



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

4 September 2023

EMA/53385/2022

EVVET – Data Warehouse User Manual

Version 2.0

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1. Introduction

1.1. About this User Manual

This user manual is prepared to support the use of the business intelligence tool EVVET3-DWH. The document is composed by the following chapters

- **Chapter 2:** presents a Login overview of DWH application and how to access the catalog.
- **Chapter 3:** presents the *AER received over a period of time and Organisation* dashboard.
- **Chapter 4:** presents the *Adverse event overview* dashboard.
- **Chapter 5:** presents the *Signal detection* dashboard.
- **Chapter 6:** presents the *Signal evaluation* dashboard.
- **Chapter 7:** presents the *Adverse event comparison between 2 periods* dashboard.
- **Chapter 8:** presents the *Data stratification* dashboard.
- **Chapter 9:** presents the *Signalling for reactions linked to a product or ingredient* dashboard
- **Chapter 10:** presents the *Line listing* dashboard
- **Chapter 11:** presents the *List of products* dashboard
- **Chapter 12:** presents how to group data for different products
- **Chapter 13:** provides an oversight of the different dashboards implemented
- **Chapter 14:** elaborates on KPI's and ROR calculation.

Therefore, the scope of this user's manual is to provide detailed explanation on each of the reports that have been implemented and its behavior.

2. EVVET3 DWH

2.1 DWH Login

EVVET3 Data Warehouse is accessible by clicking on the production URL: <https://bi.ema.europa.eu> by using any modern browser:

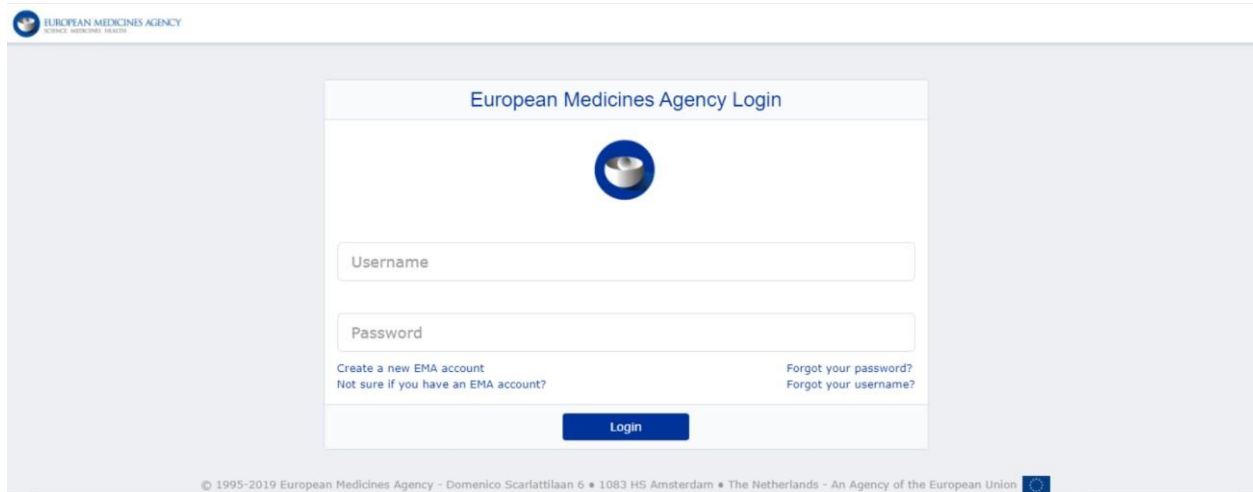


Image 1: Login to DWH application

User entering credentials to login, user ID (no mail account) and password:

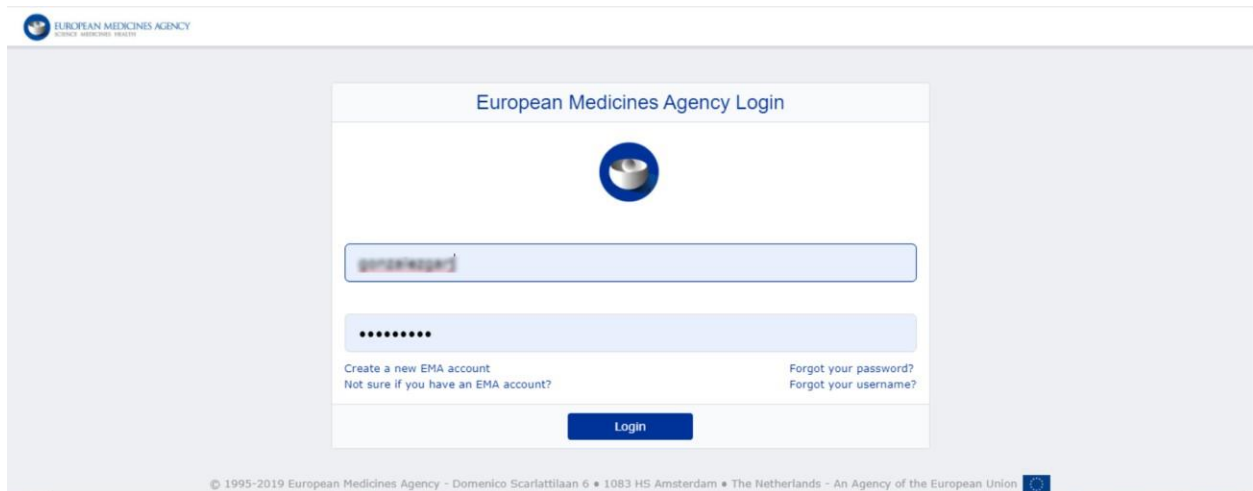


Image 2: Enter credentials

When user logs in, user is prompted to Home page from EMA Business Intelligence tool, where Oracle BI standard features are displayed (i.e.: user's recent dashboards or analysis among other options):

