Human and veterinary pharmaceuticals regulation

Towards EU accession: Serbia's regulatory challenges, expectations and opportunities

29-30 November 2010

Hotel Holiday Inn, Belexpo Convention Centre, Belgrade, Serbia

Republika Srbija
Ministarstvo zdravlja
Ministarstvo poljoprivrede, šumarstva i vodoprivrede,
Uprava za veterinu

Republic of Serbia
Ministry of Health
Ministry of Agriculture, Forestry and Water Management,
Veterinary Directorate

alims
Agencija za lekove i medicinska sredstva Srbije
Medicines and Medical Devices Agency of Serbia

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance

Veterinary pharmacovigilance

Outline of the EU pharmacovigilance system

Presented by: Peter Ekström, CVMP, Sweden

Pharmacovigilance

From Wikipedia, the free encyclopedia

Pharmacovigilance (abbreviated **PV** or **PhV**) is the pharmacological science relating to the detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines.[1]

[1] Source: The Importance of Pharmacovigilance, WHO 2002

Pharmacovigilance

Generally speaking, pharmacovigilance is the science of collecting, monitoring, researching, assessing and evaluating information from *healthcare providers* (veterinarian) and *patients* (animal owner) on the adverse effects of medications, with a view to:

- identifying new information about hazards associated with medicines
- preventing harm to patients.

Spontaneous reporting

Spontaneous reporting is the core data-generating system of pharmacovigilance, relying on veterinarians and other animal health professionals, animal owners to identify and report any suspected adverse drug reaction to the Marketing Authorisation Holders or the National Competent Authority.

Improve reporting

Information

- Veterinarians
- Students

Feedback

- Publications of reports
- Access to data base

Promotional effort

Make reporting easy

- Easy forms, electronic

Community legislation

Directive 2001/82/EC, as amended by Directive 2004/28/EC

Title VII Pharmacovigilance

Article 72 - 79

Regulation (EC) No 726/2004

Chapter 3 Pharmacovigilance

Article 46 – 54, Article 57 (d)

The EU pharmacovigilance system

www.ema.europa.eu

The veterinary pharmacovigilance system in the European Union (EU) operates with the management and involvement of national competent authorities, the European Commission as the competent authority for medicinal products authorised centrally for the whole EU and European Medicines Agency, in collaboration with the marketing authorisation holders (MAHs) for the medicinal products.

The Agency has a co-ordinating role within the EU veterinary pharmacovigilance system and provides advice to ensure the safe and effective use of veterinary medicinal products.

Post-authorisation monitoring

- What is monitored?
- How frequent / which procedures?
- What are the tools?
- Future

What is monitored?

Adverse reaction:

A reaction to a veterinary medicinal product which is harmful and unintended and which occurs at doses normally used in animals for the prophylaxis, diagnosis or treatment of disease or to restore, correct or modify a physiological function

What is monitored?

Serious adverse reaction:

An adverse reaction which results in death, is life-threatening, results in significant disability or incapacity, is a congenital anomaly / birth defect, or which results in permanent or prolonged signs in the animals treated.

What is monitored?

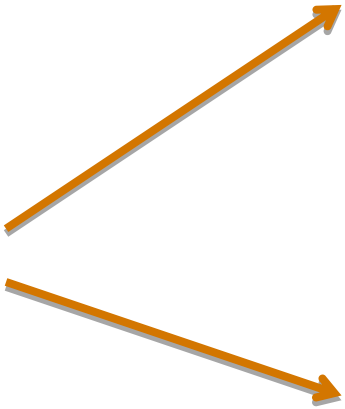
Human adverse reaction:

A reaction which is noxious and unintended and which occurs in a human being following exposure to a veterinary medicine.

What else is monitored?

- Lack of expected efficacy
- Adverse reaction reports related to off-label use
- Violations of approved residue limits validity of withdrawal times (consumer safety)
- Potential environmental problems

How frequent / which procedures?



