Brussels Update on Proposed Medical Device and IVD Regulations

September 2013
2013 BSI Healthcare Roadshow
Who are these men, and what do they know?

Donald Rumsfeld
13th and 21st United States Secretary of Defense

Major General HR McMaster
As commander of the 3rd Armored Cavalry Regiment secured the Iraqi city of Tal Afar in 2004
Many of You are the Regulatory Affairs Leaders on the Front Line
How Can You Guide your Corporate Leadership and Overcome the New European Requirements?
The Current Regulatory Landscape: PIP Fallout

- Clinical data, PMS and PMCF
- Enforcement
- Commission Implementing Regulation on Designation and Supervision of Notified Bodies
  - Central oversight
  - Generalists to Specialists
- Commission Recommendation on UDI
- Commission Recommendation on Notified Body Audits
  - 24 September
Topics to Cover

• 24 September: Commission Recommendation
• Medical Device Regulation
• In Vitro Diagnostic Device Regulation
24 September 2013

COMMISSION RECOMMENDATION on the audits and assessments performed by notified bodies in the field of medical devices
Commission Recommendation Recitals 1

• Instructs Notified Bodies to Perform Unannounced Audits
  • In addition to product assessments and quality system assessments
  • To verify the continuous compliance with legal obligations

• “...In the absence of established practice for unannounced audits it is important to determine the practicalities for such audits, as well as to provide advice on the arrangements needed for facilitating these audits”
Commission Recommendation Recitals 2

• Provides specific advice to Notified Bodies on requirements for
  • Medical Devices: Clinical Evaluation and Post Market Clinical Follow-up
  • IVD Devices: Performance Evaluation and Post Market Follow-up
• Provides specific advice to make sure Notified Bodies do not provide any exceptions for outsourced production compared to in-house production
  • Must include the most important subcontractors and suppliers in the conformity assessment procedures
Commission Recommendation: Recitals 3

...Though regarded as two independent exercises, it is necessary to strengthen the link between the quality system review and the review of the technical documentation on a sampling basis.
GENERAL GUIDELINES FOR AUDITS AND ASSESSMENTS

Where the manufacturer has applied for a design dossier examination or for a type examination (hereinafter jointly referred to as "product assessment"), notified bodies should verify the conformity of the device under all product related aspects referred to in Directive 90/385/EEC, Directive 93/42/EEC and Directive 98/79/EC for detecting any non-compliance of the device and should apply Annex I.

Annex I Product Assessment:
- Reinforces Current Good Practice
GENERAL GUIDELINES FOR AUDITS AND ASSESSMENTS

Where the manufacturer has applied for an assessment of its quality system, notified bodies should verify the conformity of the quality system with all system related requirements contained in Directive 90/385/EEC, Directive 93/42/EEC and Directive 98/79/EC for detecting any non-compliance of the quality system and should apply Annex II.

Annex II Quality System Assessment:
- Mainly Reinforces Current Good Practice
- Gives advice in case of outsourcing of the production via subcontractors or suppliers
General advice in case of outsourcing of the production via subcontractors or suppliers

- Critical subcontractors or crucial suppliers may be suppliers of suppliers or even suppliers further down the supply chain

- Notified bodies should refrain from signing arrangements with manufacturers unless they receive access to all critical subcontractors and crucial suppliers and thus to all sites where the devices or its crucial components are produced, regardless of the length of the contractual chain between the manufacturer and the subcontractor or supplier
GENERAL GUIDELINES FOR AUDITS AND ASSESSMENTS

To verify the day-to-day compliance with legal obligations, notified bodies should, in addition to the initial, surveillance or renewal audits, visit the manufacturer or ... one of its subcontractors in charge of processes which are essential for ensuring compliance with legal requirements ("critical subcontractor") or a supplier of crucial components or of the entire devices (both: "crucial supplier") without prior notice ("unannounced audits") in accordance with Annex III.

Annex III: Unannounced Visits

• Significant New Obligations
Annex III: Unannounced Visits

- Unannounced audits at least once every third year
- Increased frequency of unannounced audits if the devices bear a high risk, if the devices of the type in question are frequently non-compliant or if specific information provides reasons to suspect non-conformities of the devices or of their manufacturer
- The timing of the unannounced audits should be unpredictable
- An unannounced audit should not take less than one day and should be executed by at least two auditors
Annex III: Unannounced Visits 2

- Notified bodies may ... visit one of the premises of the manufacturer's critical subcontractors or crucial suppliers if this is likely to ensure more efficient control.