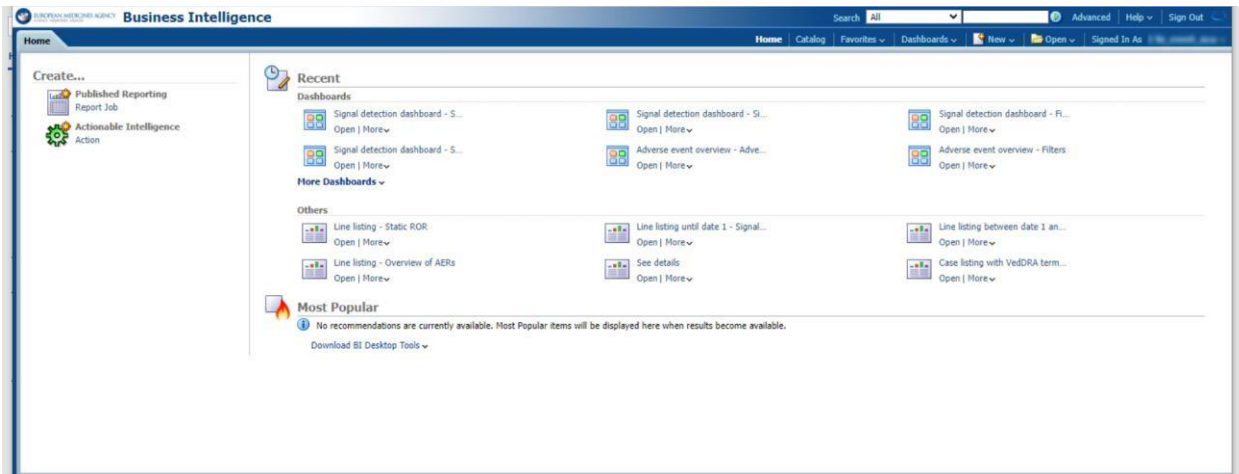


Image 3: BI Home page

2.2 Catalog access

Over the main menu located on the top of the screen, the user can access to the data warehouse catalog of reports:

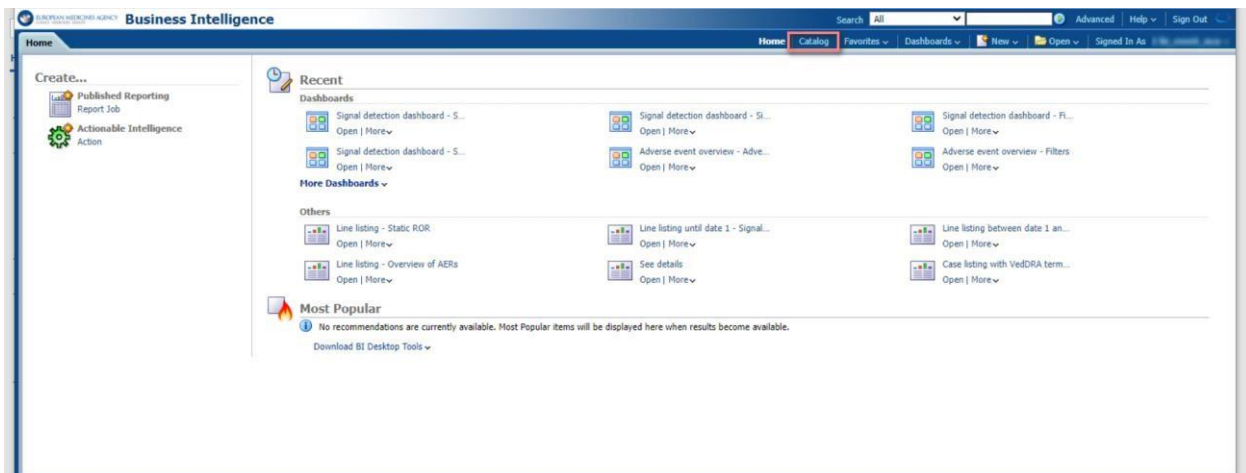


Image 4: Access catalog

Once in the catalog section, in the left side of the screen, user will see the folder 'EVVET3 DWH', containing a subfolder 'Dashboards', followed by each of the reports user has access to

