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# **CLINICAL DATA REQUIREMENTS**

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AHC-AHWP Joint Workshop  
Seoul, Republic of Korea, November 18, 2014

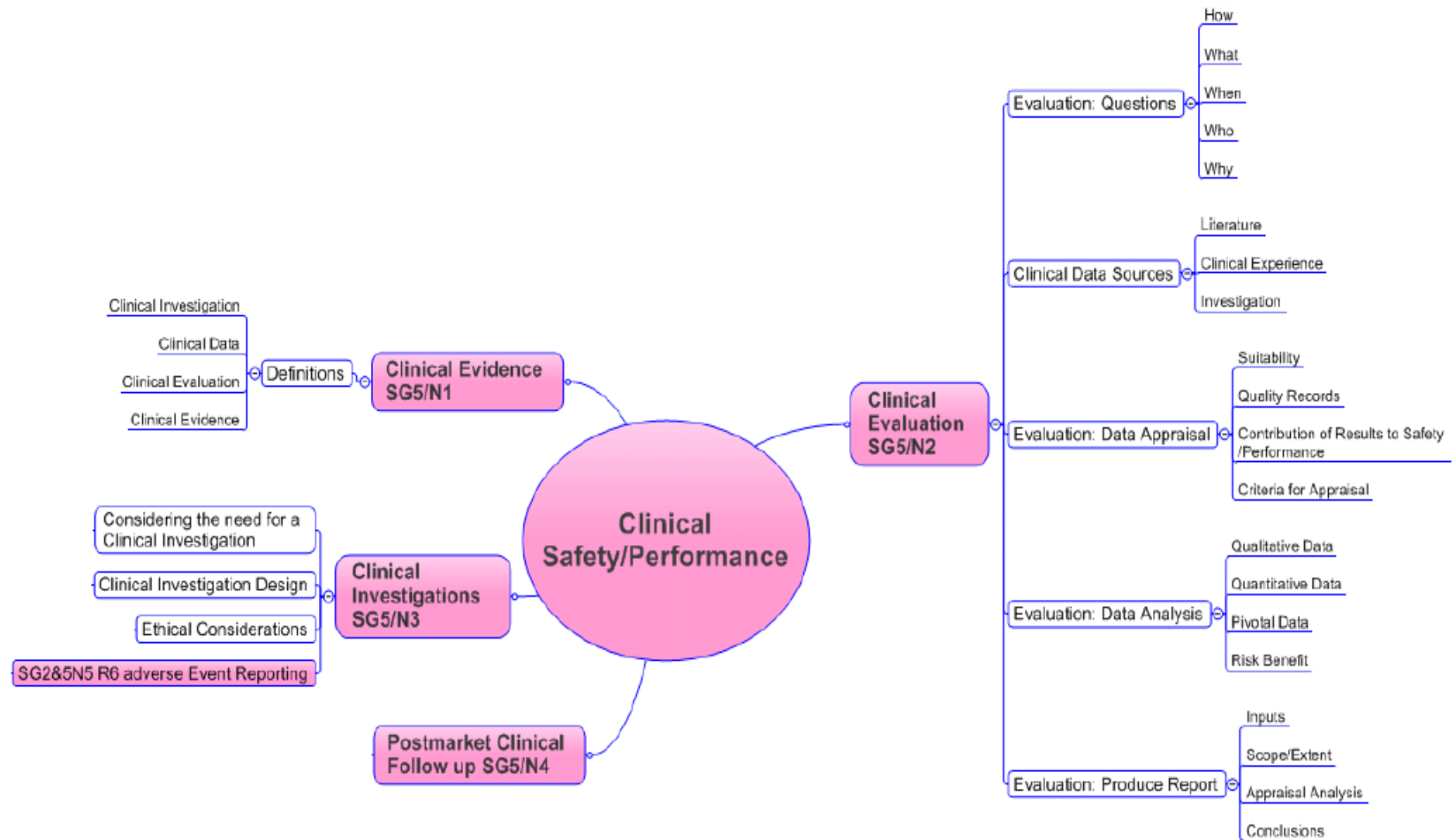
# ACKNOWLEDGEMENTS AND DISCLAIMERS

- Acknowledgements
  - Catherine Vitols, Medtronic Corporate Regulatory Affairs
  - Amra Racic, Medtronic Corporate Regulatory Affairs
  - Kyung-Ja Lee, Medtronic Republic of Korea Regulatory Affairs
  - AdvaMed PMA Working Group
  - Staff of US FDA Center for Devices and Radiological Health
    - Center for Devices and Radiological Health 2014-2015 Strategic Priorities
- Disclaimer
  - Errors are attributable to the author
  - All opinions are those of the author

