EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update on EMA role in implementation of new legislation for medical devices (MDR) and in vitro diagnostics (IVDR)

Annual PCWP/HCPWP meeting with all eligible organisations
20 November 2019

Presented by Zaide Frias
Head of Human Medicines Evaluation Division

PIP breast implant scandal
Metal-on-metal hip implant recall

In 2010, the French AFSSAPS withdrew PIP (Poly Implant Prothèse) implants from the market, after surgeons reported a higher-than-usual rate of rupture.

In 2010, Johnson & Johnson recalled metal-on-metal hip systems with higher than expected revision rates.


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PIP breast implant boss Jean-Cl… faces charges

27 January 2012

The owner of a French breast implant maker that sparked a safety scare faces charges of "involuntary injury", his lawyer says.

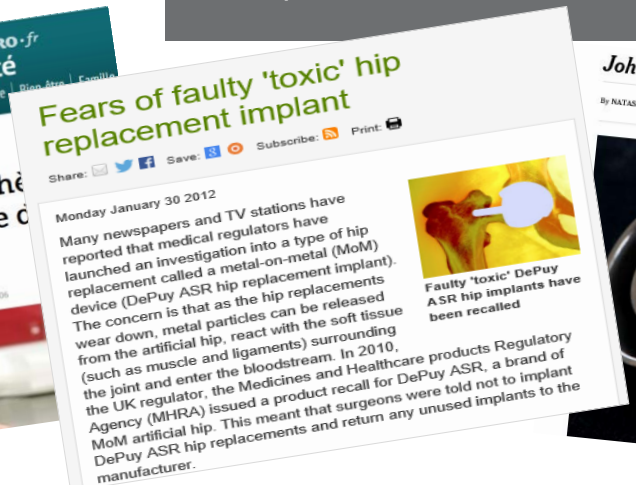
He said Poly Implant Prothese (PIP) founder Jean-Claude Mas, 72, had been freed on bail of 100,000 euro ($130,000).

In 2010, France banned PIP implants made with the low-grade silicone,

LE FIGARO.fr santé

Médecine | Santé Publique

Dangerosité des prothè… PIP: l'Afssaps alertée … 2008

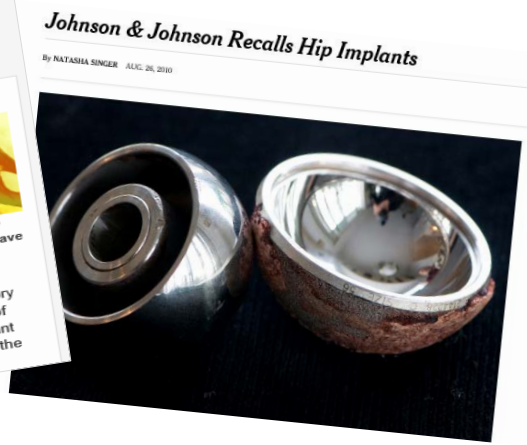

Fears of faulty 'toxic' hip replacement implant

Share: Save: Subscribe: Print:

Monday January 30 2012

Many newspapers and TV stations have reported that medical regulators have launched an investigation into a type of hip replacement called a metal-on-metal (MoM) device (DePuy ASR hip replacement implant). The concern is that as the hip replacements wear down, metal particles can be released from the artificial hip, react with the soft tissue (such as muscle and ligaments) surrounding the joint and enter the bloodstream. In 2010, the UK regulator, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a product recall for DePuy ASR, a brand of MoM artificial hip. This meant that surgeons were told not to implant DePuy ASR hip replacements and return any unused implants to the manufacturer.