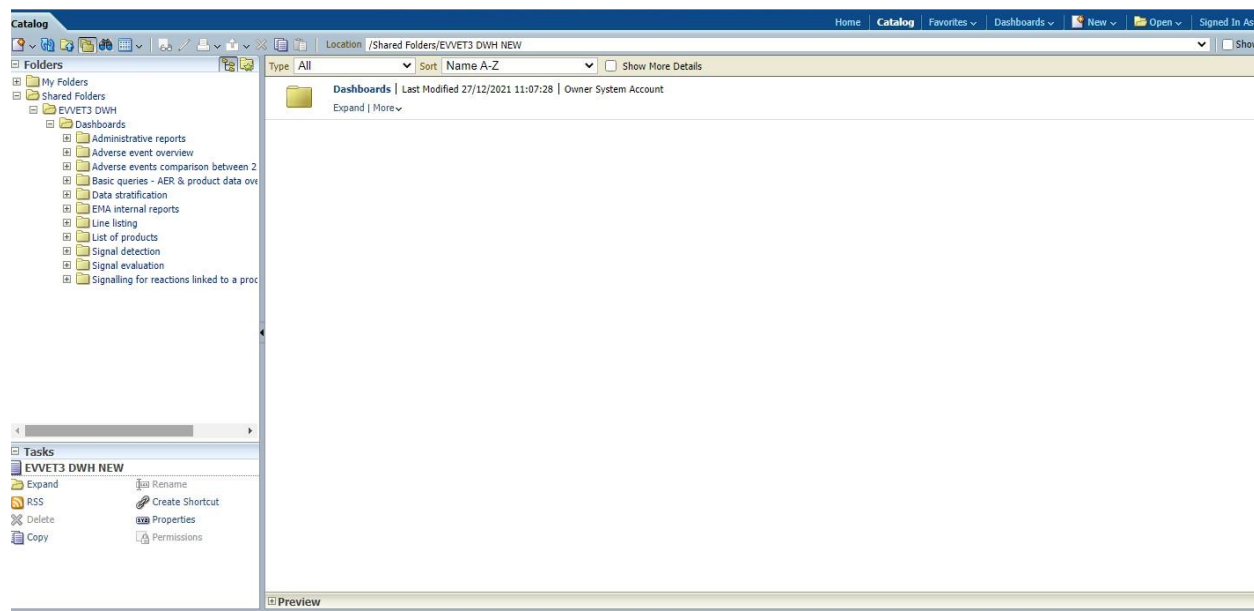


Image 5: Dashboard of reports

The next chapters of this user's manuals will guide the user through each of the above dashboards.

Note: each dashboard can be accessed through different ways on top the above explained, such as: searching on the top menu by the name of the dashboard or adding it to your favorites and consult the tab Favorites.

3. AER received over a period of time and Organisation compliance

This dashboard displays several Number of AERs metrics, so the user will be able to get an overview of the data based on correctness, classification or message received date, as well as get the organization compliance report related to the information set in the filters page.

The dashboard is divided in two tabs, the 'AER received over a period of time' and the 'Organisation compliance report'.

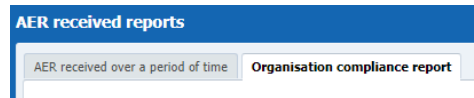


Image 6: AER Received reports



AER received over a period of time and Organisation compliance | Last Modified 19/08/2021 14:17:29 | Owner BI Administrator Role

Expand | Open | Edit | More v

Image 7: AER received reports

3.1 Filters

Filters for this dashboard are distributed in the following sections:

1. Timing Filters

In this prompt, the user should select the received date range to apply to the dashboards.

2. Geographic Filters

In this prompt the user can select:

- Region: EEA or non EEA countries
- Occurrence country

3. Organisation filters

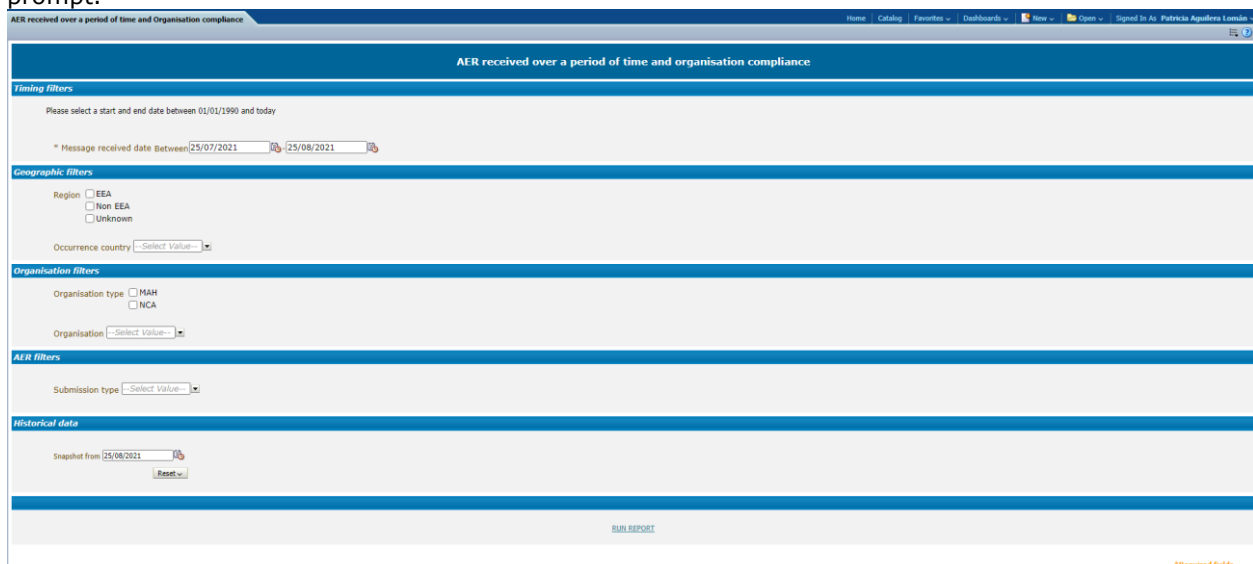
Non-mandatory prompts for selecting the organization type (MAH or NCA) or a specific organization.

4. AER filters

Non-mandatory prompt for selecting the submission type.

5. Historical data

No answer is required for this prompt. By default, a snapshot of the day will be set. In case the user needs to have the information as it was in a past date, then it's needed to inform this date in this prompt.



The screenshot shows a web interface with a blue header and a white content area. The title is 'AER received over a period of time and organisation compliance'. Below the title, there are five filter sections:

- Timing filters:** A prompt 'Please select a start and end date between 01/01/1990 and today' with two date input fields. The first field is labeled '* Message received date Between' and contains '25/07/2021'. The second field contains '25/08/2021'.
- Geographic filters:** A 'Region' section with radio buttons for 'EEA', 'Non EEA', and 'Unknown'. Below it is an 'Occurrence country' dropdown menu with a placeholder '- Select Value -'.
- Organisation filters:** An 'Organisation type' section with radio buttons for 'MAH' and 'NCA'. Below it is an 'Organisation' dropdown menu with a placeholder '- Select Value -'.
- AER filters:** A 'Submission type' dropdown menu with a placeholder '- Select Value -'.
- Historical data:** A 'Snapshot from' input field containing '25/08/2021' and a 'Reset' button.

