



EudraVigilance and use of MedDRA

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**MedDRA User Group Meeting
Lisbon, Portugal 2005**



Overview

- **MedDRA and Regulatory Background**
- **MedDRA and ICH E2B(M)**
- **Current Implementation Status in EudraVigilance**
- **EudraVigilance and MedDRA Versioning**



MedDRA

Regulatory Background In the European Economic Area (EEA)



Regulatory Background

- **Regulation (EC) No. 726/2004**
 - Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency
- **Directive 2001/83/EC as amended**
 - Community Code relating to Medicinal Products for Human Use

Use the medical terminology accepted at international level: MedDRA

Save in exceptional circumstances, adverse reactions shall be transmitted electronically

Applicable as of 20 November 2005



Regulatory Background

- **Volume 9 Notice to Marketing Authorisation Holders**
 - **MedDRA should be used**
 - **Mandatory for single case reports received electronically from January 2002**
 - **For regulatory reporting of all adverse drug reactions from January 2003**
 - **Use of the appropriate **Lowest Level Terms****
 - **Use of the **latest version** of MedDRA**



Regulatory Background

- **Directive 2001/20/EC**

- **Implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use**

- **Implementing Texts**

Reporting of suspected unexpected serious adverse reactions (SUSARs) and serious adverse reactions (SARs)

- **The latest version of MedDRA should be applied**
- **Lowest Level terms (LLT) should be used**
- **Where medically appropriate, signs and symptoms can be lumped into diagnoses**



MedDRA

ICH E2B(M) Guideline Version 4.4.1 of 5 February 2001



ICH E2B(M) Guideline

- **Version 4.4.1 of 5 February 2001 and Use of MedDRA**
 - **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 E2B(M) Guideline

- **Version 4.4.1 of 5 February 2001**
 - **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)

