Patients' organisations roles in pharmacovigilance

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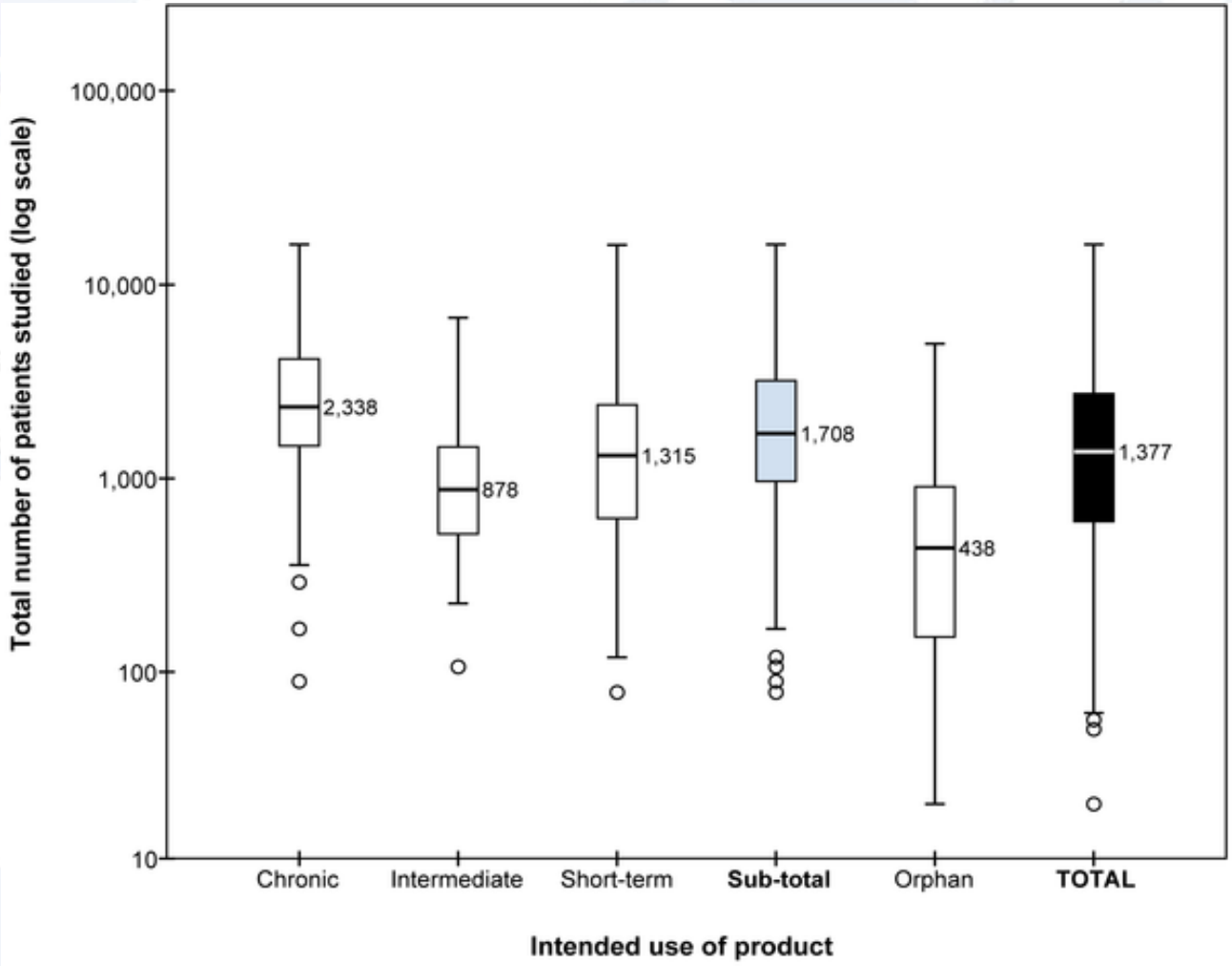
Why? - To Further Strengthen Pharmacovigilance

- 5% of all hospital admissions are for Adverse Drug Reactions (ADRs)
- 5% of all hospital patients suffer an ADR
- ADRs are the 5th most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU societal cost of ADRs amounts to Euro 79 Billion per year

Figure 1. Boxplots with medians of the number of patients studied before approval.



Duijnhoven RG, Straus SMJM, Raine JM, de Boer A, et al. (2013) Number of Patients Studied Prior to Approval of New Medicines: A Database Analysis. PLoS Med 10(3): e1001407. doi:10.1371/journal.pmed.1001407
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001407

What's new for the patients in the pharmacovigilance landscape?

- Coordination / lists of medicines / ▼
- Risk Management Plans
- Effectiveness of risk minimisation
- Post-Authorisation Studies (Safety and Efficacy)
- www.adrreports.eu
- Public hearings
- National authorities web portals
- Periodic Safety Update Reports
- Scientific Committees / decision-making
- Transparency and communication
- SCOPE/Web-RADR

PSURs

Periodic Safety Update Reports

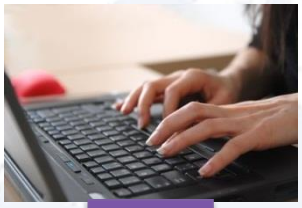
ADRs unlikely to be identified in clinical trials

Dr Stella Blackburn, EMA Risk Management Development and Scientific Lead, 29/11/2011

- ADRs which have a long latency
- ADRs which need prolonged exposure
- ADRs due to cumulative effects
- ADRs which are rare
- ADRs which mimic common diseases

