Vaccines, reporting of adverse events: transparency and independancy

Vaccine Academy

BRUSSELS

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Agenda

1. FAMPH and EMA
2. LEGAL CONTEXT
3. VACCINOVIGILANCE
4. ADVERSE EVENT FOLLOWING IMMUNISATION
5. SPONTANEOUS REPORTING IN BELGIUM
6. TRANSPARENCY

Federal Agency for Medicines and Health Products

The FAMHP is a public interest organisation with legal personality, classified under category A*, as referred in the law of March 16 1954 relating to the control of certain public interest organisations

The FAMHP plays an essential role in the **protection of public health**. One of these missions is :

Ensuring, from development to use, the **quality**, **safety** and **efficacy** of medicines for human, including vaccines

* Law concerning the establishment and functioning of the Federal Agency for Medicines and Health Products of July 20 2006 (B.S. - M.B. of September 8 2006)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The EMA is a decentralised agency of the European Union (EU), located in London. It began operating in 1995. The Agency is responsible for the scientific evaluation, supervision and safety monitoring of medicines developed by pharmaceutical companies for use in the EU

EMA protects public and animal health in 28 EU Member States, as well as the countries of the European Economic Area, by ensuring that all medicines available on the EU market are safe, effective and of high quality

LEGAL CONTEXT

Reinforcement of the pharmacovigilance for the human medicines, at the European level:

The new pharmacovigilance legislation, which came into effect in **July 2012**, was the biggest change to the regulation of human medicines in the European Union (EU) since 1995

- Adoption of new Directive and Regulation by the European Parliament and Council of Ministers in **December 2010**, bringing about significant changes in the safety monitoring of medicines across the EU: **DIRECTIVE 2010/84/EU** and **REGULATION (EU) No 1235/2010**
- In October 2012, the pharmacovigilance legislation was further amended following review of the withdrawal of the medicine Mediator (benfluorex). The amendments aimed to further strengthen of the protection of patient health by allowing prompt notification and assessment of safety issues: **Regulation (EU) No 1027/2012** (applicable since 05.06. 2013) and **Directive 2012/26/EU** (applicable since 28.10.2013)
- Practical measures to facilitate the performance of pharmacovigilance in accordance with the legislation are available in the **Guideline on Good Pharmacovigilance Practices (GVP)**

Transposition in the Belgian legal framework :

- **LAW modifying the Law of 25 March 1964 concerning the medicinal products**, published on 03.08.2012, and related **Royal Decrees**

VACCINOVIGILANCE

Activities related to :

Detection

Assessment

Prevention

Communication

of adverse events of vaccines

SAFETY

VACCINOVIGILANCE

Objectives of vaccinovigilance

- Early detection of **new** adverse events
- Detection of any **increase of the frequency** of known adverse events
- Identification of **risk factors** and **potential mechanisms** for adverse events
- Assessment and communication of the **benefit/risk balance** of authorised vaccines

VACCINOVIGILANCE

Why Vaccinovigilance?

The complete safety profile of a vaccine is known at the time of its marketing authorisation

No !