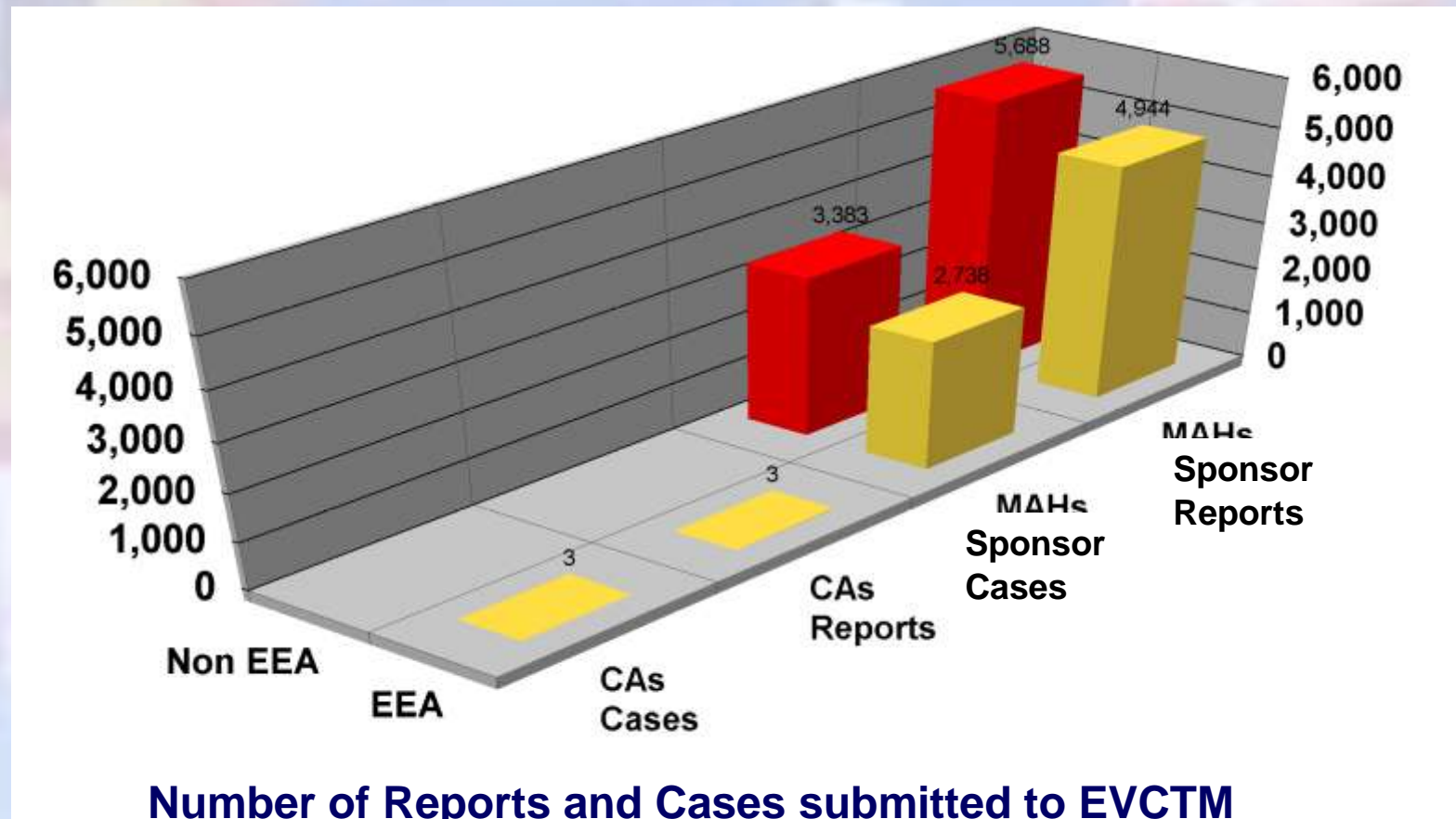


MedDRA

Current Implementation Status of Electronic Reporting and EudraVigilance



