EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Access to EudraVigilance data to Patients and Health Care professionals

Implementation of the revised EudraVigilance Access Policy

PCWP/HCPWP Joint meeting - 9 March 2016

Presented by Francois Domergue on 9 March 2016

Agenda

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1. Introduction
2. Pharmacovigilance Program and Projects
    a. EudraVigilance auditable requirement project
3. Revised EudraVigilance Access Policy
    a. Legal Background
    b. Objectives and Principles
    c. Summary and achievements
    d. New technical implementation
    e. Feedback from Patients and Healthcare professional

1. Introduction

The aim of this presentation is to provide PCWP/HCWP with an

- Overview of the Pharmacovigilance Programme and in particular the EudraVigilance (EV) auditable requirements project

- Update on the implementation of the revised EV Access Policy and in particular the new functionalities that will be made available in the ADR website (http://www.adrreports.eu/).

NOTE: screenshots included in this presentation are based on EV functionalities still under IT development/testing and might not be exactly at the go live in 2017.

2. Pharmacovigilance Programme

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Projects & Outputs	Benefits Delivered
Article 57 Database *European database of all medicinal products*	• Support PV Procedures which facilitates coordination of regulatory decisions • Supports the product index for EudraVigilance • Reduction of duplication
EudraVigilance Auditable Requirements *Enhanced adverse reaction collection and management system*	• Simplified reporting delivered • Data will be higher quality, improving searchability & analysis efficiency • Increased access to stakeholders
Medical Literature Monitoring *Delivery of literature monitoring service to MAHs*	• Improved safety monitoring of medicines through increased data quality • Reduction in costs for industry literature monitoring activities
Pharmacovigilance Fees *Collection of fees to cover costs of conduct of certain PV activities*	• Member State rapporteurs paid for certain PV assessments • Annual fees support implementation & maintenance of IT systems and services
PSUR Repository *Centralised repository for PSURs and assessment reports*	• Provides a simplification of PSUR submissions for industry • Repository will include all PSURs and assessment reports

Driven By

Effective programme management which ensures successful delivery of changes

Provides public health benefits across Europe

2.a. EudraVigilance Auditable Requirements

SCOPE:
There is a legal requirement for an **enhanced adverse reaction collection and management system** (EudraVigilance) that delivers better health protection through **simplified reporting, better quality data and better searching, analysis and tracking functionalities**. Enhanced detection of new or changing safety issues allows more rapid action to protect public health.

✓As of today, most of the IT development activities for the new EV system have now been completed

✓In October 2015, the EudraVigilance Stakeholder Change Management Plan published

✓**The revised EudraVigilance Access Policy adopted** by the EMA Management Board December 2015

✓The EudraVigilance functionalities audit is scheduled to take place in 3rd quarter 2016

✓**EMA Management Board will review the EudraVigilance System Audit outcome at its December meeting**. If the functionalities agreed at the December 2016 audit have been delivered, then the Management Board will announce the **launch of the new EV system and the start of centralised reporting in 6 months thereafter i.e. mid 2017**

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3.a Legal Background

- 2010 PV legislation requires extended access to EudraVigilance
- Article 24(2) of the Regulation defines the level of EudraVigilance access as follows:
  - EudraVigilance shall be fully accessible to the competent authorities of the Member States and to the Agency and the European Commission
  - It shall also be accessible to MAHs to the extent necessary for them to comply with their pharmacovigilance obligations
  - The Agency shall ensure that healthcare professionals and the public have appropriate levels of access to the EudraVigilance database, while guaranteeing personal data protection
- Article 28(c) of Regulation (EC) No 726/2004 further states that
  - The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the WHO

N.B. changes do not relate to Clinical Trial reports (suspected unexpected serious adverse reactions - SUSARs)

3.b. Objectives and principles (1/2)

- Providing openness to citizens, who are directly affected by the EU Regulatory Network's decisions relating to the authorisation and supervision of medicinal products, including the monitoring and assessment of the safety of medicines
- Facilitating the monitoring of the safety of medicines following their authorisation and marketing
- Supporting signal detection and evaluation activities related to all authorised medicines in the EU
- Allowing the use of adverse reaction data for research purposes to contribute to promoting and protecting public health and fostering the innovation capacity of European medical research
- Providing promptly all suspected adverse reactions occurring in the EEA to the WHO
- Strengthening of the collaboration with medicines regulatory authorities in third countries as regards the safety monitoring of medicines