VACCINOVIGILANCE

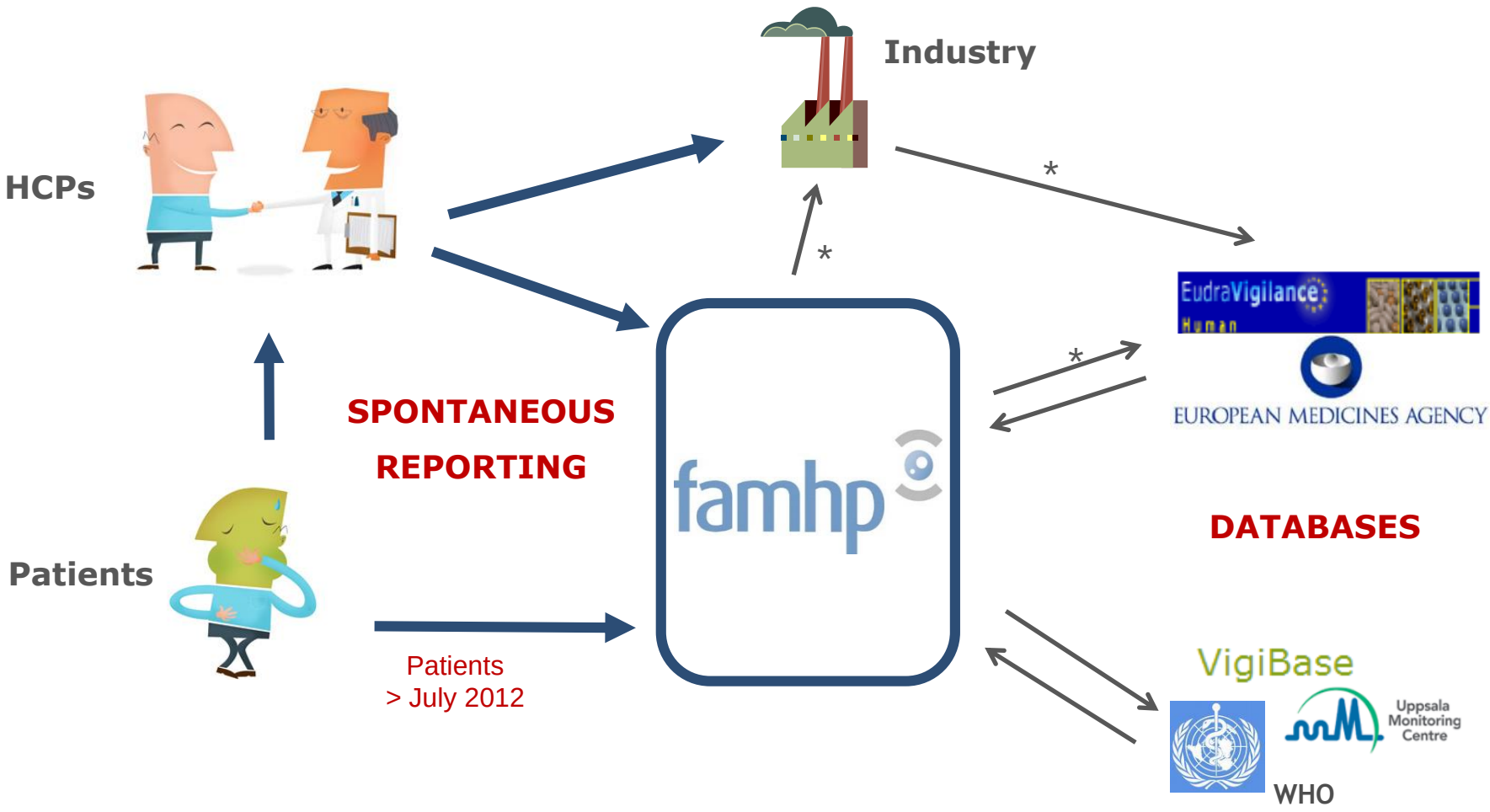
Why Vaccinovigilance?

Before marketing authorisation, evidence of safety and efficacy is limited to the results from clinical trials, where subjects are selected carefully and followed up very closely under controlled conditions for a limited length of time

After authorisation the vaccine will be used in a large number of patients and with other medicines/vaccines. Certain adverse events may emerge in such circumstances, such as **rare adverse events**

It is therefore essential that the safety of all medicines is monitored throughout their use in healthcare practice

VACCINOVIGILANCE IN BELGIUM



* Mandatory notification of AE (serious AE <15 d; non-serious AE <90d)