Benefit-Risk balance reassessment - PSUR

HCP



Patients

Studies

Literature

Pre-marketing

Initial Marketing Authorisation

e.g. 6 months

PSUR 1

e.g. 6 months

PSUR 2

All available cumulative information

Rodrigo Postigo, Pharmacovigilance and Risk Management Sector EMA

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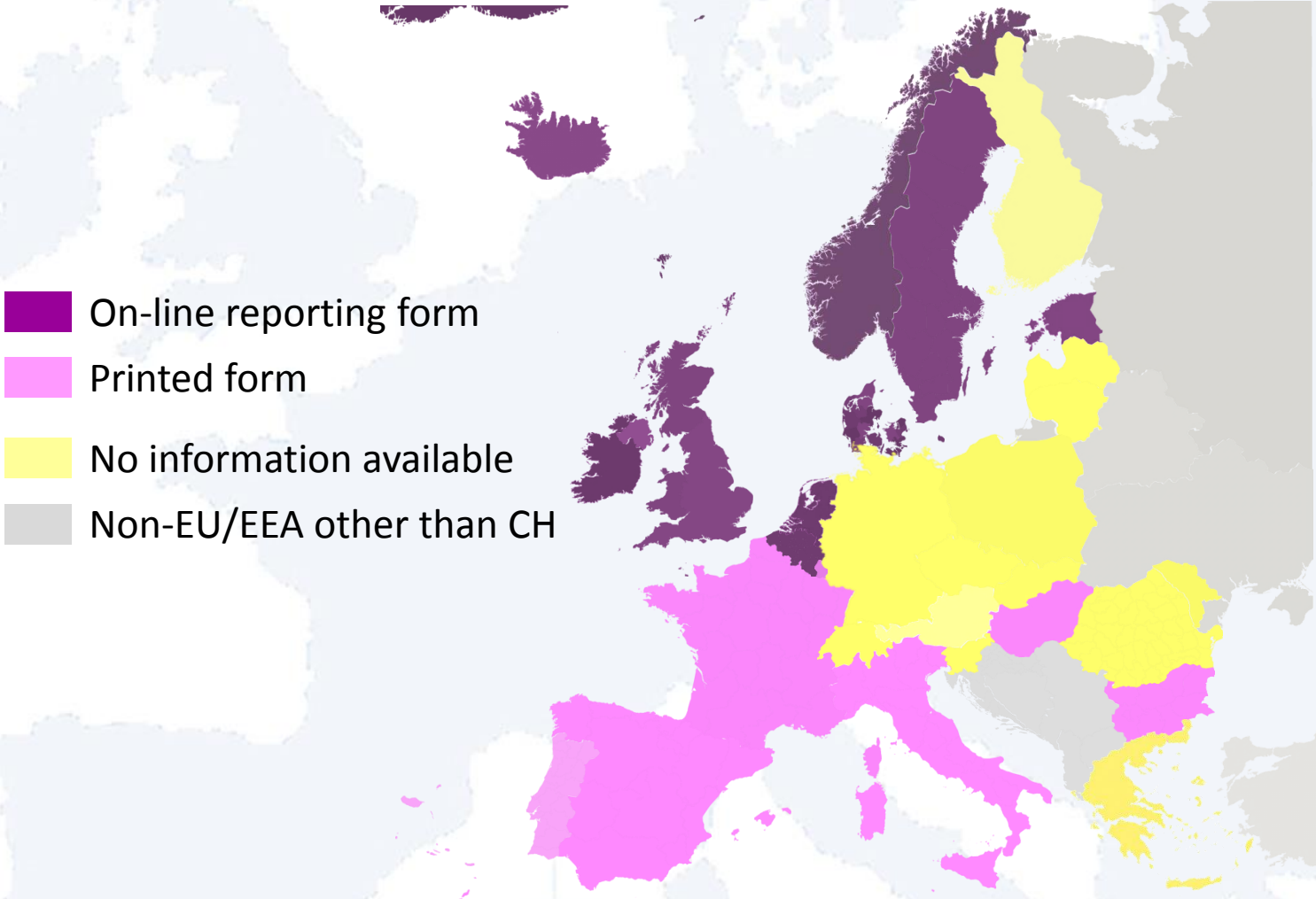
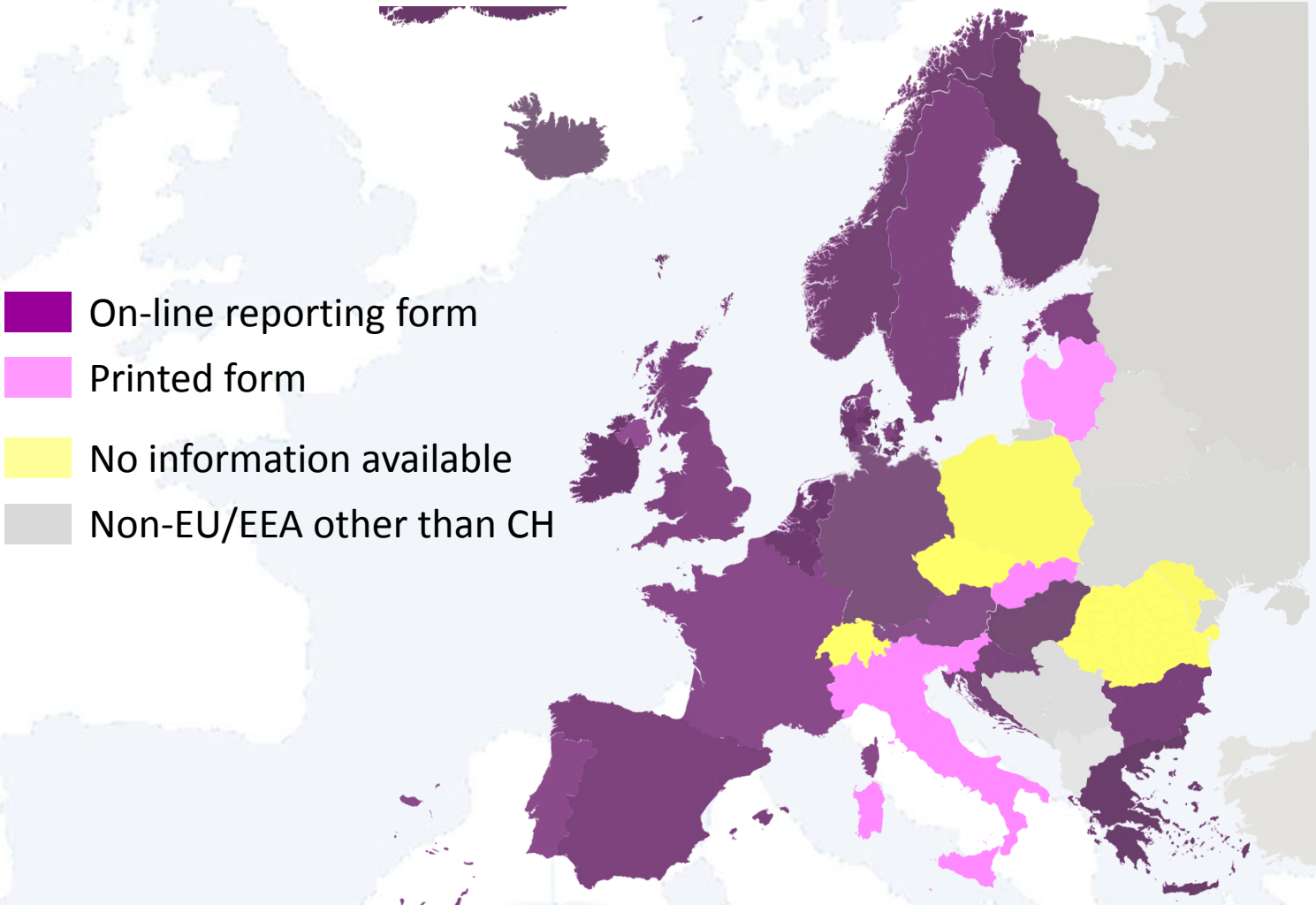
By the patients