3.b. Objectives and principles (2/2)

- The proactive and reactive disclosure of ICSR data are identical:
  - Information that is made available is the same independently, if the Agency is taking the initiative to make the data accessible through different technical solutions or if a party submits a request to the Agency to obtain such data
- Principles of transparency are put in effect:
  - Maximum data are released proactively
  - Needs of stakeholders are met
  - Requirements of personal data protection pursuant to the provisions of Regulation (EC) 45/2001 and Directive 95/46/EC are adhered to

3.c. Summary and achievements (1/4)

- Revision based on n**ew pharmacovigilance legislations** applicable as of July 2012
- **Public consultation** 4 August - 15 September 2014
- **392 organisations/individuals** have commented
- **Adopted by EMA Management Board in December 2015**
- Data elements based on **new ISO ICSR** standard
- **Access to include serious and non-serious adverse reactions**
- **Access to data for spontaneous reports on adrreports.eu website**
- **Access to data for spontaneous and solicited reports** (except interventional trials) for MAHs, academia and WHO-UMC
- **Access to SUSARs** in line with new Clinical Trials Regulation (EU) No 536/2014 to be subject to separate consultation

Note: current sender-based access maintained

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4 August 2014
EMA/759287/2009 Revision 1
Inspections and Human Medicines Pharmacovigilance Division

Revision of EudraVigilance access policy for medicines for human use
Draft

Agreement on principles of data sharing with World Health Organisation – Uppsala Monitoring Centre (WHO-UMC)[1]	22 April 2014 26 May 2014
Draft finalised by Project Team 1 "Collection of key information on medicines" of the EMA/Member States governance structure for the implementation of the pharmacovigilance legislation	2 July 2014 11 July 2014
Draft agreed for public consultation by Project Co-ordination Group of the EMA/Member States governance structure for the implementation of the pharmacovigilance legislation	16 July 2014
Draft agreed for public consultation by Pharmacovigilance Risk Assessment Committee (PRAC) Organisational Matters (ORGAM)	24 July 2014
European Commission	30 July 2014
Draft circulated to the European Risk Management Facilitation Group (ERMS-FG)	30 July 2014
Draft circulated to the Pharmacovigilance Risk Assessment Committee (PRAC)	4 August 2014
Draft circulated to the Committee for Human Medicinal Products (CHMP) and the Co-ordination group for Mutual recognition and Decentralised procedures – human(CMD-h)	4 August 2014
Draft circulated to the European Data Protection Officer	4 August 2014
Draft circulated to the European Ombudsman	4 August 2014
Draft circulated to the EudraVigilance Expert Working Group	4 August 2014
Draft circulated to the Patients' and Consumers' Working Party	4 August 2014

[1] In relation to the WHO-UMC specific arrangements

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3.c. Summary and achievements (2/4)

- Six Stakeholder Groups
  - Stakeholder Group I - Medicines regulatory authorities in EEA Member States, European Commission and the Agency
  - Stakeholder Group II - Healthcare Professionals and the Public
  - Stakeholder Group III - Marketing Authorisation Holders
  - Stakeholder Group IV - Academia
  - Stakeholder Group V - WHO Uppsala Monitoring Centre
  - Stakeholder Group VI- Medicines regulatory authorities in third countries

3.c. Summary and achievements (3/4)