# TOPICS

- Background and scope
  - United States of America
  - European Union
  - Japan
- Requirements
- Trends
- Accelerating access to medical technology

# GHTF Clinical Safety/Performance model



# **GHTF CRUCIAL STEPS IN CLARIFYING THE NEED FOR CLINICAL INVESTIGATIONS?**

- **Essential Principles**
  - Safety
  - Clinical performance
- **Clinical Evaluations**
  - Literature search sufficiency
  - Clinical experience
- **Risk Management (ISO 14971)**

# GHTF CLINICAL INVESTIGATIONS

GHTF/SG5/N3:2010

- **When should a clinical investigation be undertaken?**
  - Clinical investigations are necessary to provide the **data not available through other sources** (such as literature or preclinical testing) **required to demonstrate compliance with the relevant Essential Principles**
  - For **long established technologies**, clinical investigation data that might be required for novel technologies **may not be necessary**. The available clinical data in the form of, for example, **published literature, reports of clinical experience, post-market reports and adverse event data may, in principle, be adequate to establish the safety and performance of the device**, provided that new risks have not been identified, and that the intended use(s)/purpose(s) has/have not changed.

# GHTF ETHICAL CONSIDERATIONS

- As a general principle, “the rights, safety and wellbeing of clinical investigation subjects shall be protected consistent with the ethical principles laid down in the **Declaration of Helsinki**” (ISO 14155).
- It is ethically important in deciding to conduct a clinical investigation that it should **generate new data** and answer specific safety and/or **performance questions that remain unanswered** by the current body of knowledge.
- The desire to protect human subjects from unnecessary or inappropriate experimentation must be balanced with the need to protect public health through the use of clinical investigations where they are indicated.



# DECLARATION OF HELSINKI

- Ethical Principles for Medical Research involving human subjects, regarded as the cornerstone document on human research ethics
- The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.
- **Link:** <http://www.wma.net/en/30publications/10policies/b3/>





# EVOLVEMENT OF ETHICAL CONSIDERATIONS

Timeline of influential codes of ethics and regulations that guide ethical clinical research of today.

**1947**

**Nuremberg Code**

*Set of research ethics principles for human experimentation set*

**1979**

**Belmont Report**

*Ethical Principles and Guidelines for the Protection of Human Subjects of Research*

**1991**

**U.S. Common Rule**

*Rule of ethics regarding biomedical and behavioral research involving human subjects in the United States*

**2000**

**Declaration of Helsinki**

*Ethical Principles for Medical Research involving human subjects*

**2001**

**Acceptance of Foreign Clinical Studies**

*Industry Guidance*

**2002**

**CIOMS**

*Council for International Organizations of Medical Sciences*

# US DEVICE APPROVAL PROCESS



- Product requiring PMAs are high risk Class III devices that potentially pose a significant risk of illness or injury, or devices found not substantially equivalent to Class I and II predicate through the 510(k) process.
  - The PMA process is more involved and typically includes the submission of clinical data to support claims made for the device.
    - Device iterations may or may not require clinical data through the PMA Supplement process.
  - Some premarket notification (510(k)) submissions also require clinical study data.
- An IDE approval process allows an investigational device that otherwise would have to comply with requirements for commercial distribution to be lawfully shipped for use in a clinical trial in order to collect safety and effectiveness data.
- All clinical studies of investigational devices, unless exempt, must have an approved IDE before the study is initiated.
- Clinical studies can also include clinical evaluation of certain design modifications to, or new intended uses for, legally marketed devices.



