EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 September 2010
EMA/MB/599720/2010

2009 EudraVigilance-Human Status Report

Management Board meeting 7 October 2010

Background note

The 2009 EudraVigilance-Human Status Report was discussed at the 10 June 2010 Management Board meeting. A number of comments were made by Board Members, including the appropriateness to publish detailed information on (1) the signals detected and the follow-up given, as well as (2) compliance figures for individual Member States with respect to the legal timeframes for transmission of ICSRs to EVMP, since this is the first time such information has been made available. In addition, several Board members asked for further clarification on the information provided.

Matters for consideration

Following the June Board meeting a discussion took place at the July 2010 HMA meeting.

In view of the comments made the Agency will not include the above mentioned information in the public 2009 EudraVigilance-Human Status Report. In addition, clarification will be provided to individual Member States on the compliance figures for transmission of ICSRs to EVMP. Furthermore, a discussion will be initiated at the level of the CHMP on the follow-up by Rapporteurs on the signals communicated by the Agency and how to address the current findings.

As a consequence, the document presented to the Board in June has been revised accordingly as per the attachment. In addition, the Agency will provide the Board on a quarterly basis with updated information so that progress in this field can be monitored. It is the Agency's intention to include detailed information on both the signal management process and Member States' compliance with the legal timeframes for transmission of ICSRs to EVMP in future EudraVigilance-Human Status Reports.

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Patient Health Protection

2009 EudraVigilance-Human Status Report

Key messages

- Significant progress was made during 2009 as regards the use of EudraVigilance, illustrated by a major uptake of Member States in working with EudraVigilance.
- The EMA has been closely working with Marketing Authorisation Holders, Sponsors and Member States to improve the quality of the data submitted to EudraVigilance. Major steps of this initiative are the publication of the new Business Rules and a call for tender launched by the EMA to contract Individual Case Safety Reports and Product Dictionary cleaning.
- A 3 year IT development plan has been adopted by the EudraVigilance Steering Committee. It takes into consideration the new pharmacovigilance legislation and is subject to budget agreement for 2011 and 2012.
- Following the completion of the EudraVigilance retrospective validation study, the Management Board was informed of the strong additive role of EudraVigilance signal detection methods. The study showed significantly earlier detection of drug safety issues in about 54% of cases where a clinically important adverse drug reaction was found (compared to routine pharmacovigilance). The study also underlined the importance of established pharmacovigilance systems, and concluded that a combination of routine pharmacovigilance and statistical signal detection provides the optimal safety monitoring with earlier detection and better management of safety issues, thereby improving the protection of public health. The results of this study have been published in the peer reviewed literature (*Drug Saf 2010; 33:(6)*:475-487).
- Signal management principles were agreed at the level of the CHMP, PhVWP and HMA in 2008. The Pilot conducted in 2008-2009 was successful and showed the principles are viable and an important activity to improve pharmacovigilance work practices.
- In accordance with these agreed principles, the signal detection procedures and activities in place at the European Medicines Agency are producing regular signals and making a significant contribution to the safety monitoring of Centrally Authorised Products. The Agency, Rapporteurs, and National Competent Authorities are working together to strengthen the response and follow up to signals detected.
- The incorporation of signal detection of pandemic medicines was successful, and resulted in effective intensive monitoring and regular proactive publication of safety reports.

Table of contents

Introduction

This report consists of two main parts. The first part elaborates on signal detection and signal management activities performed in 2009. The second part provides an update on the status of implementation of EudraVigilance-Human. The signal detection / signal management activities are performed by the staff of the Signal Detection and Data Analysis Section (P-PV-SDA) of the the Patient Health Protection Unit of the European Medicines Agency. The status of Human EudraVigilance is prepared by the Section of Data Collection and Management (P-PV-CDM), also within the Patient Health Protection Unit.

This report presents a summary of routine and ad-hoc activities within the period of 1 Jan – 31 Dec 2009, and focuses on activities related to Centrally Authorized Products (CAPs). During this period, two major events had a clear impact on working practices and workload: the implementation of the restructuring of the Agency, and the onset of the novel A/H1N1 influenza pandemic, which triggered an EU-wide vaccination campaign starting in Q4 of 2009.

1. Signal Detection

1.1. Signal detection process at the EMA

A total of 1,704 potential safety issues were detected during 2009. This represents an increase of 377 signals[1], i.e. an increase of approx. 28% compared to 2008. These signals are presented below in an aggregated form. Of these, 37 signals were communicated to the Rapporteurs.

As described in the relevant SOPs and other working documents of the European Medicines Agency (EMA), products are classified according to the periodicity of their safety monitoring in:

- **Weekly monitored products**: Products for which, in the opinion of the EMA, a continuous monitoring of the safety profile is critical to protect patient health in Europe. This procedure includes the following steps:
  - the weekly production of a monitoring report that includes a compilation of all serious adverse reactions received in EudraVigilance for that product
  - an immediate screening of this report by a member of the EMA Signal Validation Team in order to identify and validate any new safety information
  - a review within 2 days of any new signal in a meeting of the EMA Signal Validation team
  - an immediate communication to Rapporteurs of new validated signals in order to allow a quick evaluation and a prompt decision-making if necessary.

  Weekly monitored products have included vaccines used in a mass vaccination campaign (such as pandemic vaccines), products with a high level of public interest (such as Tamiflu) or products for which important safety concerns have been raised (such as human papillomavirus virus vaccines).
- **Intensively monitored products**: Products for which, in the opinion of the EMA, a frequent monitoring of the safety profile is important to detect any new safety issue that may need to be reflected in the Product Information or to be further assessed. For these products, the monitoring report is produced and screened every other week. Following validation in the Signal Validation

[1] A signal is information on an adverse event that is new or incompletely documented, that may have causal relationship to treatment and is recognised as being worthy of further exploration (SOP/H/3065).

Team meeting, signals are communicated to Rapporteurs for evaluation and further action if needed.

Intensively monitored products include recent products for which the safety profile has not yet been fully characterised given their limited duration of marketing or the small number of treated patients. The safety profile needs also to be ascertained when a new indication has been granted for a new patient group. For these products, any new information needs to be identified and evaluated without delay. They include products for which an application for a marketing authorisation has been submitted to the Agency, products that have been authorised for less than 2 years, products with recent extension of indication or line extensions that could modify the target population of patients, and products that have been authorised for longer but have had a substantial recent change in labelling (< 1 year).