- This applies in particular if the main part of the design development, manufacturing, testing or another crucial process is located with the subcontractor or supplier.
Annex III: Unannounced Visits 3

- Notified bodies should check a recently produced adequate sample
- The check should encompass a file review and, if necessary in order to establish the conformity, a test
- The test may be performed by the manufacturer, its critical subcontractor or crucial supplier under observation of the notified body
Unannounced Visits: Conclusions and Next Steps

• Significant increase in oversight and workload
• A number of practical challenges
• Competent Authorities and Notified Bodies will consult soon after publication to establish rules of engagement
• BSI will brief manufacturers as soon after publication as possible and update when those rules of engagement are clear
Manufacturers’ Next Steps?

• Engage with your Notified Body to understand the rules
• Participate in regulatory forums in the EU to understand the rules
• Build a plan to facilitate unannounced audits with front line and back up personnel
• What happens when your RA/QA team are away – team building Las Vegas?

24/09/2013
26 September 2012

Proposal for a
REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

Proposal for a
REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
on in vitro diagnostic medical devices
Proposed Medical and In Vitro Diagnostic Device Regulations

• Build on the strengths of existing directives …
  • Supportive to innovation
  • Rapid access to market
  • Balance between pre- and post-market control
  • Cost-effective
  • SMEs

• … but adapt and improve, especially in terms of
  • Health and safety
  • Internal market
  • Transparency
  • Trust and confidence in the European regulatory system

• Health warning: clauses will appear, stay, change, disappear
A Key Feature: Delegating and Implementing Acts

• Proposal empowers the Commission to adopt
  • Implementing acts to ensure uniform application of the Regulation
    • Member State Committee must give positive opinion on Commission Proposals
  • Delegated acts to complement the regulatory framework for medical devices over time
    • Commission publishes the Delegated Act
    • European Parliament or Council have two months to object

• Serious centralisation of power
  • Too much say some Member States and MEPs

• Very useful tools to adapt to technical progress
Implementing Acts: Positive MS Opinion Required

• **Commission can:**
  - Establish regulatory status of products: does a specific product, or category or group of products, falls within the definitions of 'medical device' or 'accessory to a medical device'?
  - Adopt Common Technical Specifications: where no harmonised standards exist or where relevant harmonised standards are not sufficient
  - Establish and regularly update a list of categories or groups of single-use devices for critical use which may be reprocessed...
  - Lay down the modalities necessary for the development and management of Eudamed
  - Set NB application process, scope acceptability criteria and competency codes, and Notified Body De-Designation process
  - Change medical device classification criteria, conformity assessment procedures, certificates of free sale, field safety corrective action procedures
  - Procedures for dealing with non-compliant and compliant devices presenting a risk to health and safety
  - ...... and more
Delegated Acts: EP and MS Two months to object

• Commission can
  • Adopt delegated acts in the light of technical progress and taking into account the similarity between a medical device and a product without a medical purpose
  • Adapt the definition of nanomaterial in view of technical and scientific progress and taking into account definitions agreed at Union and international level
  • Amend or supplement data requirements, documentation and procedures
    • the general safety and performance requirements set out in Annex I; the information supplied by the manufacturer; the technical documentation set out in Annex II; the minimum content of the EU declaration of conformity; amend the information to be submitted as set out in Part A of Annex V, the minimum requirements in Annex VI needed for the assessment of specific devices, or categories or groups of devices; the classification criteria set out in Annex VII; the conformity assessment procedures; the minimum content of the certificates; the requirements for the documentation to be submitted with the application for the clinical investigation
  • Determine the devices, categories or groups of devices whose identification shall be based on the UDI system
  • Set out the structure and the level of the fees MS can charge NBs
  • ……And more
Key Proposals:

Device Related Changes Covered this Morning

Here are some other Proposals to Consider
### Commission proposals that Member States like

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<th>Improved coordination and cooperation between Member States</th>
<th>Alignment with the 'New Legislative Framework'</th>
<th>Rules-based system to classify IVDs</th>
<th>More rigorous designation and audit of notified bodies</th>
<th>Increased regulation of reprocessing of single-use devices</th>
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<td>More effective governance structure of Member State experts</td>
<td>More traceability – UDI and implant cards</td>
<td>More information available on the quality and safety of devices on the market</td>
<td>Central reporting of serious incidents and field safety corrective actions</td>
<td>Clearer requirements for clinical evidence</td>
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### Proposals that cause some Member States Concern