**U.S. Food and Drug Administration**  
Protecting and Promoting *Your* Health

# EUROPEAN UNION REQUIREMENTS

- Conformity Assessment
  - Essential Requirements
  - Risk-based, four classifications
- Directives
  - Medical Devices
  - Active Implantable Medical Devices
- Must attain performance characteristics based upon clinical data
  - Scientific literature
  - Clinical investigations to date
- Clinical Investigation
  - EN 540—broad guidelines
  - EN ISO 14155-1, EN ISO 14155-2—precise conditions and requirements
  - EC Declaration of conformity

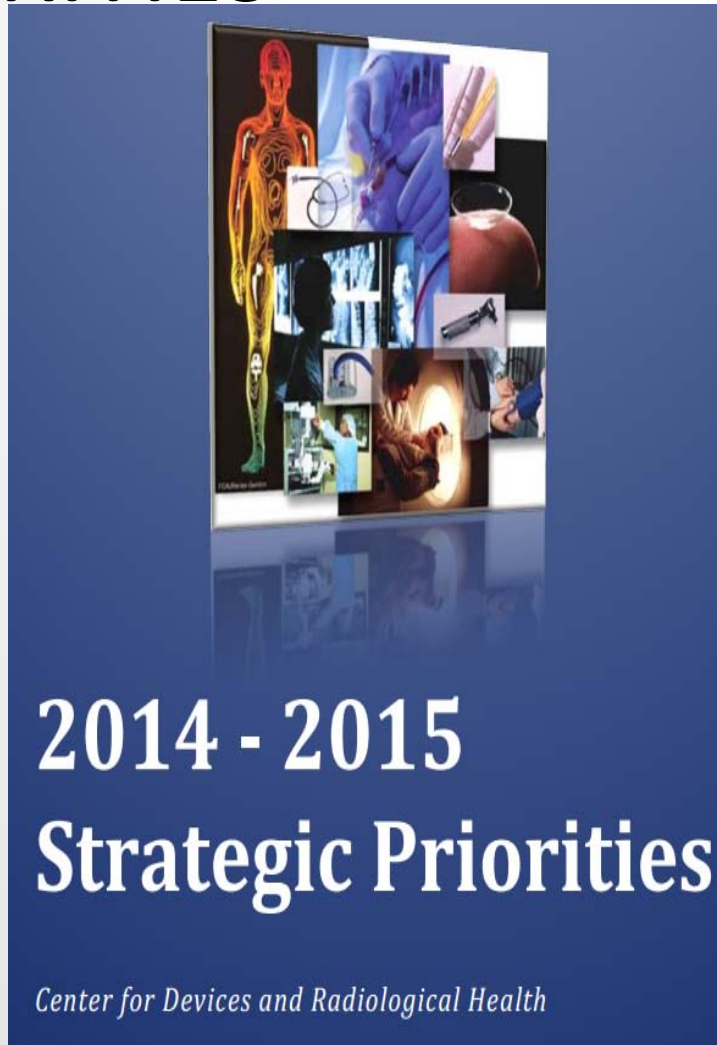
# JAPAN REQUIREMENTS

- Pharmaceutical and Medical Devices Law
  - Previously Pharmaceutical Affairs Law
- Risk-based, four class system
- Premarket Approval—Shonin

# TRENDS

- Innovation
- Smart regulation
- Mutual acceptance of clinical data

# CDRH 2014 - 2015 STRATEGIC PRIORITIES



# SMART REGULATION

- Attain the goal of protecting the public health while encouraging innovation
  - Smart, sound, science-based regulation
  - Imposes appropriate regulatory framework
  - Minimizes unnecessary burden
- Regulation done correctly can
  - Provide pathway toward meaningful innovation
  - Instill consumer confidence
  - Level the playing field for business
  - Decrease litigation (time and money in court)
  - Prevent recalls

# MISSION AND VISION

- Reset direction toward “smart regulation”.
  - Protecting public health by assuring that devices that enter and remain on the U.S. market are safe and effective
  - Promoting public health by facilitating device innovation
- Mission
  - Protect and promote public health
  - Timely and continued access to safe, effective, high-quality devices
  - Provide accessible science-based information
  - Facilitate innovation



# STRENGTHEN THE CLINICAL TRIAL ENTERPRISE

- Facilitate patient access to medical technology by streamlining the clinical trial enterprise
  - Device trials are initiated and conducted in the United States
    - Efficient and cost-effective manner
    - Maintaining appropriate patient protections
- Encourage medical device innovation particularly when alternate treatments are
  - Unavailable
  - Ineffective
  - Associated with high risk to patients

# MUTUAL ACCEPTANCE OF CLINICAL DATA

- **Canada**

- “Clinical evidence of effectiveness may comprise device-related investigations conducted in Canada or other countries. It may be derived from relevant publications in the peer-reviewed scientific literature. The documented evidence submitted should include the objectives, methodology and results presented in context, clearly and meaningfully. The conclusions on the outcome of the clinical studies should be preceded by a discussion in context with the published literature.”