ADR reporting

ADR reporting tools as of May 2012

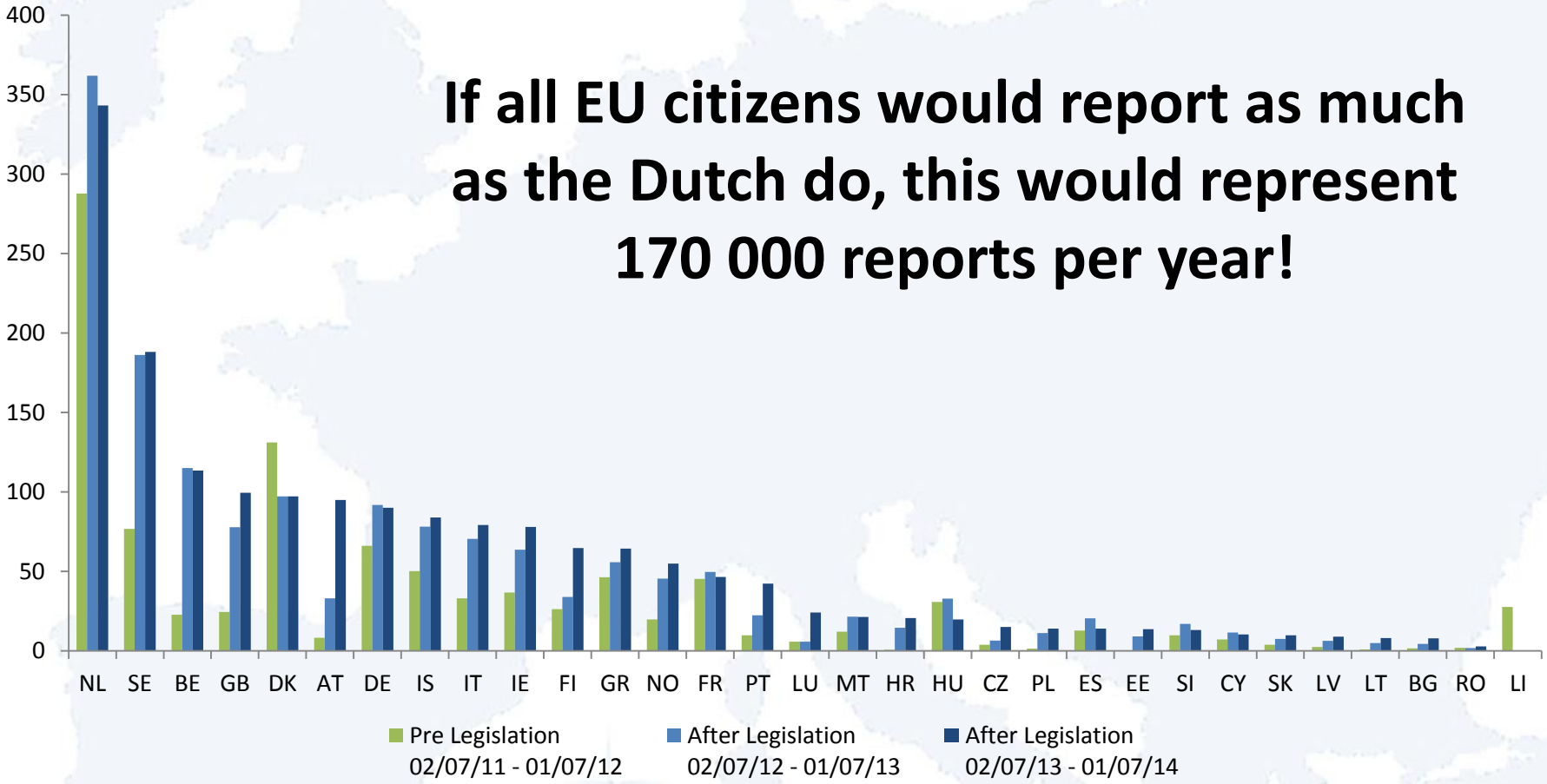


ADR reporting tools as of April 2014



www.eurordis.org/pharmacovigilance

Spontaneous reporting by patients in EEA* by country: reports by 1Mio pop. www.adrreports.eu

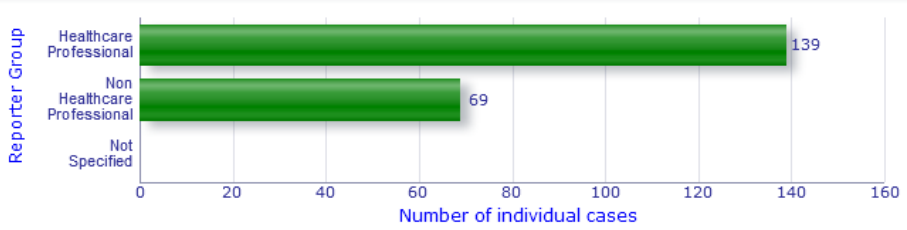


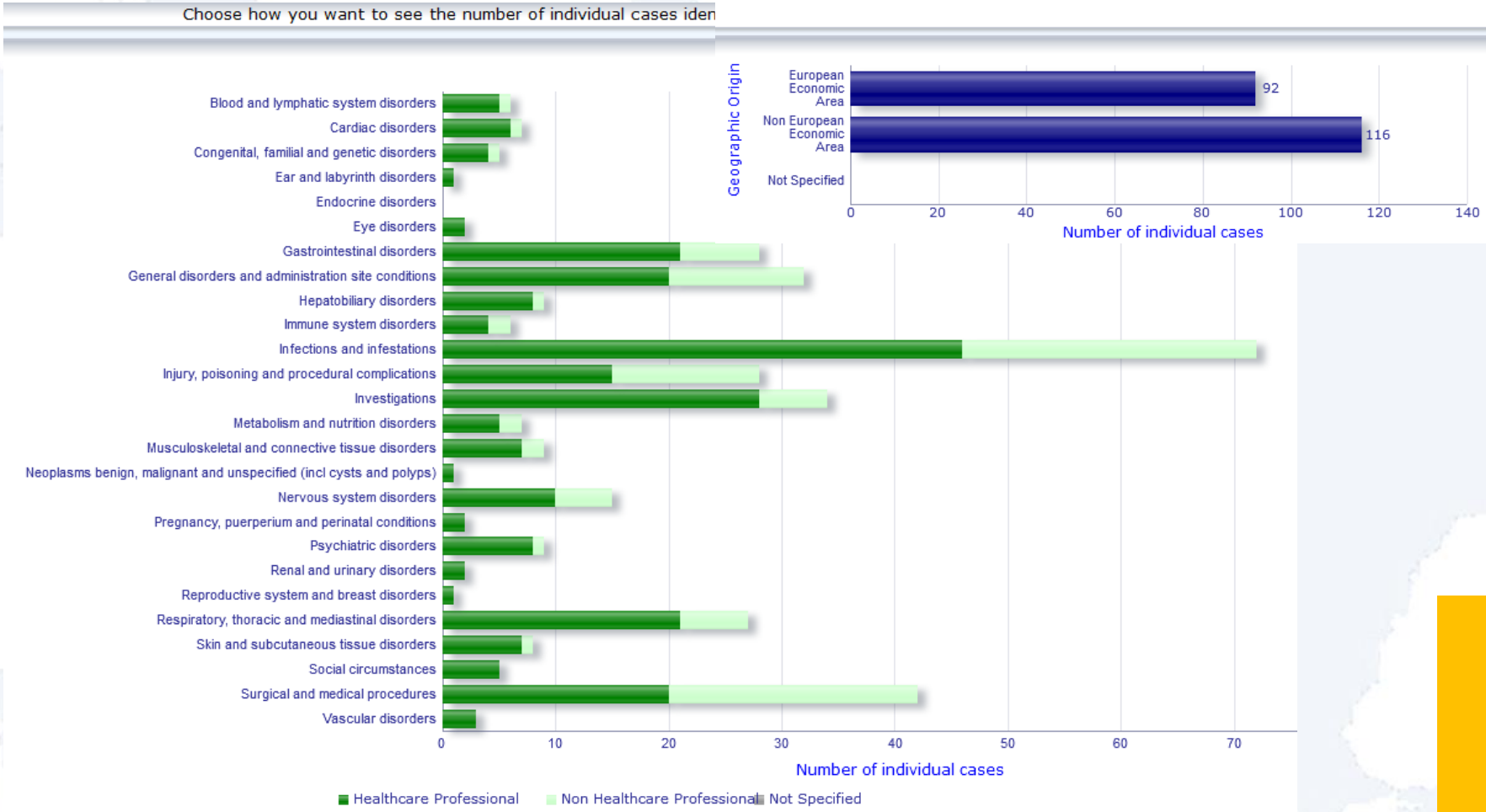
If all EU citizens would report as much as the Dutch do, this would represent 170 000 reports per year!