Faulty 'toxic' DePuy ASR hip implants have been recalled


Johnson & Johnson Recalls Hip Implants

By NATASHA SINGER AUG. 26, 2010

The New European MDR And IVD Regulations


Official Journal L 117

of the European Union

Legislation

Published on 5 May 2017

Entered into force 26 May 2017

Regulation (EU) 2017/745 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

Regulation (EU) 2017/746 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU

New rules will apply:

- For MDR starting 26 May 2020
- For IVDR will be 26 May 2022

MDR/IVDR - Increase Medical Device Safety

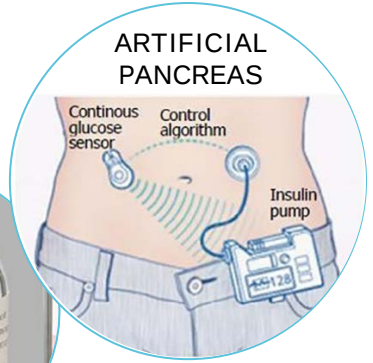
Vigilance and Post-market surveillance:

- Establish a modernised and more robust EU legislative framework to ensure better protection of public health and patient safety
- Address concerns from PIP breast implant scandals; increase confidence in the system

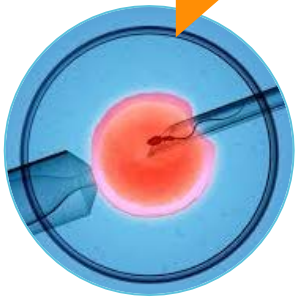
Important improvements:

Increased oversight of notified bodies, greater scrutiny of higher risk devices, improved traceability (unique device identifier - UDI)/'implant cards') and strengthening of clinical evidence and post-market surveillance requirements, EUDAMED database (partial public),..

More than 500,000 medical devices
(different sizes and models)



Higher risk medical devices



MDR/IVDR – Effectiveness of EU market & Response to technical and scientific developments

Scope expansion and re-classification of Products

While the classification system has been retained, rules have tightened and changed for some products, which will result in some devices being reclassified to higher classes. In addition, some devices that were previously exempt from the regulations are now in the scope of the new legislation.

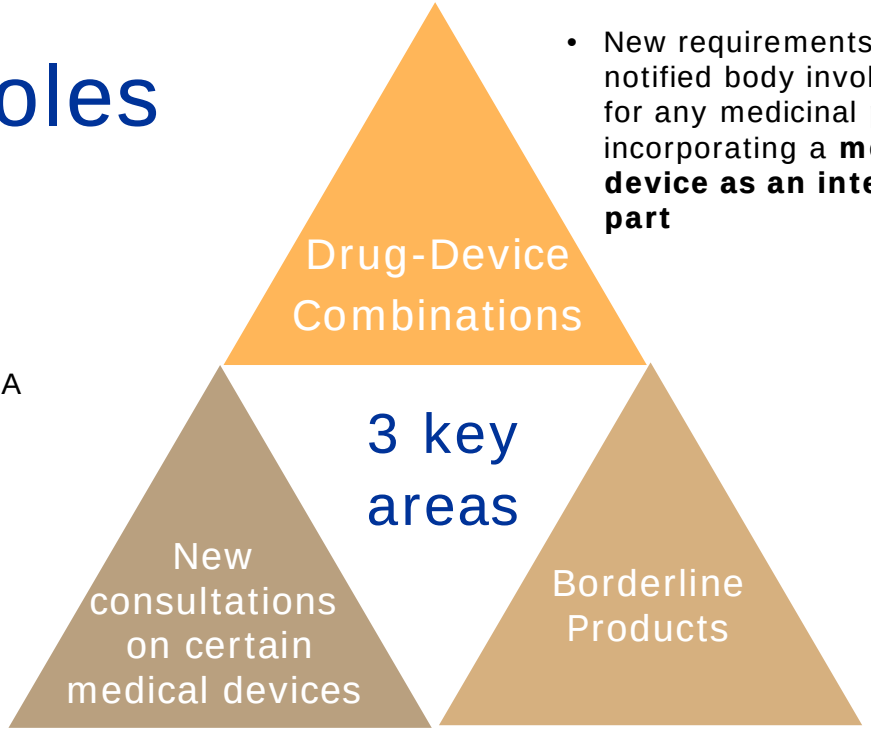
Important improvements:

Increased oversight of notified bodies, greater scrutiny of higher risk devices, continuous improvement of product on the market, expert panel assessment of clinical evaluation,..

