The changing global regulatory environment
USA & EU: brief update
Asia: Selected regulatory update
Global: AHWP, GHTF, IMDRF, WHO

Medical Devices: staying ahead of regulatory developments
Gert Bos – BSI Israel – 22 April - Herzliya
AHWP – organisation refreshment

- Association of Authorities legalised: AHWP ALS
- New leadership
  - Chair: Kingdom of Saudi Arabia
  - Co-chair: Chinese Taipei (REG) & Lindsay Tao (IND)
  - Technical Cie: Singapore, Saudi & Ming Tanakasems sub (IND)
    - WG1 pre-market / CSDT - Singapore & Singapore
    - WG2 PMS / Vigilance - Hong Kong & Hong Kong
    - WG3 QMS - Saudi & India
    - WG4 QMS auditing - Saudi & South Korea
    - WG5 Clinical - Singapore & India
    - WG6 Training - Singapore & Hong Kong
    - Nomenclature - China & China
- New member: Kuwait
AHWP and GHTF / IMDRF

- AHWP Workgroups are endorsing and improving GHTF guidance – step by step
- GHTF last chair was Japan; closed after last conference Nov 2012 Tokyo
- IMDRF (GHTF5 + Brazil + China + WHO) considers liaising with AHWP
- AHWP members considering options

- AHWP much more drive to build on GHTF model
- IMDRF coming back to stakeholder involvement in workgroups but not in management
IMDRF – progress in fast track work items

• NCAR system/PMS report improvement
  • EU – Isabelle Demade

• Roadmap for implementation of the UDI
  • EU – Laurent Selles

• Simple audit program – MD accreditation system
  • USA – Kim Trautman

• Harmonized standards
  • EU – Matthias Neumann

• Regulated product submission
  • Canada – Mike Ward
ASEAN – following EU

- 601 M inhabitants
- ASEAN Economic Community in 2020
- ASEAN Free Trade Association in 2015
- First integration 11 fields => healthcare
- Medical device legislation harmonised in 2014

- In place: CSDT, ISO 13485, ASEAN PMS, ASEAN alert
- Target: ASEAN joint alert system just completed
- Target: ASEAN MDD = AMDD:2014
Growing involvement WHO

- WHO member of IMDRF
- WHO partner of AHWP
- WHO issued report series ‘priority medical devices’
- WHO organised debate on cross-learning pharma and devices

- Main driver: emerging economies depend heavily on import and should strive to reach high standards
US Political Environment

- Pressure on FDA – new staff / retirement of staff
- Regulatory pendulum was swinging towards stronger more prescriptive environment, but, new pressures pushing back on FDA
- More push to get innovative products into USA, competition with Europe has started
US v EU Comparison

- MDMA Report – On FDA impact on innovation and comparing manufacture satisfaction with FDA to Notified Bodies
- PWC Report – Innovation scorecard
- BCG Report – US v EU device safety

- FDA under political pressure, so.....
- FDA leaked a report on unsafe EU devices to defend themselves.......
- And ......
Executive Order – FDA Rules

- All FDA rules being revisited
- Feedback on:
  - Over-burdensome
  - Ineffective
  - Outmoded
  - Insufficient
- Impediment on innovation
  - Suggestions for improvement

CDRH challenges

- **Device Performance - Not Just The Device**
  - Characteristics of the device
  - Skill of physician
  - Patient compliance
  - Device vs. Procedure
CDRH Innovation Initiative

- Facilitate the development and regulatory evaluation of innovative medical devices
- Strengthen the U.S. research infrastructure and promote high-quality regulatory science
- Prepare for and respond to transformative innovative technologies and scientific breakthroughs

- 2 out of 32 volunteering projects chosen to lead as example projects
510(k): What FDA Has Heard

Industry Concerns
The 510(k) program had become less predictable, consistent and transparent thereby stifling innovation and sending companies and jobs overseas
CDRH reviewers had become less responsive and more risk averse

Consumer, Physician and Third-Party Payer Concerns
For some devices, the 510(k) program did not provide adequate assurances of safety and effectiveness nor did it provide sufficient information for healthcare providers and patients to make well-informed treatment or diagnostic decisions

CDRH Employee Concerns
The current 510(k) program failed to adapt to the increasing complexity of devices, and reviewers’ ability to make well-informed decisions was undermined by the poor quality of 510(k) submissions
An increasing workload was straining an already overburdened Program
510(k) Implementation Plan

• 25 Action Items Implementing
• 47 Recommendations Intended to:

  Increase
  Predictability, Transparency, Consistency

• Work more closely with regulatory partners
  • Work towards the goal of Single Audit Program
  • Starting first off Health Canada pMAP Program, expanding to TGA and Brazil at this stage
  • Consider specific investigators cadre within FDA that would gain CMDCAS Certification under HC program and expand to TGA under MOU
Pilot ISO 13485 Audit Report Submission to FDA

