

# MedDRA and EudraVigilance at the EMEA



**MedDRA MSSO Users Group Meeting  
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# EudraVigilance

## I. An Overview

# I. EudraVigilance Overview

- Established through Council Regulation (EEC) No. 2309/93 and Directive 2001/83/EC.
- Represents the European data-processing network and management system developed on the basis of internationally agreed standards.
- Launched in December 2001.
- Successful implementation of the electronic data exchange and management of Individual Case Safety Reports (ICSRs) with pharmaceutical companies and National Competent Authorities (NCAs) in the post-authorization phase of marketed medicinal products.

# I. EudraVigilance Overview

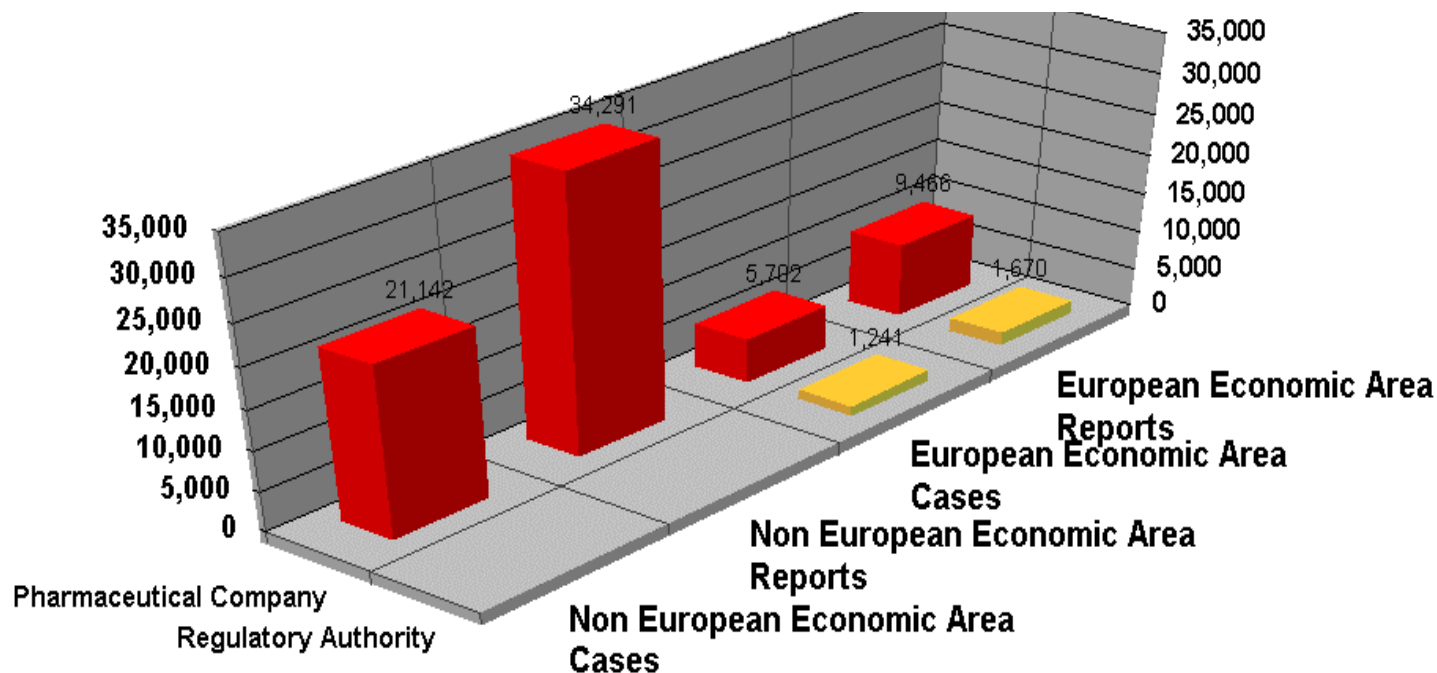
- In the time from 1 December 2001 until 15 February 2004 the following data were received from
  - ◆ 20 Pharmaceutical Companies:
    - ◆ 43,757 individual reports
    - ◆ 26,844 individual cases
  - ◆ 60 company headquarters have registered on EudraVigilance. Of those companies approximately 1/2 have registered their interest in using the EudraVigilance web-reporting tool, others are in a process of testing with the EMEA.