- **Routinely monitored products**: Well-known products for which, in the opinion of the EMA, a periodic monitoring of the safety profile is adequate to detect any new information that may need to be transmitted to the Rapporteur for further evaluation. For these products, the monitoring report is produced and screened once a month. Following validation in the Signal Validation Team meeting, signals are communicated to Rapporteurs for evaluation and further action if needed. For these products, typical steps in the validation process consist in consulting assessment reports of Periodic Safety Update Reports (PSURs) for previous evaluations of a specific issue by the Rapporteur, the list of safety issues already discussed by the Pharmacovigilance Working Party or the literature.

  Routinely monitored products are those products for which the safety profile is well known, based on data collected over several years of marketing or extensive post-authorisation studies. New serious adverse reactions are not expected to occur frequently, but the Rapporteur is quickly informed if a new signal is detected.

  Routinely-monitored products include products that are not weekly or intensively monitored. Intensively-monitored products are transferred to the list of routinely-monitored products after two years of authorisation, unless this is decided otherwise in the Signal Validation Team meeting. In such case, the product is kept in the list of intensively-monitored products for one year and re-evaluated after this period. Reasons for keeping a product as an intensively-monitored product may include a limited marketing during the two first years of authorisation, a new important identified or potential risk leading to an amendment of the Risk Management Plan (RMP), or the introduction of a new risk minimisation measure.

OVERVIEW	2009	2008
Weekly monitoring	125	N/A
Intensively monitored	733	976
Routinely monitored	846	351
Total	**1704**	**1327**

Following review of monitoring reports, signals are discussed and validated by the EMA Signal Validation Team. A validated signal is one that the Signal Validation Team decides should be communicated to the Rapporteur.

The action taken with potential signals is classified as follows:

- Closed (further investigation is not required)
- Ongoing (investigations are currently taking place)
- Monitored (not enough evidence to pursue, but will be kept under monitoring)
- Communicated to Rapporteurs (via EPITT (European Pharmacovigilance Issues Tracking Tool) and direct email)

A total of 37 signals were communicated to Rapporteurs. Type and timing of these responses have been monitored and will be used to improve the signal management process.

The feed back received from Rapporteurs is being evaluated and classified by the Agency to standardise the responses and to improve the process of signal communication across the EU.

The lessons learnt from this experience are twofold:

- For audit purposes, it is necessary to have a structured tracking system in which feed-back from Rapporteurs can be incorporated, to follow the safety issue.
- A time delay between signals raised and feed-back received was identified in some cases. This delay was very variable. Mechanisms have been put in place to improve these procedures.

1.2. Retrospective validation study

Signal detection processes at the EMA use complementary statistical and established pharmacovigilance methods.

The Retrospective Validation study (Validation of Statistical Signal detection for CAPs in EudraVigilance, presented to HMA June 2009) concluded that:

- The use of statistical tools substantially enhances the signal detection process;
- The use of Proportional Reporting Ratio (PRR) method in EudraVigilance can provide significant earlier detection of drug safety issues in about 54% of the cases where a clinically important adverse drug reaction was found (compared to routine pharmacovigilance).
- Established pharmacovigilance and PRR analysis are complementary.

The results of this study have been published in the peer reviewed literature (*Drug Saf 2010*; 33:(6):475-487).

2. Signal management in the EU

The first 6 months of 2009 saw the completion of the Pilot of Signal Management in the EU (Pilot period was 18 November 2008 – 31 May 2009).

Following the adoption of the final report on the Pilot by the Pharmacovigilance Working Party (PhVWP) on 22 July and CHMP on 18 August 2009, Signal Management Principles in the EU, as endorsed by Heads of Medicines Agencies (HMA) were considered to be viable, and an important activity to improve pharmacovigilance work practices. In September 2009, the next phase (the practical execution) of the basic premises of the Pilot were put into practice: to increase transparency between Member States and the EMA regarding signals detected and their management, and to support work-sharing principles at the level of signal assessment.

To facilitate the progression of this important aspect of EU pharmacovigilance, the PhVWP agreed on the creation of a new Drafting Group. Following a request for volunteers and a call for a new chairperson, a new group was created in January 2010, and meets on Monday evening following closure of the PhVWP plenary.

In the frame of the implementation of the Pilot, the contributions of Member States to the signal management initiative in EPITT for the period covered by this report have been monitored.

3. Pandemic influenza A/H1N1 (2009)

Following the authorisation of 3 vaccines to prevent novel influenza A/H1N1 virus in Sep 2009, and the adoption of the *European strategy for benefit-risk monitoring of influenza A/H1N1 vaccines*, weekly monitoring of safety reports for pandemic vaccines and the centrally-authorized antiviral Tamiflu was established.

In the period of this report, 10 weekly reaction monitoring reports (RMR) for pandemic vaccines were produced by P-PV-DCM and reviewed by P-PV-SDA (first RMR 29/10/2009); this led to the review of 41 potential signals: 2 for Celvapan, 17 for Focetria and 22 for Pandemrix. Procedures continued uninterrupted into the New Year.

Similarly, 34 weekly RMRs for oseltamivir and zanamivir-containing products were produced and reviewed; this led to the review of 44 potential signals for antivirals.