Implementation of the Medical Devices/IVD Regulations

EMA Roles

- New requirements for notified body involvement for any medicinal products incorporating a **medical device as an integral part**



Notified bodies must consult EMA or a competent authority for medicinal products before certifying the below types of device:

- **Medical devices composed of substances that are systemically absorbed**
- **Companion diagnostics**

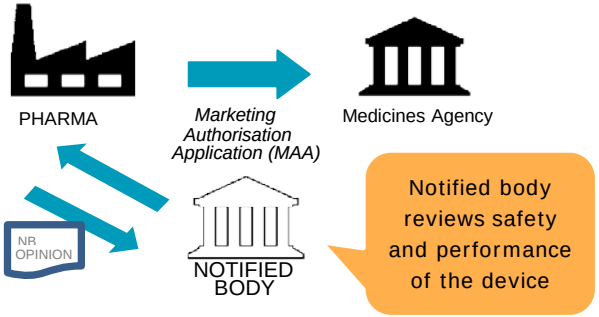
- EMA has a role in providing an opinion to European Commission on **borderline products**

1. Drug-device combinations - medicinal products with Integral device

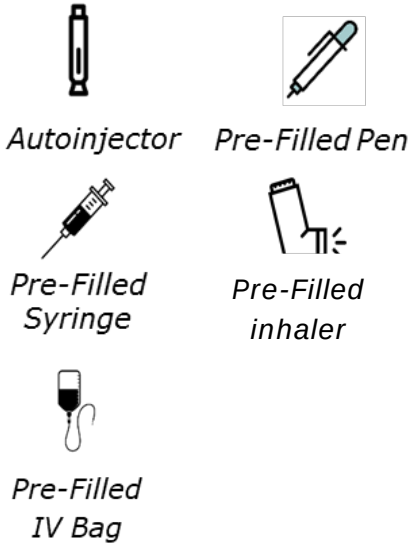
- Article 117: combination products will be reviewed by both Medicines and Device experts

Under current system

Under New Regulation



Examples of single integral product, not reusable



Notified body re-designations by EC/MS
Impact for new medicinal products availability?

- Industry letters to EMA, HMA, EC, CMDh raising concern of potential impact for medicinal products–medical device combinations (e.g. delay in NB opinion)
- 7 of 60 existing Notified Bodies designated to date

UK

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Germany

DEKRA
On the safe side.

TÜVRheinland®
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TÜV SÜD

Netherlands

DARE!!

bsi.

Italy

IMQ

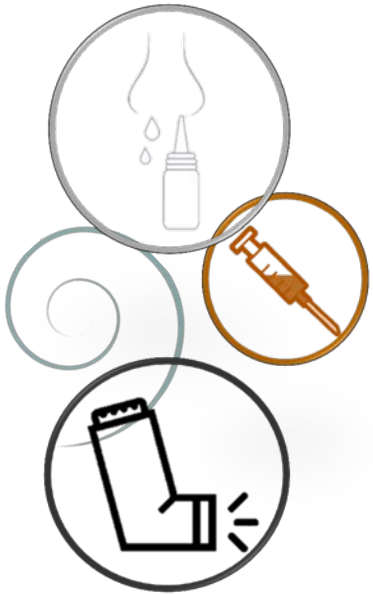
20 NB designations expected by end of 2019

Impact for centralised procedure:

- ~25 new applications with integral device in 2020*
- >100 existing CAPs with devices, some of them impacted

*Survey feedback from Industry trade associations

1. Drug-device combinations



Approximately 25% centrally authorised medicines, includes a medical device component

- Majority of combinations with medical devices:
  - ✓ pre-filled syringes / pre-filled pens (e.g. diabetes, immune therapy)
  - ✓ inhalers (Chronic Obstructive Pulmonary Disease /Asthma)
- Other, less common:
  - ✓ Nasal sprays with metered pump (measuring function)
  - ✓ Tablet delivery system with controller for pain management
  - ✓ Advanced Therapy Medicinal Products (ATMPs) (e.g. autologous cultured chondrocytes embedded in a biodegradable matrix or scaffold)

Drug-device combinations – Guidance for applicants

Guideline on the quality requirements for drug-device combinations

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CMDh

21 October 2019 Rev.1
EMA/37991/2019
Human Medicines Evaluation Division

Questions & Answers on Implementation of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations ((EU) 2017/745 and (EU) 2017/746)

This Question and Answer (Q&A) document provides practical considerations concerning the implementation of the medical devices and the in vitro diagnostic medical devices regulations.