# I. EudraVigilance Overview

- In the time from 1 December 2001 until 15 February 2004 the following data were received from
  - ◆ 3 National Competent Authorities (NCAs):
    - ◆ 1,670 individual reports
    - ◆ 1,241 individual cases
  - ◆ 5 National Competent Authorities are currently testing with the EMEA (Belgium, Sweden, The Netherlands, Finland, Paul-Ehrlich Institute-Germany)



# Overview: EU and non-EU cases and reports provided by Pharmaceutical Companies and Regulatory Authorities in the EEA



Total: 45,427 individual reports referring to 28,514 individual cases

# I. EudraVigilance Overview

- Parallel reporting through pharmaceutical companies as outlined in the Policy Paper
  - ◆ Is effective until NCAs are able to report electronically to the EMEA;
  - ◆ Contributes to efficient data collection of EU ICSRs in EudraVigilance.

*Note: The currently established data exchange between NCAs and pharmaceutical companies remains unaffected.*



# EudraVigilance

## II. Use of MedDRA

## II. EudraVigilance & MedDRA

- Mandatory use of MedDRA in pharmacovigilance post-authorisation activities in in the Community:
  - ◆ Individual Case Safety Reports (ICSRs)
  - ◆ **MedDRA Lowest Level Terms** should be provided as either text (i.e. English MedDRA term) or code according to the regional preferences until January 2003 when codes only will be used in all regions.

## ICH ICSR Patient Characteristics (B.1)

★  
★  
★  
★  
★

Structured info relevant medical history (B.1.7.1)

Relevant past drug history indication (B.1.8)

Reported cause(s) of death (B.1.9.2)

Autopsy-determined cause(s) of death (B.1.9.4)

Relevant medical history parent (B.1.10.7)

Relevant past drug history/parent indication (B.1.10.8)



## ICH ICSR Section Reaction(s) (B.2)

Reaction in MedDRA terminology (B.2.i.1)

## ICH ICSR Section Drug(s) Information (B.4)

Indication for use in the case (B.4.k.11)

Which reaction(s) recurred? (B.4.k.17.2)