VACCINOVIGILANCE IN BELGIUM

From Spontaneous Reporting to Regulatory measures

AE reports

famhp

Independant Scientific assessment

Databases

EudraVigilance Human

Uppsala Monitoring Centre

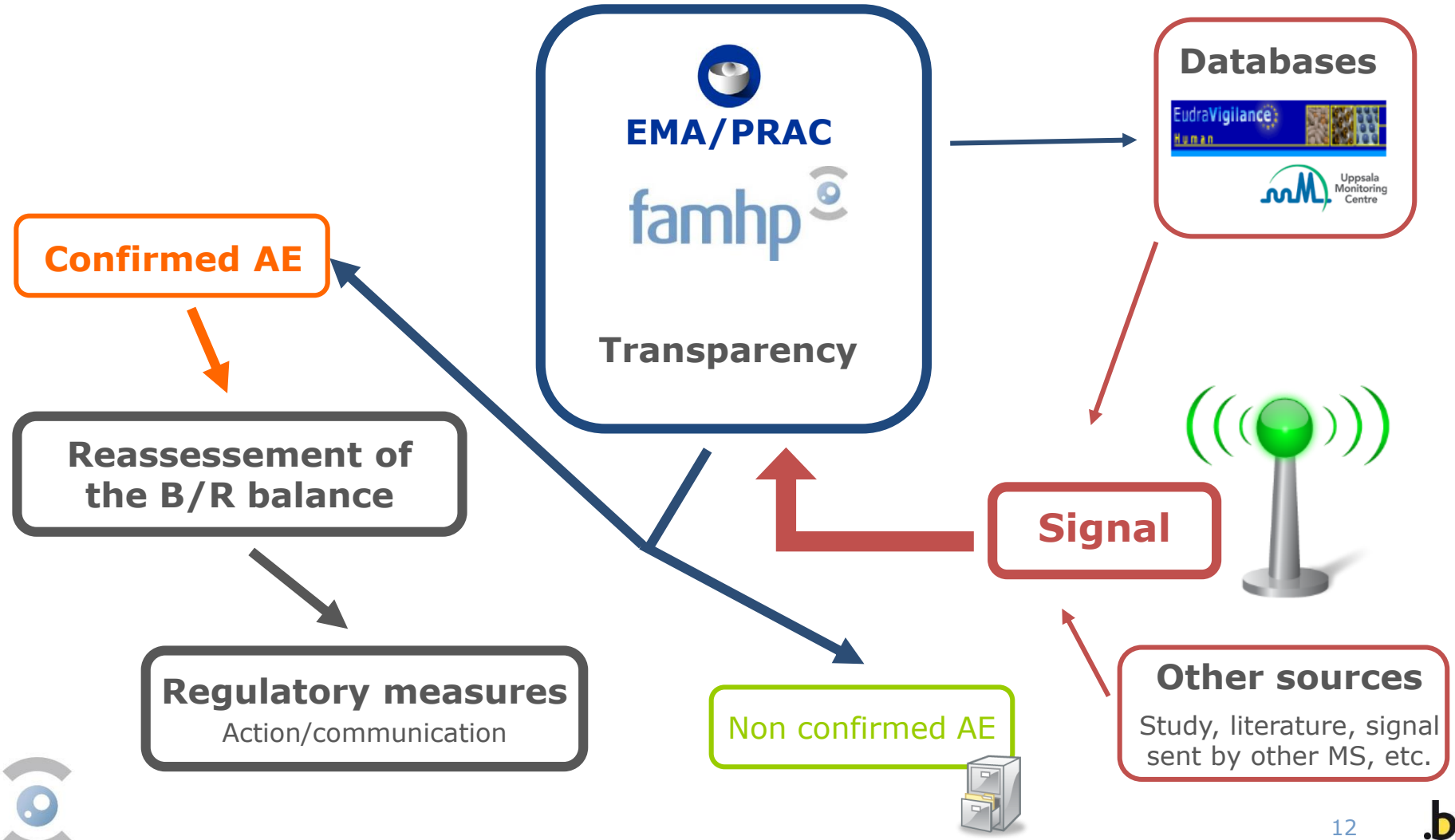
Signal

Other sources

Study, literature, signal sent by other MS, etc.

VACCINOVIGILANCE IN BELGIUM

From Spontaneous Reporting to Regulatory measures



VACCINOVIGILANCE IN BELGIUM

Independent assessment of safety data by FAMHP experts to assess the B/R balance of vaccines

Type of data

- **Regulatory tools** : PBRER, Renewal
- **Studies and statistical tools**:
  - Post-Autorisation Safety Studies (PASS):cohort study, case-control study, meta-analysis, registry, etc.
  - Observed vs expected analysis
  - Clinical/non-clinical studies, etc.
- **Case by case**: cumulative review, literature review, etc.

VACCINOVIGILANCE IN BELGIUM

Independent assessment of safety data by FAMHP experts to assess the B/R balance of vaccines

Source of data

- Spontaneous reporting and data from international pharmacovigilance databases
- Data from Marketing Authorisation Holders (MAH)
- Literature
- External experts (academic)

VACCINOVIGILANCE IN BELGIUM

Reinforcement of Vaccinovigilance in BE

- At FAMHP level, vaccine is recognised as one of the three **Domains of Excellence**
- Belgium is involved as **(Co)-Rapporteur at the Pharmacovigilance Risk Assessment Committee (PRAC)** for **20 vaccines**. This allows a close monitoring of safety and efficacy of vaccines which are authorised in the EU through the :
  - Assessment of PSUR and Renewal
  - Assessment of RMP (Risk Management Plan) and PASS (Post-Autorisation Safety Study)
  - Signal monitoring

VACCINOVIGILANCE IN BELGIUM

Reinforcement of Vaccinovigilance in BE

- Participation of FAMHP's experts at **the Superior Health Council**
- Collaboration with organisations involved in vaccine implementation in Belgium:
  - **ONE** : collection and transfer of reports of AE following vaccination to FAMHP, reinforcement of the message to parents regarding the importance to report AEs (Children Notebook)
  - **Kind & Gezin**: contact point at Vaccinet

ADVERSE EVENT FOLLOWING IMMUNISATION

Frequent and minor AEs of vaccines

General disorders:
- pyrexia
- irritability
- malaise

Local disorders:
- redness
- swelling
- pain

- Usually within 48h and of limited duration
- Nonspecific
- Variable frequency depending on the vaccine (>1%)