- ISO Audit Report from CAB certified by a GHTF regulator (GD211 compliant). Manufacturer submits report and related responses to CDRH within 90 days from close of audit.
- Office of Compliance will review per Compliance Program 7382.845
- Office of Compliance issues letter to firm confirming their inspection status with FDA and that they will be taken off routine work load plan for 1 year.
- FDA will come in for PMA pre-approval inspections and For Cause inspections where necessary.
Electronic labeling

- Regulation 207/2012 adopted 10-3-2012
- Applicable: March 1st 2013
- Scope:
  - fixed installed medical devices or AIMD or implantable;
  - devices and accessories intended to be used within same non-mobile healthcare facility;
  - devices and accessories intended for exclusive use by professional users;
  - Stand-alone software.

- Many manufacturers starting eIFU outside scope Regulation
**Animal Tissue and AIMDD**

- Regulation 722/2012 adopted 9-8-2012 to include AIMDD
  - Alignment EDQM and non-EDQM route: always Summary Evaluation Report to Competent Authorities (4 or 12 weeks)
  - 12 months until effective
  - 24 months to get AIMDD certified
  - Specific designation

- Revise MEDDEV guidance / remove and make Notified Body guidance
What will be in MD and IVD Regulations? – talk JAN

<table>
<thead>
<tr>
<th>ROADMAP</th>
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<tbody>
<tr>
<td><strong>TITLE OF THE INITIATIVE</strong></td>
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<tr>
<td>3. Communication regarding the innovation in medical devices for the benefit of patients, consumers and healthcare professionals</td>
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<table>
<thead>
<tr>
<th><strong>Type of Initiative</strong></th>
<th>X CWP act</th>
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<tbody>
<tr>
<td></td>
<td>• Non-CWP</td>
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<tr>
<td></td>
<td>• Implementing act/Delegated</td>
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<tr>
<th><strong>Lead DG – Responsible Unit</strong></th>
<th>SANCO/B2</th>
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<tr>
<td><strong>Expected Date of Adoption</strong></td>
<td>Month/Year: 2nd quarter 2012</td>
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<tr>
<td><strong>Version of Roadmap</strong></td>
<td>No: 3 Last modification: Month/Year: 7.11.2011</td>
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</table>
PIP breast implant scandal

- Big case of 16 year fraud low quality silicon oil
- Stress test performed by EU Commission
- Changes needed to prevent being analysed if legislative changes will improve early detection and further prevention
- Short term changes proposed to the system:
  - Increased market surveillance
  - Additional unannounced visits on top of regular audits
  - Product responsible person
Device cases in the EU media

- Alert systems MHRA (UK), AFSAPPS (France), etc.
- No overview, no detailed analysis
- In the news:
  - Breast implants (PIP and M-implants)
  - Metal on Metal hip implants
  - Pacemaker leads
  - Soft tissue reconstructive meshes

Overview Interim measures

- Functioning of Notified Bodies
- Market Surveillance
- Coordination
- Communication and transparency

The following section/document has been added/updated

Title:

Medical Device Alert: Left ventricular cardiac resynchronization therapy (CRT) leads manufactured by St Jude Medical (MDA/2012/021)

Summary

This Medical Device Alert has been issued as there is a risk of worsening heart failure symptoms due to wear and/or abrasion of lead insulation after implantation.

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TEAM-NB—Code of Conduct under revision

- Currently endorsed by 29 NoBo’s (mandatory)
- **Rev 3.1 endorsed 16 April 2013**
- Changes and additions:
  - Extension to IVD
  - **Unannounced visits**
  - **Product Verification**
  - Supervisory Structure
  - Peer assessment

- **Consistent quality between Notified Bodies**

www.team-nb.org
ISO 13485 3rd Revision Status - ISOTC 210 – WG1

- April 2011, Justification Study & New Work Item Proposal (NWIP)
- Oct 2011, review results of NWIP, areas for consideration include:
  - Publication of 2007/47/EC
    - Clinical Data
    - Post Market Surveillance
      - Software as a Medical Device, including requirements for validation
  - Swedish Competent Authority formal objection to ISO 13485
- 2012 – several meetings - 24 different topics/subject areas
  - EU objections, impact revision ISO 9001, scope revision, reinforce focus on QMS, product life cycle, organisation to include manufacturer, re-processor, distributor etc.
  - Expand Risk Management requirements and provide greater clarity
  - Emerging markets; other regulatory regimes, geographic areas requirements
  - Management responsibility, personnel competence etc
  - In all 24 different topics/subject areas have been highlighted
- March 2013, preparing draft for consultation, expected for comment soon
- 2014 – standard expected to be published
Meanwhile: EN ISO 13485:2012

- To overcome formal objection Sweden
- Adding details to Annex ZA, ZB, ZC
- Focus on presumption of conformity from MDD, IVD and AIMD
- Normative text not changed
- EN ISO 13485:2012 will be the harmonized version
- ISO 13485 covers circa 50% of QMS requirements EU legislation
## Registration Time Frame