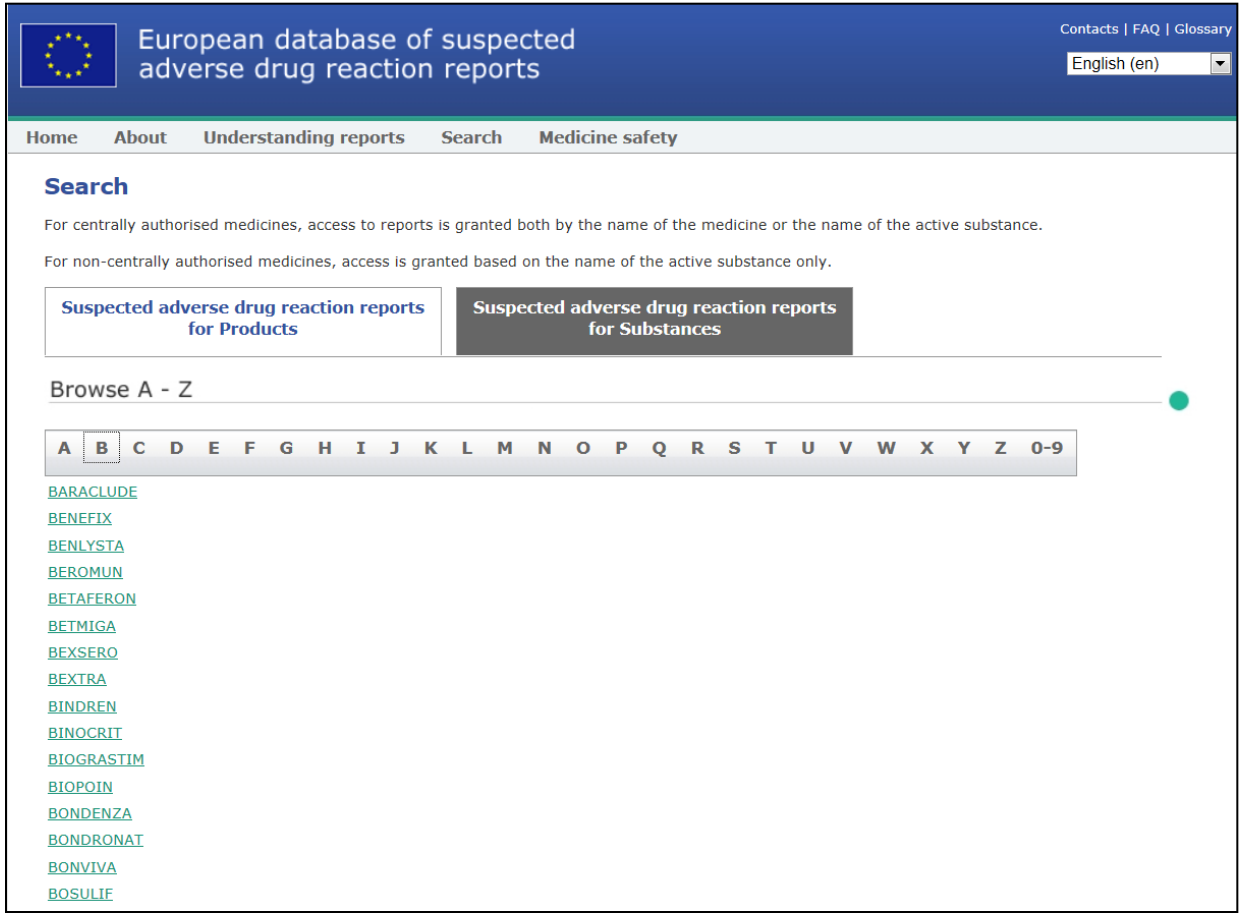
Stakeholder	Access given (summary)
Regulators in EEA	Complete access to all data via data Warehouse
General public	All spontaneous reports as aggregated data + line listings based on restricted data elements via adrreports.eu
MAHs	1. Access to all data elements for cases sent 2. Access to restricted data set for substances in their products (for signal detection) 3. Access to extended data set based on confidentiality undertaking (for signal validation. N.B. includes free text narratives)
Academia	Aggregated access as general public + access on request + study protocol to extended data set based on confidentiality undertaking. No pre-scrutiny of publications
WHO-UMC	Extended data set – agreed with WHO – sent electronically every day
3rd country regulators	Data set as WHO but reactive access (i.e. on request)

3.c. Summary and achievements (4/4)