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<td>Additional pre-market scrutiny of high-risk devices by a centralised committee</td>
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<td>Expanding the scope of the IVD Regulation to include Class D devices manufactured and used in-house</td>
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<td>Where the default assumption is confidentiality rather than transparency</td>
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<td>Erosion of national competence and too much left to tertiary legislation?</td>
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Obligations of Authorized Representative, Importers, Distributors

- Manufacturer designates by written mandate a single authorized representative confirmed in writing by the authorized representative
  - Prescriptive requirements for authorized representative
  - Written process for changing authorized representative

- General obligations of importers & distributors
  - Confirm: conformity assessment, authorized representative, technical documentation, devices CE Marked, labeled in accordance with regulation
  - Identify themselves, registration, storage & transportation, records, complaints, responsibilities

- Relabeling / repackaging devices
  - Assumes responsibilities of the manufacturer
Manufacturer - Qualified Person

- Manufacturers need a qualified person available within their organisation who has medical device expertise
  - Either education requirements plus two years medical device RA / QA experience or five years medical device RA / QA experience
- Protected when properly fulfilling responsibilities
- Responsibilities include
  - Statements regarding clinical investigation devices essential requirement compliance and protection of subjects
  - Conformity of devices confirmed before batch release
  - Technical documentation and declarations of conformity are current maintained
  - Reporting obligations are met
- EU Representatives shall also have qualified person
  - Expert knowledge of EU medical device regulations
Single Use Devices and Reprocessing

- Considered to be the manufacturer
- Reprocessing of single-use devices for critical use is prohibited (intended for surgically invasive procedures)
- EC has power to change definition of devices for critical use
- Removal of OEM’s name from label
- National provisions may be maintained or introduced
Implant Card

• Manufacturers of implantable devices shall provide implant card for particular patients
  • Identifies device implanted including UDI
  • Warning, precautions, measures to be taken with reciprocal interference with external influences (e.g. compatibility with diagnostic devices)
  • Information on expected life cycle and follow-up
Parts and components

- New requirement for suppliers of parts or components.
- Responsibility to determine the part or component does not adversely affect the safety and performance of the device.
  - Substantiating evidence available to CA's
- Part or component that significantly changes the performance or safety characteristics of a device shall be considered a device in its own right.
Identification within the Supply Chain

- Economic operators shall identify the following (available to CA’s):
  - Economic operator to whom they supplied a device
  - Economic operator who supplied them a device
  - Any health institution or healthcare professional to whom they have supplied a device
Electronic System on Registration of Devices and Economic Operators

- The EC will set up and manage an electronic system
- Manufacturers will submit information in electronic means
- Importers will submit information in electronic means
  - All changes updated within one week
- Accuracy confirmed at least every 24 months
- Data shall be publicly available
- Fees may be collected
Notified Bodies

- Significant new requirements regarding the designation, competence, scope, monitoring and maintenance of notified bodies
- Requirement to issue certificates and status in database
- Procedure for changing notified bodies
- Current notified bodies will need to apply for and achieve designation under the new regulation
  - National Authority shall notify to the EC, MS and MDCG
  - Scopes of NB’s will be competence specific
Conformity Assessment

• Notified bodies shall notify the Commission and MDCG of new applications for class III devices
• Notified body shall rotate the members of the audit team (no more than three years per auditor)
Clinical Evaluation & Clinical Investigation

• Regulation combines and incorporates current guidance on clinical evaluation and clinical investigation

• Significant requirements on clinical
  • General requirements – sponsor responsibilities
  • Application
  • Registration
  • Electronic system
  • Post market clinical investigation requirements
  • Substantial modification
  • Sponsor information obligations regarding suspension / termination
  • Event reporting
Vigilance & Market Surveillance

- Regulation combines and incorporates current vigilance guidelines
  - Electronic system
- Member State market surveillance activities
  - Procedures for problem / non-compliant devices uniformly
  - Action against economic operators
European MS Co-operation