EVCTM



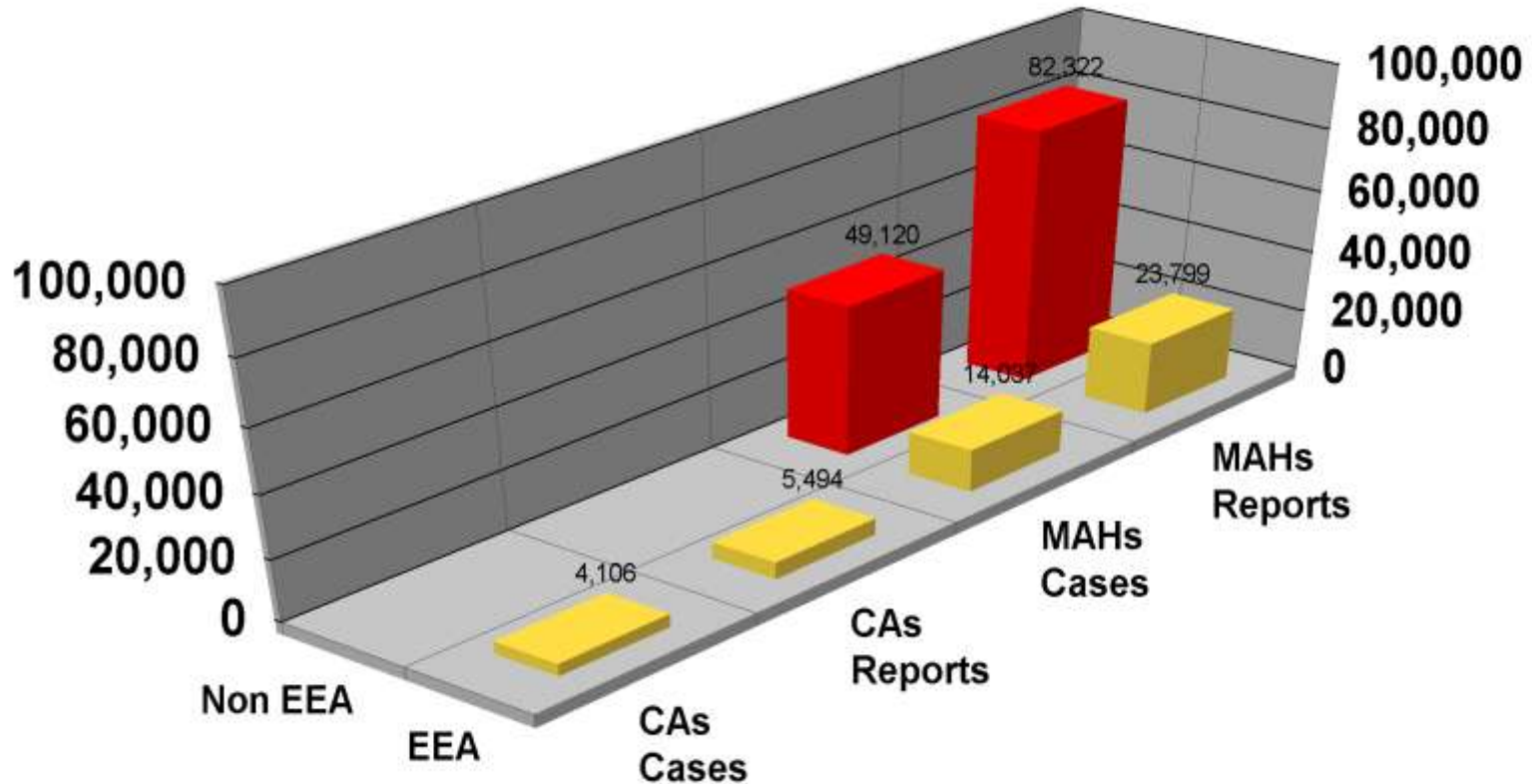
Number of Reports and Cases submitted to EVCTM

