CORE-MD

Coordinating Research and Evidence for Medical Devices

Exploiting IT tools to retrieve alerts and reports of high-risk medical devices

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Medical Device Regulation (2017/745): towards increased safety of MD

Reinforce **surveillance** and **management** of the entire MD **life cycle**

Reduce ambiguity with clear **classifications** and **definitions**

European Database on Medical Devices (**EUDAMED**)

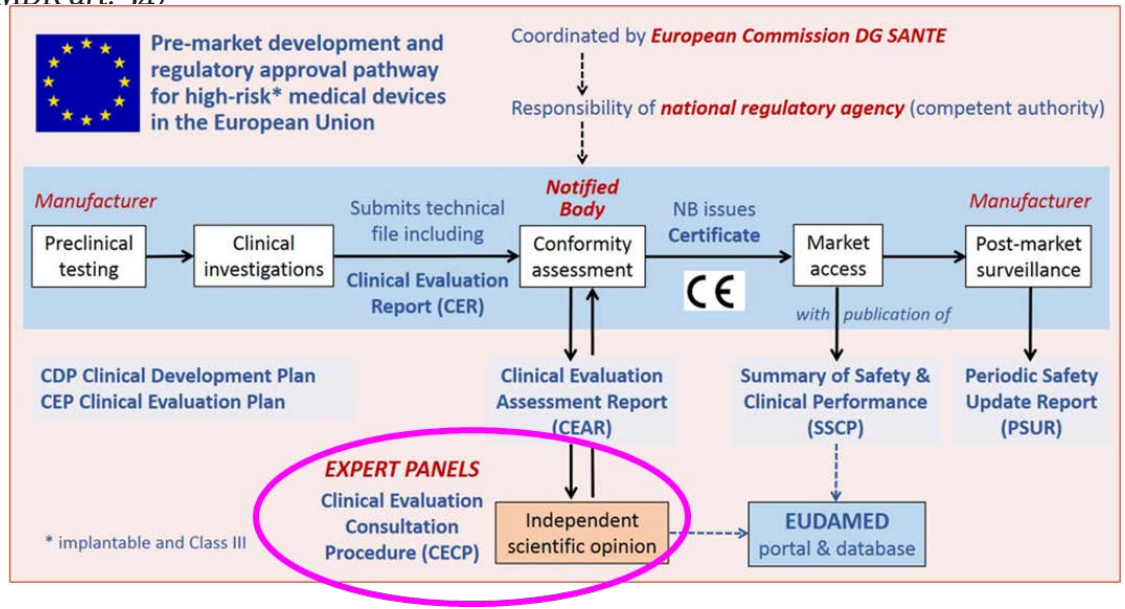
Unique Device Identifiers (**UDI**s)

Increase **clinical investigation requirements** and manage risk to ensure **patient safety**

Improve **transparency** and **traceability**

Increase investigation requirements: role of Expert panels

Expert Panels will scrutinize the clinical evidence submitted by manufacturers for Class III implantable medical devices and Class IIb active medical devices intended to administer and/or remove a medicinal product *(MDR art. 54)*

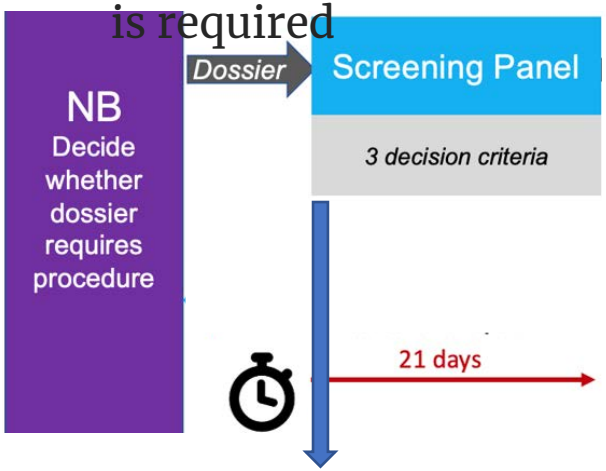


[Fraser et al. Eur Heart J 2020; 41(27):2589–2596]

