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EU Medical Devices: the changing enforcement landscape

The International Pharmaceutical Compliance Congress and Best Practices Forum, May 10-12, 2016, Warsaw, Poland

Maurits Lugard, Sidley Austin LLP, Brussels

Overview

- **From PIP to 2015**
  - Joint Action Plan
  - Commission Initiatives
- **Regulatory Enforcement**
  - Concrete Examples
  - Takeaways
- **Why new rules?**
  - New EU; New Needs
- **Latest Developments on MDR & IVDR**

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From PIP to 2015 (1)

- Recently, European medical device regulatory & enforcement environment **has changed drastically**
- Triggered by major **scandals** in 2010-2012:
  - **PIP**: French company for many years used industrial-grade silicone in breast implants sold globally
    - 400,000 women affected world-wide
  - **MoM**: reports in the UK regarding exposure of patients to failing implants causing damage
- Led to **strong reactions across Europe**, demanding much stricter rules & oversight

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- Led to **call by EC** Health Commissioner Dalli in February 2012 **for immediate actions**
  - Proposed **Joint Action Plan** to EU Member States (MS) within existing framework to "**tighten controls**"
    - Verifying **designations Notified Bodies** (NBs) in light of their expertise & competence
    - Ensuring NBs use their powers within conformity assessments, incl. **conduct of unannounced audits**
    - Reinforcing **market surveillance** by national competent authorities (NCAs), incl. in particular "spot checks"
    - Improving functioning of MD **vigilance regime**

From PIP to 2015 (3)

- Further reinforced by **EP Resolution** regarding PIP scandal (June 14, 2012)
  - Called on EU MS and EC to introduce measures aimed at ensuring safety of MD/IVD & bring back trust of patients
  - Requested **immediate measures**, incl.:
    - Stricter controls on medical devices on the market
    - Increased focus on designation and activities NBs
    - Reinforcement of market surveillance
    - Improvement of MD vigilance reporting system
- On 26 September 2012, Commission proposed **two new Regulations** (more on that later)

From PIP to 2015 (4)

- In September 2013, EC published interim two measures:

  1. **Commission Recommendation (2013/473/EU)**
     - NBs should perform **unannounced audits** in addition to regular product & quality assessments
     - **EU MS responsible for supervision** relevant NB activities

  2. **Comm. Implementing Regulation (920/2013/EU)**
     - Increased **focus on**
       - **Competence of Notified Bodies**; and
       - Monitoring by responsibilities EU Member States

From PIP to 2015 (5)

Commission Recommendation (2013/473/EU)

Whereas clause (3):

– "The interpretation of those provisions [*i.e.* the medical device directives] and the behaviour of notified bodies designated in the field of medical devices differ.

From PIP to 2015 (5)

Commission Recommendation (2013/473/EU)

Whereas clause (3):

- "The interpretation of those provisions [*i.e.* the medical device directives] and the behaviour of notified bodies designated in the field of medical devices differ.
- Therefore, this Recommendation should **set benchmarks** for (1) assessments and (2) unannounced audits by notified bodies and
- respond to the **most frequent shortcomings** of the current practices."

From PIP to 2015 (6)

Commission Recommendation (2013/473/EU)

1. PURPOSE:

– "To facilitate the consistent application of the conformity assessment provisions contained in [the MDDs], the NBs should apply the provisions of this Recommendation when they perform product assessments, quality systems assessments and unannouced audits. [...]

From PIP to 2015 (6)

Commission Recommendation (2013/473/EU)

1. PURPOSE:

– "To facilitate the consistent application of the conformity assessment provisions contained in [the MDDs], the NBs should apply the provisions of this Recommendation when they perform product assessments, quality systems assessments and unannouced audits. [...]

– By providing general guidelines [...] this Recommendation should facilitate the work of the NBs as well as the MS' evaluation thereof.

From PIP to 2015 (6)

Commission Recommendation (2013/473/EU)

1. PURPOSE:

– "To facilitate the consistent application of the conformity assessment provisions contained in [the MDDs], the NBs should apply the provisions of this Recommendation when they perform product assessments, quality systems assessments and unannouced audits. [...]

– By providing general guidelines [...] this Recommendation should facilitate the work of the NBs as well as the MS' evaluation thereof.

– This Recommendation does not create any new rights and obligations."

From PIP to 2015 (7)

Commission Recommendation (2013/473/EU)

Annex III – Unannouced audits

– "Notified bodies should carry out unannounced audits at least once every third year.

From PIP to 2015 (7)

Commission Recommendation (2013/473/EU)

Annex III – Unannouced audits

- "Notified bodies should carry out unannounced audits at least once every third year.
- Notified bodies should **increase the 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.