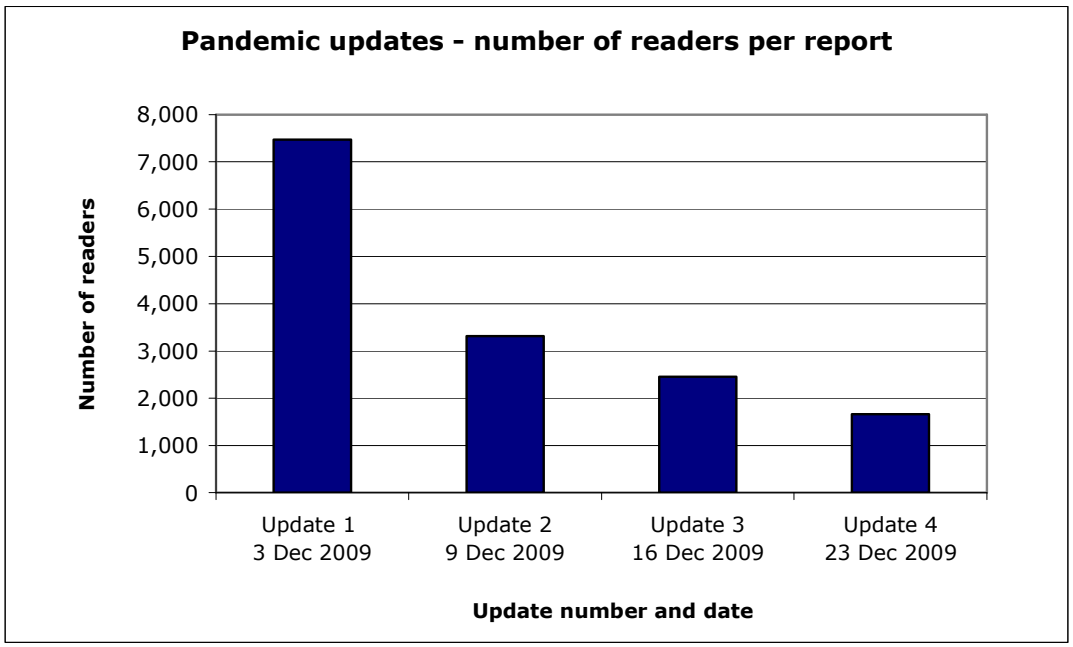
Responding to the Pandemic situation has provided important experience in vaccine signal detection and in the production of proactive information of safety data from EudraVigilance for external publication.

3.1. Pandemic pharmacovigilance update

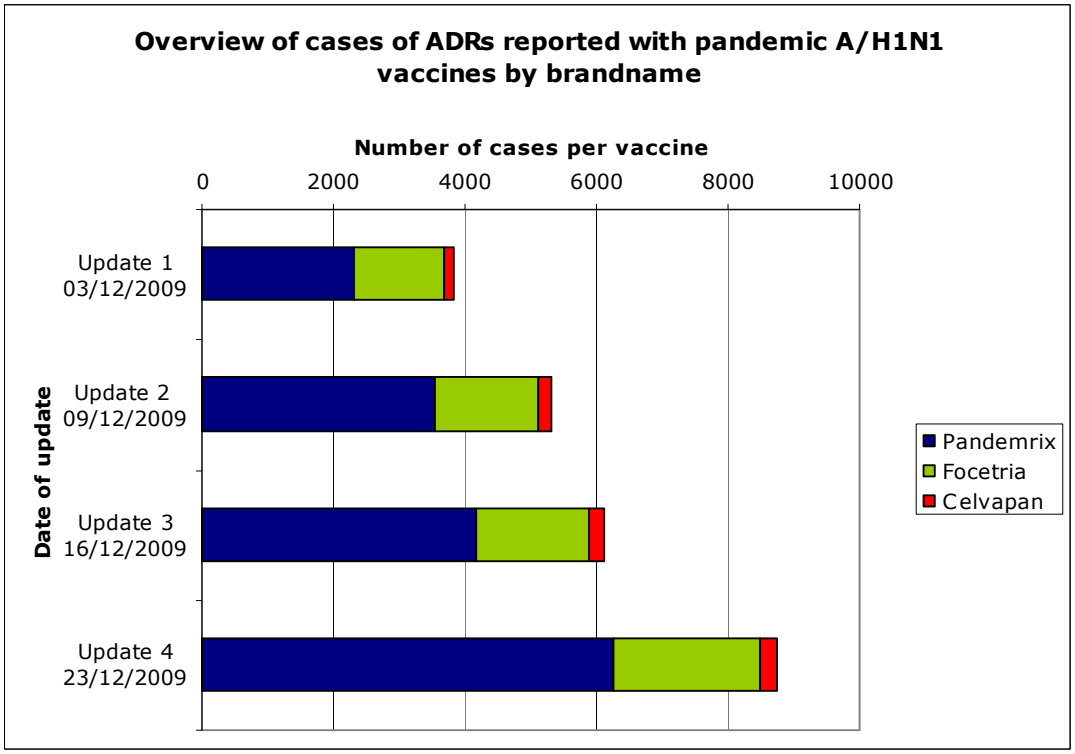
A weekly update to make safety information available to the public was implemented in late 2009, with the first Pandemic Pharmacovigilance Update published on Dec 3 2009, on the EMA website. A list of the published reports is available on the EudraVigilance website.

These reports contain key safety messages related to pandemic medicines, an overview of the pandemic situation in the EEA including summaries of new information from the European Centre for Disease Prevention and Control (ECDC) and the World Health Organisation (WHO), an overview of safety information of centrally authorised vaccines including exposure data, and detailed reporting activity of the centrally authorised vaccines and Tamiflu, with numbers of reports per System Organ Class (high level grouping per organ systems), list of most frequently received adverse events per product and updated safety information including deaths for each product.

Four updates were published by the end of 2009, with positive feedback received from stakeholders. The following chart documents the public interest in the pandemic weekly updates in the initial phases of the vaccination campaign (number of visits received to the relevant section of the website, presented as number of readers):



The distribution of reported cases of ADRs for the 3 centrally authorised A/H1N1 pandemic vaccines received during the period covered by this report is presented here, by brandname.



An overview of the issues reviewed was published as part of the Pandemic pharmacovigilance update and is presented below.

Update date	Celvapan	Focetria	Pandemrix
1st Update 3 Dec 2009		Cerebral haemorrhage	Fever, local reaction and drowsiness following 2nd dose in children 6-35 months old Pregnancy-related events Anaphylactic reactions in children Guillain-Barré syndrome Heart transplant rejection
2nd Update 9 Dec 2009	Paraesthesia Anaphylaxis, angioedema, hypersensitivity	Pregnancy-related events Guillain-Barré syndrome	Anaphylactic shock Pregnancy-related events Transplant rejection
3rd Update 16 Dec 2009	Circulatory collapse	Anaphylactic shock Acute Disseminated Encephalomyelitis (ADEM) Encephalitis	Transplant rejection Injection site necrosis Guillain-Barré syndrome Paralysis and paresis Cerebral infarction
4th Update 23 Dec 2009	Guillain-Barré syndrome Eye disorders	Guillain-Barré syndrome	Guillain-Barré syndrome Idiopathic thrombocytopenic purpura (ITP) Sudden hearing loss Seizures with fatal outcome.