16 Sponsors, 10,635 ICSRs-SUSARs, 6,124 Cases

Reporting Period: 1 May 04-28 February 05



EVPM

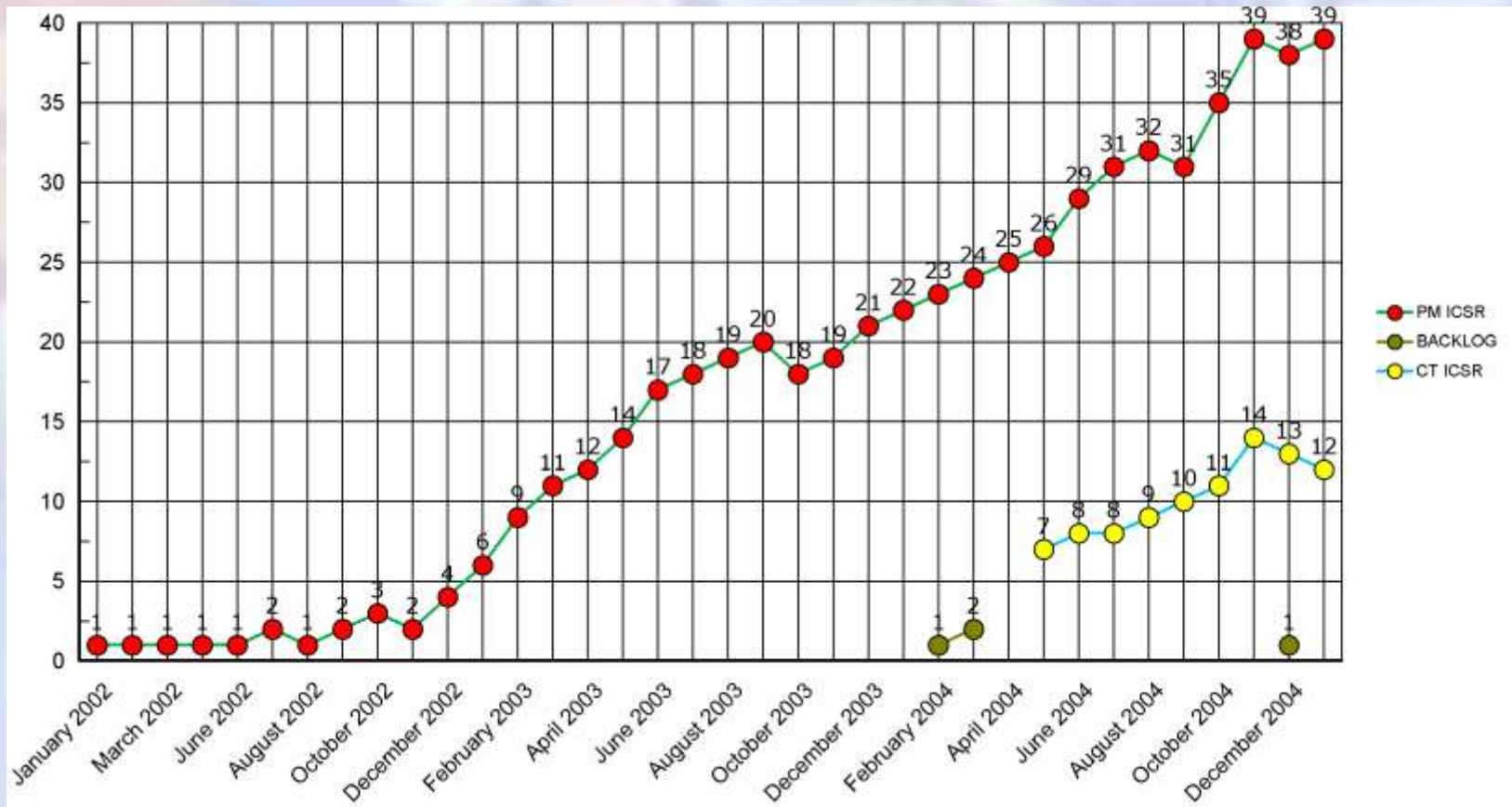


Number of Reports and Cases submitted to EVPM
39 MAHs, 6 CAs 106,121 ICSRs, 63.157 Cases
Reporting Period: 1 January 04 - 28 February 05



EVDBMS

Number of Organisations Reporting per month EVPM and EVCTM





MedDRA

Version Handling in EudraVigilance



EudraVigilance and MedDRA

- **EMEA follows the MedDRA® MSSO's Recommendations for Single Case Reporting using **Semi-annual Version Control****
 - All reporting should be done using the **most recently released version of MedDRA**
 - The version number of the MedDRA release used to code the report should be included in all reports
 - A new version of MedDRA should become the reporting version on the **first Monday of the second month** after it is released i.e. midnight GMT, Sunday to Monday, for the switchover



EudraVigilance and MedDRA

EMA supports

- **Recommendations for MedDRA™ Implementation and Versioning for Clinical Trials (Option 5 and 6)**
- **Option 5** - Freeze version at the beginning of each trial within a project and optionally re-code data with the latest version at the conclusion of the trial. Always output the data utilizing the most recent version of MedDRA.
- **Option 6** – Re-code the trial data for all trials in a project on an ongoing basis with the most recent version of MedDRA.



EudraVigilance and MedDRA

- **EMA supports since January 2005 Supplemental Terms in line with the MedDRA® MSSO's Recommendations for the Implementation of MedDRA Supplemental Terms**
- **Policy to be developed at ICH level to address version handling for supplemental terms**
- **Current EMA approach: reported version in ICSRs should always be the next official version when a supplemental term is used**
 - (e.g. current version 7.1 but if supplemental term is reported, version 8.0 should to be specified)



EudraVigilance and MedDRA

- **MedDRA Versioning** in EudraVigilance Post-Authorisation and Clinical Trial Modules:
 - Previous version for a period of 6 months (e.g. version 7.1)
 - Current version (e.g. version 8.0)
 - Current version plus supplemental terms (version 8.1)



EudraVigilance and MedDRA

- **MedDRA Versioning and Duplicate Detection and Management (Master Reports) in EudraVigilance:**
 - **Currently tested with**
 - **Last six versions (e.g. vs. 5.0, 5.1, 6.0, 6.1, 7.0, 7.1)**
 - **Current version (vs. 8.0)**
 - **Current version plus supplemental terms (vs. 8.1)**