<table>
<thead>
<tr>
<th>Registration Process</th>
<th>Classification</th>
<th>Class I (First registration &amp; Renewal/ Re-registration)</th>
<th>Class II &amp; III</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>First registration</td>
<td>Renewal / Re-registration</td>
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<tr>
<td>Step 1: Dossiers request (between manufacturer and his distributor)</td>
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<td>2-3 months</td>
<td>2-3 months</td>
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<tr>
<td>Step 2: Translation, Product registration standard compilation and IFU modification or creation (between manufacturer and his distributor)</td>
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<td>1-2 months</td>
<td>1-2 months</td>
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<tr>
<td>Step 3: Technical dossiers submission and standard scrutiny by MD Standardization Technical Committee – step deleted</td>
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<td>Step 4: Sample tested by National Laboratory</td>
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<td>3 months</td>
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<td>Clinical Trial or clinical data evaluation</td>
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<td>TBC</td>
<td>N/A</td>
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<tr>
<td>On-Site Inspection (For Class III only) at overseas manufacturing sites</td>
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<td>Class III only</td>
<td>N/A</td>
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<tr>
<td>Step 5: Registration dossiers submission &amp; censored and approved by SFDA</td>
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<td>5 months</td>
<td>8 months</td>
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<tr>
<td>IFU reviewed and approved by SFDA</td>
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<td>8 months</td>
<td>8 months</td>
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<tr>
<td><strong>Total</strong></td>
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<td>7-8</td>
<td>12-14</td>
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Highlighted Changes Nov 2011

- SFDA Issued the "Notice on the Issuance of the Directory of Class II Medical Devices Exempted from Submitting Clinical Trial Data"
  - Product fall into the list can be exempt from clinical trials
  - Submit Product Comparison like US 510(k) instead
  - Comparison with similar product on market:
    - Operation Principle
    - Product Materials specifications
    - Structural Design and Characteristics
    - Technical Performance Factors
    - Sterilization or Disinfection method (if applicable)
    - Intended Use
    - Whether the product is Self-Use, etc.
Notice on the Issuance of the Directory of Class II Medical Devices Exempted from Submitting Clinical Trial Data

• For the 21 types of Class II devices eligible for waiver, see the list below

  • Basic surgical instruments
  • Operative orthopedic surgical instruments
  • Injection and puncture instruments
  • Devices for general examination
  • Medical electrical devices
  • Medical optical and endoscopic devices
  • Medical ultrasonic devices
  • Medical and surgical electrodes
  • Traditional Chinese medical devices
  • Medical X-ray auxiliary parts and equipment
  • Devices for clinical lab tests (hematology, etc.)
  • Equipment for clinical laboratories
  • Equipment for cardiopulmonary bypass and blood circulation
  • Equipment for surgical and ER rooms
  • Equipment for dentistry and stomatology
  • Equipment for ward rooms
  • Equipment for sterilization
  • Equipment for medical cold therapy / low temperature storage
  • Materials for dentistry and stomatology
  • Medical dressing and garments
  • Medical polymer materials and products (one-time disposable)

Please cross check the original notice (in Chinese) before registration!

Guidelines for the Medical Devices Adverse Events Monitoring

- Issued on 16 Sept 2011
- Using “Report Form for Suspected Medical Device Adverse Events”

- Timeline of reporting
  - Lead to Death – Within 5 Working days
  - Serious injuries, or may possibly cause serious injuries or death – Within 15 Working days
  - unexpected and mass medical devices adverse events – Within 24 hours
  - Complete the “Supplementary Report Form for Medical Device Adverse Events” within 20 working days after submitting the report of suspected medical device adverse events
  - Complete and submit (for class 2 & 3) the “Annual Summary Report Form for Medical Devices Adverse Events” at subsequent year but before the end of January
Measures for Administration of Medical Device Recall (Interim)

• Issued on 20 May, 2011; Effective on 1 July 2011

• Ch2, Rule 13 - Severity Class of Recall (Risk Based)
  • Class 1 Recall – Possibly or already cause serious threat to health (notice made within 1 day)
  • Class 2 Recall – Possibly or already cause temporary or reversible threat to health (notice made within 3 days)
  • Class 3 Recall – Low possibility to cause harm but require recall (notice made within 7 days)

• Complete and submit recall report form within 5 days
• Regular provide Recall Status report
• Complete and Submit Recall Summary Report within 10 days after recall completed
• Missing timeline will cause money penalty and even worse may cause license suspension or other penalty
Malaysia

- Legislative Bill in place
- Implementing legislation finalised
- Third party audit and dossier reviews
- CABs working on designation

- Part of ASEAN, so 2014/2015 might see AMDD

- Warning on not allowing GDP consultancy/certification
The END ....
For further information

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