

# Global and Regulatory Environment in Medical Device Industry



ASQ Austin, November 11, 2009

Evangeline D. Loh, Ph.D., RAC (US,EU), Vice President Regulatory Affairs

[Evangeline@emergogroup.com](mailto:Evangeline@emergogroup.com)

## Overview of medical device requirements :



USA



Canada



Mexico



Japan



China



Brazil



Australia



Russia

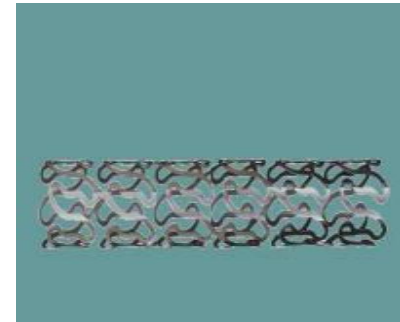


Europe

Emphasis on US and Europe markets, and also discuss:

- Quality system requirements: ISO 13485 versus ISO 9001 and FDA GMP
- Additional regulatory requirements

# What is a Medical Device?





## Compliance Requirements - USA

- Food and Drug Administration (FDA) regulatory agency
- FDA has authority for medical devices, IVDs, biologics, and drugs manufactured and sold in the U.S.
- Center for Devices and Radiological Health (CDRH) is division within FDA that oversees medical devices
- Products divided into three classes: Class 1, 2 and 3, classification determined identifying specific product code
- Must implement quality system and register device

# A Quality Management System must be established for the **USA**



- Most companies must comply with 21 CFR Part 820 “Quality System Regulations”
- These are also known as cGMP (current Good Manufacturing Practices) or simply GMP
- Implement quality system, conduct training, maintain records
- Ongoing compliance is **mandatory** to market devices in the USA
- There is no certification program as with ISO - FDA conducts **periodic** inspections of increasing frequency depending on classification of products
- Medical companies fail because of non-understanding and implementation of quality systems

## Quality System Elements: USA



- Management responsibility defined
- Document control for the organization – paperwork !
- Maintenance of Quality Records for objective evidence
- Design controls depending on the class of device
- Production and process controls are implemented
- Packaging and labeling control – sterilization
- Complaint management by the organization
- Corrective Action and Preventive Action (CAPA) feedback



## FDA Mandates Compliance in the US

- Manufacturers outside US must appoint a **U.S. Agent**
- Regulatory pathways in U.S. are complex
- Compliance is managed via different methods:
  - Device submissions for sale in U.S.
  - Inspections conducted of manufacturing facilities
  - Issuance of Form 483 and Warning Letters for non-compliance
  - Adverse event reporting system

# How Do I Register Products in the USA?



- FDA 510(k) Clearance process
  - Applies to some Class I devices, sterile or measuring instruments
  - Most Class II devices and very small number of Class III devices
  - Predicate device must be identified
  - FDA has 90 days to review your application
  - Certain devices are 510(k) exempt, especially Class I products
  - Approval process generally takes 4-8 months.
- FDA Pre-Market Approval (PMA) process
  - Class III devices
  - New devices with new technology or no predicate
  - Approval process takes 1 year or more due to clinical requirement

NOTE: FDA 513(g) process allows classification of a device. Often needed for new technology.

# Determining Device Classification for devices sold in the **USA**



- Each device has a three letter product code
- New combination devices with drugs or drug substances
- New technologies and applications of devices
- May include a device in a current product category
- FDA has the ultimate responsibility for device classification and how you must submit
- Process is explained step by step at:
  - <http://www.fda510k.com/approval-process/>

# Compliance Requirements for Europe



- The European Commission has published **Directives** that are transposed into national law by each country
- Implement a quality system. Most use ISO 13485
- Must create and maintain a device Technical File
- A Notified Body in Europe will be involved to review your QMS and Technical File (except Class 1 self-certified)
- 27 countries in EU plus Switzerland, Liechtenstein, Norway and Iceland – 31 total in Europe, each has own Competent Authority
- CE Marking is ultimate goal!