ICH E2B(R3) ICSR Implementation Guide ICSR sections	Total	Stakeholder Group I	Stakeholder Group II-VI	Stakeholder Group III & IV	Stakeholder Group III	Stakeholder Group III	Stakeholder Group V & VI
		Level 3	Level 1	Level 2A	Level 2B	Level 3	Level 2C
C.1 Identification of the case safety report	20	20	3	18	18	20	16
C.2.r Primary source(s)[20] of information	15	15	4	4	4	15	4
C.3 Information on sender of case safety information	16	16	3	3	3	16	3
C.4.r Literature reference(s)	2	2	1	1	1	2	1
C.5 Study identification	6	6	4	5	5	6	5
D. Patient characteristics	96	96	4	87	87	96	16
E.i Reaction(s)/event(s)	21	21	11	21	21	21	18
F.r Results of tests and procedures relevant to the investigation of the Patient	13	13	0	13	13	13	0
G.k Drug(s) information	76	76	23	72	72	76	71
H. Narrative case summary and further information	7	7	0	4	7	7	0
Grand Total	272	272	53	228	230	272	134

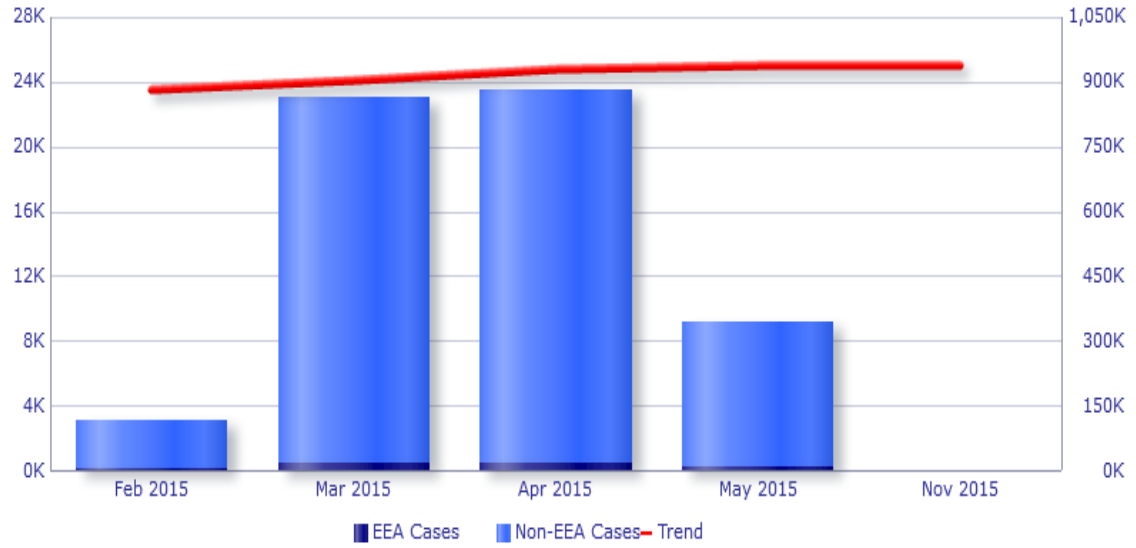
3.d. New technical implementation (1/2)

- **Weekly update** of ICSR data (currently monthly)
- **New aggregated data outputs**
  - Based on current implementation approach
  - **Country information to be disclosed**
    With additional safeguards to ensure patient data protection (if there are less than 3 cases e.g. for new drugs)


European database of suspected adverse drug reaction reports
Contacts | FAQ | Glossary
English (en)
Home
About
Understanding reports
Search
Medicine safety
Search
For centrally authorised medicines, access to reports is granted both by the name of the medicine or the name of the active substance.
For non-centrally authorised medicines, access is granted based on the name of the active substance only.
Suspected adverse drug reaction reports for Products
Suspected adverse drug reaction reports for Substances
Browse A - Z
A B C D E F G H I J K L M N O P Q R S T U V W X Y Z 0-9
BARACLUDE
BENEFIX
BENLYSTA
BEROMUN
BETAFERON
BETMIGA
BEXSERO
BEXTRA
BINDREN
BINOCRIT
BIOGRASTIM
BIOPOIN
BONDENZA
BONDRONAT
BONVIVA
BOSULIF