This document has been produced to provide guidance to Applicants as regards aspects falling within the scope of the Agency's activities and should be read in conjunction with the new medical devices Regulation (EU) 2017/745, and the new in vitro diagnostic medical devices Regulation (EU) 2017/746. The medical devices regulation (MDR) and in-vitro diagnostics regulation (IVDR) replace the three existing Directives (93/42/EEC, 98/79/EC and 90/385/EEC) for medical devices. The Regulations entered into force on 25 May 2017; however, they will have a transition period to allow manufacturers, notified bodies and authorities to comply with the changes and will come into full application on 26 May 2020 for medical devices and 26 May 2022 for in vitro diagnostics. These regulations lay down roles and responsibilities for EMA and National Competent Authorities (NCA) for medicinal products, as follows:

- For medical devices incorporating a medicinal substance (with action ancillary to the device)[1] the notified body shall seek a scientific opinion from either the NCAs or EMA. The notified body shall seek the opinion of EMA for medicinal products falling exclusively within the scope of centralized procedure[2], or that incorporate human blood or plasma derivatives
- For devices that are composed of substances or of combinations of substances that are systemically absorbed by the body in order to achieve their intended purpose, the notified body shall seek a scientific opinion from either the NCAs or the EMA[3]
- For companion diagnostics, the notified body shall seek a scientific opinion from either the NCAs or the EMA[4]
- The European Commission may consult EMA when deliberating on the regulatory status of products in borderline cases involving medicinal products[5].

[1] Regulation 2017/745 Annex IX 5.2
[2] Annex 1, Regulation (EC) No 726/2004
[3] Regulation 2017/745 Annex IX 5.4
[4] Regulation 2017/746 Annex IX 5.2, Annex X 3(b)

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Draft guideline on quality requirements released on 3 June 2019

- Scope: drug-device combinations (integral, co-packaged or referenced in the medicinal product information)

Q&As published February and October 2019

- Scope: drug-device combinations, scope to be expanded as further updates are published