EudraVigilance and MedDRA

- **MedDRA Versioning and retrospective population of**

EudraVigilance Post-Authorisation Module

- **All versions of MedDRA accepted as of version 4.0**
- **Current version plus supplemental terms**

EudraVigilance Clinical Trial Module

- **All versions of MedDRA accepted as of version 6.0**
- **Current version plus supplemental terms**



EudraVigilance and MedDRA

- **EMA is testing the MedDRA Versioning and non-expedited ICSRs submissions referred to in**
- **PSURs**
 - **All versions of MedDRA accepted as of version 6.1**
 - **Current version plus supplemental terms**
- **Annual Safety Reports in Clinical Trials**
 - **All versions of MedDRA accepted as of version 4.0**
 - **Current version plus supplemental terms**



MedDRA

EudraVigilance Licensing Policy and Current Status



EudraVigilance and MedDRA

- **EVWEB facilitates the use of MedDRA in electronic reporting for**
 - **Small and Medium Size Enterprises (SMEs)**
 - **Sponsors of Non-Commerical Trials conducting clinical trials in the EEA**
- **Special EudraVigilance MedDRA Licensing Policy was extended by MedDRA Management Board until November 2005**
- **No license fee for Non-Commerical Sponsors organisations**



EudraVigilance MedDRA License Current Status

Registered MAHs/Sponsors:

TEST ENVIRONMENT:

- **177 Full MedDRA Subscriber**
- **22 EudraVigilance MedDRA Fee Waiver**
- **8 EudraVigilance MedDRA Low Revenue Subscriber**

PRODUCTION ENVIRONMENT:

- **57 Full MedDRA Subscriber**
- **7 EudraVigilance MedDRA Fee Waiver**
- **2 EudraVigilance MedDRA Low Revenue Subscriber**