- Competent authorities (CA)
- Medical Device Coordination Group (MDCG)
  - Oversight and contribute: NB designation / Class III certification / Guidance / Assist CA’s (vigilance, clinical investigations) / Assist EC / Harmonization
- Scientific Advisory Board (SAB)
- European Union Reference Laboratories (EURL)
  - EC will facilitate access to manufacturers and NB’s to advice provided by SAB and EURL’s
- Union shall support the establishment of registers for certain devices to evaluate long term safety and performance
Budgetary Implications: Costs

- Development of the Eudamed database (one-off costs and maintenance)
- Commission staff organising and participating in 'joint assessments' of notified bodies
- National assessors participating in 'joint assessments' of notified bodies
- Commission staff supporting the MDEG and its sub-groups
- Commission staff managing the Regulation and developing the delegated/implementing acts
- Organisation of meetings of the MDEG and its sub-groups, of the advisory committee on borderline issues, and of the Committee under Regulation 182/2011, including reimbursement of the members appointed by the Member States
- Reporting members of the MDEG preparing opinions on notified bodies' preliminary conformity assessments of high risk devices
- Organisation of meetings of the Scientific Advisory Committee, including reimbursement of its members
- The functioning of the EU reference laboratories
- Participating in international regulatory cooperation
Budgetary Implications: Finding the Money

- The Commission, the Member States or and the designated EU reference laboratories will charge fees for various activities
- The Commission will use implementing acts to set the level and structure of fees
- The Commission
  - Fees for the registration of medical devices in the central database
- The Member States
  - Fees for the designation and monitoring of notified bodies
  - Transfer a portion to the Commission to finance the 'joint assessments' and the scrutiny mechanism for high risk devices
- EU Reference Laboratories
  - Fees for scientific opinions provided to notified bodies and manufacturers
The Parties Trying to Reach Agreement

- **European Commission**
  - Prepared proposal 26 Sep 2012

- **European Parliament** – representing the citizens of Europe
  - Committees working on counter proposals
  - IMCO (113 IVD and 212 MDR amendment proposals), voting done on consolidated amendments
  - EMPL (20 IVD and 60 MDR amendment proposals), voting done on consolidated amendments
  - ENVI (399 IVD and 907 MDR amendment proposals), voting Sept 18
  - First vote full Parliament – November 22/23
  - Re-elections May 2014

- **European Council of Ministers** – representing EU Member States
  - 11 workgroup meetings so far, 60% through proposal
  - Plan to complete counter proposals before end of 2013, more likely March 2014

25 September
From Proposal to Regulation: The Normal Procedure

**European Parliament**
- Proposal
  - First Reading
  - Second Reading
  - Third Reading

**Council of Ministers**
- First Reading
  - Common Position (or adopts EP Text)
  - Commission Opinion on Amendments
  - Conciliation Committee Joint Text (within 6+2 weeks)
  - No agreement proposal lapses

**European Parliament**
- Committees Recommendation
  - 3 (+ 1) Months

- Report from lead Committee

- Accepts or modifies amendments by QMV or unanimous vote (depending on COM position)

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2012 View of Best Case Timelines

- **EU Presidency**
  - European Commission
    - Draft the legal text
    - Jul - Dec 2011

- **Denmark**
  - European Commission
    - Publish the Proposal
    - April 2012

- **Cyprus / Ireland**
  - EU Parliament and Council
    - 1st Reading: Assess and amend the Proposal
    - 2012 / 2013

- **Lithuania / Greece**
  - EU Parliament and Council
    - 2nd Reading: Negotiate agreeable text
    - 2013 / 2014

- **Italy**
  - Member States
    - Implement
    - 2014
Timelines: Current Status

**European Commission**
- **Draft the legal text**
  - Jul - Dec 2011

**European Commission**
- **Publish the Proposal**
  - April 2012

**EU Parliament and Council**
- **1st Reading: Assess and amend the Proposal**
  - 2012 / 2013

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- **2nd Reading: Negotiate agreeable text**
  - 2013 / 2014

**Member States**
- **Implement**
  - 2014

**EU Presidency**

**Denmark**

**Cyprus / Ireland**

**Lithuania / Greece**

**Italy**
European Parliament Amendments

- 19 September ENVI Committee Rapporteurs proposed “Compromise Amendments” for the MDR and IVDDR on which ENVI Committee will vote on 25 September.
- Amendments that survive the vote will be voted on by the European Parliament in November.
- Those that survive the vote will go forward to the Commission and Council of Ministers.
ENVI Committee Compromise Amendments: MDR