3.2 Collection of exposure data

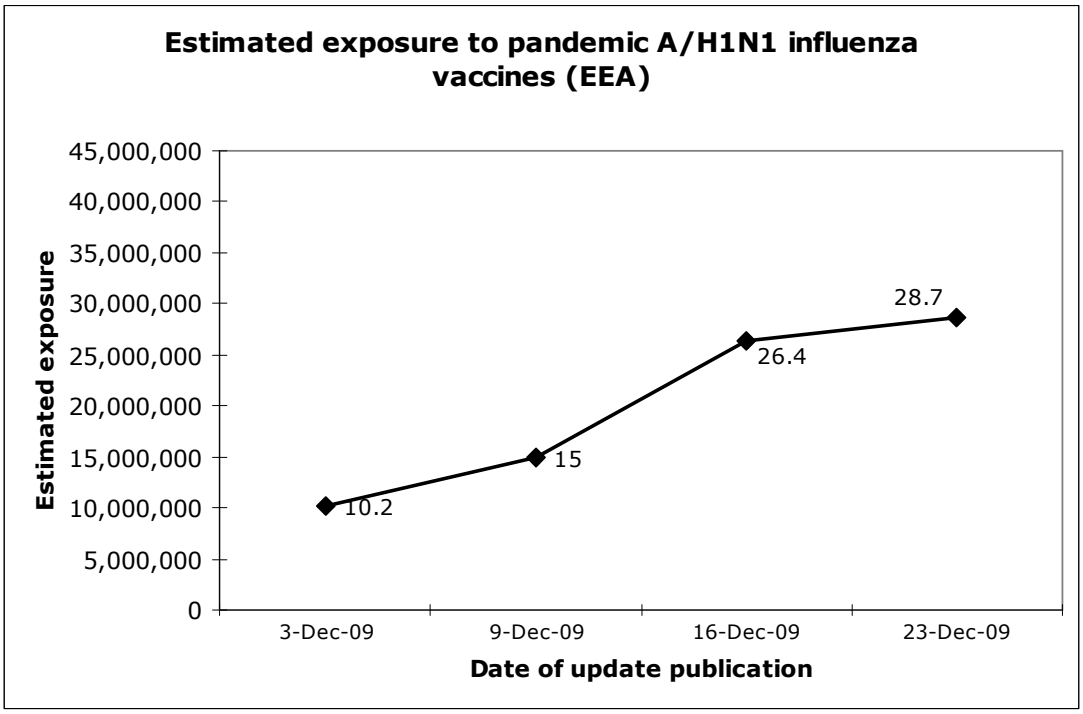
Exposure data to pandemic vaccines was required for assessment of safety data. The need for a 'live' collection of exposure data was identified, and implemented via a Non-Urgent Information request, an established exchange mechanism system between Agencies in the European Network. Every week a table with up-to-date available exposure data was circulated to PhVWP members with a request for national data.

The Agency collated the information from the Member States and from the monthly PSURs.

Following some initial adjustments and formatting modifications, the exposure table was distributed to all relevant stakeholders weekly from 2 December 2009 onwards. The information was stratified per vaccine brandname, separating number of distributed doses from vaccinated individuals. It also allowed for collection of exposure data regarding specific patient population (i.e. pregnant women), sex and age distribution.

Although the information collected was by no means complete, it proved very useful for data analysis purposes and become the exposure reference point for pharmacovigilance activities in the EU.

A graph summarising exposure data received during the period of this report is presented below. The times presented are as per publication date of pandemic pharmacovigilance update.



3.3. PREG

Following consultation of the PhVWP and the CHMP, a Pandemic Pharmacovigilance Rapid Response Expert Group (PREG) was created on 29 Oct 2009. The PREG remit included:

- To look into serious safety issues and information arising with potential to impact on the balance of risk and benefits;
- To review both new information and emerging information on known risks, since the possibility that data on adverse events already listed will impact on benefits risk could not be excluded (e.g. frequency of reporting);
- To address issues referred to the PREG by a member or a Member State;
- To provide advice on the collection of additional information and not specifically only on design of clinical trials.

In the period covered by this report, 8 PREG teleconferences took place between 5 Nov 2009 and 30 Dec 2009, including two teleconferences during the Christmas break period.

3.4. Reporting of batches

According to EU Pharmacovigilance guidelines cases concerning biologicals should be reported with the invented name and batch number of the medicinal product involved in the safety issue. This is of particular relevance for potential safety issues with pandemic vaccines in the context of mass vaccination across the EEA.

An analysis of data received in EudraVigilance during the period of this report showed that two thirds (7,543) of the 11,272 identified cases related to pandemic vaccines had one or more batch numbers reported (the batch numbers reported can not be guaranteed as valid; the values provided by the reporters were not always in accordance with the E2B guidelines and the most obvious data quality

issues were excluded. Therefore, it is likely that the batch number reporting rate as provided in this report is over-estimated). In about one third of the cases (3,729) the batch numbers were missing. The distribution per brandname is presented below.

Vaccine product(s)	Total EV cases 31/12/2009	No of cases with batch/lot	No of cases without batch/lot	% of cases with batch/lot
Pandemrix	8,187	5,896	2,291	72
Celvapan	212	144	68	68
Focetria	2,667	1,365	1,302	51
Total (CAPs)	11,066	7,405	3,661	67
Other*	206	138	68	67
All vaccines	**11,272**	**7,543**	**3,729**	**67**

* Other refers to vaccines other than Celvapan, Focetria, and Pandemrix reported to EudraVigilance during vaccination campaign 2009/10. This could include Arepanrix, Cantgrip, Celtura, Fluval P, Humenza, Panenza, and cases with vaccines under development sent to EV CTM module.