At the bottom of the page, there is a 'BUIL REPORT' link and a '*Required fields' note.

Image 8: Filter options

3.2 AER received over a period of time

In the first tab the user will navigate to the AER received over a period of time, with the following structure:

At the top of the dashboard, two dropdowns for the user to select Correctness and Classification.

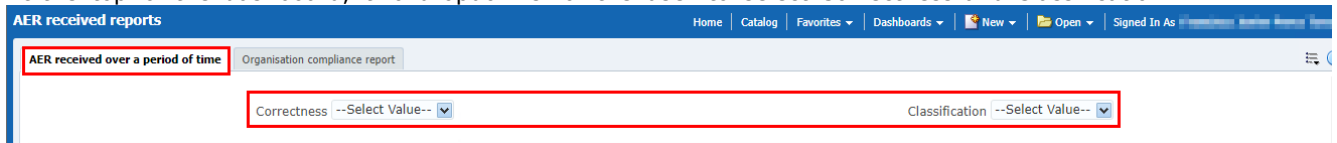


Image 9: Correctness and Classification dropdowns

Right below, 2 pie charts will be displayed:

- Number of AERs by correctness: Displaying Correct reports in green, Report with errors in red and Report with warning in yellow.
- Number of AERs by classification: Displaying Case report in green, Error report in red, Nullified report in white and Replaced report in yellow.



Image 10: Correctness and Classification charts

Right below, 2 more charts will be displayed with the following information:

- Number of AERs by message received date: Showing number of AERs per message received date on a monthly basis.
- Number of AERs by message received year (last 5 years): Showing number of AERs per message received date on a year basis, always for the last 5 years span.

Right below, 2 links: Switch to table, for the user to visualize the information in table format, and Return to filters to go back to filters page and edit the query or start over.

In addition, the user will see the filters applying to the charts by looking at the bottom, as follows:

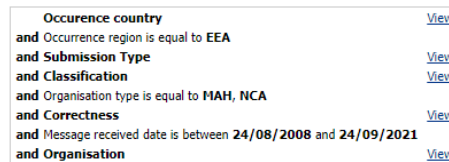


Image 11: Filters set

3.3 Organisation compliance report

In the second tab the user will navigate to the Organisation compliance report, with the following structure:

At the top of the dashboard, a series of checkbox for the user to select: Animal/Human, Seriousness and Information Type.

Right below, two pie charts will be displayed:

- Message received date to original received date
- Message received date to most recent info date

Both representing Compliant in green and Non-compliant in red.

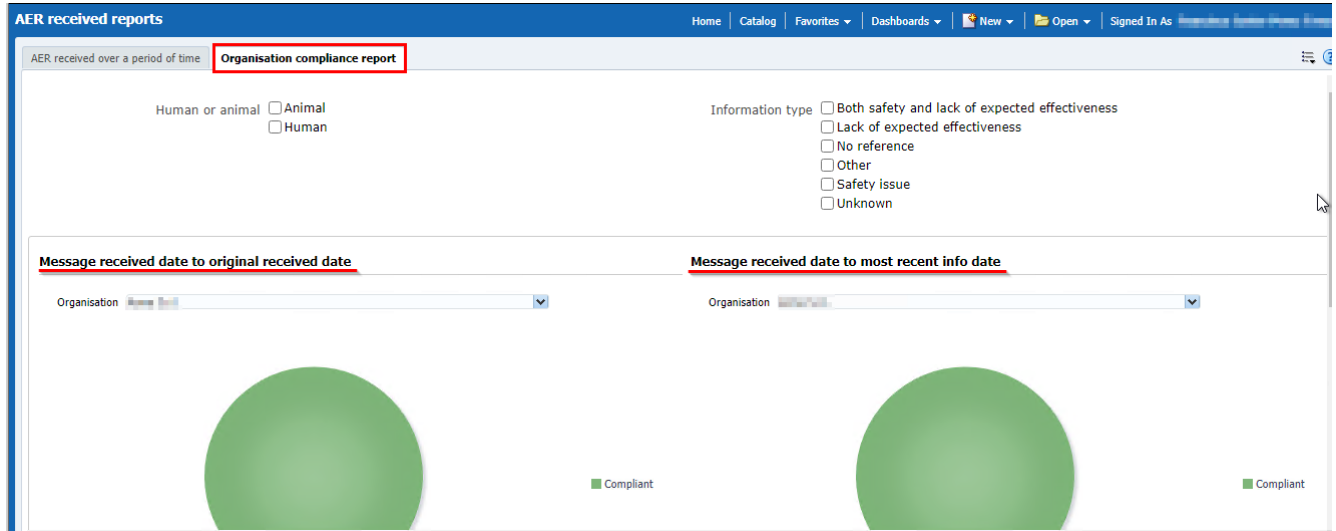


Image 12: Received date to original and most recent charts

Above the charts, the user will find a dropdown to jump between organisations. Right below, 2 links: 'Switch to table', for the user to visualize the information in table format, and 'Return to filters' to go back to filters page and edit the query or start over. In addition, the user will see the filters applying to the charts by looking at the bottom, as follows:

```

Submission Type
and Occurrence region is equal to EEA
and Organisation type is equal to MAH
and Occurrence country
and Human/Animal
and Information type
and Seriousness
and Organisation
and Message received date is between 24/08/2016 and 24/09/2021
and Number of cases is greater than 0
and Organisation is not null
and (VALUEOF(NQ_SESSION.GROUP) LIKE '%r_bi_evvet_mah_dashboards%' and "Organisation"."Organisation" = 'EUDRAVIGILANCE VETERINARY United Kingdom') OR (VALUEOF(NQ_SESSION.GROUP) NOT LIKE '%r_bi_evvet_mah_dashboards%')
  