From PIP to 2015 (7)

Commission Recommendation (2013/473/EU)

Annex III – Unannouced audits

- "Notified bodies should carry out unannounced audits at least once every third year.
- Notified bodies should **increase the 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."

From PIP to 2015 (8)

- In September 2013, EC published interim two measures:

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     - NBs should perform **unannounced audits** in addition to regular product & quality assessments
     - **EU MS responsible for supervision** relevant NB activities

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     - Increased **focus on**
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From PIP to 2015 (9)

Commission Implementing Regulation (920/2013)

– A MS shall only designate or re-designate a NB after a joint assessment conducted with experts from the Commission and other MS.

From PIP to 2015 (9)

Commission Implementing Regulation (920/2013)

- A MS shall only designate or re-designate a NB after a joint assessment conducted with experts from the Commission and other MS.
- MS are required to carry out surveillance and monitoring of the NBs at certain intervals to ensure that they continuously live up to requirements. If this is not the case, the MS must withdraw the designation as NB.

From PIP to 2015 (9)

Commission Implementing Regulation (920/2013)

- A MS shall only designate or re-designate a NB after a joint assessment conducted with experts from the Commission and other MS.
- MS are required to carry out surveillance and monitoring of the NBs at certain intervals to ensure that they continuously live up to requirements. If this is not the case, the MS must withdraw the designation as NB.
- Knowledge and experience requirements of the staff of the NBs are clarified.

From PIP to 2015 (10)

- EC Staff Working Document of June 13, 2014 indicated substantial progress on Joint Action Plan
  - EU MS re-assessment of NBs led to **corrective measures** in at least 8 countries
  - By May 2014, EC and MS had conducted **joint audits of NBs** in 22 of 23 relevant countries
    - In all cases non-conformities were found, and in about half of the countries these were major non-conformities
  - NBs initiated **unannounced audits**
  - EC and MS have **monthly telephone conferences** to **coordinate vigilance matters**
    - In June 2014, **more than 70 specific cases** had been presented for coordination

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Regulatory Enforcement (1)

- EC and MS measures have **significantly changed** European **regulatory enforcement landscape**

  - **NBs are under stricter supervision** by NCAs and EC
  - NBs are increasingly subject to **pressure from NCAs** with respect to specific topics / manufacturers
  - Directly **impacts NBs interaction** with and position towards **manufacturers**

  - **Could lead to some unexpected changes in position by NBs…**

Regulatory Enforcement:
Concrete Example: Vigilance Reporting (1)

- **Key area for regulatory enforcement has been vigilance (*i.e.*, safety) reporting**
  - **EC and NCAs are increasingly coordinating** their concerns re: specific issues and manufacturers
    - Facilitated by monthly telephone conferences NCAs/EC
  - "**Task Force**" of NCAs led by 1 NCA will raise concerns with manufacturer and request detailed info, e.g. on
    - ***Complaint handling approach***
    - ***Number of complaints and Incidents in EEA***
    - ***Risk analysis and argumentation on specific issues***
    - ***Justification for marketing of specific products***

Regulatory Enforcement:
Concrete Example: Vigilance Reporting (2)

- In many cases, NCA or Task Force will **expect** to see a swift and **significant increase** in Incident **reporting**
- NCA or Task Force will **pressure NB to audit** and take action with respect to manufacturer concerned
- Typically involves **threats of enforcement** or consequences for marketing of specific products

- **NCA concerns are often unexpected** by manufacturers due to lack of supervision by NBs
  - **Not unusual for NBs to have completed multiple audits with no or only minor findings on issue concerned**

Regulatory Enforcement:
Concrete Example: Vigilance Reporting (3)

- Process to address questions and concerns can take **more than year** and requires **significant resources**
  - Short term pressure to provide detailed response to questions that require input multiple departments
  - Subsequent pressure to increase reporting results in more questions to answer
  - Often requires overcoming internal resistance and an **overall culture change**
- **Expectation** is **continued push** by in particular certain NCAs for increased Incident reporting
  - Part of reason is lack of trend reporting by industry

Regulatory Enforcement:
Concrete Example: Certification (1)

- ***First illustrative example***:
  - Manufacturer unexpectedly is asked by NB to re-confirm or supplement clinical evidence for CE marked device
  - Manufacturer resistant because device is on the market and was certified by same NB
  - Situation escalates and manufacturer later learns that
    - NB was under pressure from responsible NCA, and
    - Responsible NCA had in turn been encouraged by other NCA from main market for the device concerned
  - Manufacturer is presented with situation to either present additional clinical evidence or lose certification

Regulatory Enforcement:
Concrete Example: Certification (2)