The batch reporting rate for the 26 EEA countries was as follows:

- 60% or more for 18 countries;
- 70% or more for 16 countries;
- 80% or more for 10 countries;
- 100% for 4 countries with relatively small total number of cases reported.

The population of the batch field was not uniform with fewer batches reported in CT than in spontaneous reports: A total of 11,254 cases were reported to EVPM ICSR(s), 67% of which had batch number, and 6 were reported to EVCTM ICSR(s), with 50% having batch number. Batch number reporting was also higher in non health care professionals group, as detailed below.

Number of cases	Qualification	With Batch/Lot Number	Without Batch/Lot Number	% of cases with batch/lot
4,452	Health Care Professional	2,644	1,808	59
6,798	Consumer or other non health professional	4,890	1,908	72
22	Not Specified	9	13	41
11,272	All	7,543	3,729	67

Finally, compliance with batch reporting was uneven among different senders. A total of 21 National Competent Authorities and 9 companies or other organisations were reporting batches as of 31 December 2009.

4. Status of Human EudraVigilance

An average of 48,000 reports were received per month and made available for analysis to the EMA and the Member States. There was a major uptake of Member States in working with EudraVigilance. Since 2007, 90% of NCAs have analysed data in the system (as of 31 Dec 2009, there were 134 regular users from the NCAs). An average of over 2,000 data analyses using the EudraVigilance Data Analysis System were conducted per month. Availability of the database for analysis by the Member States and the EMA is on average more than 98%.

EudraVigilance supports signal detection and data analysis by Member States including regular notification of Reaction Monitoring Reports in the context of the EudraVigilance Support Programme, which was extended to include all pandemic influenza vaccines for circulation to all Member States and the ECDC.

In the context of making the data in EudraVigilance accessible to the Member States and, in the future, to all stakeholders, the EMA has undertaken work in relation to the quality of the ICSRs reported by NCAs, Marketing Authorisation Holders (MAHs) and clinical trial sponsors. In addition to performing "data cleaning" of medicinal product data and checking the quality of the reported ICSR data the EMA in 2009 published an Invitation to Tender to perform ICSR data quality checks on data transmitted to EudraVigilance by all stakeholders, to detect and remove duplicate cases from EudraVigilance, to populate the EudraVigilance Medicinal Product Dictionary (EVMPD), to recode the medicinal product data transmitted in ICSRs against the EVMPD and, when required, to translate case narratives into English. This will ensure that all the data in EudraVigilance is of the highest possible quality and consistency, to provide the most accurate possible results for the pharmacovigilance analysis.

In addition to the "data cleaning" efforts undertaken by the EMA on the data currently in EudraVigilance, the EMA has introduced, after consultation with all stakeholders, a series of measures designed to ensure that data received in the future is of the highest standard. These measures, including notifications on expedited reporting compliance, support to pharmacovigilance inspectors and recently enhanced business rules, will further benefit the protection of public health as the analysis of the adverse reaction data in EudraVigilance will be further strengthened.

Looking to the future, the EMA is actively engaged in harmonisation activities at ICH in the context of the ongoing international standardisation work and has produced a 3-year development plan, intended to ensure compliance with the new pharmaceutical legislation and technical developments, which was adopted by the EudraVigilance Steering Committee. The development plan incorporates the following amendments to the system: making the appropriate data available to all EU citizens in line with the EudraVigilance Data Access Policy (currently being finalised following public consultation), upgrading the EVMPD to incorporate the Medicinal Product ID (MPID) fields (see section 5.2.2 for more information relating to the MPID) and upgrading the system infrastructure to ensure, amongst other benefits, compliance with the EMA's Business Continuity Plan.

4.1. Current Status of Implementation of EudraVigilance-Human Covering the Period 1 January 2009 – 31 December 2009

Activities focused on:

- The continuation of the EVDAS roll-out to the NCAs. The EudraVigilance Support Programme was launched, sending bi-weekly reaction monitoring reports to NCAs to aid routine pharmacovigilance. 13 NCAs signed up for this during 2009.

- Ensuring that MAHs for CAPs and NCAs are complying with the mandatory electronic reporting of ICSRs:
  - By end-2009 all Member States were in production with EudraVigilance for the electronic reporting of ICSRs in the post-authorisation phase.
  - By end-2009 two MAHs for CAPs were not yet in production with EudraVigilance and the EMA continues its efforts to ensure that those companies meet their obligations within the shortest possible timeframe.
  - Retrospective population of EudraVigilance continued to increase; 187,824 backlog ICSRs and SUSARs were submitted during the period 1 January 2009 – 31 December 2009.

9 EudraVigilance Expert Working Group and 2 EudraVigilance Steering Committee meetings were held during 2009.

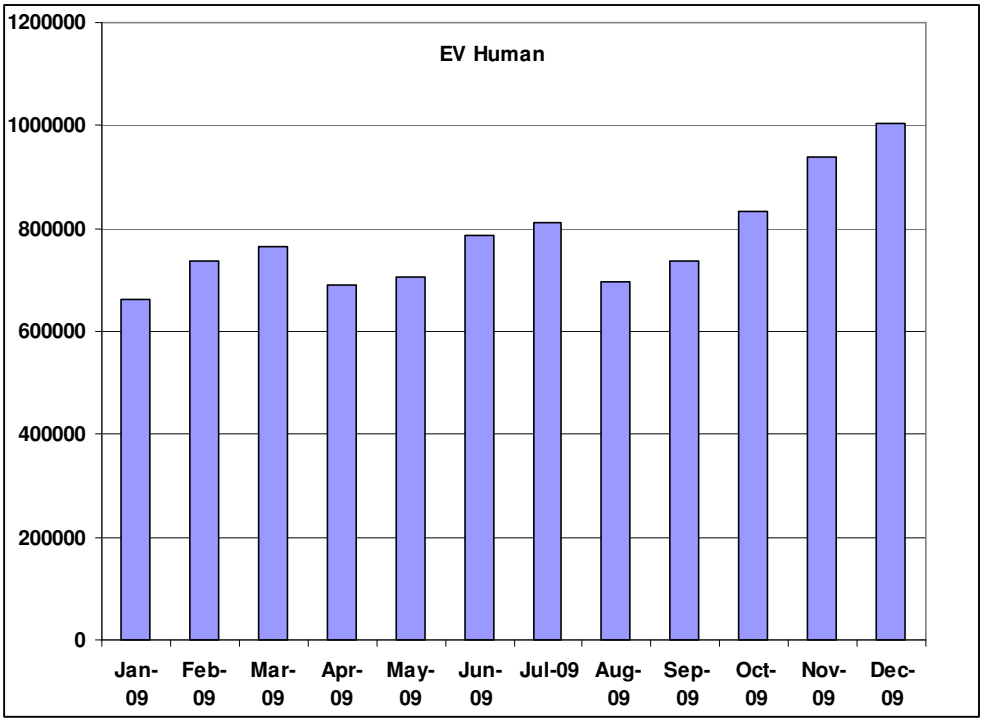
The three-day user training courses for the EVWEB application, the one-day training course for the EVMPD and the three-day EVDAS training course for NCAs continued during the reporting period.