Expert panels: Clinical Evaluation and consultation procedure

Step 1: decision by two experts whether opinion is required

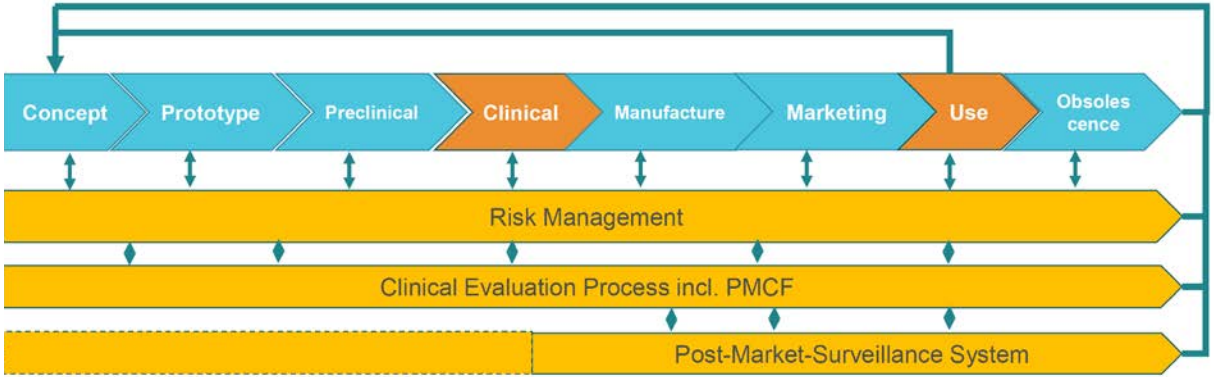
Step 2: scientific opinion on CEAR



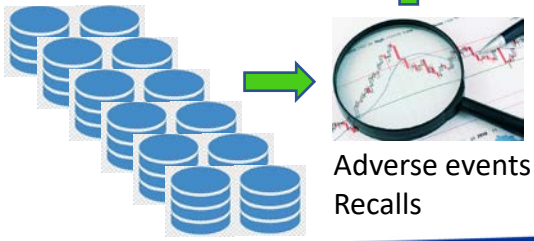
1) **Novelty** of the device/clinical procedure **and possible major clinical/health impact**
2) Significant adverse **change in the benefit-risk profile** of a specific **category or group** of devices, due to scientifically valid health concerns (MDR Annex IX, paragraph 5.1.c)
3) Significant **increased rate of serious incidents** reported for a specific **category of group** of devices

Reinforce surveillance and management of the entire MD life cycle

Post-Market Surveillance seen in the context of the entire medical device life cycle, where safety (positive acceptable Benefit-Risk-Ratio) needs to be assessed in multiple scenarios in a continuous way.



*The post-market surveillance system shall be suited to **actively** and **systematically** gathering, recording and analysing relevant data on the quality, performance and safety of a device throughout its **entire lifetime**, and to drawing the necessary conclusions and to determining, implementing and monitoring any preventive and corrective actions (MDR Art. 83).*



Adverse events
Recalls

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Need for **data aggregation** tools to generate **new value** for **regulatory purposes** from existing open access information relevant to **medical device malfunctions**!

- Different definitions
- Different reporting criteria
- No common reporting forms
- Multiple languages and alphabets
- Different reporting timelines
- Different nomenclatures
- Multiple UDIs systems