MedDRA

EudraVigilance - Data Analysis and Examples

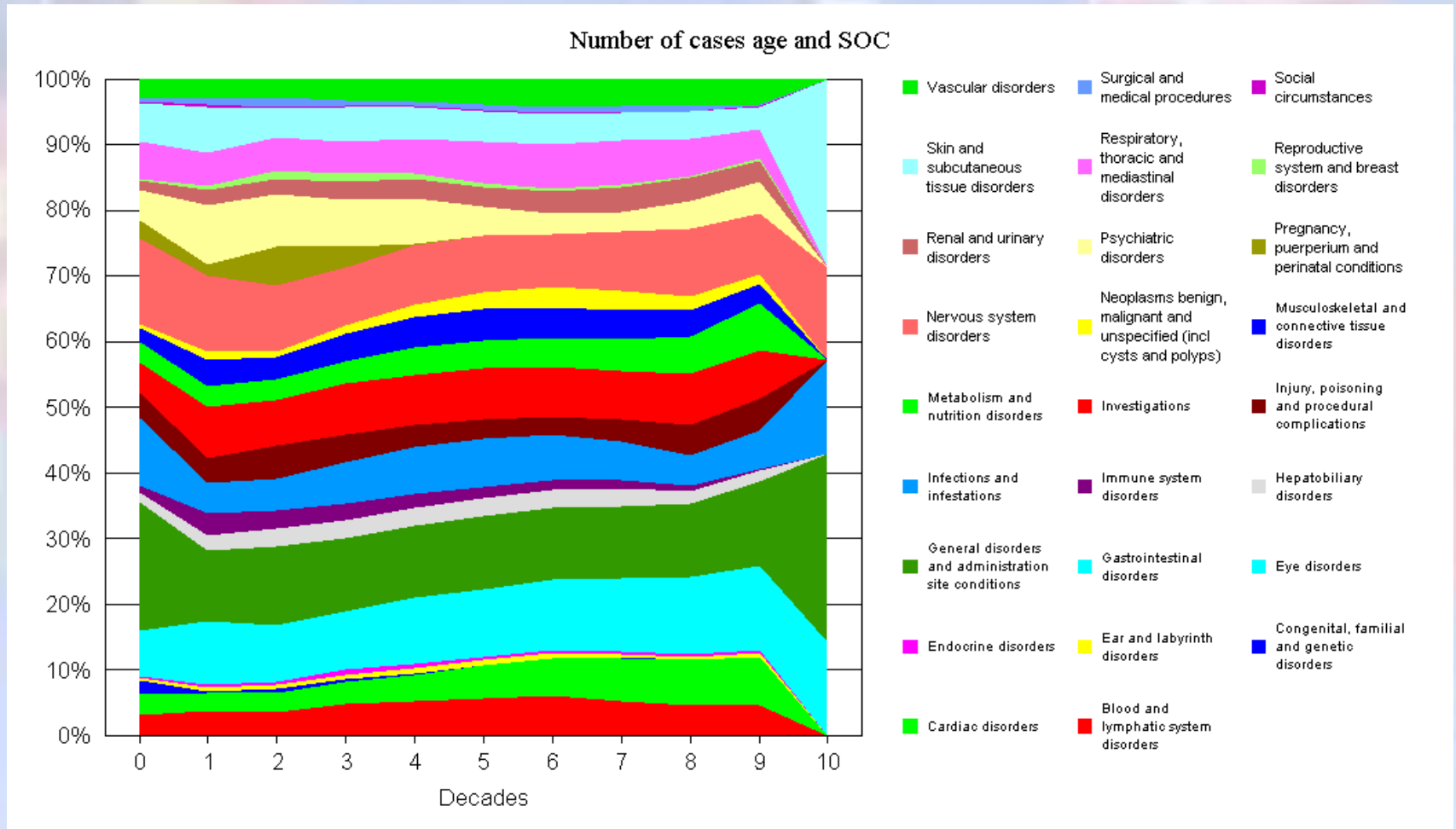


EudraVigilance and MedDRA

The main emphasis besides data coding with MedDRA in line with E2B(M) is now put on **data analysis**

- Appropriate coding practises in line with the MedDRA Points to Consider guideline are fundamental for proper data analysis (MedDRA Training is essential)**
- MedDRA SMQs have been tested and will be implemented in EudraVigilance**
- Currently most of the scientific queries are based on the use of MedDRA**