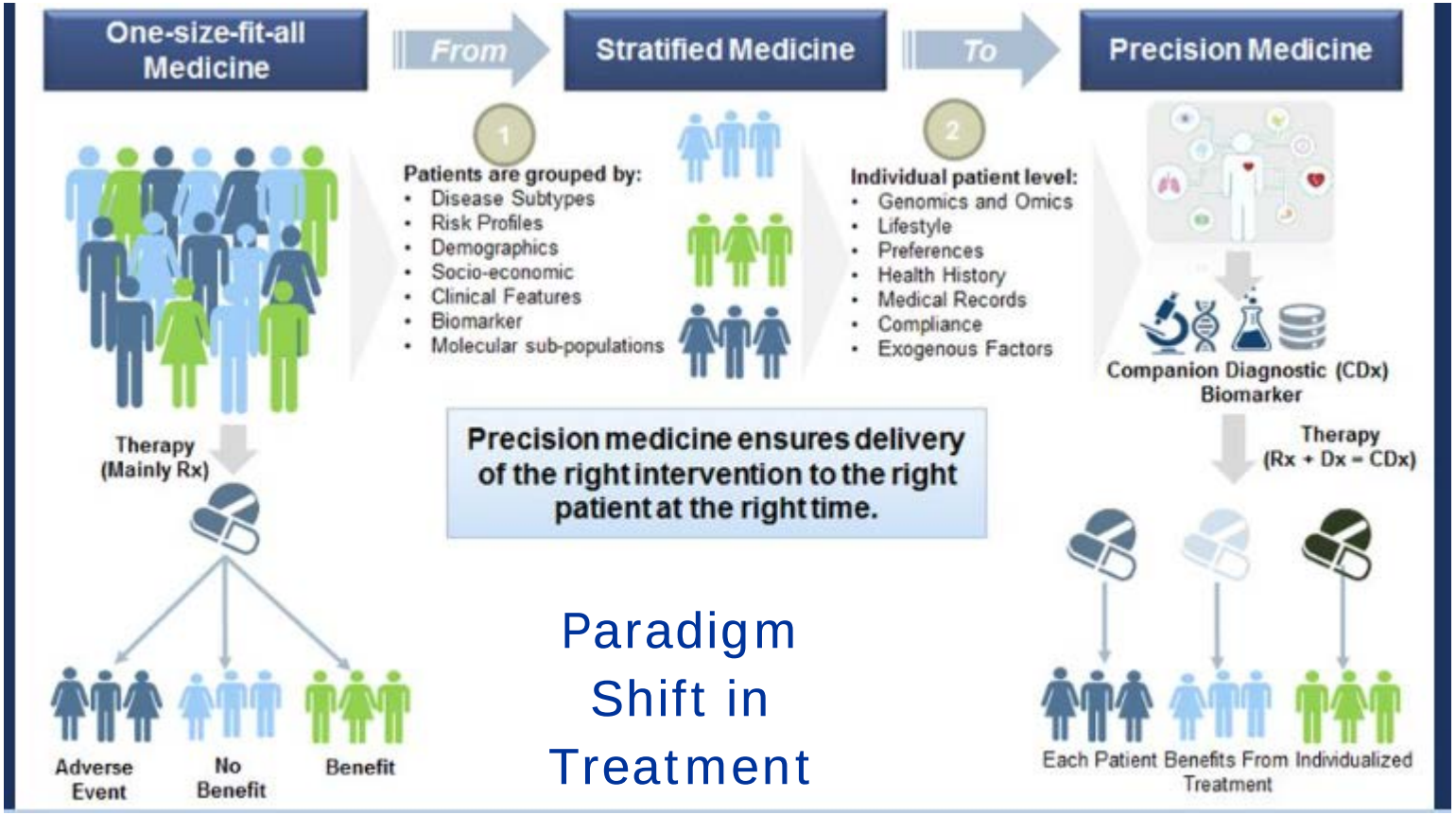
2. NEW EMA consultation procedure: Medical devices composed of substances that are systemically absorbed to achieve the intended action

- Formulation similar to a medicine (e,g: some cough syrups, laxatives, fat binding etc)
- Principal intended action is not achieved by a pharmacological, immunological or metabolic means

Increased safety and requirements as considered “higher risk”:

- By Notified body review
- Compliance with Directive 2001/83/EC for absorption, metabolism, toxicity etc
- If systemic absorption - additional scrutiny by medicines authorities

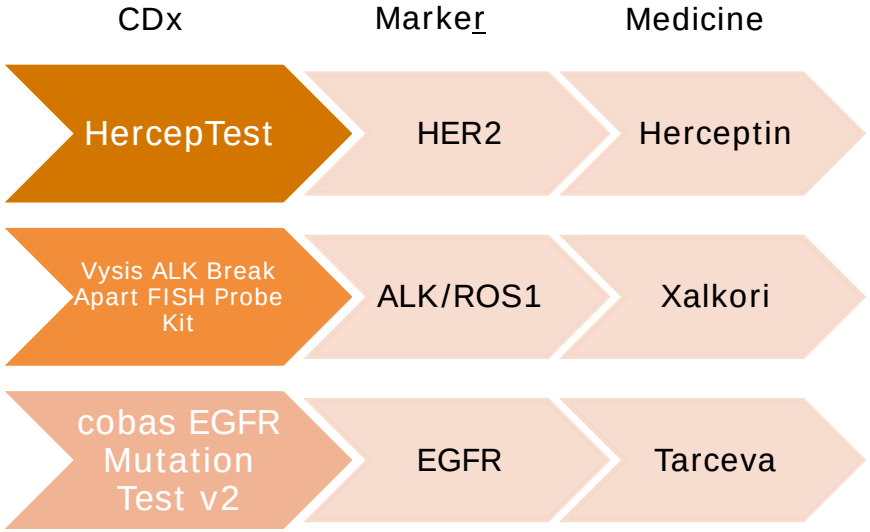
2. NEW EMA consultation procedures: Companion diagnostics