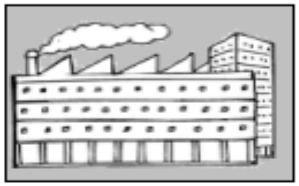
Expedited reporting SAR
(suspected serious adverse reaction report)

Periodic reporting PSUR
(periodic safety update report)

Expedited reporting

- Serious Adverse reaction reports
- Human Adverse reactions
- 15-day reporting
- also for SARs from third countries

- **Primary Source: veterinarian, owner, health care professional, reports directly to MAH**

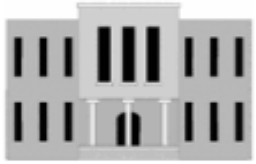


MAH suspect product A

(a)

A C K

- send within 15 days



Competent Authority on whose territory the SADR occurred

(b) ACK

(C) ACK

EVVet DB

MAH suspect product B

PSURS

- All SARS and other information
- Sales figures / calculation of incidence
- Overall Safety information
- Benefit /Risk evaluation

PSUR timing

- 6-monthly before on the market
- 6-6-6-6 monthly after placing on the market
- then yearly for the next two years
- thereafter at three-yearly intervals

Reporting tools

- Expedited reports

  Electronic reporting since November 2005

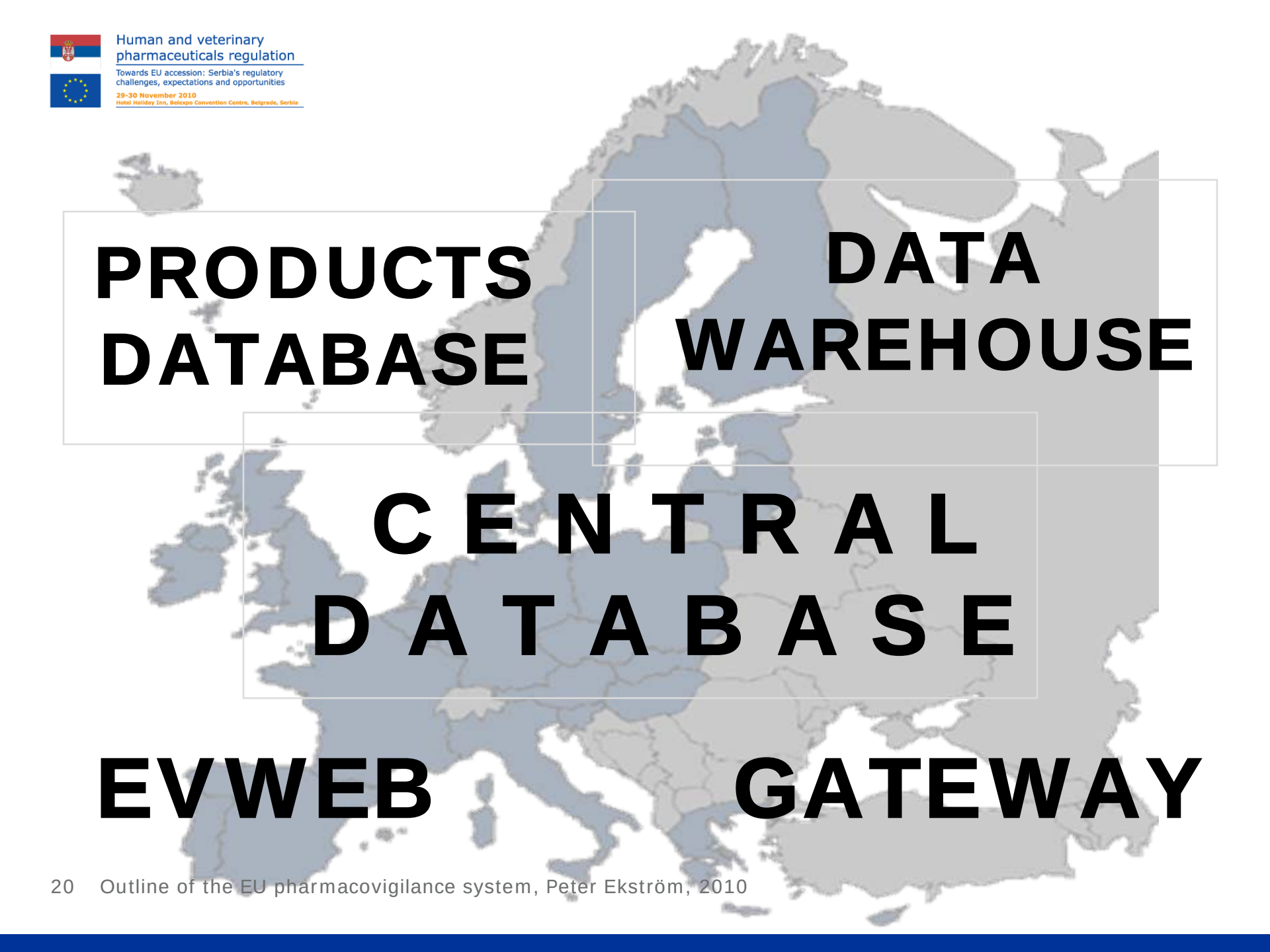
PSUR reports

paper reporting

electronically/CD

TOOLS

EUDRAVIGILANCE VETERINARY (EVVet)