```

Image 13: Filters set

Lastly, by clicking in the sections of both pie charts the user will get the chance to navigate to the line listing reports:



Image 14: Line listing view

And the Reports and duplicates:

ABO ID	In	Affected	Duplicate report list
5248	No	5248	
5511	No	5511	
5547	No	5482, 5547	
6022	No	6022	
6086	Yes	6086, 6086	
7603	No	7603, 6857	
18091	No	18091, 2270	
19622	No	19622, 22136, 4674	
19623	No	19623, 22140	
20205	No	20205, 22136	
20469	No	20469	
20471	No	20471	
20476	No	20476	
20476	Yes	20476, 20476, 2058	
20478	No	20478, 20478, 2058	
21837	No	21837, 4403	
22848	No	22848	
22923	No	22923, 4289	
22923	No	22923	
22224	No	22224, 5134	
22132	No	22132, 5448	
22138	No	22138	
22138	Yes	19622, 22136, 4674	

Image 15: Detailed view

4. Adverse event overview

This dashboard displays several quantitative metrics, so the user is able to get an overview of the data for a product, substance or group of products in terms of number of cases, animals affected, animals died or fatal cases for the selected period.

The dashboard also contains links that allow the user to navigate to Signal Detection dashboard, Current Product and Associated Products detail tables as well as getting ROR-based calculations also related to the parameters previously set in the filters page.

The dashboard is broken down in two tabs, the 'Filters' tab and the 'Adverse Event Overview' tab, in which the user gets to see the result of the query.

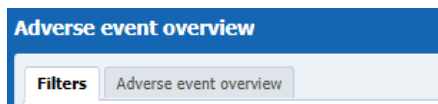


Image 16: Adverse event overview menus

4.1 Filters

1. Choose from all attributes in the Product Information (Required)

In this prompt you select at what level of the product hierarchy you want to run your query. These levels are:

- Active substance level: Results will be related to AERs for products that contain the selected active substance(s).
- Product Short name: Results will be related to AERs for selected product(s) grouped by the product short name.
- ATCVET Vet code level: Results will be related to AERs for products that belong to the selected ATCVET Vet Code.
- Reported Brand Name: Results will be related to AERs for a selected Product Brand Name as reported in the AER verbatim, prior to standardization.
- Product Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number stated in the product dictionary.
- Reported Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number as reported in the AER.
- Product composition level (Composition, Strength, Formulation, Pharma Product): Results will be related to AERs for products that are composed solely of the selected active substance(s), active substance(s) + strength(s), Active substance(s) + Pharmaceutical form(s), Active substance(s) Strength + Pharmaceutical form. This enables users to group products based on their composition, regardless of the trade names of the products.

1. Product information (Required)

Active substance --Select Value--

Product short name --Select Value--

ATC vet code --Select Value--

Reported brand name --Select Value--

Product authorisation number --Select Value--

Reported authorisation number --Select Value--

Product composition (Type = Composition) --Select Value--

Product composition (Type = Strength) --Select Value--

Product composition (Type = Formulation) --Select Value--

Product composition (Type = Pharma Product) --Select Value--

Image 17: Filter criteria

2. Message received date range (Required)

In this prompt you select a range of dates.

2. Message received date range (Required)

Message received date Between 03/08/2021 - 03/09/2021

Image 18: Message received date filter

3. VeDDRA hierarchy

In this prompt you select one or multiple VeDDRA terms at different levels.

3. VeDDRA hierarchy

VedDRA Term SOC --Select Value--
 VedDRA Term HLT --Select Value--
 VedDRA Term PT --Select Value--
 VedDRA Term LLT --Select Value--

OR

VedDRA Term SOC --Select Value--
 VedDRA Term HLT --Select Value--
 VedDRA Term PT --Select Value--
 VedDRA Term LLT --Select Value--

*Use the drop down on the left side to filter by one or multiple VeDDRA terms. When selecting only one term in each level, the query will return all cases where the VeDDRA Terms selected have been reported simultaneously (AND).
*Using the drop downs on both sides will return all cases where at least one of the VeDDRA terms selected has been reported (OR).
*In both sides, if more than one term is selected in the same level, the query will return all cases where at least one of the VeDDRA terms selected has been reported (OR).

Image 19: VeDDRA hierarchy filter

4. Report filter (Required)

Select whether your result should contain only **Animal** or **Human** AERs by ticking the relevant option, or both by selecting both Animal and Human.

4. Report filter (Required)

Human or animal Human Animal

Image 20: Human or animal filter

5. All cases or new cases (Required)

In this prompt you have to select one of the two options, being "All Cases" selected by default. Selecting "New cases" will return data related only to **new** reports received in EVVET during the selecting period, and will exclude from the data set follow ups to reports initially received in EVVET prior to the selected period.