* Number of ICSRs received in EudraVigilance before de-duplication

▼ MA: 2012 cystic fib.

www.adrreports.eu





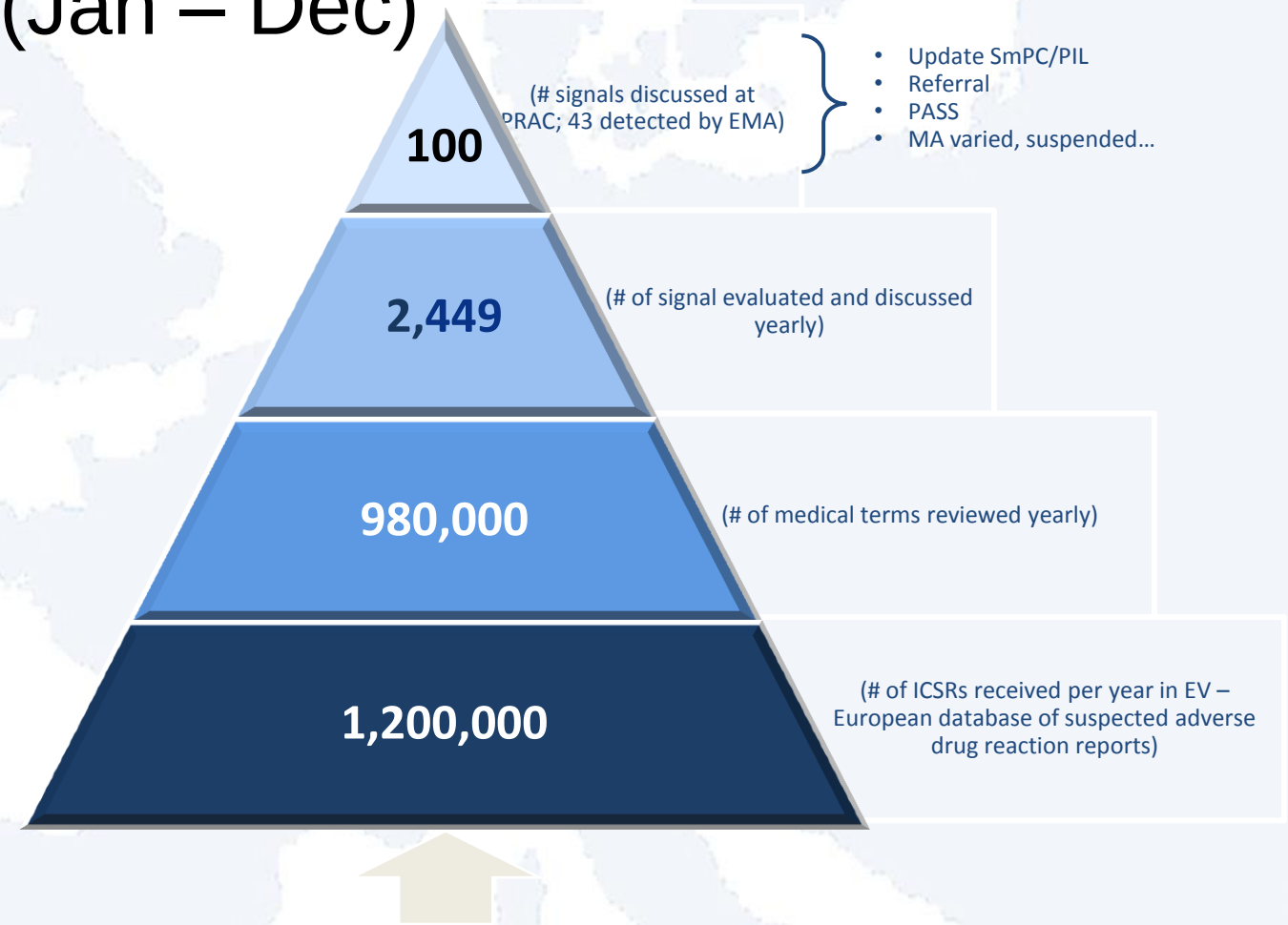
Issues with reporting forms

- Often outdated, design > 10 years
  - Not taking the best of available technologies (Web-RADR)
- Often a rough adaptation of the form for HCPs
  - Technical words
  - No tools to translate the text as described by patients into regulatory information (e.g. MedDRA terms)
- Patients consulted for the creation of the form: rarely
- Hard to find on authorities' web sites
- Poorly publicised
- Usually no help line to assist when reporting
- Web-RADR

Patients' organisations membership list

- Is a source of information, rarely used
- Benfluorex (proposed for obesity in type 2 diabetes)
  - Risk of heart valve disease (fenfluramine-like cardiovascular side-effects) greater than their benefits
  - Other fenfluramines withdrawn 1997
- In France benfluorex marketed until 2009 and is thought to have caused 500 – 2,000 deaths
  - 2 Mio people treated since 1976
- 2006: only 7 spontaneous reports to authorities
- In HTAP-France membership list: how many had been using benfluorex?