PRODUCTS DATABASE
DATA WAREHOUSE
CENTRAL DATABASE
EVWEB
GATEWAY

REPORTING ROUTES

- Gateway
- EVWEB (EudraVigilance Web application)
- Simplified Electronic Reporting Form
- Future

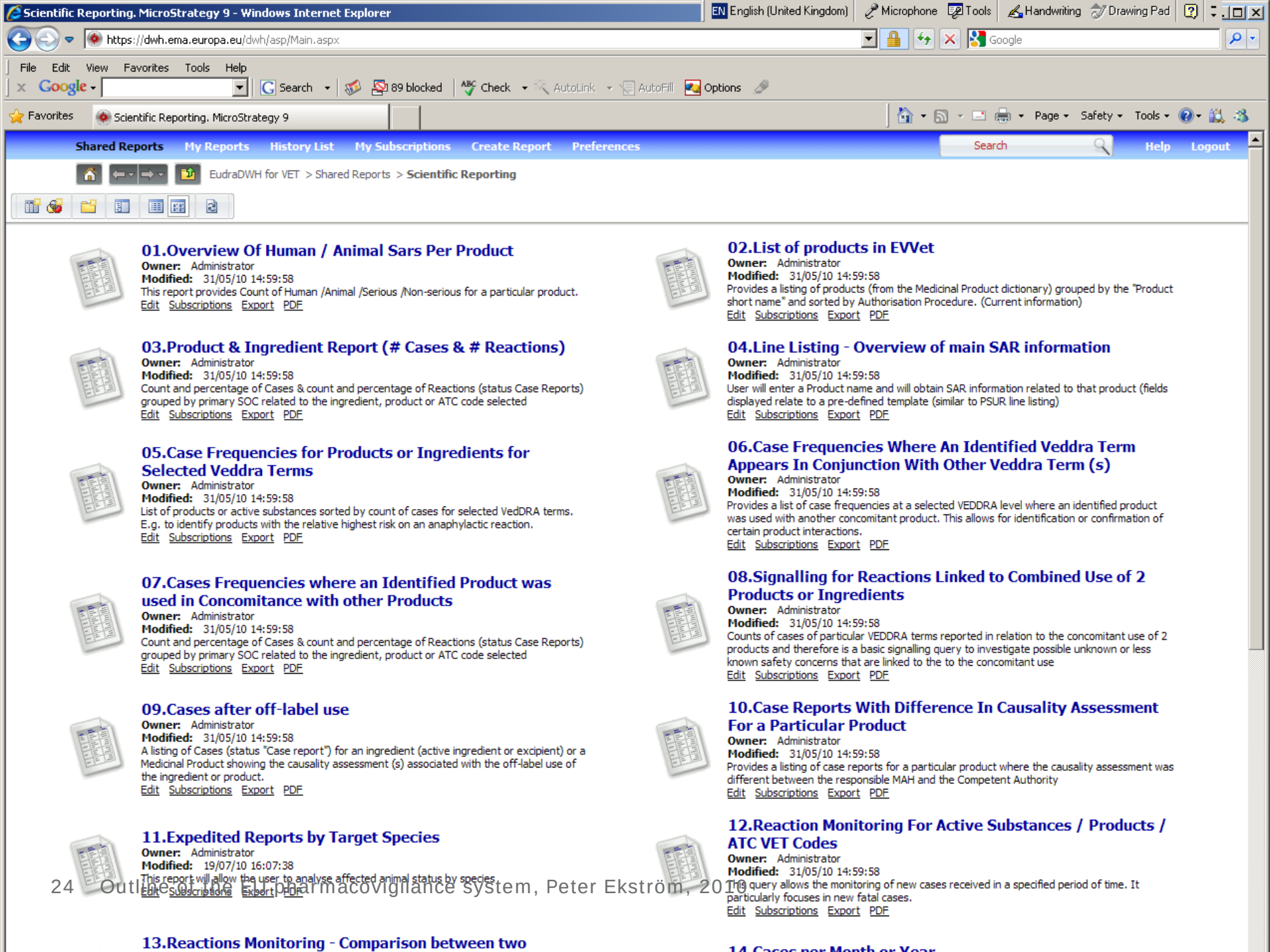
  Electronic reporting tool for Veterinarians?