- Two types of Notified Body
  - Regular Notified Bodies
  - ‘Special Notified Bodies’ to review high risk devices
  - EMA to designate SNBs

- Qualification Requirements
  - Qualification for competent authority auditors supervising notified bodies identical to those of notified bodies

- Reprocessing of Medical Devices
  - Manufacturer to prove non-reusability before claiming single-use only

- Many proposals on transparency and data to make available to public

- Strong focus on clinical trials
  - Including comparative studies for new devices and new materials

- Electronic Implant Cards
ENVI Committee Compromise Amendments: IVDDR

• Three year transition
  • IVDDR Proposal has five year transition for IVDDR
  • Notified Bodies, Manufacturers, Commission and Competent Authorities will have a lot to do

• Annual unannounced visits as with MDD

• Clinical Evaluation Proposals
  • Lots of wording imported from MDD
European Parliament Conclusions

• Very Public Debate by Lobbyists and Politicians
• Amendments drafted by Enthusiastic Lay People
• It will be difficult to implement well-meaning impractical proposals
Council of Ministers - Interim report

• Council Working Party on Pharmaceuticals and Medical Devices
• Met Four times in 2012, and Seven times in 2013
  • Chapters IV of both Proposals – Notified Bodies,
  • Chapters V of both Proposals – Classification and Conformity Assessment,
  • Chapters VI – Clinical Evaluation & Clinical Investigation (MD Proposal) and Clinical Evidence (IVD Proposal), and
  • Chapters VIII of both Proposals - Cooperation between Member States, Medical Device Coordination Group, EU Reference Laboratories.

• Seven Technical expert meetings
  • Annexes VI of both Proposals – Minimum Requirements for Notified Bodies
  • Annexes VII of both Proposals – Classification
  • Annexes XIII & XIV of the Medical Devices Proposal – Clinical Evaluation and Post-Market Clinical Follow-Up and Clinical Investigations
  • Annexes XII & XIII of the IVD Proposal – Clinical Evidence and Post-Market Follow-Up and Clinical Interventional Clinical Performance Studies and other Clinical Performance Studies involving risks for the subjects of the Studies
Council of Ministers: Positions Taken So Far

• Did not split legislation and proposals to expedite agreement in areas of consensus

• Unresolved Differences of Position on Scrutiny of Notified Body Reviews and Decisions
  • delete, keep, improve...

• Not yet clarified position on How Member States and Commission should supervise Notified Bodies

• Agreed to align IVD classification GHTF principles
  • Move from list based to risk based regulation

• Agreed on a Longer Clinical Trial Approval Process
  • detailed ethical requirements and approvals procedure

• Proposal to require clinical trials on all class III products
Timelines

• European Parliament publish report in November 2013

• Member States

  • Official Position
    • Formal counter proposals before end 2013 or early 2014 and seek agreement before June 2014 European Parliament elections

  • Unofficial Position
    • Council Working Group and Experts not far enough through the text to make that deadline
    • Still major differences of opinion in some areas already discussed
      o Chapter VIII Cooperation between Member States, Medical Device Coordination Group, EU reference laboratories, Device registers
Political change on the horizon

**July 2013**
Lithuanians chair Member State meetings

**January 2014**
Greeks chair Member State meetings

**July 2014**
Italians chair Member State meetings

**Spring 2014**
European Parliament campaigns

**June 2014**
European Parliament elections

**October 2014**
New European Commissioners
### Timelines:

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- **European Parliament 1<sup>ST</sup> Reading – November 2013**
- **2<sup>nd</sup> Reading – either Q1 2014 or Q3/Q4 2015**
- **Designation of Notified Bodies**
- **3 Year Transition**
- **5 Year Transition**

**Regulation covering MD & AI MD**

**Regulation covering IVD**
Conclusions and Manufacturers’ Next Steps?

- There are huge costly changes on the way
- There may be some delay
- But “soft law” will introduce some provisions now
- Unannounced visits; Clinical Evaluation …
- Decide what is best for your business
- Influence to best defend your business
- React to make sure your systems meet the needs of new regulations
- Commit to best prepare your business
- Wait and respond to regulations and play catch up
- Invest
- Specialist regulatory and quality system professionals who understand the theatre of operations
- Bigger regulatory and compliance budgets
- Engage, based on understanding