Trends in Adverse Event reports and signals in 2013 (Jan – Dec)



Adverse Reactions reported by:
Patients, HCPs, Pharmaceutical companies

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Some examples of signals discussed at PRAC

- Adalimumab (Humira®) - Missed dose due to **malfunction** of the pre-filled pen device
- Leuprorelin (Prostap®) - **Medication errors** (wrong technique in drug usage process)
- Clopidogrel (Clopidogrel®) - **Eosinophilic pneumonia** *
- Docetaxel (Docefrez®) - Serious/fatal **drug interactions** *
- Bevacizumab (Avastin®) - **Anaphylactic shock**
- Roxithromycin (Roxithromycin ®) - **Hearing disorders** *
- Temozolomide (Temodal®…) - **Hepatic failure** *
- Ticagrelor (Brilic®, Possia®) **- Interaction** with grapefruit juice *
- Cinacalcet (Mimpara®, Parareg®)- **QT prolongation / ventricular arrhythmias** *

* Represents those resulting in labelling changes

How does the RMP affect patients?

Dr Stella Blackburn, EMA Risk Management Development and Scientific Lead, 29/11/2011

- As a patient
  - Routine risk minimisation
  - Additional risk minimisation
- Providing input into the RMP
  - Is the risk too great or should patients have the choice?
  - Balancing needs for access with needs to minimise risk
  - Is the educational material understandable?

First RMP summary for the public: here

public hearings

Towards rules of procedures for

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PRAC decision to hold a public hearing

Proposal for a public hearing

- Referral procedures in accordance with Art. 20 of Regulation (EC) 726/2004, Art. 31 or Art. 107i of Directive 2001/83/EC
- Proposal to hold a public hearing – can be submitted by any PRAC member
- Content of proposal
  - Purpose of the public hearing (what is intended to be achieved?)
  - Specific questions on which public opinion should be sought
  - Any additional information as appropriate

Evaluating the need

- Who: PRAC

Agreement to hold a public hearing

- Who: PRAC
  - By consensus
  - Or by majority vote

Modalities of participation

Participants can attend **in person to speak**

Participants can submit their contribution **in writing**

Participants can watch a **live video-stream**

Summary of actions

You and/or your organisation can lead

2012-14: ANSM calls for project specific to patients' organisations – ADRs reporting

- Encouraging self-reporting of adverse reactions by patients (medicines & medical devices)
  - Self-reported adverse events related to Gylenia (fingolimod, MS)
  - Self-reported adverse effects linked to the exposure to diethylstilbestrol (DES) to assess the risk of breast cancer in women exposed to DES in utero in France (2nd generation) and to point out other risks over 3 generations
  - Support to help line as telephone assistance for patients when reporting ADRs (Maladies Rares Info Service)
  - Self-reported ADRs with coagulation factors (inhibitors++)
  - **Funds allocated: 114 456 € + ANSM expertise**

http://ansm.sante.fr/L-ANSM2/Appels-a-projets-Associations/Appels-a-projet-Association-2014/(offset)/0

Building your pharmacovilance expertise

Vis à vis your members/peers

- When renewing membership, survey your members to learn more on their treatment (all the ones they can use, including off-label)
- Explain the signification of ▼ in package leaflet
- Advertise the importance to report suspected ADRs

Vis à vis your national competent authority

- Test the online reporting tool in your country. Feedback to your NCA
- Review useful ADR reports with your NCA experts
- Review and discuss risk communication channels in your country. Do they work?

Vis à vis EMA

- Review Risk Management Plan summaries for medicines of interest to you. Feasability? Constrains?
- Register to EMA RSS feeds/monthly highlights
- See PRAC agendas / minutes

Conclusions

- Patients' organisations play an active role in pharmacovigilance
- Patients are no longer passive receivers of medicines
- We need to exchange information on safety/efficacy with regulators on a broader scale

Thank you!

If we have time for questions…

EURORDIS Drug Information Transparency and Access 'DITA' task force members

- Claudie Baleydier, Friedreich Ataxia, FRA
- Juan Fuertes, Primary Pulmonary Hypertension, SPA
- Ellen van Veldhuizen, Addison Disease Org., NLD
- Rainald von Gizycki, Pro Retina, GER
- Danijela Szili, Rett synd., HUN
- Luc Matthyssen, Pulmonary Hypertension, BEL
- Sigurður Jóhannesson, Alternating Hemoplagia of Childhood, ICE
- Isabel Fernandez, FEDER, SPA
- François Houÿez, Anne-Mary Bodin, EURORDIS, Paris
- Rob Camp, EURORDIS, SPA
- Lise Murphy, Marfan syndrome, SWE
- Inge Schwersenz, Neuromuscular SMA, GER
- Vesna Stojmirova, Life with Challenges, FYROM
- Thomas Sannié, Association for Haemophilia, FRA
- Oliver Timmis, Alkaptonuria Society, GBR
- Christine Lavery, Muco-polysaccharidosis Society, GBR
- Dragomir Slavev, Thalassemia org., BLG
- Richard West, Behcet Society, GBR
- Tatiana Foltanova, Slovakian Alliance for RD