Data in EVVet?

- Suspected ARs
  - Serious
  - Human
  - Future
    - Non-serious
- PRODUCTS
  - CAPS
  - Future
    - Nationally authorised products

Use of EVVet

- Monthly monitoring of CAPs
  - Rapporteur/Phvig expert
- Signal detection
- Help for PSUR assessment


Scientific Reporting. MicroStrategy 9 - Windows Internet Explorer
https://dwh.ema.europa.eu/dwh/asp/Main.aspx
Scientific Reporting. MicroStrategy 9
Shared Reports
My Reports
History List
My Subscriptions
Create Report
Preferences
Search
Help
Logout
EudraDWH for VET > Shared Reports > Scientific Reporting
01.Overview Of Human / Animal Sars Per Product
Owner: Administrator
Modified: 31/05/10 14:59:58
This report provides Count of Human /Animal /Serious /Non-serious for a particular product.
Edit Subscriptions Export PDF
02.List of products in EVVet
Owner: Administrator
Modified: 31/05/10 14:59:58
Provides a listing of products (from the Medicinal Product dictionary) grouped by the "Product short name" and sorted by Authorisation Procedure. (Current information)
Edit Subscriptions Export PDF
03.Product & Ingredient Report (# Cases & # Reactions)
Owner: Administrator
Modified: 31/05/10 14:59:58
Count and percentage of Cases & count and percentage of Reactions (status Case Reports) grouped by primary SOC related to the ingredient, product or ATC code selected
Edit Subscriptions Export PDF
04.Line Listing - Overview of main SAR information
Owner: Administrator
Modified: 31/05/10 14:59:58
User will enter a Product name and will obtain SAR information related to that product (fields displayed relate to a pre-defined template (similar to PSUR line listing)
Edit Subscriptions Export PDF
05.Case Frequencies for Products or Ingredients for Selected Veddra Terms
Owner: Administrator
Modified: 31/05/10 14:59:58
List of products or active substances sorted by count of cases for selected VedDRA terms. E.g. to identify products with the relative highest risk on an anaphylactic reaction.
Edit Subscriptions Export PDF
06.Case Frequencies Where An Identified Veddra Term Appears In Conjunction With Other Veddra Term (s)
Owner: Administrator
Modified: 31/05/10 14:59:58
Provides a list of case frequencies at a selected VEDDRA level where an identified product was used with another concomitant product. This allows for identification or confirmation of certain product interactions.
Edit Subscriptions Export PDF
07.Cases Frequencies where an Identified Product was used in Concomitance with other Products
Owner: Administrator
Modified: 31/05/10 14:59:58
Count and percentage of Cases & count and percentage of Reactions (status Case Reports) grouped by primary SOC related to the ingredient, product or ATC code selected
Edit Subscriptions Export PDF
08.Signalling for Reactions Linked to Combined Use of 2 Products or Ingredients
Owner: Administrator
Modified: 31/05/10 14:59:58
Counts of cases of particular VEDDRA terms reported in relation to the concomitant use of 2 products and therefore is a basic signalling query to investigate possible unknown or less known safety concerns that are linked to the to the concomitant use
Edit Subscriptions Export PDF
09.Cases after off-label use
Owner: Administrator
Modified: 31/05/10 14:59:58
A listing of Cases (status "Case report") for an ingredient (active ingredient or excipient) or a Medicinal Product showing the causality assessment (s) associated with the off-label use of the ingredient or product.
Edit Subscriptions Export PDF
10.Case Reports With Difference In Causality Assessment For a Particular Product
Owner: Administrator
Modified: 31/05/10 14:59:58
Provides a listing of case reports for a particular product where the causality assessment was different between the responsible MAH and the Competent Authority
Edit Subscriptions Export PDF
11.Expedited Reports by Target Species
Owner: Administrator
Modified: 19/07/10 16:07:38
This report will allow the user to analyse affected animal status by species.
Edit Subscriptions Export PDF
12.Reaction Monitoring For Active Substances / Products / ATC VET Codes
Owner: Administrator
Modified: 31/05/10 14:59:58
This query allows the monitoring of new cases received in a specified period of time. It particularly focuses in new fatal cases.
Edit Subscriptions Export PDF
13.Reactions Monitoring - Comparison between two

Signal detection

Signal detection

- unexpected/unlisted SARs
- VeDDRA terms
  - System Organ Classes (SOC)
  - Preferred Term (PT)
- Proportional Reporting Ratio (PRR)
  - compare reports for a particular medical term, as the proportion of all reports

Data Warehouse

What are we looking for?