MedDRA and Data Analysis



Distribution of % of reactions per MedDRA SOC and age of patient

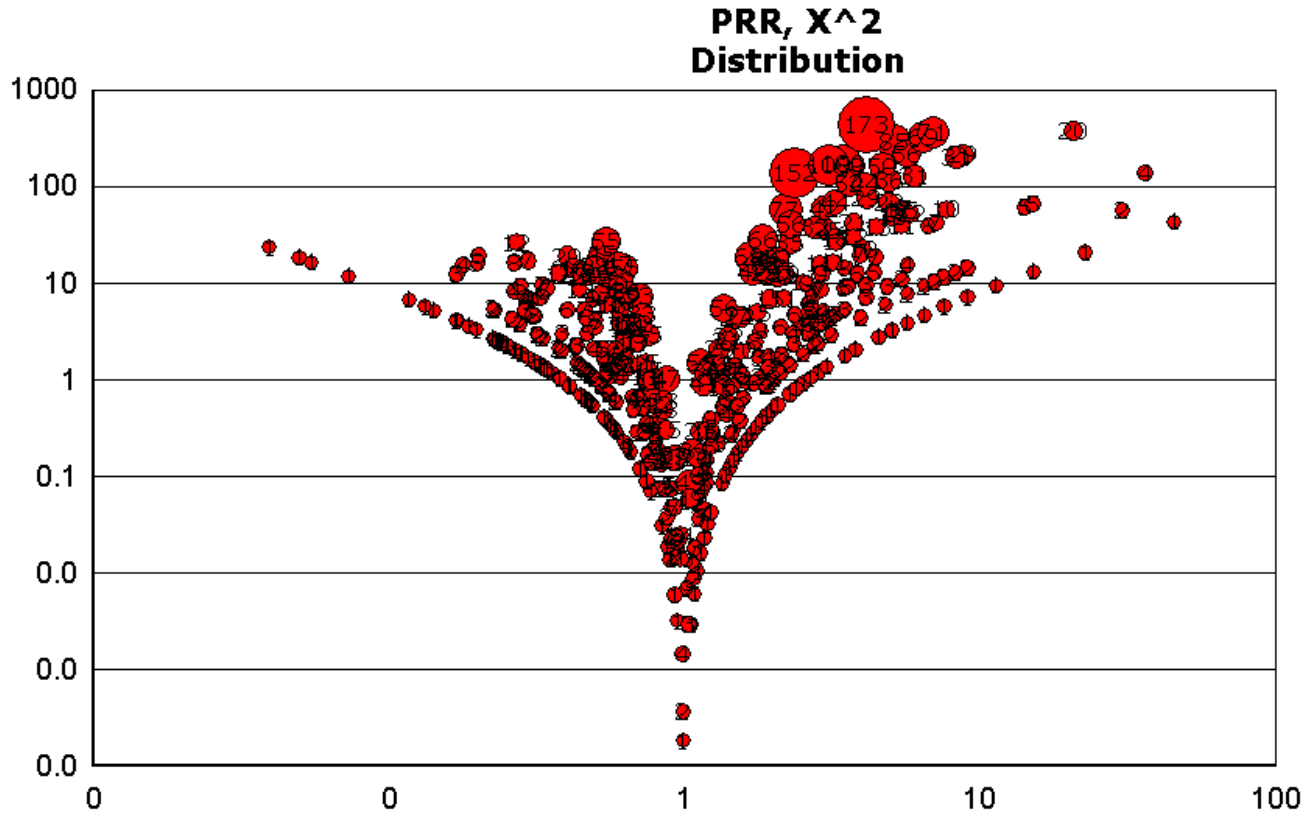
Indication PT	No ICSR	Indication studied in Clinical Trial	Most recent reaction
Schizophrenia	289	YES	02/03/2005
Bipolar disorder	88	YES	12/30/2004
Psychotic disorder	61	YES	11/18/2004
Depression	56	YES	12/02/2004
Schizophrenia, paranoid type	40	NO	12/09/2004
Schizoaffective disorder	36	NO	09/28/2004
Agitation	20	YES	01/05/2005
Schizophrenia, disorganised type	16	NO	01/07/2004
Bipolar I disorder	15	NO	09/27/2004
Drug use for unknown indication	15	NO	11/10/2004



Output

- **Report on Substance XYZ**
- **Indication at PT level**
- **Total number of ICSRs received in EVPM and EVCTM**
- **ICSRs related to the reported indication available in EVCTM for interventional clinical trials phase I-IV**
- **Red: ICSRs with fatal outcome**
- **Double line: Substance XYZ is the Suspect Drug**

EVDWH



Static PRR at HTL level



MedDRA

Revision of the E2B guideline by the ICH E2B(R) EWG



ICH E2B(R) and MedDRA

- **Currently under discussion**
 - **All fields using MedDRA will capture the term at **LLT level****
 - **Capture **single MedDRA version** in the ICSR**
 - **Delete **PT fields** (code and version)**
 - **MedDRA for **Test Names****
 - **Update user guidance in E2B(M) on the use of MedDRA**



MedDRA in the EEA

- **EU will participate at Blue Ribbon Panel discussions on Labelling**
- **MedDRA Translations**
 - **Dutch, French, German, Japanese, Portuguese and Spanish available**
 - **Italian to be released with version 8.0**
 - **Greek translation of the SOC and PT terms of MedDRA for version 4.0**
 - **Under discussion:**
 - **Czech, Hungarian, Latvian and Romanian translation**



Further Information

- **Web sites:**
- **<http://pharmacos.eudra.org>**
- **<http://eudravigilance.emea.eu.int>**
- **E-mail:**
 - eudravigilance@emea.eu.int**
 - sabine.brosch@emea.eu.int**
- **EudraVigilance Helpline:**
 - +44 (0) 207 523 7077**