product use; Creating a risk management framework; Report to the FDA Commissioner; May 1999 (Adapted)
Policy objectives – medical device regulation

• Protect and enhance public health
  • Reducing morbidity and mortality
  • Reducing burdens of chronic disability
  • Improving quality of life
Policy objectives – medical device regulation

• Timely and equitable access of patients and clinicians to appropriate diagnostic tests and therapies
• Public confidence in medical technologies
• Health as foundation for economic and social development
• Promoting continuous innovation
• Facilitating international trade
• Assuring and protecting integrity of finished and intermediate goods in supply chains
World Health Organization guidance

“Governments need to put in place policies that will address all elements related to medical devices, ranging from access to high quality, affordable products, through to their safe and appropriate use and disposal. …

Policies will be unsuccessful unless they are translated into national regulations that are enforced by legislation and correlating sanctions, and that form an integral part of the overall national health system.”

Source: Medical device regulations: Global overview and guiding principles: World Health Organization, Geneva; 2003
(At: http://www.who.int/medical_devices/publications/en/MD_Regulations.pdf)
Regulatory harmonization

Simple in concept ……

“The establishment, recognition and application of common standards and regulatory measures”
(World Trade Organization)

… more difficult in execution
Medical device regulatory harmonization

Progressive voluntary convergence in technical regulatory requirements

Not:

- International regulation
- Standardization
- Mutual recognition
- ‘Approved once, accepted everywhere’
- Verbatim adoption of same text in laws, regulation, and guidance
Medical device regulatory harmonization forums

Global Harmonization Task Force
• Began in 1992
• Voluntary forum
• Regulators and industry
• Five Founding Members:
  Australia (current Chair), Canada, EU, Japan (next Chair), USA
• Regional members
• Liaison with ISO, IEC, WHO
• Primary source of harmonized guidance documents
• Parallel to pharmaceutical International Conference on Harmonization (ICH)
Shifting sources of medical technology

2005

USA, 45%
Europe, 33%
Japan, 11%
China, 2%
Brazil, 1%

Source: Eucomed, Brussels, 2009
Research growth – Publications

Source: Thomson Reuters (Leeds); Global research report: China: Research and collaboration in the new geography of science; Nov. 2009 (adapted)

Note: During same period, USA publications increased from 265,000 to 340,000/year (~30%)

Note: Not all specific to medical technology
Research growth – Publications

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Source: Thomson Reuters (Leeds); Global research report: China: Research and collaboration in the new geography of science; Nov. 2009 (adapted)
Research growth – Publications

Note: Not all specific to medical technology

Source: Financial Times, 25 January 2010
Overview of GHTF and related medical device regulatory harmonization initiatives

China share of world publications – 2004-8

Most are in fields relevant to medical technology

Source: Thomson Reuters (Leeds); Global research report: China: Research and collaboration in the new geography of science; Nov. 2009 (adapted)
Shifting sources of medical technology

2005

USA, 45%
Europe, 33%
Japan, 11%
China, 2%
Brazil, 1%

2025

? Israel?
? Korea?
? Japan?
? China?
? Others?
? USA?
? Europe?
? Brazil?
? Malaysia?
? India?
GHTF goals

“The work of the GHTF has been guided by two overarching goals:

- First and foremost, enhancing medical device safety – thus improving public health – through information-sharing, general agreement on principles of pre-market, post-market, inspectional/regulatory enforcement activities and national import-export systems; …

Source: GHTF Steering Committee; Action Plan for 2007-2010: Path Forward for the Global Harmonization Task Force; April 2007 [emphasis as in original]
GHTF goals

“The work of the GHTF has been guided by two overarching goals: …

• Fostering medical technology innovation and facilitating global trade among major device-producing nations of the world by reducing or eliminating redundant or conflicting regulatory systems, without diminishing public health protections.”

Source: GHTF Steering Committee; Action Plan for 2007-2010: Path Forward for the Global Harmonization Task Force; April 2007 [emphasis as in original]
GHTF purpose

“…. to encourage convergence in regulatory practices related to ensuring the safety, effectiveness / performance, and quality of medical devices, promoting technological innovation and facilitating international trade . . . .