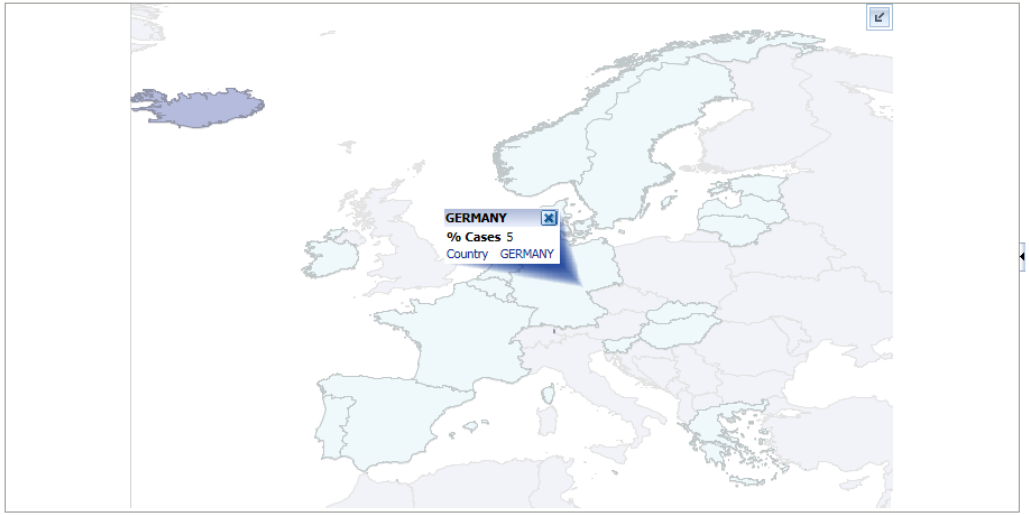
Number of Individual Cases | **Number of Individual Cases received over time** | Number of Individual Cases by EEA countries | Number of Individual Cases By Reaction Groups | Number of Individual Cases for a selected Reac

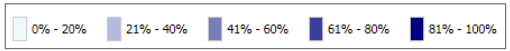
Number of Individual Cases received over time

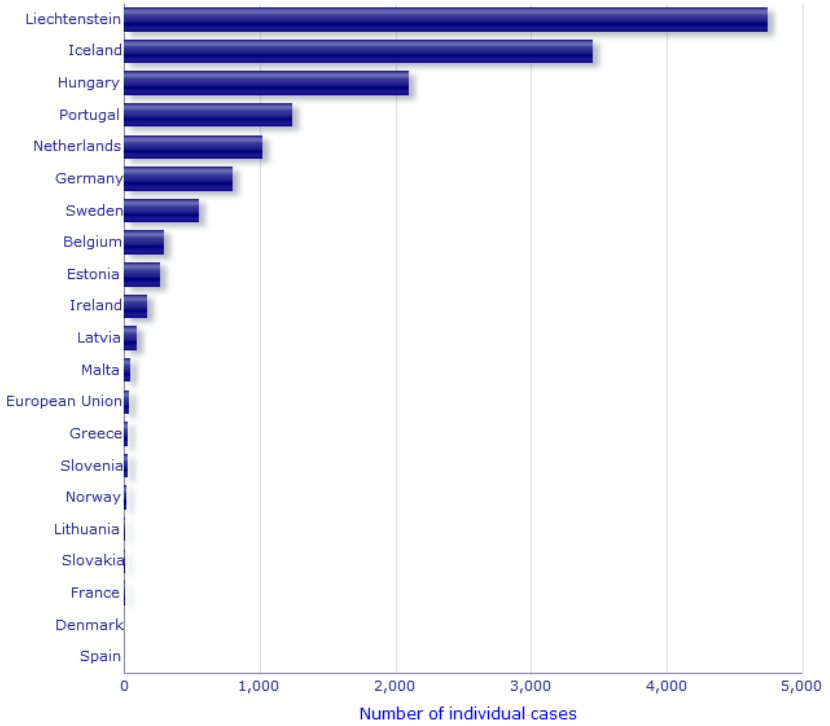


For the interpretation of the results, please refer to the key considerations at www.adrreports.eu

The country is not displayed if the number of cases is less or equal to 3 for that country