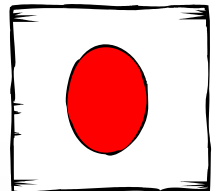
- **Europe**

- “Where the clinical investigation(s) was performed outside the EU, the manufacturer must demonstrate that the use of the device (including clinical practice and techniques) and patient population are equivalent to those for which the device will be used within the EU (if relevant).”



- **Japan**

- “MHLW/PMDA have accepted foreign clinical data for years if it is good enough to evaluate device’s clinical safety and efficacy on Japanese population under Japanese medical practice/environment.”
- “Clinical study results attached to applications for regulatory approval must be for clinical trials performed in countries or regions where the laws and regulations for clinical studies and standards for medical device studies must be at least as strict as the Japanese medical device GCP, or for clinical studies performed according to those standards or believed to have been performed according to those standards.”



# FDA CLINICAL DATA REQUIREMENTS

- In order to market class III high-risk (and some class II) medical device in the United States, companies need to demonstrate that the device is reasonably safe and effective.
- FDA will accept studies which have been conducted outside the U.S if the data constitute valid scientific evidence and the investigator has conducted the studies in conformance with the "**Declaration of Helsinki**" or the laws and regulations of the country in which the research was conducted, whichever offers greater protection to the human subjects.



# FDA ACCEPTANCE OF FOREIGN CLINICAL STUDIES

- Food and Drug Administration (FDA) regulations permit the acceptance of foreign clinical studies in support of an application for marketing approval of a human drug, biological product, or device if certain conditions are met.
  - Foreign studies performed under an investigational new drug application (IND) or investigational device exemption (IDE) must meet the same requirements of 21 CFR Part 312 or 21 CFR Part 812, respectively, that apply to U.S. studies conducted under an IND or IDE.
- A PMA based solely on foreign clinical data and otherwise meeting the criteria for approval under this part may be approved if:
  - the foreign data are applicable to the U.S. population and medical practice;
  - the studies have been performed by clinical investigators of recognized competence; and
  - the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA can validate the data through an on-site inspection or other appropriate means.
- Link: <http://www.fda.gov/regulatoryinformation/guidances/ucm124932.htm>

CAROTID

CODING

DIALYSIS

EMBOLIZATION

EVAR

LIMB SALVAGE

NEUROINTERVENTION

RENAL

SFA

THORACIC

VENOUS

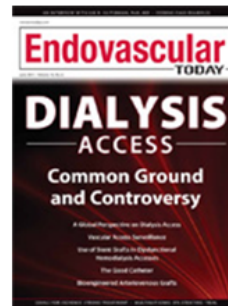
June 2011

## The Harmonization By Doing Initiative and the OSPREY Trial

An update on the evaluation of the Misago stent as part of the Harmonization By Doing regulatory collaboration between the United States and Japan.  
*By Srinivas Iyengar, MD, FACC*

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# HARMONIZATION BY DOING

- Pilot program between US FDA and Japan PMDA
  - Regulatory authorities
  - Medical community/Academic researchers
  - Sponsors
- Goal: one clinical study to satisfy requirements for two regulatory authorities
- Developed standards for global clinical trials for cardiovascular devices
- Continues in conjunction with IMDRF
  - Summit Washington, D.C., 19 September 2014

# CONCLUSION: PATIENTS FIRST

- US FDA
  - US patients will be first in the world to have access to new medical technologies
- Japan PMDA
  - Japanese patients will be first in the world to have access to new medical technologies
- Opportunities for all stakeholders to develop criteria to ensure that clinical data are applied appropriately to accelerate access to new medical technologies

# THANK YOU!

감사합니다 Natick  
 Danke Ευχαριστίες Dalu  
 Grazie Thank You Köszönöm  
 Obrigado  
 Tack  
 Спасибо Dank Gracias  
 谢谢 Merci See  
 ありがとう