5. All cases or new cases (Required)

All cases or new cases All cases New cases

Image 21: All or new cases filter

6. Choose from list of optional AE Report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

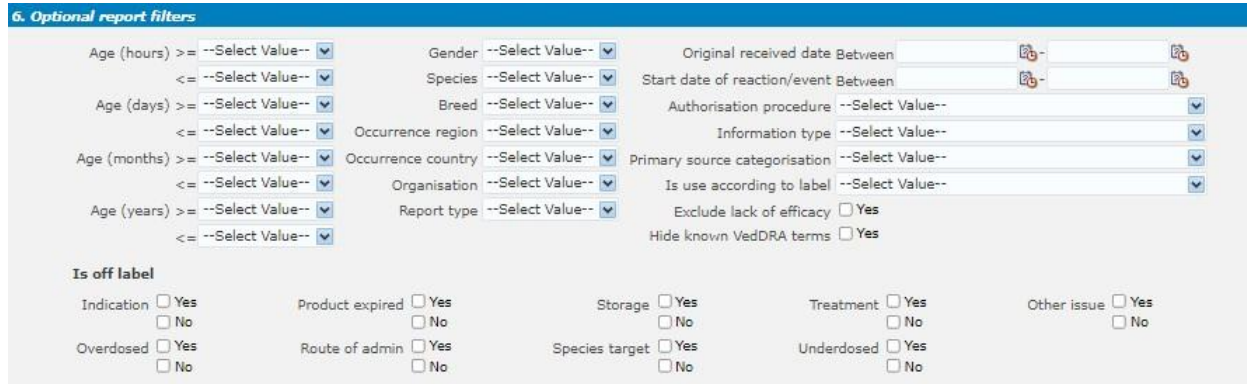


Image 22:: Additional filters

Original Received Date: The date that the MAH or NCA first received the message.

Serious: The system will return only the serious or the non-serious reports.

Information type vs Exclude lack of efficacy: If you want to exclude the lack of efficacy cases and you exclude "Lack of efficacy" within the Information type dropdown (by including all other information types), you will get the reports where LOE has been reported together with other issues/information types. However, if you tick the box "Yes" in "Exclude lack of efficacy", the system will exclude those reports where the VedDRA term "Lack of efficacy" has been reported.

7. Threshold ROR (Required)

This prompt is mandatory but filled by default with ROR \geq 2, ROR(-) \geq 1 and Number of cases \geq 3. The user is able to customize this values for the purpose of the analysis.

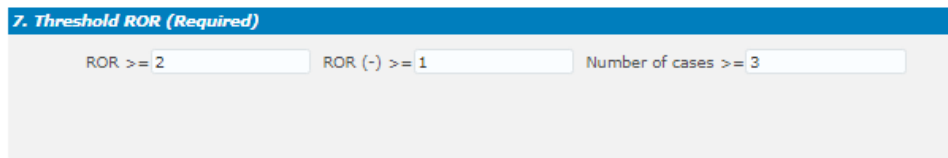


Image 23: ROR threshold

8. Historical data

No answer is required for this prompt. By default, a snapshot of the day will be set. If a different date is selected, the results will reflect the data in EVVET as per the date selecting, excluding data received after the selected date.

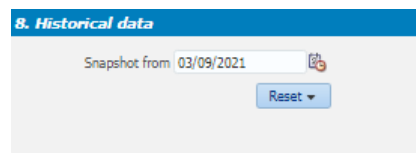


Image 24:: historical data

4.2 Adverse event overview

The Adverse Event Overview tab shows the result of the query, grouped in a series of charts of different kind, as well as a header including some key figures together with a filter for selecting Species. A summary of the filters applied is also available at the very top, so the user is able to have this information in sight while doing the analysis.

Every chart has a title on top describing the content and sometimes a clarification about the information included (between brackets) and a little disclaimer at the bottom in case additional details are required.

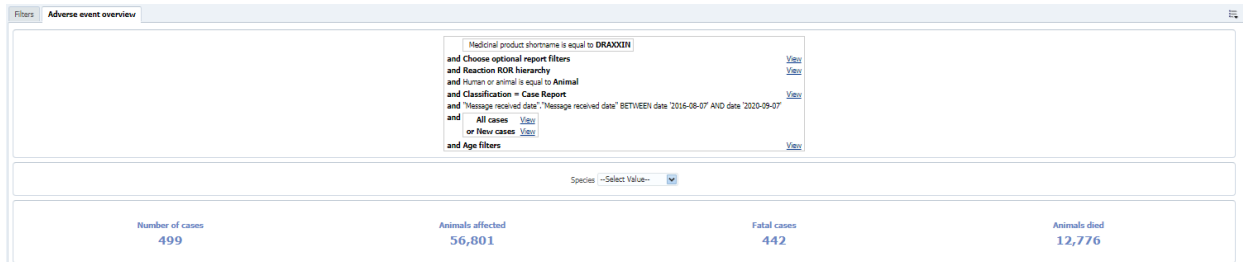


Image 25: Adverse event overview results

The charts displayed in the Adverse Event Overview tab from top to bottom are as follows:

Number of cases by region (Specified period)

Pie chart. Shows the number of cases by EEA and Non EEA for the period specified in the filters page.

Number of cases by region (All cases)

Pie chart. Shows the number of cases by EEA and Non EEA but not limited to the period specified in the filters page.



Image 26: Number of cases (period vs all time) charts

By clicking on any sector of the pie chart, the charts will break-down on EEA/Non EEA countries, with a link enabled to go back to previous state, just as follows:



Image 27: detailed chart view at country level

Number of cases and fatal cases (LAST 10 YEARS)

Bar chart. Shows the number of cases and fatal cases for the last 10 years, not applying the message received dates included in the filters page.

Number of fatal cases over average (LAST 10 YEARS)

Line chart. Shows the number of fatal cases over average for the last 10 years, not applying the message received dates included in the filters page.