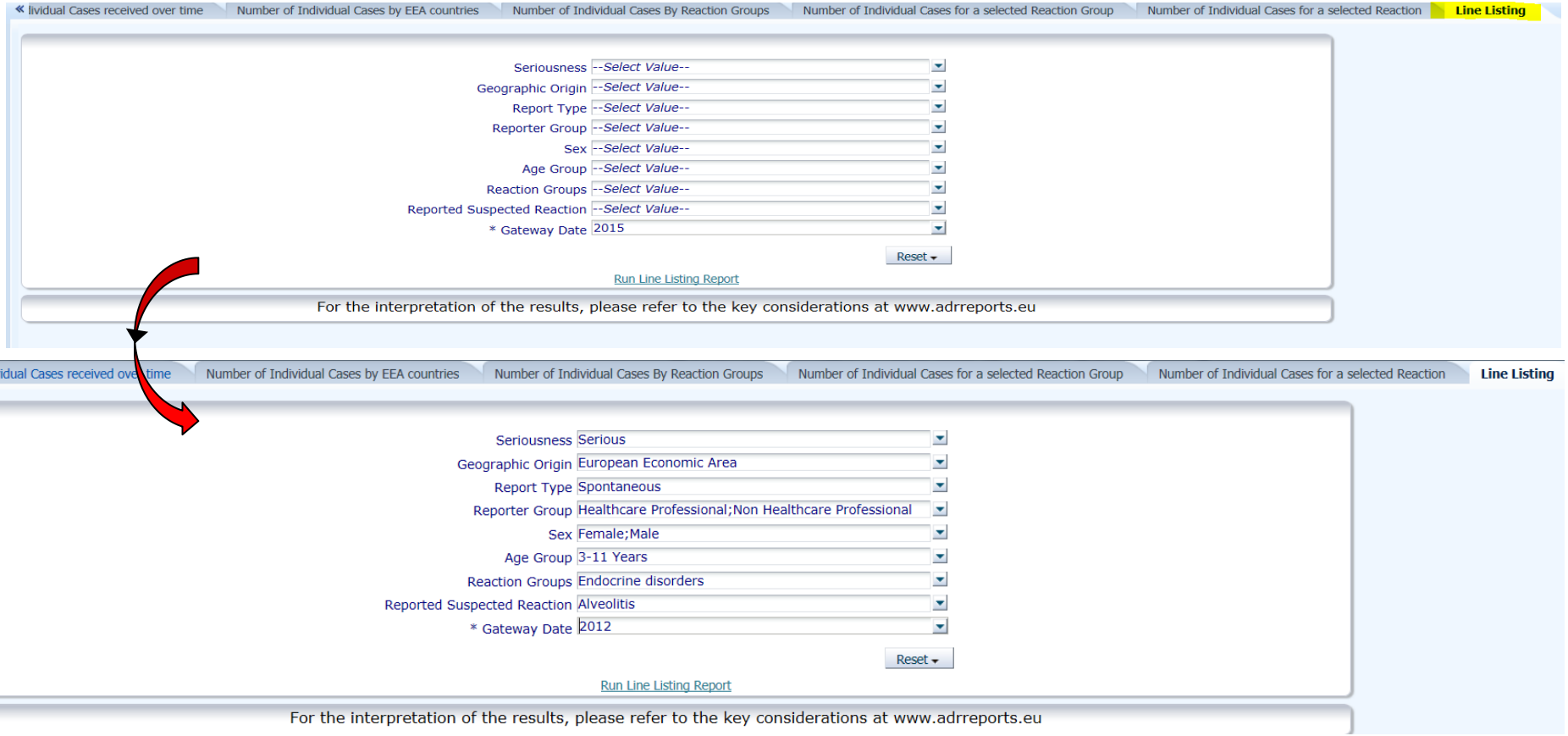






3.d. New technical implementation (2/2)

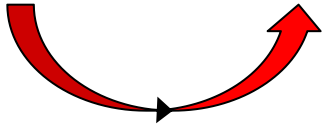
- "**Line listings**" ICSR data elements presented for each report
  - To be available from a new tab on the ADR website
  - Country specific information will not be disclosed (world-wide unique case identifier, primary source country for regulatory purposes, medicinal product name for non CAPs)
  - Search will be possible by region only i.e. EEA/mon EEA (as per current policy)
- "**ICSR form**"
  - Data elements presented in case report form (same as presented in line listing)