Paradigm Shift in Treatment

2. NEW EMA consultation procedures: Companion diagnostics and personalised medicines

- Tailor therapy to patients to obtain best efficacy response and highest safety margin
- Increased requirements for companion diagnostics:
  - Notified body review (NEW)
  - Additional scrutiny by medicines authorities on suitability (NEW)



CDx – Companion diagnostic
HER2 - human epidermal growth factor receptor 2
ALK/ROS1 - anaplastic lymphoma kinase
EGFR - Epidermal growth factor receptor

3. Borderline products
Keep up with new technology in Healthcare?

Medical device industry in EU:
675,000 employed in
27,000 companies, of which
95% are Small, medium Enterprises

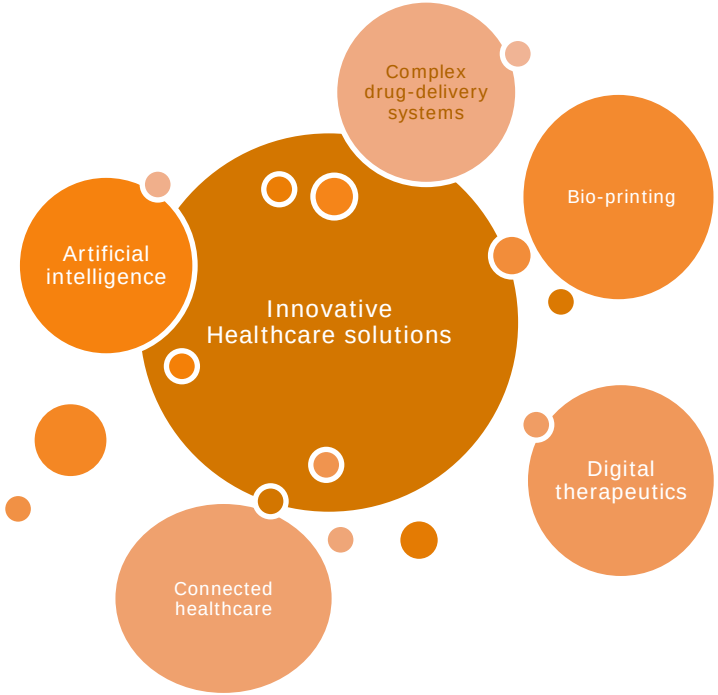
EPO technical fields with most applications 2018 (top 10)

1	2	3	4	5
Medical technology	Digital communication	Computer technology	Electr. Machinery, apparatus, energy	Transport
13 795	11 940	11 718	10 722	9 039
+5.0%	+0.7%	+3.3%	+4.7%	+5.9%
6	7	8	9	10
Measurement	Pharmaceuticals	Biotechnology	Other special machines	Organic fine chemistry
8 744	7 441	6 742	6 379	6 233
+9.3%	+13.9%	+12.1%	+10.9%	–3.6%

European Patent Office 2019

3. Borderline products

"Blurring of applicable frameworks"



- Classification challenges as product complexity increases
- Member states responsible for classification
- Mode of action of the product will determine which framework it falls under

European commission can consult EMA when deliberating the status of products on the borderline with medicines

Future Opportunities

EMA Regulatory Science Strategy 2025

Create an integrated evaluation pathway for assessment of medical devices, in vitro diagnostics and borderline products

- Mechanism for early interaction with EMA, device authorities and NBs to obtain joint advice during development
- Building a EU network of expertise to provide support throughout the continuum of product development and lifecycle
- Regulatory requirements and guidance development

EMA Medical Devices Webpages

Acknowledgements:

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