- Adverse reactions not yet in SPC
- Increased frequency of known reactions
- reactions occurring after combined use

How?

- Veddra terms frequencies
  - Per Product Name
  - Per Active Substance

Who?

- Pilot signal detection group

21a.Signal Detection Query (With PRR). MicroStrategy 9 - Windows Internet Explorer

https://dwh.ema.europa.eu/dwh/asp/Main.aspx?evt=5005&src=Main.aspx.report.5005&Main.aspx=-172*,16*,41*,120.EudraDWH+for+VET.0_&report=*

Shared Reports | My Reports | History List | My Subscriptions | Create Report | Preferences | Search | Help | Logout

EudraDWH for VET > Shared Reports > Scientific Reporting > **21a.Signal Detection Query (With PRR)**

Home | Tools | Data | Grid | Format | Last update: 28/10/10 16:08:45

PAGE-BY: Species:

Data rows: 252 | Data columns: 9

Veddra Term SOC	Veddra Term PT	Product Short Name / Metrics	# Cases until Date 1	# Animals Reacted until Date 1	# Cases between Date 1 and Date 2	# Animals Reacted between Date 1 and Date 2	# Cases until Date 2	# Animals Reacted until Date 2	PRR(-) until Date 2	PRR until Date 2	PRR(+) until Date 2
Systemic disorders	Anorexia		348	349	96	96	444	445	3.20	3.50	3.82
	Death		275	291	68	68	342	358	0.93	1.01	1.11
Digestive tract disorders	Emesis		251	263	69	69	320	332	2.31	2.57	2.86
Systemic disorders	Lethargy		262	264	59	59	321	323	1.51	1.67	1.85
Renal and urinary disorders	Renal failure		243	253	40	40	283	293	15.83	19.15	23.17
	Renal disorder NOS		182	183	78	78	259	260	15.13	18.42	22.44
Systemic disorders	Abnormal test result		145	147	37	37	182	184	5.90	7.07	8.46
	Dehydration		78	79	25	25	103	104	3.07	3.82	4.75
	Loss of condition		56	56	21	21	77	77	2.69	3.46	4.45
Neurological disorders	Ataxia		59	59	13	13	72	72	0.35	0.44	0.55
Blood and lymphatic system disorders	Anaemia NOS		48	48	14	14	62	62	2.03	2.67	3.52
Digestive tract disorders	Diarrhoea		50	50	10	10	60	60	1.03	1.34	1.74
Respiratory tract disorders	Dyspnoea		43	43	15	15	58	58	0.67	0.87	1.13
Systemic disorders	Polydipsia		46	46	10	10	56	56	5.18	7.28	10.23
Renal and urinary disorders	Urine abnormalities		36	36	17	17	53	53	7.46	10.99	16.19
Systemic disorders	Pyrexia		26	34	13	13	39	47	0.79	1.10	1.52
	Adipsia		32	33	13	13	45	46	3.13	4.43	6.27
Hepato-biliary disorders	Hepatopathy		32	32	13	13	45	45	2.42	3.37	4.71
Neurological disorders	Convulsion		26	26	10	10	36	36	0.13	0.18	0.24
Behavioral disorders	Behavioural disorder NOS		22	22	13	13	35	35	2.61	3.83	5.64
Renal and urinary disorders	Polyuria		28	28	5	5	33	33	4.88	7.66	12.03
Systemic disorders	Hypothermia		25	25	5	5	30	30	0.40	0.58	0.83