4.1.1. EudraVigilance Gateway

With regard to the reporting period from 1 January 2009 – 31 December 2009 a total of 9,366,731 transactions (including message disposition notifications) were performed by the EudraVigilance Gateway (production). These transactions included messages exchanged between the EMA, pharmaceutical companies, sponsors of clinical trials and NCAs and rerouted messages to and from NCAs, sponsors of clinical trials and pharmaceutical companies.

Overall, between the establishment of the EudraVigilance Gateway in November 2001 and 31 December 2009, a total of 22,657,967 transactions have been performed.

Graph 1 gives an overview of the number of transactions for the EudraVigilance Gateway (Production) from 1 January 2009 – 31 December 2009.



Graph 1: Total number of transactions performed per month at the level of the EudraVigilance Gateway from 1 January 2009 – 31 December 2009.

4.1.2. EudraVigilance Database (EV)

E-reporting status for MAHs and Sponsors of Clinical Trials

- A total of 297 MAHs (at headquarter level) have sent reports to EVPM in the period between 1 December 2009 and 31 January 2009.
- A total of 300 sponsors of clinical trials (at headquarter level) have sent reports to EVCTM in the period between 1 January 2009 – 31 December 2009.
- Tables 1 and 2 below show the total (both expedited and non-expedited) number of unique cases and ICSRs transmitted by MAHs and Sponsors to EVPM and EVCTM and the 15-day reporting compliance of MAHs and Sponsors of Clinical Trials when reporting to EVPM.

EVPM	ICSRs	399,136
	Individual Cases	259,308
	Backlog cases	90,744
EVCTM	ICSRs	69,718
	Individual Cases	28,945
	Backlog cases	1,140

Table 1: Number of ICSRs and unique cases transmitted by MAHs & Sponsors to EVPM & EVCTM during 2009

% of ICSRs transmitted to EVPM within 15 days	92.7

Table 2: Combined 15-day reporting compliance to EVPM for all MAHs and Sponsors

E-reporting status for NCAs

- All 31 NCAs have been authorised to enter into production with EudraVigilance.

  EVPM: All NCAs have reported ICSRs to EVPM, except for AFLUV (Liechtenstein) & the Division de la Pharmacie et des Médicaments (Luxembourg), for whom special arrangements are in place:

  - All ICSRs occurring in Liechtenstein are transmitted to EudraVigilance by MAHs
  - The NCA for Luxembourg has their reports transmitted by AFSSAPS.
- During 2009, the following 11 NCAs transmitted SUSARs to EVCTM:

Federal Agency for Medicines and Health Products	Belgium
Danish Medicines Agency	Denmark
National Agency for Medicines	Finland
Federal Institute for Drugs and Medical Devices	Germany
Paul-Ehrlich-Institut	Germany
National Organisation for Medicines	Greece
Medicines Authority	Malta
College ter beoordeling van geneesmiddelen	Netherlands
Norwegian Medicines Agency	Norway
Infarmed	Portugal
Medicines and Healthcare Products Regulatory Agency	United Kingdom

- Backlog: During 2009, the following 18 NCAs transmitted backlog cases to EVPM & EVCTM

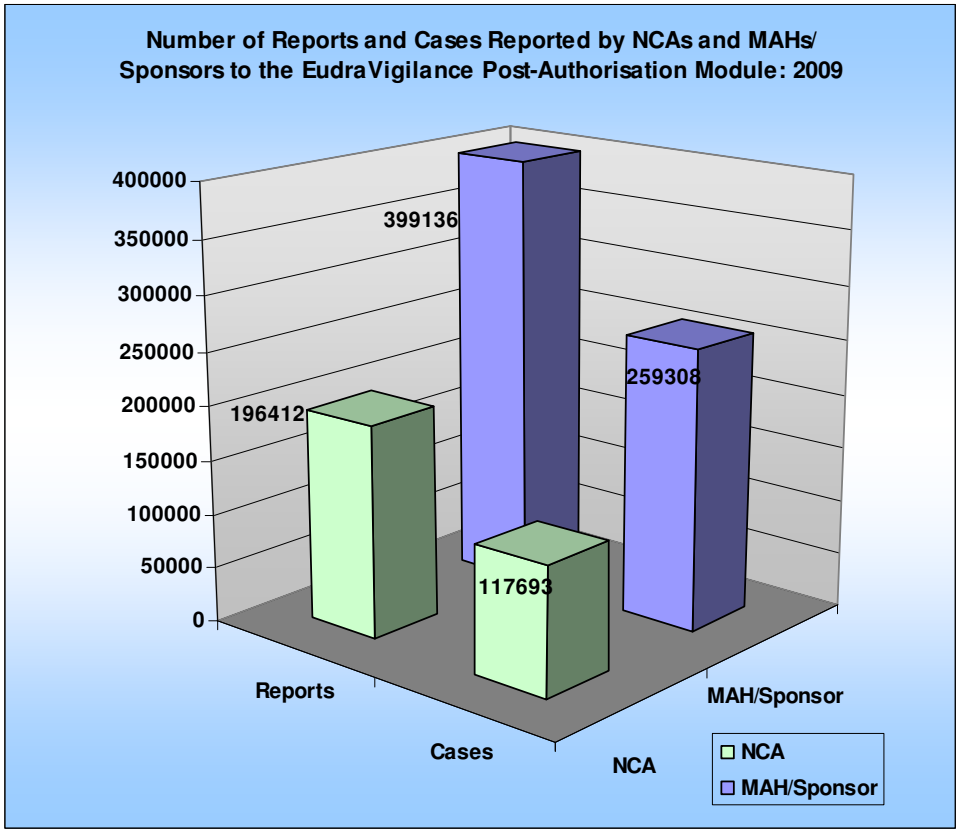
Agentur für Gesundheit und Ernährungssicherheit	Austria
Federal Agency for Medicines and Health Products	Belgium
Bulgarian Drug Agency	Bulgaria
State Institute for Drug Control	Czech Republic
Danish Medicines Agency	Denmark
Federal Institute for Drugs and Medical Devices	Germany
Paul-Ehrlich-Institut	Germany
National Organisation for Medicines	Greece
National Institute of Pharmacy	Hungary
AIFA	Italy
State Agency of Medicines of the Republic of Latvia	Latvia
State Medicines Control Agency	Lithuania
College ter beoordeling van geneesmiddelen	Netherlands
The Office For Registration of Medicinal Products	Poland
Infarmed	Portugal
State Institute for Drug Control	Slovakia
AGEMED	Spain
Medical Products Agency	Sweden