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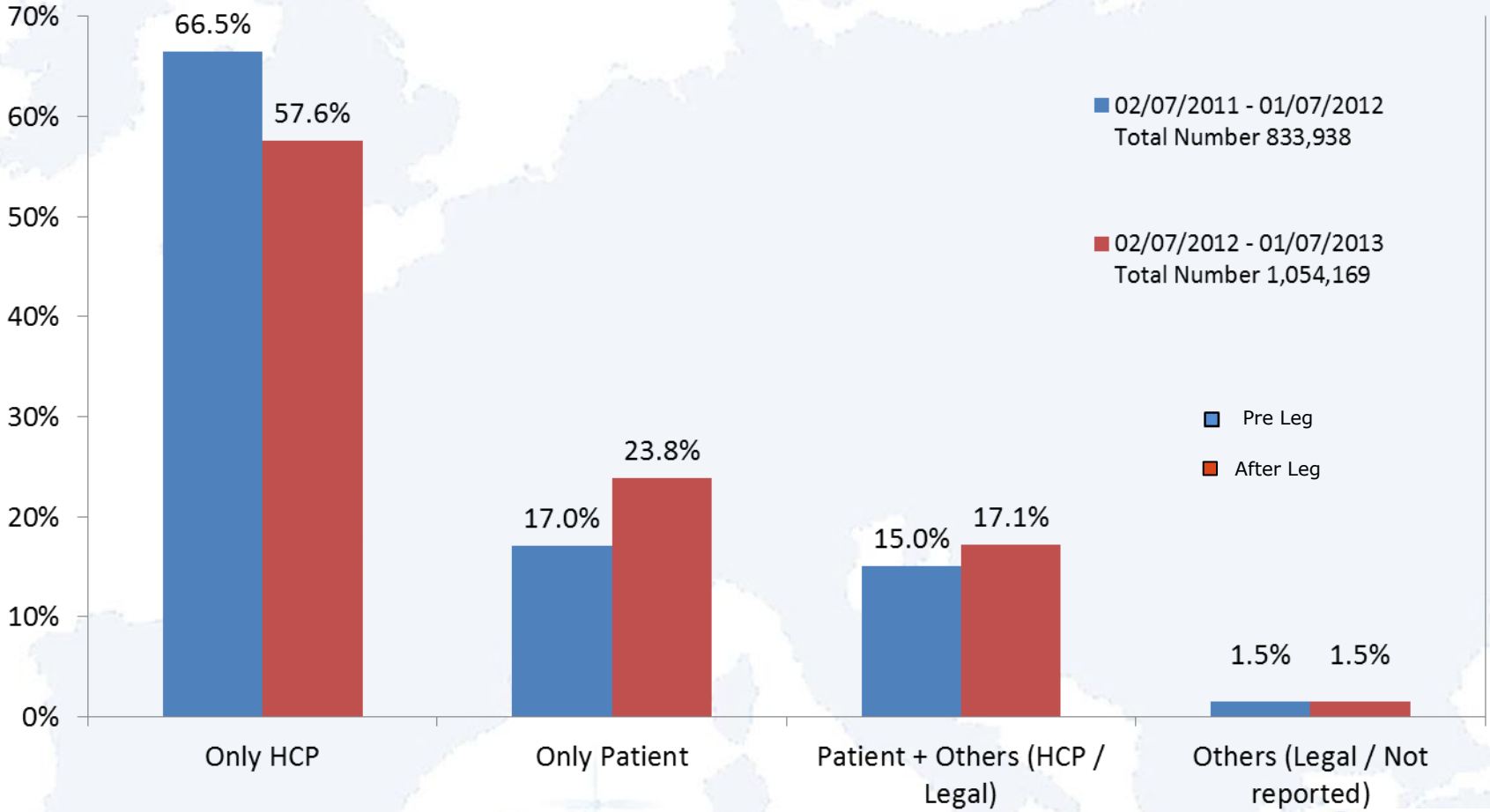
Proportion of ICSR reporting pre- and post new PV legislation



Organisation of a public hearing
Before the hearing

Announcement of the public hearing

- A **summary of the** safety concern
- A **list of specific questions**
- Information on **date, time and location** of the public hearing
- **Registration information**
- Information on how to **submit written contributions**
- Contact email address and phone number
- Information about **live-broadcast/ webstream**

Submitting a request to speak

- **Name** & **Affiliation** (e.g. patient, carer, physician, etc.…)
- Name of the **organisation/group** he or she is representing if applicable
- Contact information
- **outline of the planned presentation/intervention**, specifically how it addresses the questions on which the PRAC is seeking public opinion
- **Declaration of interest** pertaining to the medicine(s) to be discussed at the public hearing.

Review of requests to speak

- All requests will be **reviewed**.
- Efforts to **accommodate all speaking requests**
- Speaking requests may be **declined only if clearly unrelated to subject matter** of pubic hearing
- **Priority to speakers representing groups, organisations or institutions**
- **Confirmation** of attendance as a speaker **at least 10 days in advance** of the public hearing

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PRAC recommendation as a result of PSUR assessment

- Maintenance of the marketing authorisation (MA)
  - Balance of benefits and risks remains favourable
- Variation of the MA
  - Balance of benefits and risks remains favourable
  - Clear proposals for amendments to SPC and PL
  - Scientific Rationale clearly described in assessment
- Suspension of the MA
  - Balance of benefits and risks are negative
  - Grounds for action have been clearly justified in report
  - Grounds for lifting suspension have been identified
- Revocation of the MA
  - Balance of benefits and risks are negative
  - Grounds for action have been clearly justified in report