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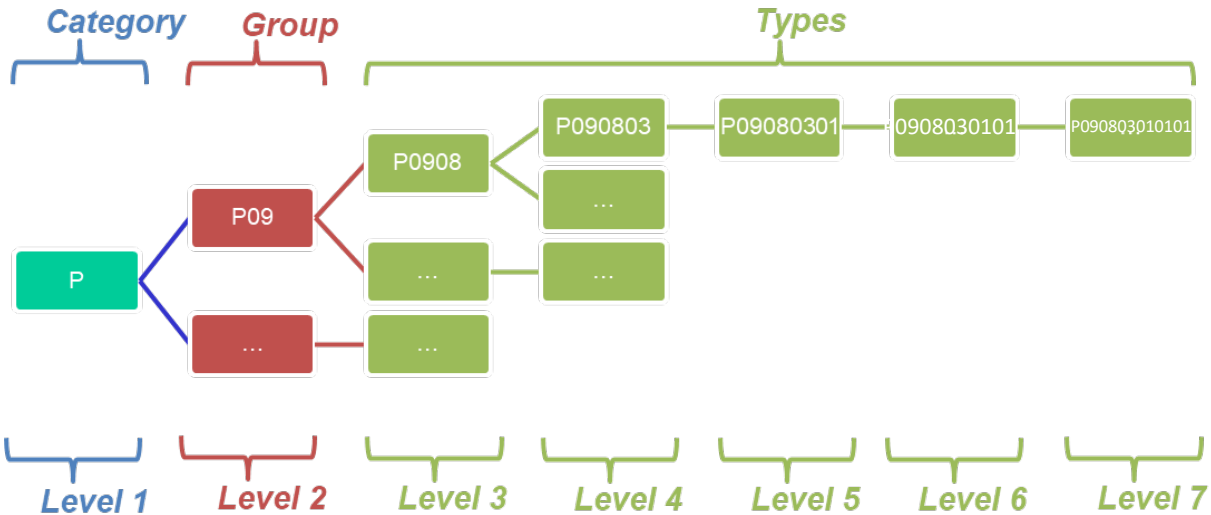
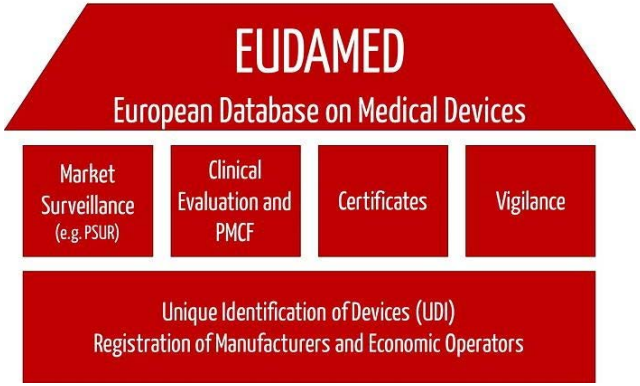
Reduce ambiguity: European Medical Device Nomenclature

The Italian **“Classificazione Nazionale Dispositivi medici” (CND)** has become the basis for the **European Medical Device Nomenclature (EMDN)**



Enhance transparency and coordination: EUDAMED database



1. Actors registration
2. UDI/Devices registration
3. Notified Bodies and Certificates
4. Clinical Investigations and performance studies
5. Vigilance and post-market surveillance
6. Market Surveillance

EUDAMED Limitations

No historical data will be present

Only EU data, no links with other regulatory jurisdictions outside EU

*"the European Commission, in collaboration with the Member States, shall put in place systems and processes to actively **monitor the data available** in order to **identify trends, patterns or signals** that may reveal new risks or safety concerns." (MDR, article 90)*

The aim of the CORE-MD PMS tool

- To **automatically collect** publicly available curated regulatory information on **alerts and recalls** from the official websites of EU competent authorities, as well as from non-EU regulatory authorities, in a single database

- To attribute proper **EMDN classification** to the medical devices relevant to each of these records

- To allow **multiple queries** to the generated database

- To display **results** in both an **aggregated way,** for **capturing possible trends**, as well as **in detail** for **further analysis.**

EU countries with available data

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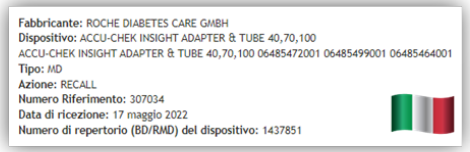
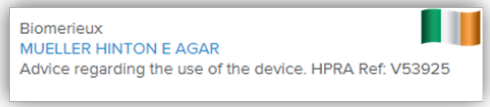
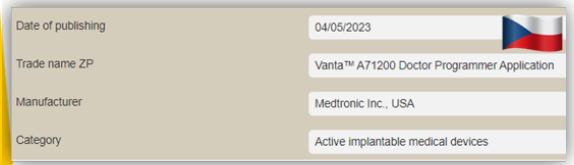
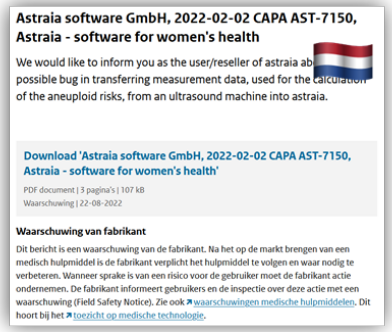
Countries with **periodically updated** safety notices: **15/27 +1**

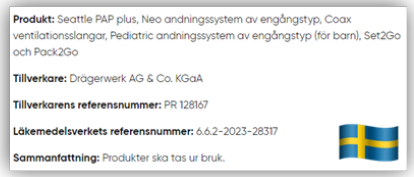
Data in input: Safety notices published from official National Authorities websites