- Few impact regarding mordidity
- Moderate impact in terms of acceptance

ADVERSE EVENT FOLLOWING IMMUNISATION

Infrequent AEs of moderate severity of vaccines

Acute clinical picture of variable severity ($<1/10^2$ to $1/10^5$)

- Pyrexia> 40°c
- Febrile convulsions
- Hypotonic-hyporesponsive episodes

Low morbidity, no sequelae

- Few impact regarding mordidity
- Significative impact in terms of acceptance

ADVERSE EVENT FOLLOWING IMMUNISATION

Rare but severe AEs of vaccines

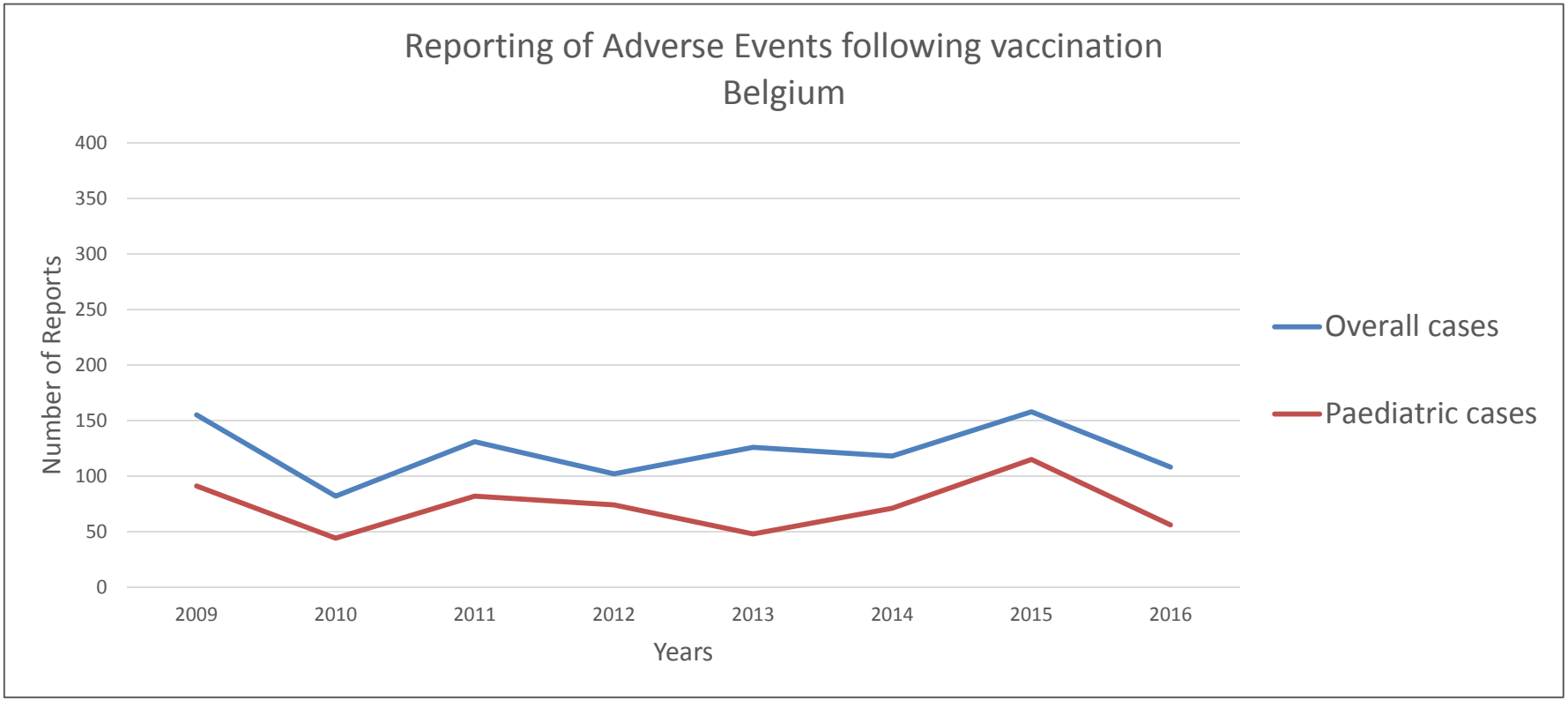
Acute clinical picture of variable severity ($<1/10^4$ to $1/10^7$)

Important morbidity, potentially life-threatening and/or resulting in sequelae or death

- Intussusception following rotavirus vaccination
- Narcolepsy following H_1N_1-AS03 vaccination
- Anaphylactic shock