« lividual Cases received over time
Number of Individual Cases by EEA countries
Number of Individual Cases By Reaction Groups
Number of Individual Cases for a selected Reaction Group
Number of Individual Cases for a selected Reaction
Line Listing
Seriousness --Select Value--
Geographic Origin --Select Value--
Report Type --Select Value--
Reporter Group --Select Value--
Sex --Select Value--
Age Group --Select Value--
Reaction Groups --Select Value--
Reported Suspected Reaction --Select Value--
* Gateway Date 2015
Reset
Run Line Listing Report
For the interpretation of the results, please refer to the key considerations at www.adrreports.eu
lividual Cases received over time
Number of Individual Cases by EEA countries
Number of Individual Cases By Reaction Groups
Number of Individual Cases for a selected Reaction Group
Number of Individual Cases for a selected Reaction
Line Listing
Seriousness Serious
Geographic Origin European Economic Area
Report Type Spontaneous
Reporter Group Healthcare Professional;Non Healthcare Professional
Sex Female;Male
Age Group 3-11 Years
Reaction Groups Endocrine disorders
Reported Suspected Reaction Alveolitis
* Gateway Date 2012
Reset
Run Line Listing Report
For the interpretation of the results, please refer to the key considerations at www.adrreports.eu

EU Local Number	Worldwide Unique Case Identification	EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Literature Reference	Patient Age Group	Patient Age Group (as per reporter)	Patient Sex	Parent Child Report	Reaction List PT (Duration – Outcome - Seriousness Criteria)	Suspect/interacting Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	Concomitant/Not Administered Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	ICSR Form
EU-EC-9286623	Non EEA-EMA-20150513-pdevhumanwt-093119502	13/05/2015	Spontaneous	Healthcare Professional	Non European Economic Area	Not available	More than 85 Years	Not Specified	Male	No	Confusional state (n/a) - Recovered/Resolved - Caused/Prolonged Hospitalisation, Disturbance in attention (n/a) - Recovered/Resolved - Caused/Prolonged Hospitalisation, Hyponatraemia (n/a) - Recovered/Resolved - Caused/Prolonged Hospitalisation	(Suspect - Bipolar disorder - Drug withdrawn - (n/a - n/a-30 -ORAL), (n/a - n/a-n/a -ORAL)) (Suspect - Bipolar disorder - Drug withdrawn - (n/a - n/a -300 -ORAL), (n/a - n/a-n/a -ORAL)), V (Suspect - Bipolar disorder - Drug withdrawn - (n/a - n/a -300 -ORAL), (n/a - n/a-n/a -ORAL))	) (Concomitant - - (n/a n/a) - Unknown), (Concomitant - - (n/a - n/a) - Unknown), Concomitant - - (n/a - n/a) - Unknown), (Concomitant - - (n/a - n/a) - Unknown), TRIATEC /00116401/ (Concomitant - - (n/a - n/a) - Unknown)	ICSR
EU-EC-9286624	Non EEA-EMA-20150513-pdevhumanwt-094042786	13/05/2015	Spontaneous	Healthcare Professional	Non European Economic Area	Not available	More than 85 Years	Not Specified	Female	No	Death (n/a) - Fatal - Results in Death, Life Threatening, Caused/Prolonged Hospitalisation, Hepatitis (13d) - Not Recovered/Not Resolved - Results in Death, Life Threatening, Caused/Prolonged Hospitalisation		Not reported	ICSR
EU-EC-9286625	Non EEA-EMA-20150513-antarvp-101119983	13/05/2015	Spontaneous	Healthcare Professional	Non European Economic Area	Not available	More than 85 Years	Not Specified	Male	No	Metastases to liver (n/a) - Unknown - Results in Death, Other Medically Important Condition, Pancreatic carcinoma metastatic (n/a) - Fatal - Results in Death, Other Medically Important Condition		Not reported	ICSR
EU-EC-9286627	Non EEA-EMA-20150513-antarvp-101732199	13/05/2015	Spontaneous	Healthcare Professional	Non European Economic Area	Not available	3-11 Years	Not Specified	Male	No	Aphasia (n/a) - Not Recovered/Not Resolved - Caused/Prolonged Hospitalisation, Cerebral atroph (n/a) - Not Recovered/Not Resolved - Caused/Prolonged Hospitalisation, Constipation (n/a) - Unknown - Caused/Prolonged Hospitalisation, Developmental delay (n/a) - Not Recovered/Not Resolved - Caused/Prolonged Hospitalisation, Dyskinesia (n/a) - Unknown - Caused/Prolonged Hospitalisation, Epstein-Barr vir infection (n/a) - Not Recovered/Not Resolved - Caused/Prolonged Hospitalisation, Fatigue (n/a) - Unknown - Caused/Prolonged Hospitalisation, Feeding disorder (n/a) - Not Recovered/Not			ICSR