- ***Second illustrative example***:
  - Manufacturer has been marketing particular medical device across Europe for multiple years
  - No major issues with device, however NB unexpectedly challenges classification of device (higher risk)
  - NB refuses renewal of expiring certificate supporting marketing of device due to classification disagreement
  - Manufacturer discovers that NCA backs NB, and is prevented from marketing device until requirements related to higher risk classification are met

Regulatory Enforcement:
Concrete Example: Certification (3)

- ***Third illustrative example***:
  - Manufacturer developed and agreed device development plan with NB and worked towards certification
  - NB repeatedly confirms agreement with development plan and steps taken by manufacturer
  - After several years, upon completion of final step of plan, manufacturer requests certification
  - NB refuses certification and requests additional clinical evidence to support safety of device
  - Manufacturer discovers that change of position NB in part is due to pressure from NCA

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Regulatory Enforcement:
Takeaways (1)

- Practices and arrangements that were common and **acceptable** for many years **no longer** are
  - Several NCAs view industry overall as non-compliant with e.g. Vigilance obligations
  - Response "*but our approach is in line with industry practice*" does no longer work
- Different regulatory enforcement landscape requires **different approach** towards NBs and NCAs
  - **NBs should be dealt with more like a regulator, as opposed to service provider**

Regulatory Enforcement:
Takeaways (2)

- In many cases, issues escalate due to **lack of transparency** / **lack of diligence** in responses
  - Questions, incl. in particular *unexpected* questions require diligence and accurate response
  - Place information in appropriate context, e.g.
    - mention sales volume for high volume product to contextualize number of complaints / Incidents
    - highlight benefit-risk balance and/or reference material supporting value of device (e.g. publications)

Regulatory Enforcement:
Takeaways (3)

- **Building trust is key**
  - This takes time and requires living up to commitments (even small ones, like "minor" deadlines)
- Important to **be ahead of the curve**
  - Better to analyze gaps now and address them proactively, then to wait for NCA/NB scrutiny
- **Potential impact** is **significant**
  - Identification of systems/process issue by NCA/NB can impact sale of all of manufacturer's devices

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Why New Rules? (1)

- **Existing EU rules**
  - Medical Devices Directive (1993)
  - Active Implantable Medical Devices Directive (1990)
  - *In Vitro* Diagnostic Medical Devices (1998)
- **Enlarged EU**
  - From 12 to 28 (+ 5) Member States
  - Different implementation
- **Advances in technology**

Why New Rules? (2)

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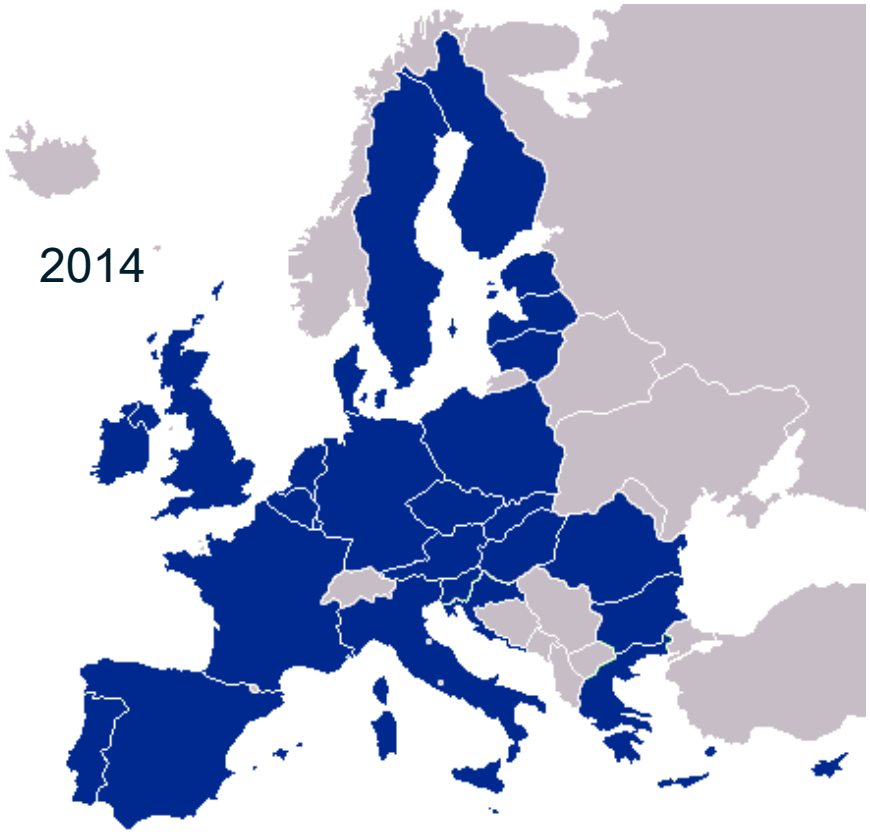
Why New Rules? (3)