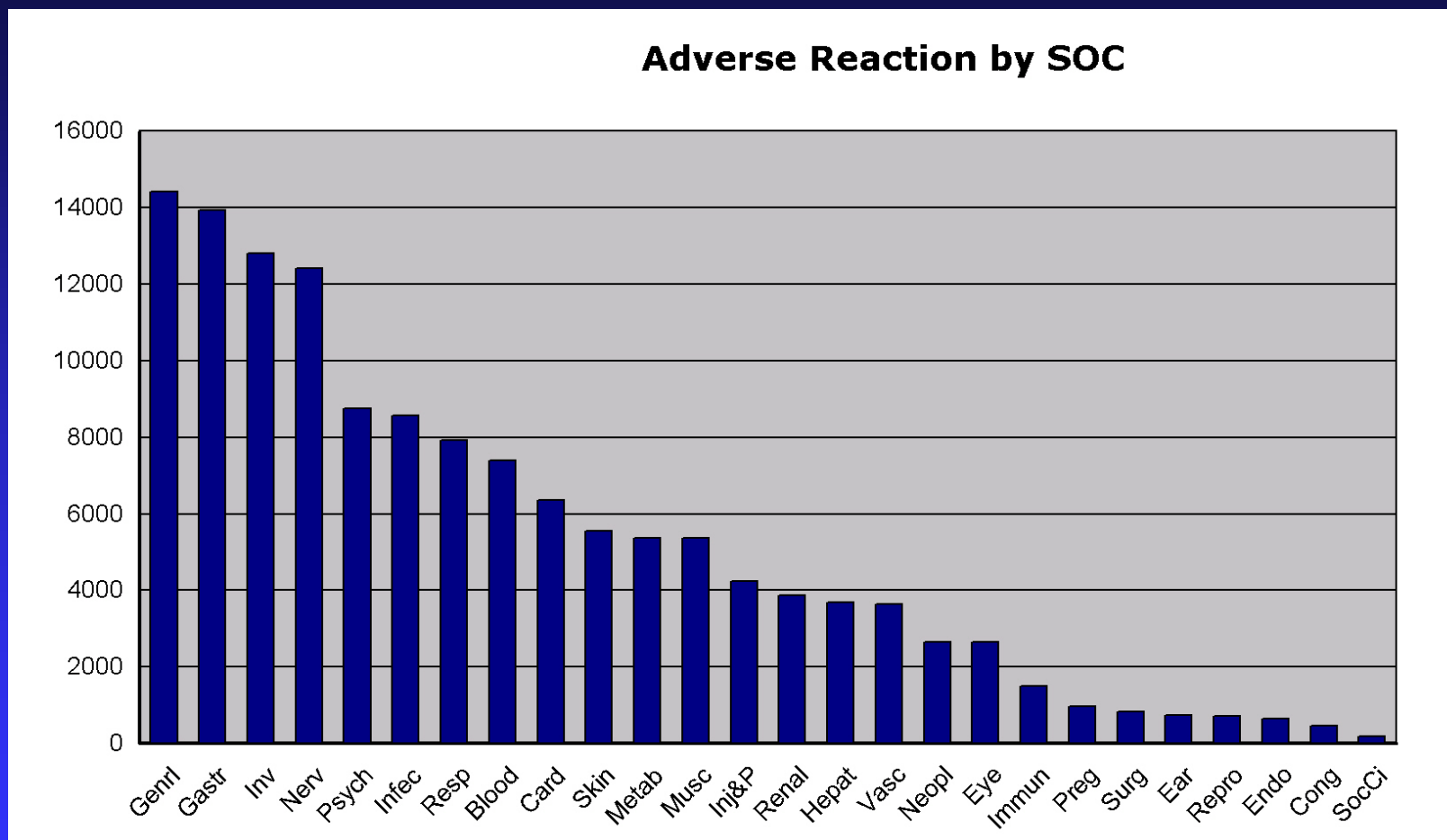
## ICH ICSR Section Narrative case summary (B.5)

Sender's reclassification of reaction (B.5.3)

## ICH ICSR Section Tests and Procedures (B.3)

Tests/investigation of the patient (B.3.1)