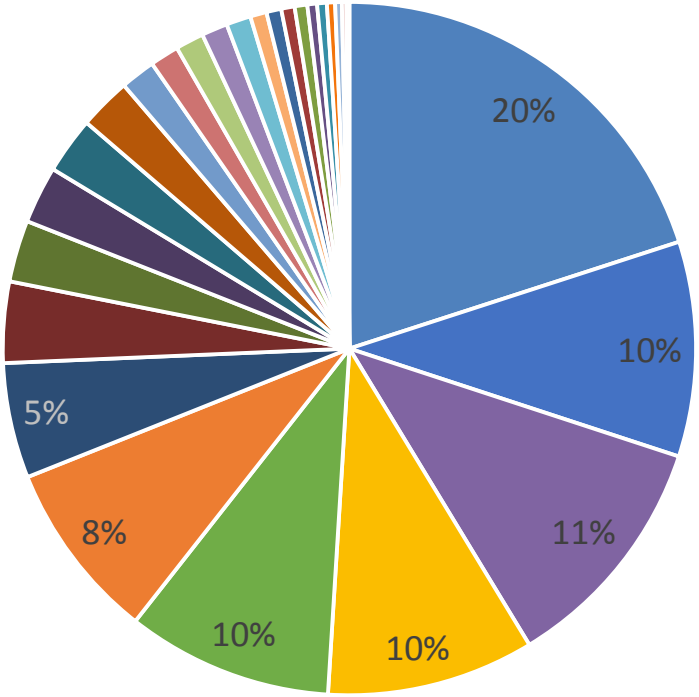
- High impact regarding mordidity
- Major impact in terms of acceptance

SPONTANEOUS REPORTING IN BELGIUM



SPONTANEOUS REPORTING IN BELGIUM

Mostly reported adverse events following vaccination are disorders such as:



- General disorders, administration site conditions
- Injury, poisoning and procedural complications

Pyrexia, fatigue, headache, pain, injection site reactions, incl. Extensive limb swelling

- Infections and infestations
- Nervous system disorders
- Gastrointestinal disorders
- Skin and subcutaneous tissue disorders
- Musculoskeletal and connective tissue disorders
- Respiratory, thoracic and mediastinal disorders

SPONTANEOUS REPORTING IN BELGIUM

Example: Infections as adverse events

In Belgium, **about 11% of reported AEs are related to infections and infestations, and mainly gastroenteritis** (~3% of total adverse events)

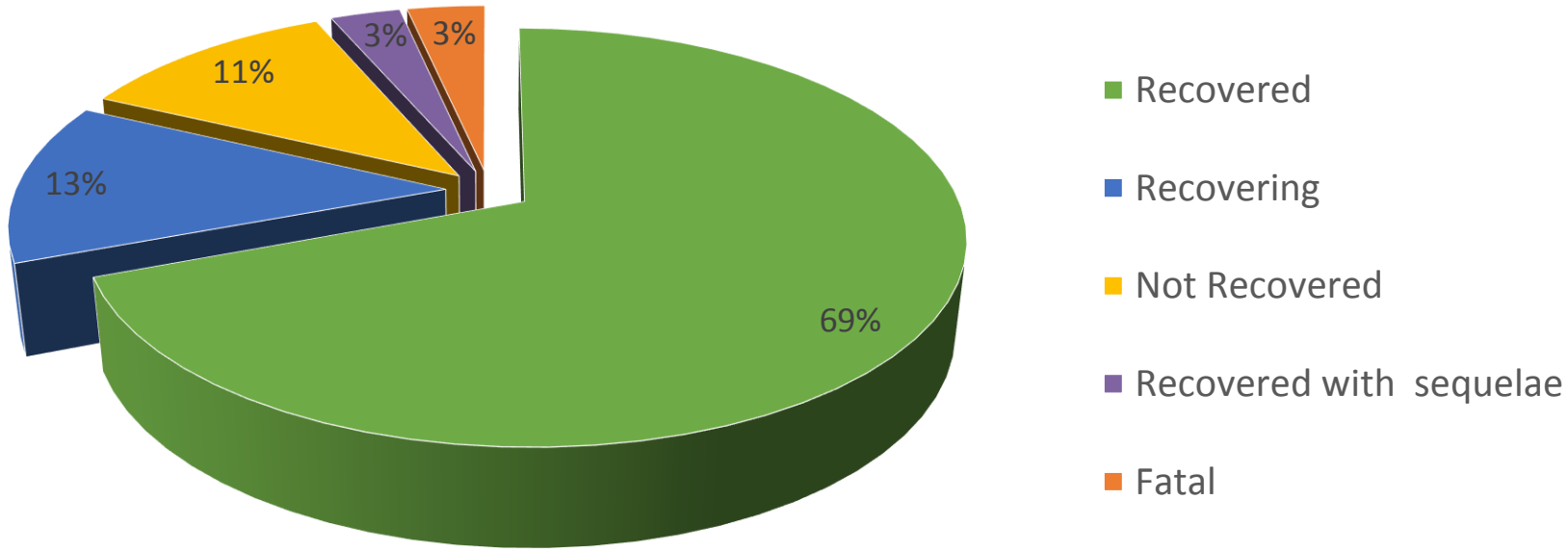
*Rotavirus vaccine**	Flanders	Wallonia	Brussels
Coverage (2012/2015)	94%	90%	77%
Impact†	89%	83%	75%