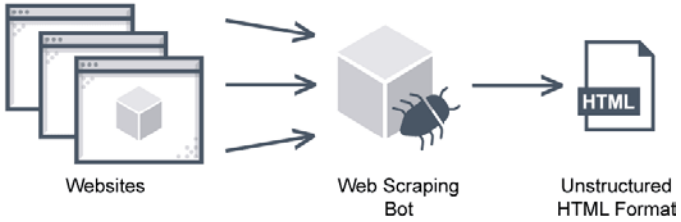








Country-specific
Web-scraping approaches
with automated update



- **Unstructured information** about manufacturers and devices
- **Unavailability** of a reference list of devices on the market
- **Different adopted nomenclatures** for devices, i.e. GMDN
- **Different languages**

Need to identify:
Manufacturer name
Device name

Need to attribute
EMDN code

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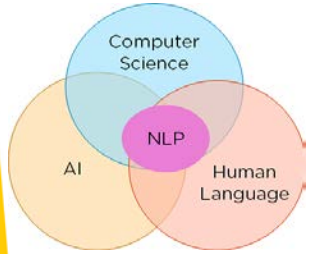
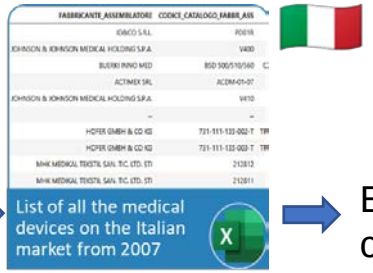
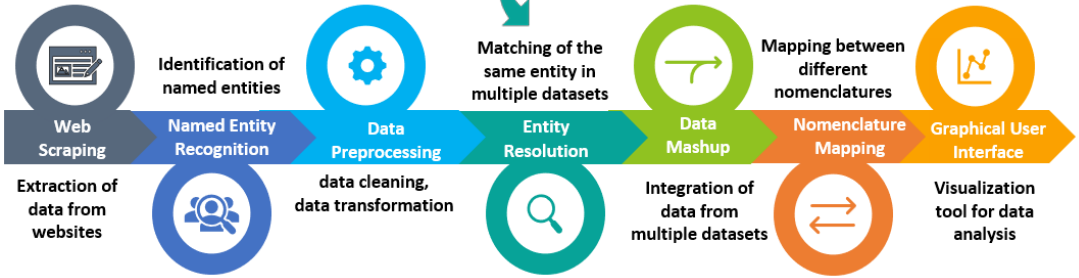
Natural Language Processing helps!



If a reference list of devices on the market was not available for that specific country, we considered the list of devices for Italy.



EMDN code



If **manufacturer and device name** were not clearly retrievable:

- Regular Expressions
- Transformer models

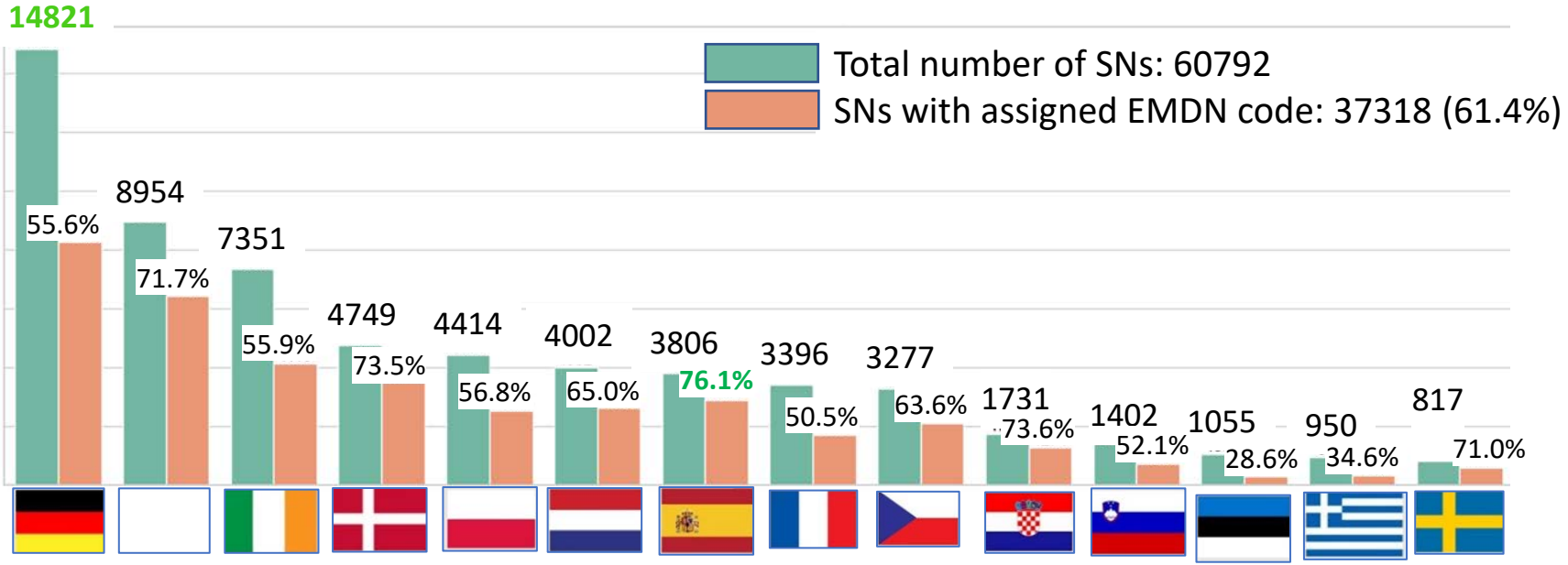
If the adopted **nomenclature** differs from EMDN:

- nomenclature mapping algorithm (GMDN→EMDN)
- manual mapping

[Ren et al. Ther Innov Regul Sci 2023]

[Ren and Caiani. Proc. IEEE BHI Conf. 2023]

Safety notices from EU in PMS CORE-MD Database



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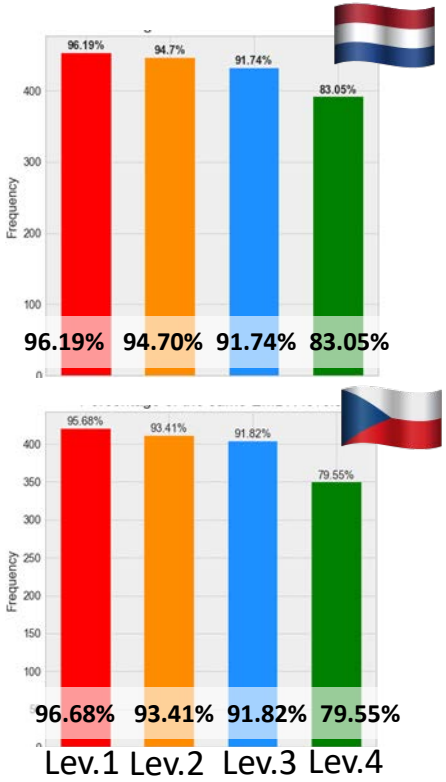
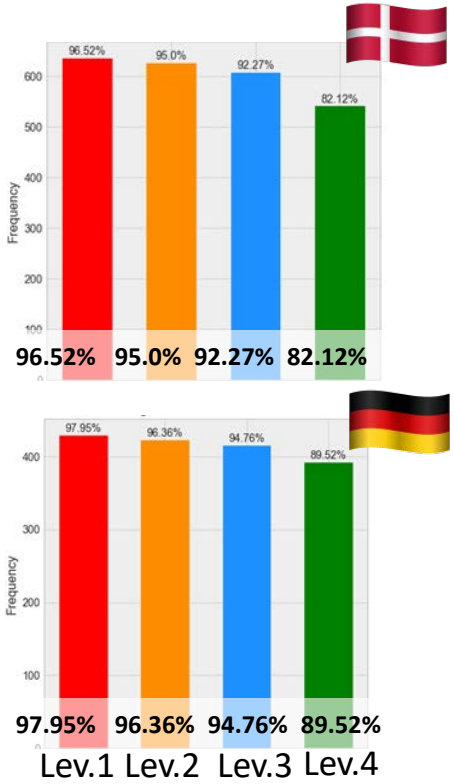
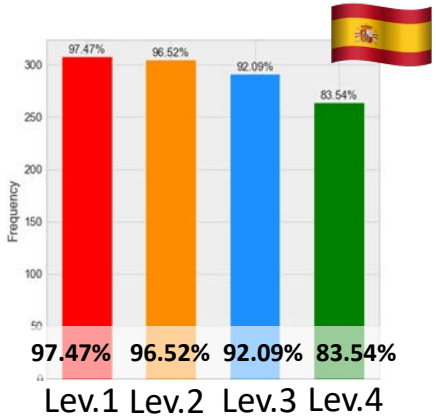
Example of validation of EMDN code attribution