## II. Reported Reactions by MedDRA SOC

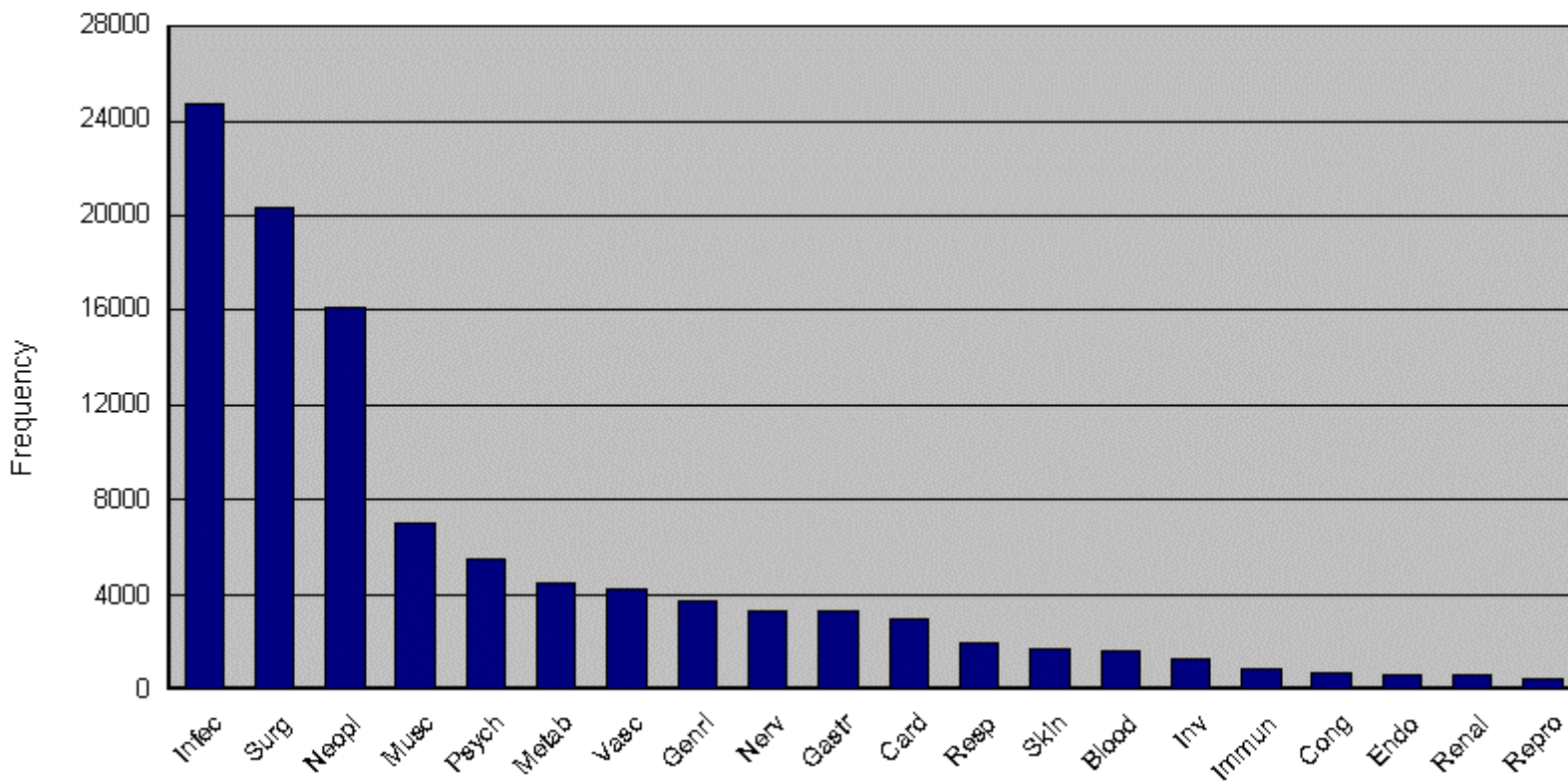


Reaction SOC 6.1		Count (Distinct Reaction ID)
Blood	Blood and lymphatic system disorders	7,385
Card	Cardiac disorders	6,358
Cong	Congenital, familial and genetic disorders	472
Ear	Ear and labyrinth disorders	729
Endo	Endocrine disorders	654
Eye	Eye disorders	2,646
Gastr	Gastrointestinal disorders	13,926
Genrl	General disorders and administration site conditions	14,428
Hepat	Hepatobiliary disorders	3,687
Immun	Immune system disorders	1,498
Infec	Infections and infestations	8,564
Inj&P	Injury, poisoning and procedural complications	4,245
Inv	Investigations	12,817
Metab	Metabolism and nutrition disorders	5,374
Musc	Musculoskeletal and connective tissue disorders	5,360
Neopl	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2,648
Nerv	Nervous system disorders	12,426
Preg	Pregnancy, puerperium and perinatal conditions	967
Psych	Psychiatric disorders	8,753
Renal	Renal and urinary disorders	3,880
Repro	Reproductive system and breast disorders	704
Resp	Respiratory, thoracic and mediastinal disorders	7,931
Skin	Skin and subcutaneous tissue disorders	5,551
SocCi	Social circumstances	181
Surg	Surgical and medical procedures	838
Vasc	Vascular disorders	3,629
<b>Total</b>		<b>135,651</b>

## II. Reported Indications by MedDRA SOC



**2.3.20 Drug Indication**





## 2.3.20 Drug Indication Complete SOC Desc

Indication SOC 6.1	Count (Drug ID)
Infections and infestations	24,718
Surgical and medical procedures	20,320
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	16,117
Musculoskeletal and connective tissue disorders	7,036
Psychiatric disorders	5,462
Metabolism and nutrition disorders	4,483
Vascular disorders	4,255
General disorders and administration site conditions	3,752
Nervous system disorders	3,310
Gastrointestinal disorders	3,284
Cardiac disorders	2,982
Respiratory, thoracic and mediastinal disorders	1,953
Skin and subcutaneous tissue disorders	1,709
Blood and lymphatic system disorders	1,609
Investigations	1,297
Immune system disorders	863
Congenital, familial and genetic disorders	655
Endocrine disorders	579
Renal and urinary disorders	566
Reproductive system and breast disorders	425
Injury, poisoning and procedural complications	389
Hepatobiliary disorders	267
Eye disorders	263
Social circumstances	122
Pregnancy, puerperium and perinatal conditions	59
Ear and labyrinth disorders	46
<b>Total</b>	<b>106,521</b>