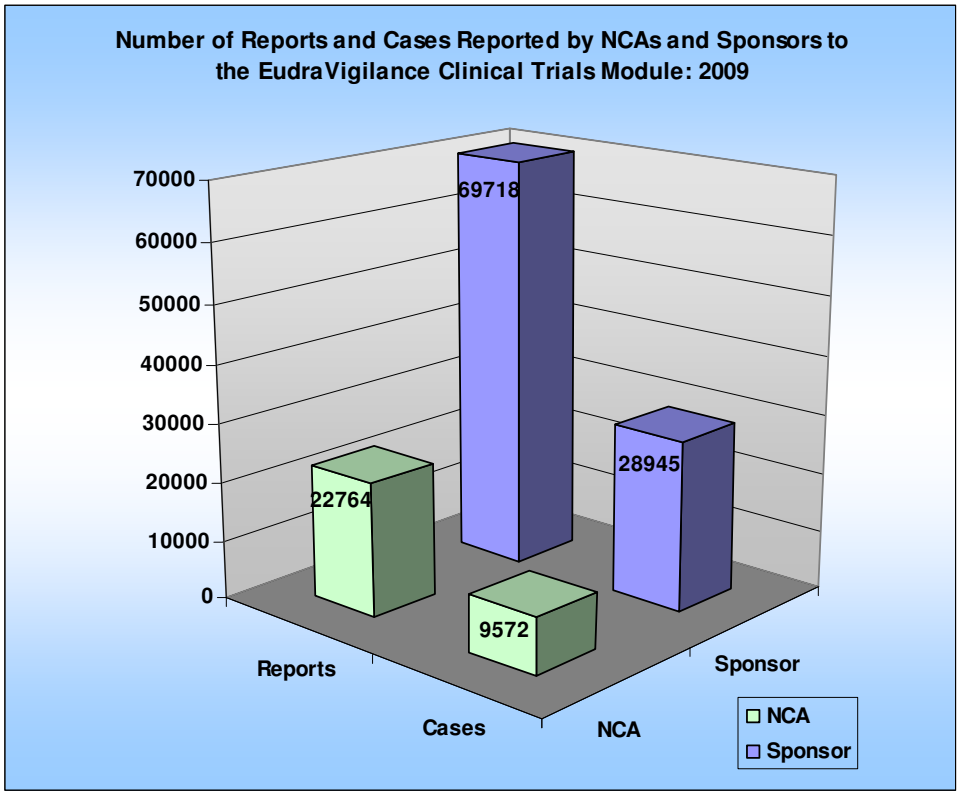
- Table 3 below shows the total (both expedited and non-expedited) number of unique cases and ICSRs transmitted by NCAs to EVPM and EVCTM.

EVPM	ICSRs	196,412
	Individual Cases	117,693
	Backlog cases	95,776
EVCTM	ICSRs	22,764
	Individual Cases	9,572
	Backlog cases	164