Source: GHTF Steering Committee; Lubeck, June 2006
GHTF purpose

“…. the primary way in which this is accomplished is via the publication and dissemination of harmonized guidance documents on basic regulatory practices. These documents …. Can then be adopted / implemented by member national regulatory authorities …”

Source: GHTF Steering Committee; Lubeck, June 2006
GHTF purpose

“…. GHTF also serves as an information exchange forum through which countries with medical device regulatory systems under development can benefit from the experience of those with existing systems and/or pattern their practices upon those of GHTF founding members”

Source: GHTF Steering Committee; Lubeck, June 2006
GHTF Strategic Direction – Goals (1)

Emerging regulatory challenges

- GHTF will encourage and support timely identification of opportunities to promote regulatory convergence in addressing regulatory challenges including those of emerging public health risks and new medical technologies
- GHTF will implement a process to identify these new risks and technologies in order to achieve regulatory convergence in their management

Source: GHTF Steering Committee; Lubeck, June 2006 [emphasis added]
GHTF Strategic Direction – Goals (2)

Implementing guidance documents

• GHTF will encourage the adoption of timely and clear guidance suitable for implementation in national/regional regulatory systems

Source: GHTF Steering Committee; Lubeck, June 2006 [emphasis added]
GHTF Strategic Direction – Goals (3)

Mutual acceptance by regulators

- GHTF will seek to evolve beyond convergence of regulatory requirements to embrace **mutual acceptance** of common data submissions, pre-market conformity assessment (including clinical evidence) processes, quality systems, quality systems auditing results, and a broad sharing of post-marketing experience.

- The objective will be to allow presentation of data that are acceptable in principle to relevant authorities as the basis for meeting regulatory requirements.

*Source:* GHTF Steering Committee; Lubeck, June 2006 [emphasis added]
GHTF Strategic Direction – Goals (4)

Evolving regulatory systems

• GHTF Steering Committee will support and advocate the adoption of the global regulatory model in their own systems and those of other countries/regions

Source: GHTF Steering Committee; Lubeck, June 2006 [emphasis added]
GHTF organization structure

Steering Committee

Study Group 1
Regulatory systems
Premarket assessment

Study Group 2
Vigilance reporting
Market surveillance

Study Group 3
Quality system requirements

Study Group 4
Quality systems auditing

Study Group 5
Clinical evidence
Overview of GHTF and related medical device regulatory harmonization initiatives

GHTF organization structure

- **Asian Harmonization Working Party**
- **Steering Committee**
- **Study Group 1**
  - Regulatory systems
  - Premarket assessment
- **Study Group 2**
  - Vigilance reporting
  - Market surveillance
- **Study Group 3**
  - Quality system requirements
- **Study Group 4**
  - Quality systems auditing
- **Study Group 5**
  - Clinical evidence
- **ISO TC/210**
- **ISO TC/194**
- **ISO, IEC**
- **WHO**
- **GMDN**
- **PAHO**
- **Latin American Harmonization Working Party**
- **ISO TC/194**
GHTF overview

GHTF proposed and final guidance documents publicly available free of charge via Internet

www.ghtf.org
GHTF guidance document topics

- Definition of “medical device”
- Principles of medical device classification
- Principles of conformity assessment
- Labeling
- Essential principles of safety and performance
- Role of standards in assessment
- Summary technical documentation (“STED”)
- Adverse event reporting (“medical device vigilance”)
- Post-marketing surveillance: content of field safety notices
- National competent authority report exchange programme (“NCAR”)
- Quality management system requirements
- Risk management
- Process validation
- Regulatory auditing strategy
- Clinical evidence and clinical evaluation
Adoption of GHTF harmonized guidance

GHTF guidance forms substantial basis for:

• Medical device provisions of Australia Therapeutic Goods Act
• Canada Medical Devices Regulations
• EU medical device directives and guidance
• Medical device provisions of Japan Pharmaceutical Affairs Law
• USA FDA medical device regulations (partial, e.g., QMS, STED, standards)
Adoption of GHTF harmonized guidance

GHTF guidance forms substantial basis for regulatory systems in:

• Singapore (2007)
• Malaysia medical device regulation bill (2011?)
• Kingdom of Saudi Arabia (2011) (Arab HP?)
• ASEAN medical device directive (2015)
• India draft Schedules M-III, M-IV (201X?)
• Pakistan (2011?)
• South Africa (201X?)
GHTF Vision

Enhancing the health of the public worldwide and facilitating innovation by harmonizing the global regulatory environment
Medical device regulatory harmonization forums

- GHTF
- PAHO
- LAHWP
- APEC
- AHWP
- ACCSQ MDWPG (ASEAN)

WHO
Questions?
Medical device regulatory harmonization forums

Asian Harmonization Working Party
- Began in 1998
- Voluntary forum
- Regulators and industry
- 22 members
- Chair: China; Vice-Chair: India
- Liaison with GHTF
- 5 working groups mirror GHTF study groups
- Developer of harmonized regional guidance documents based on GHTF
  - www.ahwp.info
AHWP member economies

- Abu Dhabi
- Brunei Darussalam
- Cambodia
- Chile
- Chinese Taipei
- Hong Kong SAR, China
- India
- Indonesia
- Jordan
- Kingdom of Saudi Arabia
- Korea
- Lao PDR
- Malaysia
- Myanmar
- Pakistan
- People’s Republic of China
- Philippines
- Singapore
- South Africa
- Thailand
- Vietnam
- Yemen
Overview of GHTF and related medical device regulatory harmonization initiatives

AHWP guidance

www.ahwp.info
AHWP Purpose

To study and recommend ways to harmonize medical device regulation in the Asian region with global trends and to work in coordination with the Global Harmonization Task Force and APEC

Source: AHWP Terms of Reference
**AHWP Purpose**

AHWP will strive to:

Examine the use of quality system requirements around the world and prospects for **adopting a quality system standard** based on internationally recognized and accepted quality system standard for medical devices

Work toward building a common regulatory consensus based on **acceptance of international standards** as the chief means of ensuring product safety and assurance

Move toward **recognition of a common audit** that can be accepted throughout the Asian region

Work toward a **harmonized system of medical device vigilance reporting** for adoption within the region and information sharing …..

Source: AHWP: Terms of Reference [emphasis added]
AHWP guidance

- Safety Alert Dissemination System (SADS)
- Draft Common Submission Document Template (CSDT)
- Other guidance under development
Overview of GHTF and related medical device regulatory harmonization initiatives

- Established 1989
- 21 Member Economies
- 40.5% of world population
- 54.2% of world GDP
- 43.7% of world trade

Source: APEC Secretariat
APEC Life Sciences Innovation Forum

• In 2002, APEC Leaders endorsed proposal to establish LSIF

• Reflected belief that life sciences innovation is important in promoting public health and economic development

• Annual forum to promote policy discussions and projects aimed at advancing life sciences innovation

• From outset, harmonization seen as prerequisite to promoting life sciences innovation
Medical device regulatory harmonization forums

Asia-Pacific Economic Cooperation
Life Sciences Innovation Forum

- Began in 2002
- Mandate from APEC Leaders
- 21 member economies
- Government, industry, academia
  - [http://www.apec.org/apec/apec_groups/other_apec_groups/life_sciences.html](http://www.apec.org/apec/apec_groups/other_apec_groups/life_sciences.html)

- USA host for APEC in 2011; then Russian Federation
APEC Life Sciences Innovation Forum

• Since 2000, APEC-funded regional medical device regulatory training and capacity-building workshops
  • Singapore, Bangkok, Santiago, Kuala Lumpur, Toronto
  • Often in conjunction with AHWP meetings
  • 2009-10 included visits to Health Canada and US FDA CDRH