By clicking on the ICSR link in the line listing, the users will get the ICSR form

	Suspect/interacting Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	Concomitant/Not Administered Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	ICSR Form
ed - tion, ion, nged (n/a) -	(Suspect - Immunisation - Not applicable - n/a-n/a - UNKNOWN))	Not reported	ICSR



EVPM **Individual Case Safety Report Form** EudraVigilance

Worldwide Unique Case Identification Number
Sender type
Senders Organisation
Type of Report
Primary Source Country
Reporter's qualification
Case serious?

Patient

Age/Age Group	Sex
5 – 15 years old/adolescent	Female

Reaction / event

MedDRA LLT	Duration	Outcome	Seriousness*
Drug reaction with eosinophilia and systemic symptoms		not recovered/not resolved/ongoing	death, life threat., hospital., congen.
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes		not recovered/not resolved/ongoing	death, life threat., congen.
End stage liver disease		fatal	death, disability, other
B-immunoblastic lymphoma (Kiel Classification) refractory		recovered/resolved	life threat., other

Drug Information

Role†	Drug	Duration	Dose	Units in Interval	Action taken
S	B 5 mg/ml		10 mg/kg	1 per 2w	Drug withdrawn
C	[illegible] mg				Dose reduced

Drug Information *(cont.)*

Info‡	Drug	Indication	Pharm. form	Route of Admin.	Parent Route of Admin.
	25 mg/ml	Non-small cell lung cancer	Concentrate for solution for infusion	transplacental	intravenous
	200 mg RECODED	Clonic seizures	Prolonged Release Tablets		

Reaction / event

MedDRA LLT	Drug	Rechallenge
Drug reaction with eosinophilia and systemic symptom		No/na
		Yes/yes
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes		Yes/no
		Yes/unk
End stage liver disease		No/na
		Yes/yes
B-immunoblastic lymphoma (Kiel Classification) refractory		Yes/no
		No/na

Literature Reference

Mudalel ML, Dave KP, Humme JP, Solga SF. N-acetylcysteine treats intravenous amiodarone induced liver injury. World Journal of Gastroenterology 21: 2816-2819, No. 9, Mar 2015

Information concerning the parent for a parent-child/foetus report

Parent

Age	Sex
30-40 years old	Female

* **death**=results in death; **life threat.**=life threatening; **hospital.**=requires hospitalization/prolongation of hospitalization; **disability**=results in disability/incapacity; **congen.**=congenital anomaly/birth defect; **other**=other medically important information; **(blank)**=non-serious
† S=suspect; C=concomitant; I=interacting; N=not administered
‡ 1=Counterfeit; 2= Overdose; 3=Drug taken by the father; 4=Drug taken beyond expiry date; 5=Batch and lot tested and found within specifications; 6=Batch and lot tested and found not within specifications; 7=Medication error; 8=Misuse; 9=Abuse; 10=Occupational exposure; 11=Off label use; **(blank)**=no additional information

Report run: 20/11/2015 09:36:42 Page 1 of 1

3.e. Feedback from Patients and Healthcare professional

- Mock-ups of the proposed line listing and ICSR form have been shared with PCWP and HCPWP on 23rd of February in advance of this meeting to collect feedback

- Questions can be sent directly to
  - Rodrigo Postigo: rodrigo.postigo@ema.europa.eu
  - Francois Domergue francois.domergue@ema.europa.eu

Thank you for your attention

Further information

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