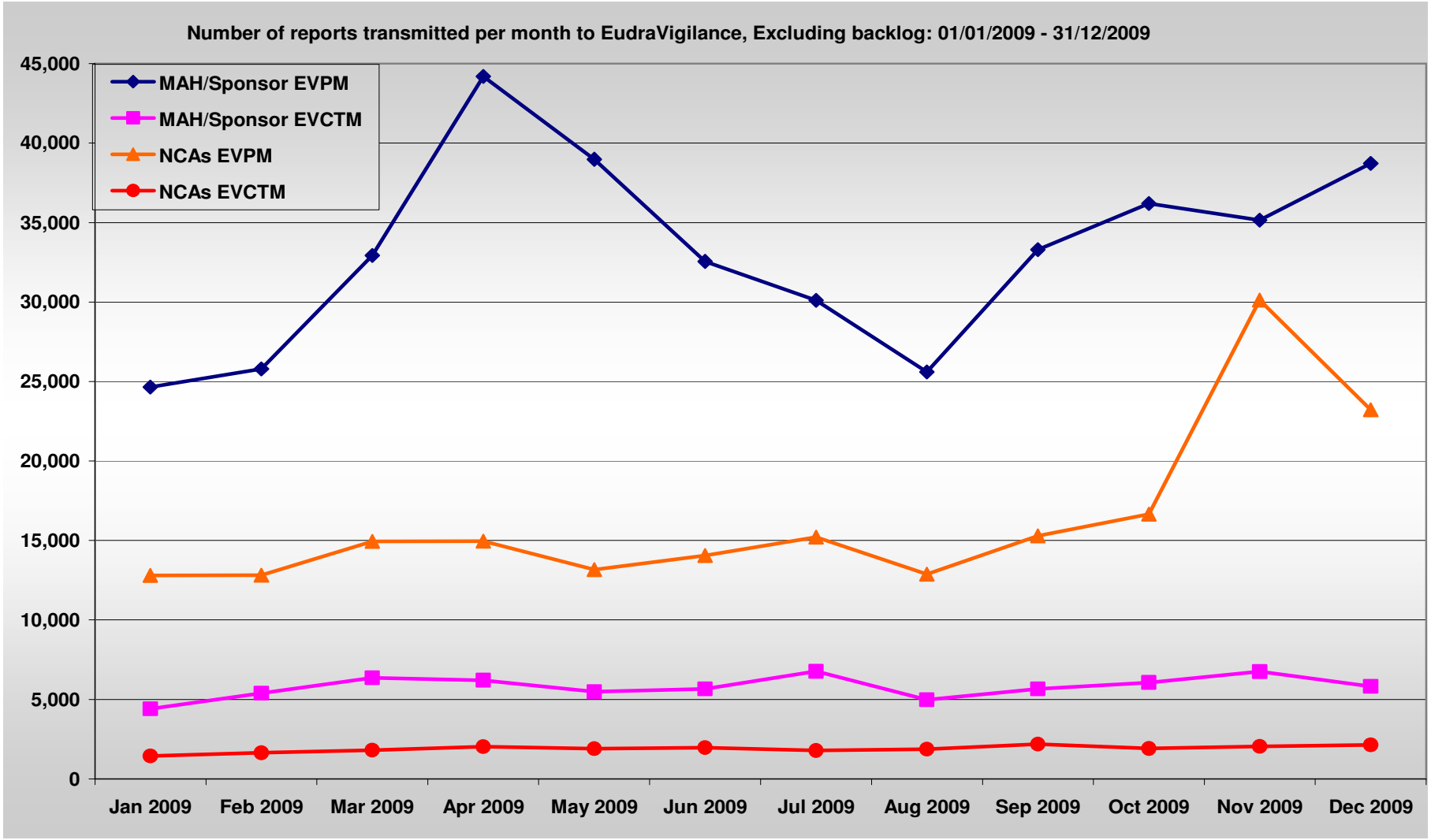
Table 3: Total number of ICSRs and unique cases transmitted by NCAs to EVPM & EVCTM during 2009, including both serious and non-serious cases & ICSRs

Number of reports and cases reported to EudraVigilance during the reporting period, excluding backlog




Number of Reports and Cases Reported by NCAs and Sponsors to the EudraVigilance Clinical Trials Module: 2009
70000
60000
50000
40000
30000
20000
10000
0
69718
28945
22764
9572
Reports
Cases
NCA
Sponsor
NCA
Sponsor

Number of reports submitted per month to EudraVigilance, excluding backlog



Summary of e-reporting status by all Stakeholders (NCAs, MAHs and Sponsors of Clinical Trials), excluding backlog

In the period from 1 January 2002 to 31 December 2009 a total, including both expedited and non-expedited cases & ICSRs, of:

- 2,103,713 ICSRs were reported to the EVPM referring to 1,281,682 individual cases.
- 316,671 ICSRs were reported to the EVCTM referring to 140,302 individual cases.

Summary of e-reporting status by all Stakeholders (NCAs, MAHs and sponsors of Clinical Trials) to EVPM split by EEA and Non-EEA, excluding backlog

In the period from 1 January 2002 to 31 December 2009 a total, including both expedited and non-expedited cases & ICSRs, of:

- 853,244 EEA ICSRs were reported to EVPM referring to 511,056 EEA individual cases.
- 1,250,469 non-EEA ICSRs were reported to EVPM referring to 770,626 non-EEA individual cases.

Summary of e-reporting status by all Stakeholders (NCAs and Sponsors of Clinical Trials) to EVCTM split by EEA and Non-EEA, excluding backlog

In the period from 1 May 2004 to 31 December 2009 a total, including both expedited and non-expedited cases & ICSRs, of:

- 174,164 EEA ICSRs were reported to EVCTM referring to 67,184 EEA individual cases.
- 159,716 non-EEA ICSRs were reported to EVCTM referring to 62,890 non-EEA individual cases.

4.1.3. EudraVigilance Medicinal Product Dictionary

During the period 1 January 2009 – 31 December 2009:

596 presentations for Investigational Medicinal Products and 11,447 presentations for Authorised Medicinal Products were entered into EVMPD and checked by the DCM Section.

4.1.4. EudraVigilance Help Desk Support Provided by the PhV-RM Sector

During the period 1 January 2009 – 31 December 2009, the EMA PhV-RM Sector handled 6,179 written help desk requests and 697 telephone requests.

4.2. EMA Initiatives to Progress with the implementation of EudraVigilance in the Field of Human Medicines

4.2.1. EVDAS Training for NCAs

During 2009, EVDAS training was held at the agency on 8 occasions, training 60 experts from 22 different NCAs.

4.2.2. Activities related to the International Standardisation Work in the context of the International Conference on Harmonisation (ICH) and the International Standards Organisation (ISO)

In the context of the ISO Technical Committee (TC) 215 'Health Informatics' Working Group 6 'Pharmacy and Medicines Business' activities the following important developments have occurred:

April 2009: ISO TC215/WG 6 Plenary Meeting in Edinburgh

- Resolution approved the release of Identification of Medicinal Products (IDMP) Committee Drafts (CDs) for ballot

June 2009: IDMP was recognised as joint initiative (JI) project by the following Standards Development Organisations (SDOs)

- European Committee for Standardization (CEN)
- International Organization for Standardization (ISO)
- Health Level 7 (HL7)
- Clinical Data Interchange Standards Consortium (CDISC)
- International Health Terminology Standards Organisation (IHTSDO)

June- September 2009: ICH testing of the ISO IDMP CD was performed.

September 2009: IDMP Committee Draft (CD) ballot was closed and successful for all five work items

September– March 2010: ISO IDMP Draft International Standard (DIS) preparation:

- IDMP was fully aligned with HL7 Common Product Model (CPM), which will serve as the basis for the messaging model of the Medicinal Product ID (MPID) and Pharmaceutical Product ID (PhPID)
- Project proposal for developing a substance messaging model was submitted and was accepted by HL7
- ISO IDMP/HL7 CPM are also being fully integrated in the ISO ICSR DIS standard

4.2.3. EudraVigilance Information Day

Two EudraVigilance Information Days were held during 2009.