* Rotavirus vaccination is recommended by the Superior Health Council since 2007
† Impact: reduction of RV infection (laboratory-confirmed) in 2013-2014 compared to 2005-2006

Data from (1) WIV-ISP. Maladies infectieuses pédiatriques à prévention vaccinale, 2014; (2) ULB-Ecole de Santé Publique. Enquête de couverture vaccinale des enfants de 18 à 24 mois en Région de Bruxelles-Capitale, 2012; (3) WIV-ISP. Infectieziekten invlanderen; Trendsen ontwikkelingen, 2010-2012; (4) Vaxinfo. Enquête de couverture vaccinale en Wallonie, 2016

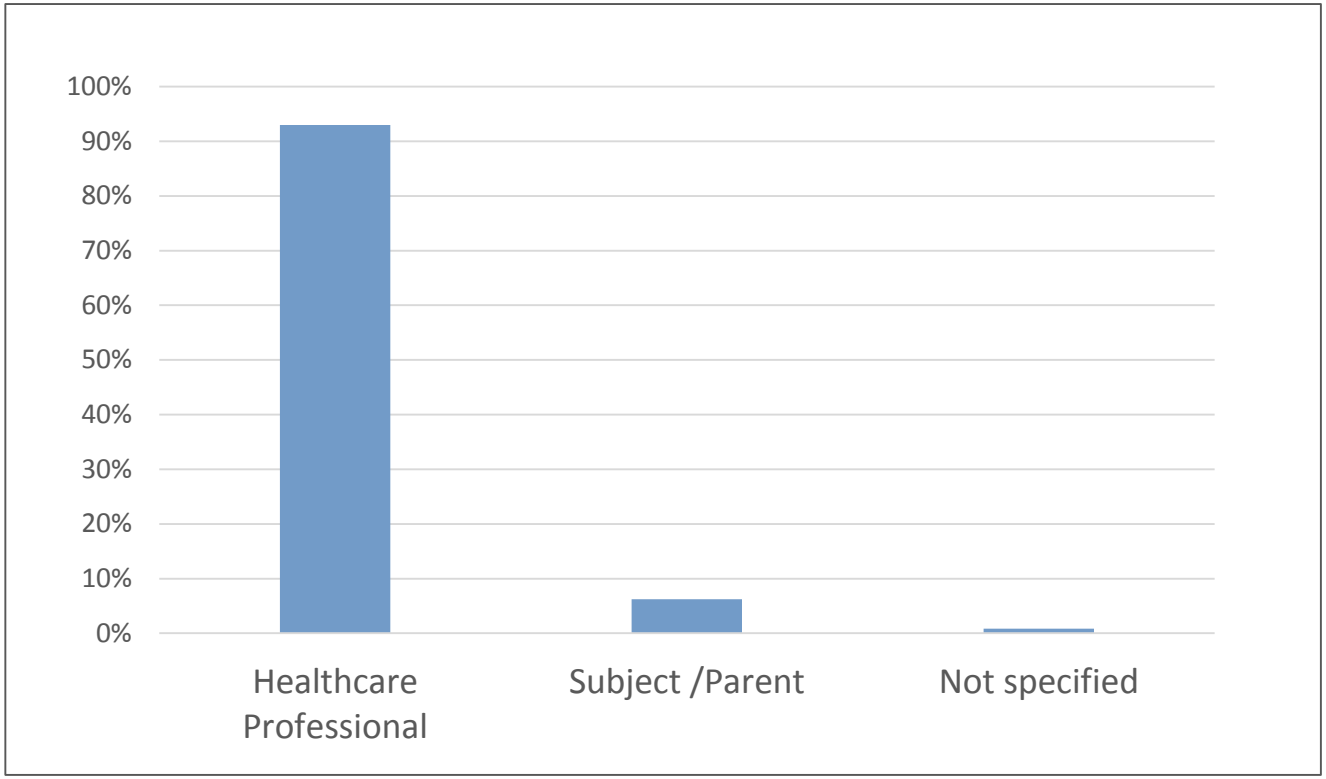
SPONTANEOUS REPORTING IN BELGIUM

The outcome of Adverse Events following vaccination is known for about 59% of reports



SPONTANEOUS REPORTING IN BELGIUM

Who reports adverse events following vaccination ?