• In 2010, APEC Leaders endorsed goal of medical device regulatory harmonization by 2020
APEC Life Sciences Innovation Forum

- 2008 proposal from Korea to establish APEC Harmonization Center
- Approved 2008
- APEC Harmonization Center established in 2009 in Seoul
  - http://www.apec-ahc.org/
- First workshop held June 2009
- Regulatory Harmonization Steering Committee and Advisory Board established and held first meeting March 2010 (medicines and medical devices)
Association of Southeast Asian Nations (ASEAN)

- ~592 mio. Population
- US$1.5bio GDP 2009

Source: ASEAN Secretariat
Medical device regulatory harmonization forums

Association of Southeast Asian Nations Medical Device Product Working Group

ASEAN

- Formed August 1967
  - 5 founders
  - Now 10 Member States

- ASEAN Community agreed 2003
  - ‘Single market and production base, highly competitive and fully integrated into global community by 2015’

- Three pillars
  - Political-Security Community
  - Economic Community
  - Socio-cultural Community
ASEAN economic integration

- Economic integration goals include
  - Elimination of tariffs, free movement of professionals, freer movement of capital, and streamlined customs clearance procedure
  - Elimination of non-tariff barriers to trade through harmonization of standards, technical regulations and conformity assessment procedures
Overview of GHTF and related medical device regulatory harmonization initiatives

**ASEAN harmonizing standards and regulations**

- **ASEAN Economic Minister Meeting**
- **ASEAN Senior Economic Official Meeting (SEOM)**
- **ASEAN Consultative Committee on Standards and Quality (ACCSQ)**

- **WG 1** Working Group on Standards and Mutual Recognition Arrangements (MRAS)
- **WG 2** Working Group on Accreditation and Conformity Assessment
- **WG 3** Working Group on Legal Metrology
- **JSC EE MRA** Joint Sectoral Committee for ASEAN Sectoral MRA for Electrical and Electronic Equipment
- **ACC** ASEAN Cosmetic Committee
- **PPWG** Pharmaceutical Product Working Group
- **PFPWG** Prepared Foodstuff Product Working Group
- **APWG** Automotive Product Working Group
- **TMHSPWG** Traditional Medicines and Health Supplements Product Working Group

**WG 1**
- **WG 2**
- **WG 3**
- **JSC EE MRA**
- **ACC**
- **PPWG**
- **PFPWG**
- **APWG**
- **TMHSPWG**

9 of these sectors account for 50% of ASEAN trade
ASEAN Medical Device Product WG

• Chair: Malaysia; Co-Chair: Singapore

• Government and industry from 10 Member States

• Scope of activities
  • Develop common submission dossier template (CSDT) for product approval in ASEAN
  • Explore feasibility of abridged approval process for devices which regulators of benchmarked countries or recognized regulators have approved
ASEAN Medical Device Product WG

• Scope of activities (cont’d)
  • Explore feasibility of adopting harmonized system of placement of devices into ASEAN markets, based on a common product approval process
  • Formalize post-marketing alert system for defective or unsafe medical devices
  • All ASEAN countries to consider joining AHWP and work in parallel with GHTF on technical harmonization efforts
ASEAN Medical Device Product WG

- Timeline
  - 2008-09: Implement ASEAN CSDT
  - 2013: Adopt ASEAN medical device directive
  - Dec. 31, 2014: Transposition into laws of Member States completed
  - Jan. 1, 2015: Entry into force across ASEAN

- Probability unknown

- Different Member States moving at different paces, with different priorities and resources
Pan American Health Organization

• “Resolves: …

• 2. To support the proposal for form an ad hoc group to promote and facilitate the medical devices harmonization processes in the Americas

• 3. To urge the Member States to:
  (a) develop and strengthen their programs for the regulation of medical devices;
  (b) promote and support the participation of their regulatory authorities the general meetings of the [GHTF] and those of its four study groups, while promoting the use of GHTF documents for the regulation of medical devices …”

World Health Organization guidance

“With the exception of commercial activities including advertising and sales, …, the GHTF Study Groups are involved in all aspects that have direct impact on the safety and performance of medical devices.