# Quality Management System must be Established for **Europe**



- ISO 13485:2003 quality management system preferred method of compliance with Directive
- Similar to the US FDA Quality System Regulation
- ISO 13485 is certified by a third party: **Registrar**
- Implementation and maintenance of the quality system is done by the organization
- Certification is renewed on an annual basis
- ISO 13485 standard becoming **widely** recognized internationally: EU, Canada, Australia, China, Japan, etc.



# How Devices are Classified in Europe

- First select the directive that is applicable to device
  - Medical Devices Directive (MDD 93/42/EEC)
  - In Vitro Diagnostic Medical Devices Directive (IVDD)
  - Active Implantable Medical Devices Directive (AIMDD)
- Class I non-measuring or non-sterile – drapes, wheelchairs
- Class I measuring or sterile – blood glucose monitors, band-aids
- Class IIa – invasive catheters, stimulation devices
- Class IIb – blood bags, contraceptive devices
- Class III – implantable devices, pacemakers
- Rules are defined in the directives for classification

## How Do I Register Devices in Europe?



- Select a Conformity Assessment route – how the Notified Body will inspect your product
- Prepare a **Technical File** or Design Dossier
- Appoint an Authorized Representation (**EC REP**) within the EU
- Class I products (non-sterile, non-measuring) do not require Notified Body intervention

# CE Mark / Technical File Process for Europe



- Essential Requirements of device
- Risk management and risk analysis of device
- Labeling and language requirements
- Technical File is approved by the Notified Body
- Design Dossier is required for Class III devices – includes the design control information

# Contents of the Technical File for **Europe**



- Created for product family or product group
- Device description: mechanical, electrical, biological
- Classification decision for device
- Critical suppliers of components
- Manufacturing process and testing aspects
- Risk analysis for the device
- **Clinical evaluation** (will be very important for all devices starting March 21, 2010)
- Packaging and labeling of device, instructions

## Compliance Requirements for **Japan**



- Organizations must have Quality Management System certified to ISO 13485: 2003
- Pharmaceutical Affairs Law (PAL) and MHLW Ordinance No. 169 compliance for the quality system/submission
- Marketing Authorization Holder (MAH) in Japan
- Creation of the Summary Technical Documentation (STED) by product family

# How Do I Register Medical Devices in **Japan**?



- Classification of the device:
  - Class I - General medical devices
  - Class II - Controlled medical devices
  - Class III - Specially controlled medical devices
  - Class IV - High risk / high control medical devices
- Identify and appoint a Market Authorization Holder (MAH) in Japan. Best to select a **D**-MAH (not a distributor) to maintain complete control over device registration
- Submit application for foreign manufacturer – may require a JPAL inspection
- Submit Pre-Market Submission in the STED format

# Japanese Device Submission Process



- The documents must be in Japanese (translated)
- **S**ummary **T**echnical **D**ocumentation (STED) created
- Must provide the Seihin Hyojun Sho or the Device Master Record – how the product is made
- Once approved this is called a Shonin or when you receive certificates is called a Ninsho
- Long process, be patient...

# Compliance Requirements for China



- State Food & Drug Administration (SFDA) medical device approval through the government
- Provide evidence of compliance with ISO 13485 or FDA QSR
- Must complete a submission to SFDA for approval
- Only low risk Class I devices may apply for Import Medical Device Certificate
- Legal Agent/After Sales Agent representation required within mainland China. Hire independent LA/ASA to maintain control over device approvals

# How Do I Register a Device in **China**?



- Classification of the medical device from a schedule:
  - Class I - Low risk medical devices
  - Class II - Moderate risk medical devices
  - Class III - High risk medical devices
- CCC Mark certification required for electrical devices
- Prepare Chinese Registration Standard document – must be translated into Chinese
- Submit for approval and receive a five (5) year certificate

# Compliance Requirements for **Canada**



- Organization **must** have an ISO 13485:2003 quality system certificate (part of license)
- Additional requirements are imposed by the Canadian Medical Device Regulations (CMDR)
- Certification is provided by a CMDCAS certified **Registrar** (may be same as European Registrar– not always)
- Must apply for licenses, discussed next