Regulatory action

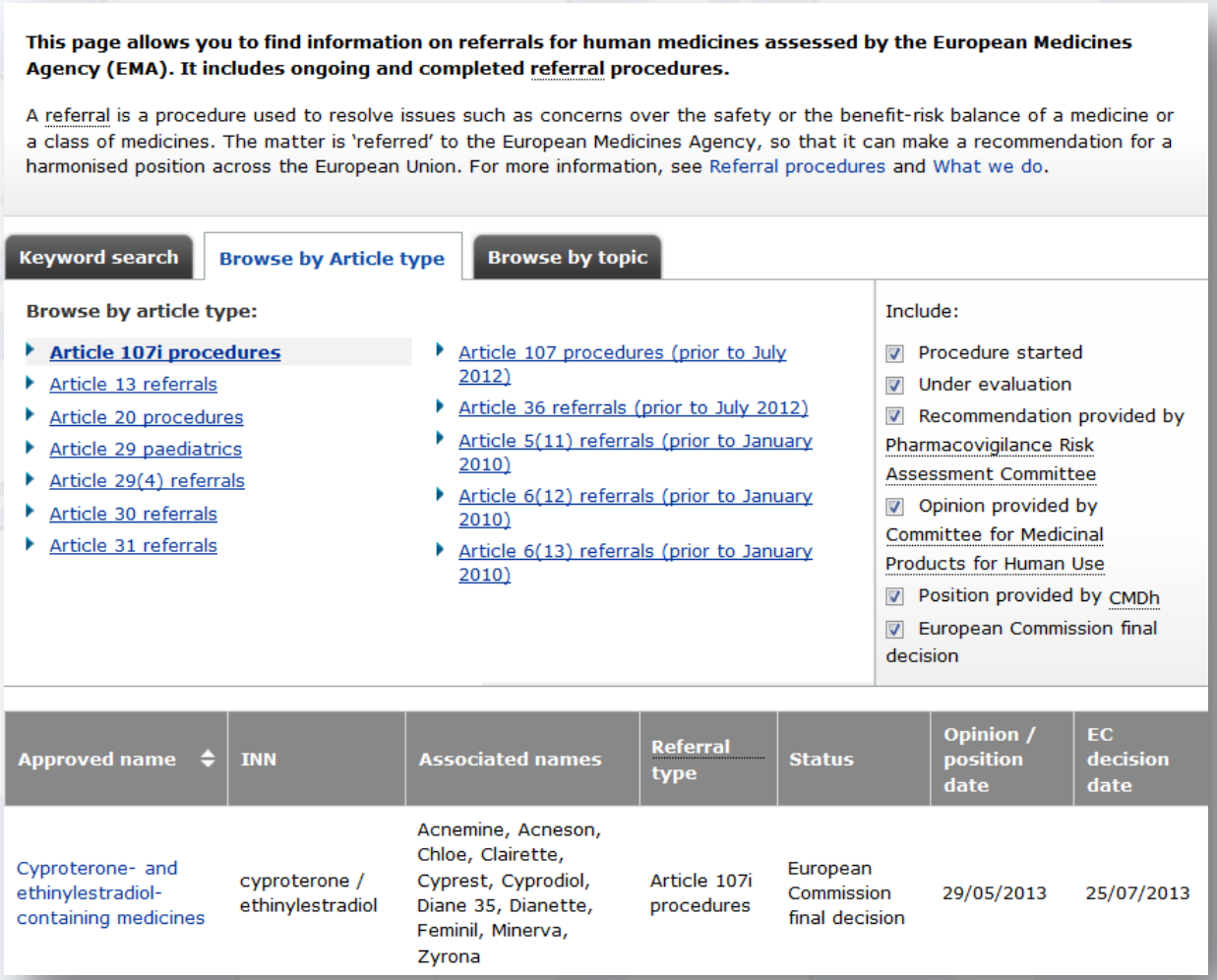
Urgent procedure

Referrals

Article 107i Urgent Union Procedure

- This type of procedure is triggered when a Member State or the European Commission consider that **urgent** action is necessary because of a **safety issue**
- PRAC performs the assessment
- Very short timeframe (max. 60 days)
- Public hearing may be held
- SAG and ad-hoc expert meeting may be convened
- PRAC issues a recommendation
- Temporary measures can be taken at any time
- See Q&A here

All referrals: see here



This page allows you to find information on referrals for human medicines assessed by the European Medicines Agency (EMA). It includes ongoing and completed referral procedures.

A referral is a procedure used to resolve issues such as concerns over the safety or the benefit-risk balance of a medicine or a class of medicines. The matter is 'referred' to the European Medicines Agency, so that it can make a recommendation for a harmonised position across the European Union. For more information, see Referral procedures and What we do.

Keyword search | Browse by Article type | Browse by topic

Browse by article type:

- Article 107i procedures
- Article 13 referrals
- Article 20 procedures
- Article 29 paediatrics
- Article 29(4) referrals
- Article 30 referrals
- Article 31 referrals
- Article 107 procedures (prior to July 2012)
- Article 36 referrals (prior to July 2012)
- Article 5(11) referrals (prior to January 2010)
- Article 6(12) referrals (prior to January 2010)
- Article 6(13) referrals (prior to January 2010)

Include:

- Procedure started
- Under evaluation
- Recommendation provided by Pharmacovigilance Risk Assessment Committee
- Opinion provided by Committee for Medicinal Products for Human Use
- Position provided by CMDh
- European Commission final decision

Approved name	INN	Associated names	Referral type	Status	Opinion / position date	EC decision date
Cyproterone- and ethinylestradiol-containing medicines	cyproterone / ethinylestradiol	Acnemine, Acneson, Chloe, Clairette, Cyprest, Cyprodiol, Diane 35, Dianette, Feminil, Minerva, Zyrona	Article 107i procedures	European Commission final decision	29/05/2013	25/07/2013

Referrals Procedure Article 107i

- Are POs equipped to respond to PRAC questions?
- E.g.: Tetrazepam painful contractures & risk of skin reactions (Stevens-Johnson synd., toxic epidermal necrolysis and rash-with-eosinophilia-systemic-symptoms synd.)
  - Question1
    - Provide information or analysis on data (i.e. non clinical data, clinical data, epidemiological studies and published literature) that you may be aware of and which could be relevant to evaluate the risk of cutaneous ADRs with tetrazepam
  - Question 2
    - Taking into account the efficacy and in view of the cutaneous concerns, please provide your views on the use of tetrazepam in the treatment of painful muscle spasm in rheumatological disease