Therefore, recommendations from the GHTF [study groups] can provide excellent reference or guidance for countries that are establishing medical device regulation programmes.”

Source: Medical device regulations: Global overview and guiding principles; World Health Organization, Geneva; 2003
Medical device regulatory harmonization forums

- GHTF
- PAHO
- LAHWP
- APEC Funded Training Seminars
- AHWP
- ACCSQ MDWPG (ASEAN)
- APEC LSIF

Related forums:
- PAHO
- LAHWP
- APEC
- LSIF
- WHO

Overview of GHTF and related medical device regulatory harmonization initiatives
Questions?
What is the GHTF regulatory model?

- Compilation of voluntary guidance documents developed by GHTF
- Increasingly cover *in vitro* diagnostic medical devices
- Consensus view of good practices based on experience of regulators and industry
- Covers medical technology life cycle
  - Complementary pre- and post-marketing regulatory controls
Medical device product life cycle

Source: Feigal, D.W.; US Food and Drug Administration; Center for Devices and Radiological Health; CDRH Science Review: Center Perspectives; 1999
4-Mar-11
## Representative roles and responsibilities

<table>
<thead>
<tr>
<th>General</th>
<th>SG-1 Pre-market</th>
<th>SG-2 Post-market</th>
<th>SG-3 QMS</th>
<th>SG-4 QMS Audit</th>
<th>SG-5 Clinical Safety</th>
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<tbody>
<tr>
<td>National Competent Authority (NCA)</td>
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<td>Conformity Assessment Body (CAB)</td>
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<tbody>
<tr>
<td>(Not covered in GHTF guidance)</td>
<td>* Determine whether product is “medical device”</td>
<td>* Establish and maintain PMS system (part of QMS)</td>
<td>* Establish and maintain appropriate and effective QMS, including risk management</td>
<td>* Subject of periodic audits</td>
<td>* Conduct clinical evaluation (ongoing)</td>
</tr>
<tr>
<td><strong>Manufacturer</strong></td>
<td><strong>SG-1/N29</strong> national requirements</td>
<td><strong>SG-1/N065</strong></td>
<td><strong>SG-1/N41</strong></td>
<td><strong>SG1/N012, Clause 5.0; SG1/N40, etc</strong></td>
<td><strong>SG-1/N29</strong></td>
</tr>
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<td></td>
<td>Register, list</td>
<td>Investigate and evaluate complaints and product experience information (QMS CAPA)</td>
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<td>Prepare and submit vigilance reports</td>
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<td></td>
<td>Determine appropriate Essential Principles</td>
<td>Prepare, hold, and maintain technical file</td>
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<td>As appropriate safety and corrective actions</td>
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<td>Apply appropriate standards</td>
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**Notes:** Not exhaustive. * Requirements and roles vary depending on class of device(s).
What is missing?

• How to manage changes in design, manufacture, and quality management systems? (life cycle)
• How best to control products that cross traditional regulatory borderlines?
• Refurbishment and re-manufacturing?
• Alternative forms of labelling?
• Good distribution practices?
• Electronic submissions?
• Networked medical devices?
• ??
Adoption of GHTF harmonized guidance

GHTF guidance forms substantial basis for:

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- Pakistan (2011?)
- South Africa (201X?)
GHTF regulatory model

• When implemented in framework of national policies and legislation, GHTF guidance documents provide basis for comprehensive regulatory control of medical devices

• Based on risk management throughout product life cycle

• Regulator, conformity assessment body, and manufacturer have specific roles and responsibilities

• When supported by adequate resources, establishes effective and efficient controls proportionate to risks and benefits
GHTF regulatory model

- Controls are inter-connected and mutually dependent
- Accommodate diversity of medical device field
- Intended to accommodate emerging technologies and advances in state of the art
- To the extent regulatory systems converge, fosters mutual confidence and facilitates international trade
Questions?