Signal Detection


2.4%


2.3%


0.5%


27%


3.6%


1.8%

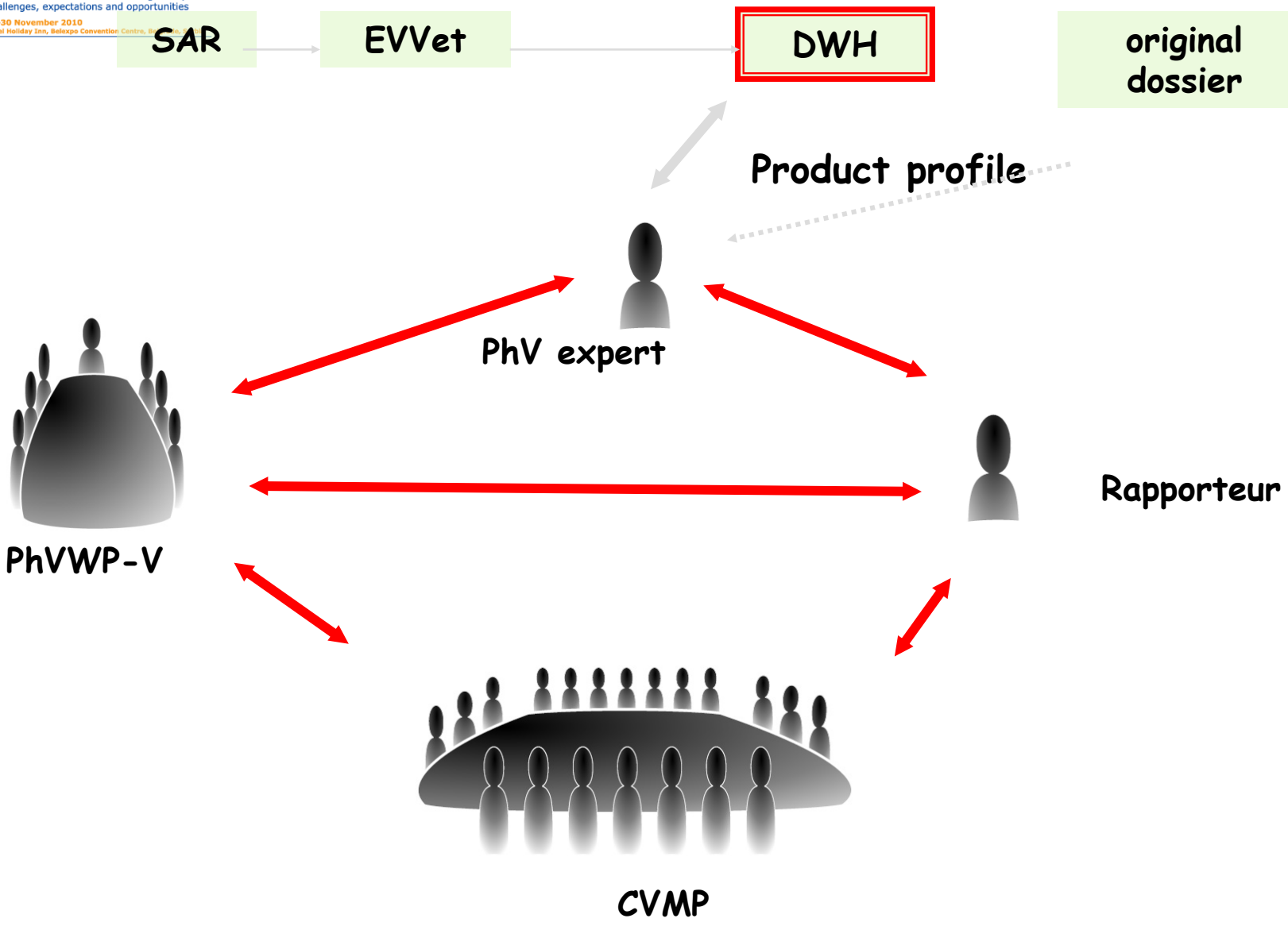

38%


19%


0.04%

CVMP Pharmacovigilance Working Party

- Core group of veterinary pharmacovigilance expertise in EU
- dual mandate, reporting to CVMP and HMA
- advice on the safety of veterinary medicinal products
- overall surveillance of the adverse reactions of veterinary medicinal products
- development of pharmacovigilance guidelines
- 6 meetings per year


SAR
EVVet
DWH
original dossier
Product profile
PhV expert
PhVWP-V
Rapporteur
CVMP

Regulatory actions on basis of pharmacovigilance data

- Continued surveillance
- Requests for data
- Recommendations for amendments of the authorisation / product literature
- Suspension of authorisation
- Withdrawal of authorisation
- Referral procedures

Thank you for your attention

http://www.ema.europa.eu/