Up to Level 3:
correctness > 90%

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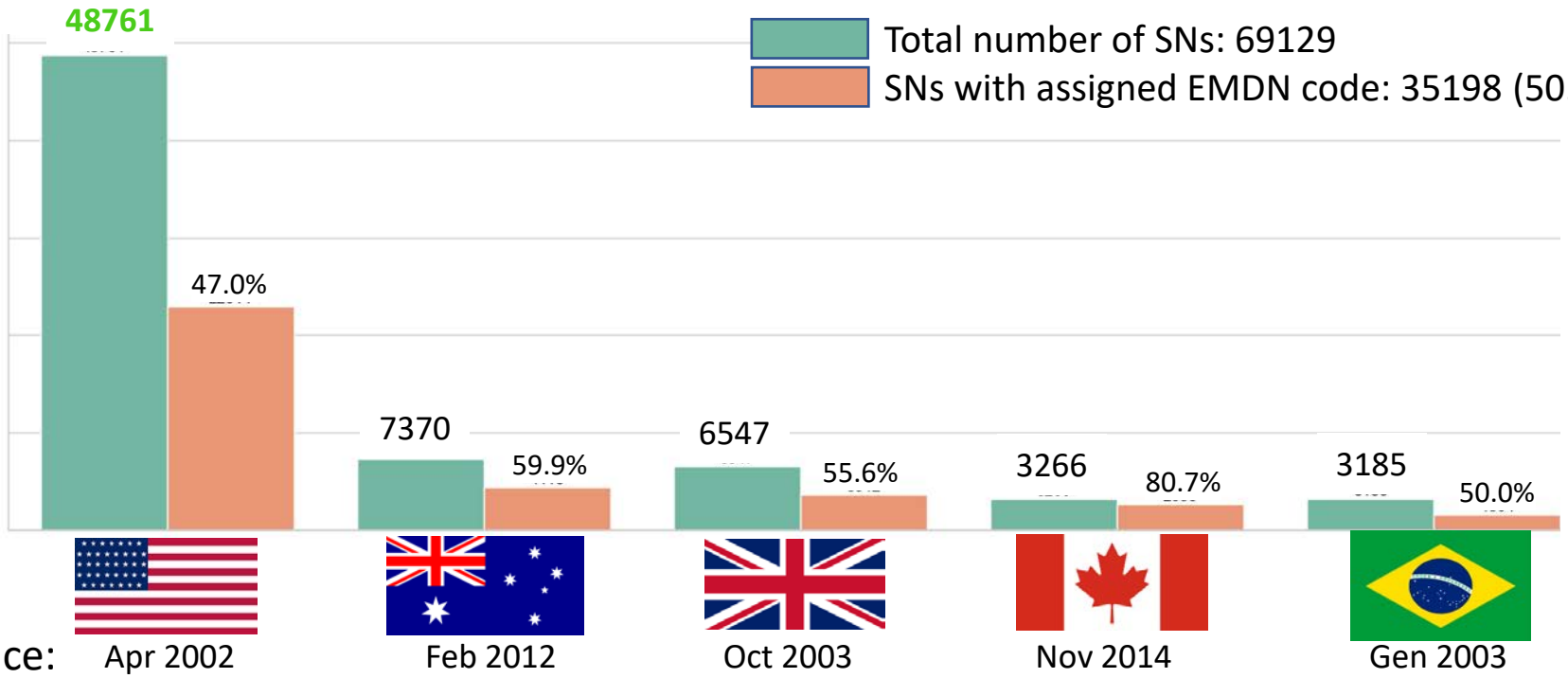
Safety notices from extra-EU in PMS CORE-MD Database