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Why New Rules? (4)

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Latest Developments on MDR & IVDR
State of Play

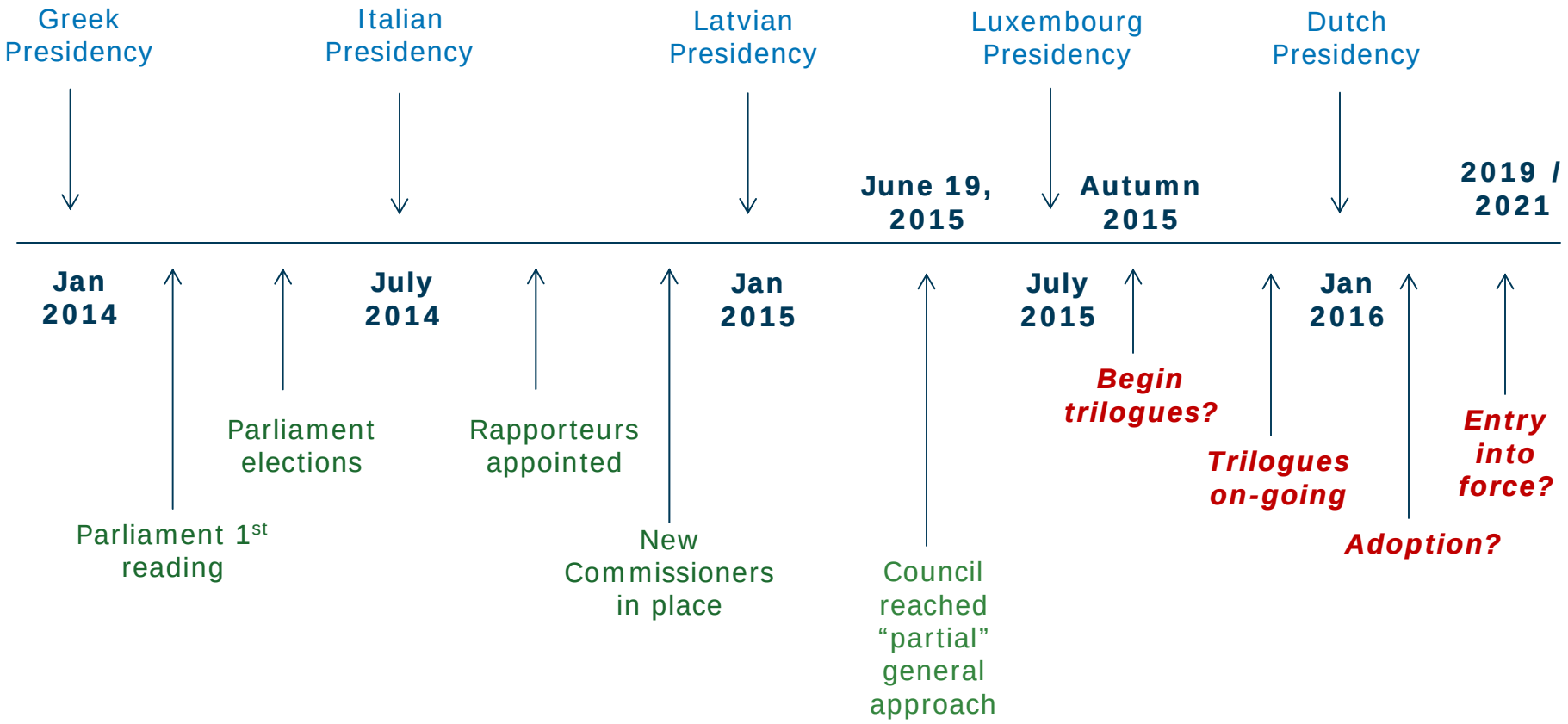
- Existing Medical Devices Directive dates back to **1993**
  - EC first raised review of directives in 2004
  - Several consultations followed
- EC issued **proposed MD Regulation** and **IVD Regulation** in **September 2012**
  - EP proposed significant amendments in October 2013
  - EP adopted first reading position in April 2014
- On June 19, 2015, Council reached a "**partial general approach**" on the legislative proposal
- **Trilogues are on-going…**

EU legislative decision making

"Laws are like sausages.
It's better not to see them
being made."

Otto von Bismarck (1815–1898)

Political Timetable



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Questions/Comments

Maurits J.F. Lugard
Head, European Life Sciences Regulatory, Compliance & Enforcement Practice

Sidley Austin LLP
51, Rue Montoyer
1000 Brussels, Belgium
mlugard@sidley.com
+322.504.6417

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