## II. MedDRA Term Recoding

- Data Administration and recoding of MedDRA terms:
    - ◆ Indication for use in the case (B.4.k.11): 2,727
    - ◆ Tests/investigation of the patient (B.3.1): 3,298
- Test names that are currently not included in MedDRA are forwarded to the MedDRA MSSO for further discussion regarding a possible integration in the MedDRA terminology.



# EudraVigilance

## III. MedDRA and EudraVigilance Data Warehouse (EVDWH)

## III. EudraVigilance DWH Project

- EudraVigilance data warehouse (EVDWH) and pharmacointelligence project:
  - ◆ Implementation of sophisticated analytical tools for decision making support and data interpretation focused on large volume of data covering the whole life cycle of medicinal products.
  - ◆ Establishment of the EudraVigilance Data Warehouse and Pharmacointelligence Group in May 2003 and initiation of a pilot with experts from NCAs and pharmaceutical industry.

## III. EudraVigilance DWH Project

Development of:

- ◆ Export Transformation and Loading (ETL) procedures and data normalization standards
- ◆ Data Warehouse Standard Query Library
- ◆ Signal detection methodologies
- ◆ EudraVigilance Data Warehouse database and report generation tools
- ◆ Data mining tools
- ◆ Access and security policies

## III. EudraVigilance DWH Project

- ◆ MedDRA is the key element as part of the methodology development for signal detection, data analysis and case assessment.
- ◆ SMQs will be integrated to support the data analysis aspects.
- ◆ Appropriate MedDRA coding in line with the MedDRA Points to Consider guideline is a critical component to assure reliable data output.



# EudraVigilance

IV. MedDRA, EudraVigilance Web Application (EVWEB) and Small and Medium Size Enterprises (SMEs)

# IV. EudraVigilance for SMEs



SME Office



Online Access  
via the Internet  
*Internet Explorer  
vs. 5.5 or superior*

Internet  
https

E  
U  
D  
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I  
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C  
E

- Use of EV Gateway & secure data transmission
- ICSR generation
- Message generation
- Message sending & receiving
- Access to complete MedDRA terminology
- Medicinal Product Dictionary
  - ✓ Access to complete data set
  - ✓ Update of products
  - ✓ Variation of products

## IV. EudraVigilance for SMEs

- Service provided by the EMEA to support e-reporting by SMEs to EMEA and NCAs in the EEA allowing for
  - ◆ Easy access to the EVWEB application via the Internet;
  - ◆ Fast and secure processing of safety and acknowledgement messages;
  - ◆ Standardised fully ICH compliant creation of ICSRs.

## IV. EudraVigilance for SMEs

- Secure communication over the Internet for SMEs without a local Gateway solution:
- Use of the EudraVigilance Gateway through integrated “Web Trader” functionality allowing
  - ◆ Sending and receiving of safety and acknowledgment messages in full compliance with the ICH M2 standards;
  - ◆ Saving of all received messages;
  - ◆ Standardisation of message receivers:
    - ◆ EMEA and NCAs

## IV. EudraVigilance for SMEs

- Online function to create fully ICH E2B(M) and M2 compliant safety and acknowledgement messages and ICSRs (initial and follow-up);
- Access to all relevant standard terminology:
  - ◆ MedDRA in the latest version;
  - ◆ EudraVigilance Medicinal Product Dictionary (EVMPPD);
  - ◆ Other ICH defined terminology.
- Query functions with restricted access to data submitted by SMEs to EMEA.