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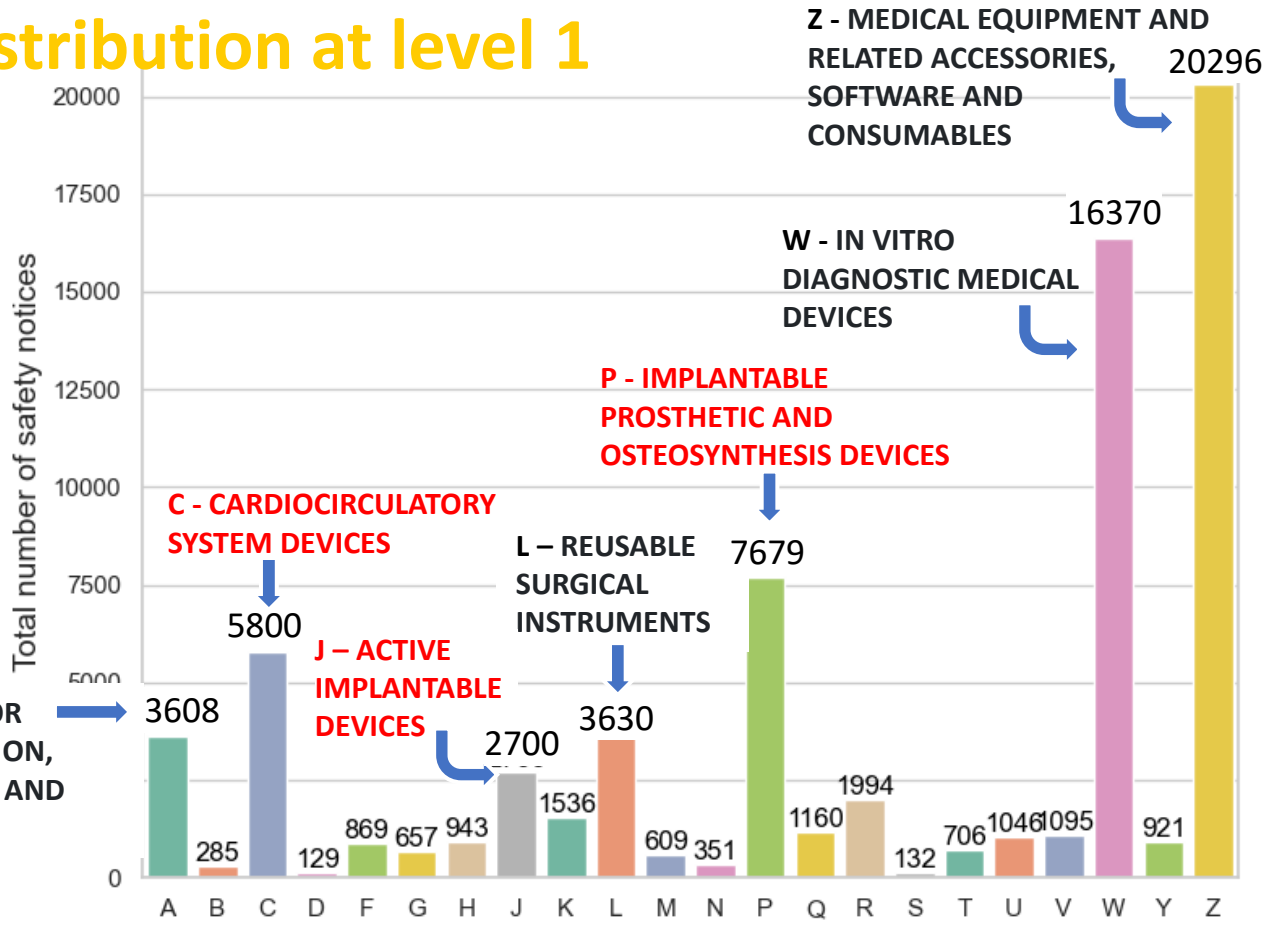
EMDN code distribution at level 1

Total number of Safety Notices with assigned EMDN code: **72516**



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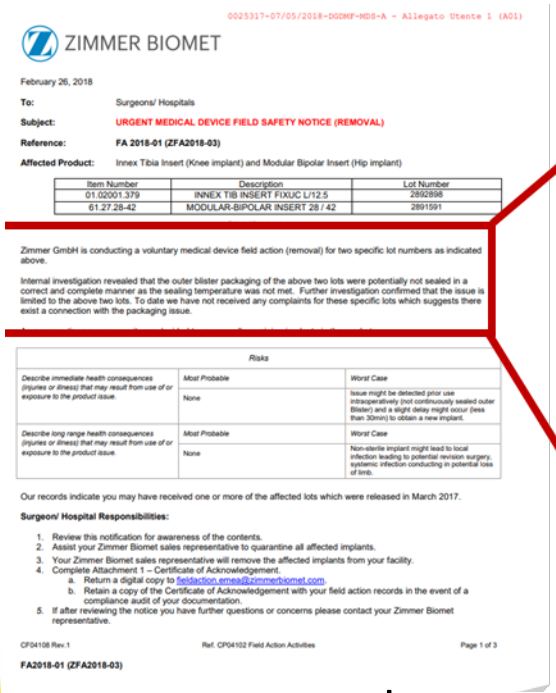
- Live Demo

Possible utilization of Query results



0025317-07/05/2018-DGDMF-MDS-A - Allegato Utente 1 (A01)

ZIMMER BIOMET

February 26, 2018

To: Surgeons/ Hospitals

Subject: URGENT MEDICAL DEVICE FIELD SAFETY NOTICE (REMOVAL)

Reference: FA 2018-01 (ZFA2018-03)

Affected Product: Innex Tibia Insert (Knee implant) and Modular Bipolar Insert (Hip implant)

Item Number	Description	Lot Number
01.02001.379	INNEX TIB INSERT FIXUC L/12.5	2892898
61.27.28-42	MODULAR-BIPOLAR INSERT 28 / 42	2891591

Zimmer GmbH is conducting a voluntary medical device field action (removal) for two specific lot numbers as indicated above.