## How Do I Register a Device in **Canada**?



- Medical Device License (MDL) required for Class II, III, and IV devices – renewed annually
- Class I devices require a Medical Device Establishment License (MDEL) only
- Classification of the medical device:
  - Class I - Lower risk devices that do not require license
  - Class II - Measuring devices, invasive devices
  - Class III - Moderate risk devices, special controlled devices
  - Class IV - Implants, biologics, active medical devices
- Submit Medical Device License (MDL) to Health Canada
- Approval process similar to FDA

# Compliance Requirements for **Australia**



- Implement a quality management system
- Australian Sponsor required in Australia
- Complete Summary Technical Document (STED)
- Therapeutic Goods Administration (TGA)
- All devices must be listed in the Australian Register of Therapeutic Goods (ARTG)

## How Do I Register a Device in **Australia**?



- Classify the device – similar to the European Union with Class I, Class IIa, Class IIb, and Class III
- Vast **majority of companies achieve CE Marking first** since CE is recognized in Australia – much easier
- If no CE, prepare and submit a Summary Technical Document (STED) or Technical File – similar to Europe
- Appoint a regulatory representative called a “Sponsor” within Australia
- Sponsor submits the Technical File and Medical Device Application for approval to the TGA

## How Do I Register a Device in **Mexico**?



- Medical device registration with COFEPRIS, the Mexican Ministry of Health
- There is no requirement for quality system, but expected compliance to FDA Quality Regulations
- The device approval consists of material similar to a 510(k) or a Technical File
- Best to work with an independent company to register company (instead of a distributor) and act at your “Registration Holder” within the country
- Lengthy process; device must be approved in home country



## How Do I Register a Device in **Brazil**?

- Devices regulated by ANVISA
- There is no consistent regulatory approval process for other countries in South America
- GMP compliant and FDA 510(k) often accepted
- In all instances, applications must be translated



## How Do I Register a Device in **Russia**?

- Devices regulated by Roszdravnadzor
- Devices classified much like Europe: I, II, III, IV
- Testing required for all products within Russia, regardless of whether product has already met international standards
- All products need Registration and GOST-R Certificates
- Some require Hygienic Testing
- Very difficult and cumbersome process
- MUST have local consultant in Moscow to register products – in person meetings are the norm!

# How Do I Register a Medical Device in the Rest of the World?

- Each country will have their specific requirements or regulations for device approval
- Some countries do not have any requirements
- Other countries use the approval process from United States or European Union
- Must provide information in the Technical File or Device Master Record
- If you have a Technical File, generally have what is needed for submission

## Compliance is Essential in the Global Environment to Ensure Success

- Understand the regulatory environment within each country or region
- Utilize regulatory consultants to navigate properly
- Without the knowledge or expertise approval can take significantly longer
- Global harmonization of submission is still being applied
- Assure design aspects are complete for submission

# What is the Difference Between **ISO 13485** and **ISO 9001** in the Global Market?

- ISO 9001 is intended for all industries and focuses more on process improvement and customer satisfaction
- ISO 13485 is specific to the medical device industry and focuses almost solely on regulatory compliance
- ISO 13485 is based from ISO 9001 with additions:
  - Cleanliness claims of the device and sterilization
  - Active implantable and implantable device requirements
  - Risk Management is required for the devices / processes
  - Post Market Surveillance activities
- Some organizations may have to certify to both

# What is the Difference Between **ISO 13485** and **FDA Quality System Regulation**? Not much!

- Organizations must be compliant to both – marketing areas, i.e. European Union, Canada, Japan
- ISO not recognized in US, and QSR not recognized in EU, Canada or Japan. China recognizes both.
- There are slight differences between them:
  - Packaging and labeling requirements
  - Complaint management and adverse event reporting
  - Inspection activities and acceptance status of product
  - Post Market Surveillance activities
- Compliance with one is 95% of the other
- One is “**free**” the other you have to pay for (audits)

Download the **regulatory process** charts found in your handout for:



USA



Canada



Mexico



Japan



China



Brazil



Australia



Russia



Europe

[www.EmergoGroup.com/literature](http://www.EmergoGroup.com/literature)

Thank you for your time.