## IV. EudraVigilance for SMEs

- Prerequisite for use of EVWEB:
  - ◆ Company and User Registration:

All MAHs and users of EVWEB must register with the EMEA through the qualified person for pharmacovigilance;
  - ◆ MedDRA Licensing Process

Indicate MedDRA licence type during registration process

    - ◆ Full MedDRA Subscriber
    - ◆ Low Revenue MedDRA EudraVigilance Subscriber
    - ◆ Low Revenue MedDRA EudraVigilance Fee Waiver

## IV. EVWEB Low Revenue MedDRA Subscription (1)

- Provides access to MedDRA through EVWEB
- Intended for use by SMEs
  - ◆ Available to Small and Micro Sized Enterprises based on the definition of the European Commission

Enterprise category	Headcount	Turnover	Or	Balance sheet total
Small	< 50	≤ € 10 million		≤ € 10 million
Micro	< 10	≤ € 2 million		≤ € 2 million

## IV. EVWEB Low Revenue MedDRA Subscription (2)

### ■ Process

- ◆ Specify MedDRA license category during the registration process for EVWEB
- ◆ License Category
  - ◆ Low Revenue MedDRA EudraVigilance Subscriber:  
More than 100 ICSRs per year – contact MedDRA MSSO for Low Revenue subscription
  - ◆ Low Revenue MedDRA EudraVigilance Fee Waiver  
100 or fewer ICSRs per year to EMEA– EMEA will grant free access to MedDRA through EVWEB
  - ◆ Full MedDRA license if not qualified for Small or Micro Enterprise.

## IV.EVWEB Low Revenue MedDRA Subscription (3)


- Qualification
  - ◆ Meet the criteria for a definition of a small or micro enterprise as defined by the EC;
  - ◆ Small or micro company must be located in the EEA or an Accession Country.
- Pricing
  - ◆ Low Revenue Subscription (\$1,000 per year)
  - ◆ Fee exemption, if small/micro company submits 100 or fewer ICSRs per year directly to EMEA. ICSRs to NCAs are not counted.



# EudraVigilance

V. EudraVigilance Clinical Trial  
Module (EVCTM) and MedDRA

## V. EudraVigilance & Clinical Trials

- 
- A vertical blue bar on the left side of the slide, containing five yellow stars arranged vertically.
- EVCTM will become an integrated part of EudraVigilance to support the electronic reporting of suspected unexpected serious adverse reactions (SUSARs) in the frame of Clinical Trials.
  - EVWEB component will be made available to interested commercial and non commercial sponsors to facilitate e-reporting to
    - ◆ National Competent Authorities
    - ◆ EVCTM

## V. EudraVigilance & Clinical Trials

- E-reporting of SUSARs & MedDRA
  - ◆ LLTs in the latest version (following the MedDRA policy on version control) for all E2B(M) applicable fields including test names.
  - ◆ This policy should apply as of 1 May 2004.
  - ◆ Discussed and approved by the Clinical Trial Expert Working Group established at the level of the European Commission during its meeting on 13 February 2004.

## V. EudraVigilance & Clinical Trials

- MedDRA Licensing Policy
  - ◆ EMEA and European Commission need to address the license fee policy for non commercial sponsors at the MedDRA Management Board level.
  - ◆ Approach similar to SMEs EVWEB licensing policy would be a desired solution.



# EudraVigilance

## VI. Conclusions

## VI. Conclusions



- Current experience based on the electronic reporting has shown that high quality of data can be collected through EudraVigilance.
- MedDRA is a key component of EudraVigilance and the EU pharmacovigilance activities.
- The use of MedDRA will now be stepwise extended to SUSAR reporting in Clinical Trials.

## VI. Conclusions

- The value of data standardisation based on the MedDRA terminology becomes fully evident through the activities in the frame of the EVDWH and the methodology development for data analysis and signal detection.
- Through the EVDWH and a common medical terminology such as MedDRA the scientific experts will be able to effectively evaluate and analyse adverse reaction data covering the whole life cycle of a medicinal product (i.e. pre-and post-authorisation phase).

# Further information

- Web site: <http://eudravigilance.emea.eu.int>
- E-mail: [Eudravigilance@emea.eu.int](mailto:Eudravigilance@emea.eu.int)
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