SPONTANEOUS REPORTING IN BELGIUM

Campagne européenne relative à la notification d'effets indésirables

L'agence fédérale des médicaments et des produits de santé (afmps) participe à la campagne européenne de sensibilisation relative à la notification d'effets indésirables suspectés de médicaments. Un plus grand nombre de notifications d'effets indésirables suspectés permet de découvrir plus rapidement un éventuel problème et d'intervenir plus vite.

Découvrez en vidéo comment fonctionne la notification et comment vous contribuez ainsi à accroître la sécurité des médicaments.

TRANSPARENCY

At the EMA level

- Publishing on the EMA website (EPAR, SmPC, RMP summaries, meeting minutes, recommendations from PRAC, …)
- Since 2010 ATD (Access To Document) Policy (Policy 0043) - "reactive" release of any documents upon request
- Answering to questions asked by stakeholders by using a single webform to ask a question or request a document
- Inviting patients to committee meetings
- Since 2014 Clinical data publication (Policy 0070) – "proactive" publication of Clinical data

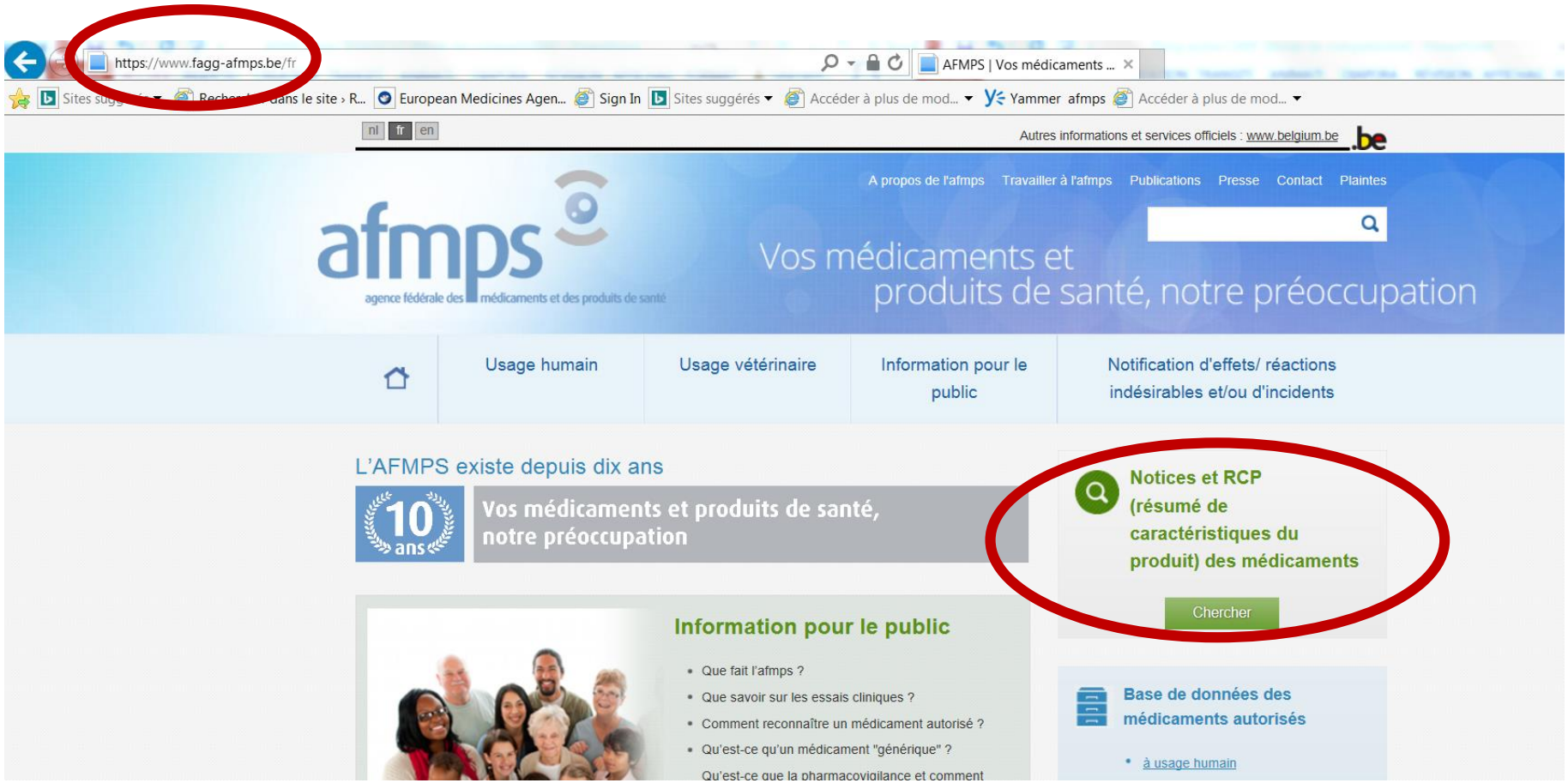
TRANSPARENCY

At the FAMHP level

- Information available on the FAMHP website:
  - RCP /Notice
  - DHPC
  - VigNews (communication to HCPs)
  - PRAC highlights
  - Vaccines under additional monitoring (▼)
  - Links notification
- Answer to questions from HCPs and citizen
- Evaluation report sent to HCPs who report adverse event
- Information exchange with other public institutions

TRANSPARENCY

Example: RCP/Notice are available on the FAMHP and CBIP-BCFI websites



TRANSPARENCY

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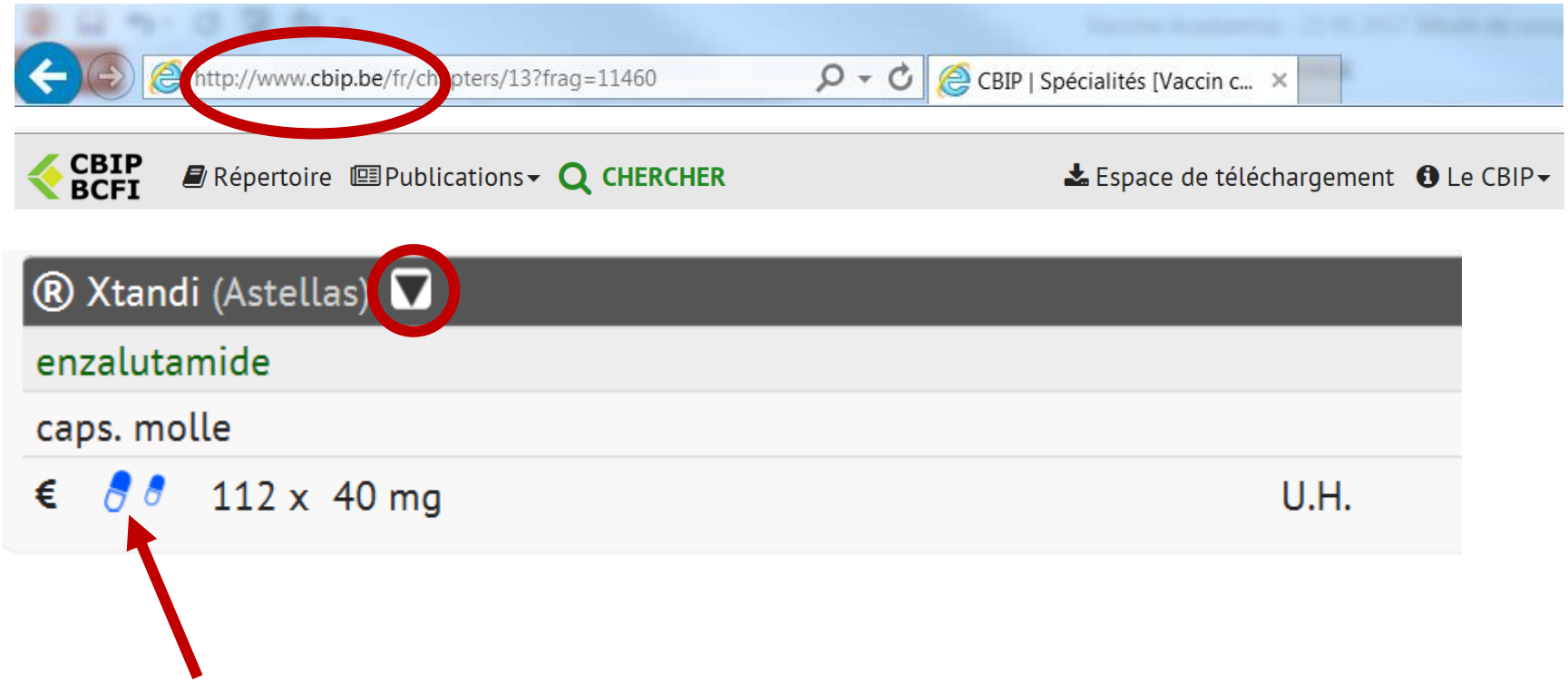

TRANSPARENCY

Example: How to notify AEs on the FAMHP website

TRANSPARENCY

Example: VigNews

Contact

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