Internal investigation revealed that the outer blister packaging of the above two lots were potentially not sealed in a correct and complete manner as the sealing temperature was not met. Further investigation confirmed that the issue is limited to the above two lots. To date we have not received any complaints for these specific lots which suggests there exist a connection with the packaging issue.

Risks

Describe immediate health consequences (injuries or illness) that may result from use of or exposure to the product issue.	*Most Probable*	*Worst Case*
	None	Issue might be detected prior use intraoperatively (not continuously sealed outer Blister) and a slight delay might occur (less than 30min) to obtain a new implant.
Describe long range health consequences (injuries or illness) that may result from use of or exposure to the product issue.	*Most Probable*	*Worst Case*
	None	Non-sterile implant might lead to local infection leading to potential revision surgery, systemic infection conducting in potential loss of limb.

Our records indicate you may have received one or more of the affected lots which were released in March 2017.

Surgeon/ Hospital Responsibilities:

1. Review this notification for awareness of the contents.
2. Assist your Zimmer Biomet sales representative to quarantine all affected implants.
3. Your Zimmer Biomet sales representative will remove the affected implants from your facility.
4. Complete Attachment 1 – Certificate of Acknowledgement.
   a. Return a digital copy to fieldaction.emea@zimmerbiomet.com.
   b. Retain a copy of the Certificate of Acknowledgement with your field action records in the event of a compliance audit of your documentation.
5. If after reviewing the notice you have further questions or concerns please contact your Zimmer Biomet representative.

CF04108 Rev.1 Ref. CP04102 Field Action Activities Page 1 of 3

FA2018-01 (ZFA2018-03)

Attribution of IMRDF – Adverse Event nomenclature

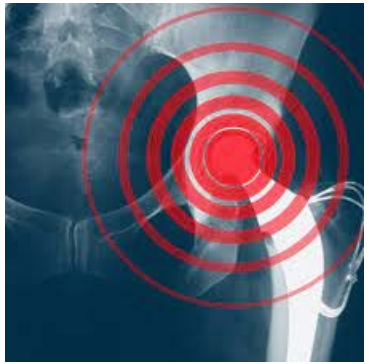
Zimmer GmbH is conducting a voluntary medical device field action (removal) for two specific lot numbers as indicated above.
Internal investigation revealed that the outer blister packaging of the above two lots were potentially not sealed in a correct and complete manner as the sealing temperature was not met. Further investigation confirmed that the issue is limited to the above two lots. To date we have not received any complaints for these specific lots which suggests there exist a connection with the packaging issue.

A020503 – Unsealed Device Packaging

- Improved understanding of risks related to a specific MD category
- Safety signal detection?

Possible utilization of Query results

Combined analysis with Medical Registry Data



Outlier detection

Features for early detection

Conclusions

- The availability of tools based on **Natural Language Processing** can help dealing with **partially unstructured** and **partially incomplete** information, such as those provided by the safety notices, to generate new potential value for regulatory purposes.

- Such tools could fill the temporal gap until **Eudamed** would become fully operational, **and beyond** by linking different jurisdictions.

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Acknowledgments


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MS student


Prof. Maristella Matera


Prof. Cinzia Cappiello

CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945260

For more information, visit: www.core-md.eu

ESC
EFORT
Biomedical Alliance in Europe
European Academy of Paediatrics
EPF European Patients Forum
Leiden University Medical Center
University of Oxford
Region Uppsala
RCSI University of Medicine and Health Sciences
INSELSPITAL Universitätsspital Bern Hôpital universitaire de Berne
KU LEUVEN
UMIT TIROL
University of Gothenburg
Politecnico Milano 1863
HPRA
LÆGEMIDDELSTYRELSEN Danish Medicines Agency
National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport
Istituto Superiore di Sanità
aihta HTA Austria Austrian Institute for Health Technology Assessment GmbH
AETSA
TEAM NB

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