Image 28: number of fatal cases and average chart

By clicking on any bar, the chart will give the user access to a see details functionality. A new tab will open up with a detailed table containing several metrics for that specific year and product at VeDDRA PT level, just as follows:

See details

Product Hierarchy Level: Medicinal product shortname: VeDDRA Hierarchy Level: VeDDRA PT name:

Species:

Medicinal product shortname	VeDDRA SOC name	VeDDRA PT name	ROR (+)	ROR (-)	ROR (?)	Number of animals affected	Number of cases (period specified)	Number of NON EEA cases (period specified)	Number of EEA cases (period specified)	Number of cases (Total ALL)	Number of NON EEA cases	Number of EEA cases	Number of cases (Total ALL reactions)	Number of fatal cases (period specified)	Number of fatal cases	Reaction count	Case count by product (filter applied)	Case count (filter not applied)	Reaction count total	Percentage of reactions	Percentage of cases	
DRAXOZIN	Application site disorders	Injection site haemorrhage	N/A	N/A	N/A	1	1	1	0	1	3	2	1	1115	0	0	1	80	1566	43	2%	1%

[Return](#) - [Analyze](#) - [Refresh](#) - [Print](#) - [Export](#) - [Create Bookmark Link](#)

Image 29: VeDDRA level detailed line listing

At the same time, by clicking in the blue line of the right chart, for a specific year, the user navigates into a that years' 12 month-span, just as follows:

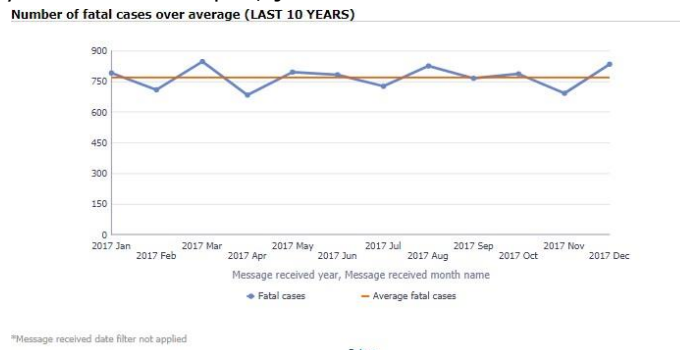


Image 30: 12 month-span chart

Number of cases by species and VeDDRA SOC over product

Heat map. Shows the cases classified by species and VeDDRA SOC for the product selected in the filters page. This table uses a different tone of blue depending on the number of cases. The larger the quantity of cases for that species and reaction, the darker the blue.

Number of animals affected and animals died (LAST 10 YEARS)

Bar chart. Shows the number animals affected and died over the last 10 years, not applying the message received dates included in the filters page.

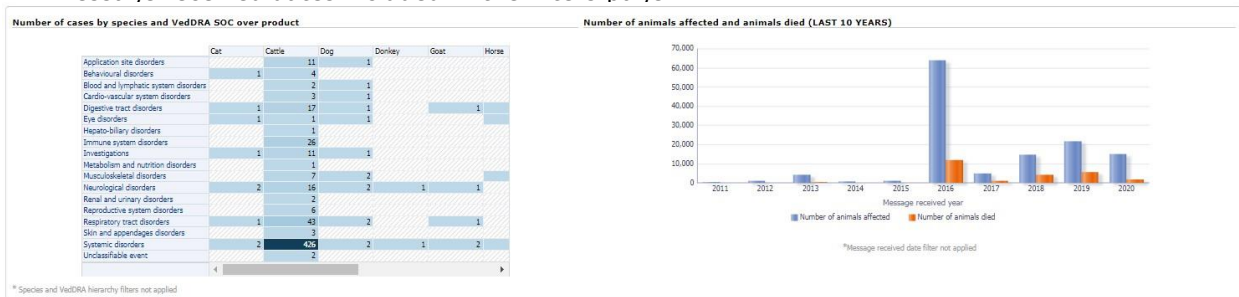


Image 31: Number of cases by species and VedDRA SOC over product and animal affected over diedcharts

Both charts have second level reports:

In regards of the heatmap, the user will get access to the See Details table with detailed information, to the Signal Detection dashboard through the Animal/Human adverse events overview as well as to the Associated medicinal products & VeDDRAs in the last of the options displayed in the dropdown. All the three second level reports will show the information in regards of that set of specific cases.

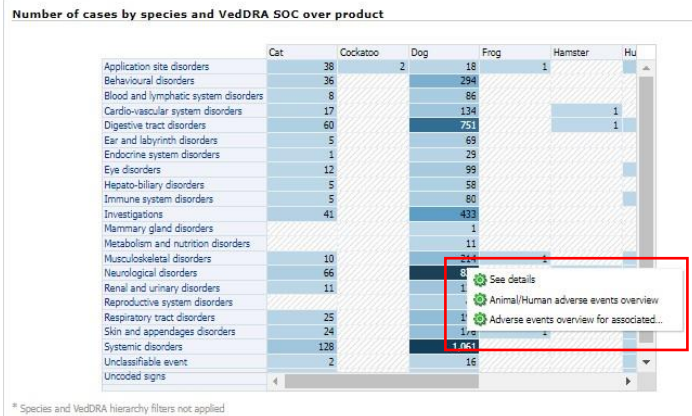


Image 32: Number of cases by species and VedDRA SOC over product

By clicking on any of the bars of the bar chart, the user gets to navigate to the ROR calculation using animals affected for the year selected:

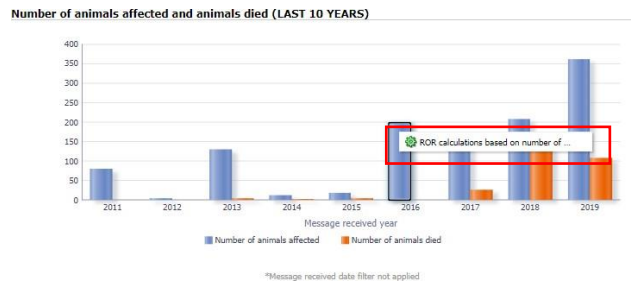


Image 33: Animal affected over died chart

ROR calculation using animals affected

Species: Cattle

Medicinal product shortname	VeDDRA SOC name	Animals affected ROR - A	Animals affected ROR - B	Animals affected ROR - C	Animals affected ROR - D	Animals affected ROR (-)	Animals affected ROR (+)	Message received date
DRAOXIN	Application site disorders	20	44	9	33	N/A	N/A	N/A 30/08/2016
	Application site disorders	100	0	0	53	N/A	N/A	N/A 06/09/2016
	Application site disorders	75	0	0	37	N/A	N/A	N/A 24/11/2016

Medicinal product shortname is equal to **DRAOXIN**
 and Classification code is equal to / is in **1**
 and VeDDRA SOC name is equal to **Application site disorders**
 and Human or animal is equal to **Animal**
 and Message received year is equal to / is in **2016**
 and Animals affected ROR is greater than **0**

[Return](#) - [Analyze](#) - [Refresh](#) - [Print](#) - [Export](#) - [Create Bookmark Link](#)

Image 34: detailed view

At the bottom of this tab we find a series of links with different functionalities:

4.2.1 See details

By clicking on see details the user navigates to a new window with the detailed information for the filters included in the query. At the top, the user will also find both Product Hierarchy and VeDDRA hierarchy level dropdowns as well as a Species filter to switch between potential species related to the product or products involved in the analysis.

See details

Product Hierarchy Level: Medicinal product shortname | VeDDRA Hierarchy Level: VeDDRA PT name

Species: Cat

Medicinal product shortname	VeDDRA SOC name	VeDDRA PT name	ROR	ROR (+)	ROR (-)	Number of animals affected	Number of cases (period specified)	Number of NON EEA cases (period specified)	Number of EEA cases (period specified)	Number of case (Total ALL)
DRAOXIN	Behavioural disorders	Anxiety	N/A	N/A	N/A	1	1	0	1	
	Behavioural disorders	Vocalisation	N/A	N/A	N/A	1	1	0	1	
	Digestive tract disorders	Emesis	N/A	N/A	N/A	1	1	1	0	
	Eye disorders	Abnormal vision	N/A	N/A	N/A	1	1	0	1	
	Investigations	Anaemia NOS	N/A	N/A	N/A	1	1	1	0	
	Investigations	Elevated pancreatic enzymes	N/A	N/A	N/A	1	1	1	0	
	Investigations	Elevated total bilirubin	N/A	N/A	N/A	1	1	1	0	
	Investigations	Leucopenia	N/A	N/A	N/A	1	1	1	0	
	Investigations	Other abnormal test result NOS	N/A	N/A	N/A	1	1	1	0	

Image 35: Detailed view

The see details table include the following columns:

Medicinal product shortname, VeDDRA SOC, VeDDRA PT, ROR, ROR(+), ROR(-), Number of animals affected, Number of cases (period specified), Number of non EEA cases (period specified), Number of EEA cases (period specified), Number of cases (Total ALL), Number of NON EEA cases, Number of EEA cases, Number of cases (Total ALL reactions), Number of fatal cases (period specified), Number of fatal cases, Reaction count, Case count by product (filter applied), Case count (filter not applied), Reaction count total, Percentage of reactions and Percentage of cases. What's more, the See Details table includes second level reports which is enabled at the Number

of cases (period specified) column, just as follows:

See details

Product Hierarchy Level Medional product shortname VedDRA Hierarchy Level VedDRA PT name

Species: Cattle

Medional product shortname	VedDRA SOC name	VedDRA PT name	ROR	ROR (+)	ROR (-)	Number of animals affected	Number of cases (period specified)	Number of NON EEA cases (period specified)	Number of EEA cases (period specified)	Number of cases (Total ALL)	Number of NON EEA cases	Number of EEA cases	Number of cases (Total ALL reactions)	Number of fatal cases (period specified)	Number of fatal cases	Reaction count	Case count by product applied	Case count (filter not applied)	Reaction count total	Percentage of reactions	Percentage of cases
DRA02N	Application site disorders	Injection site haemorrhage	N/A	N/A	N/A	36	1	1	0	3	2	1	1115	1	1	1	859	1566	184	1%	0%
	Application site disorders	Injection site hair change	N/A	N/A	N/A	100	1	1	0	1	1	0	1115	0	0	1	859	1566	184	1%	0%
	Application site disorders	Injection site inflammation	0.66	1.81	0.24	242	1	1	0	4	4	0	1115	1	1	2	859	1566	184	1%	0%
	Application site disorders	Injection site necrosis	N/A	N/A	N/A	11	1	0	1	4	3	1	1115	0	0	1	859	1566	184	1%	0%
	Application site disorders	Injection site lesion	N/A	N/A	N/A	200	2	2	0	5	5	0	1115	0	0	1	859	1566	184	1%	0%
	Application site disorders	Injection site necrosis	N/A	N/A	N/A	20	1	1	0	1	1	0	1115	0	0	1	859	1566	184	1%	0%
	Application site disorders	Injection site oedema	N/A	N/A	N/A	38	2	2	0	12	11	1	1115	1	1	1	859	1566	184	1%	0%
	Application site disorders	Injection site pain	N/A	N/A	N/A	2	1	1	0	3	3	0	1115	1	1	1	859	1566	184	1%	0%
	Application site disorders	Injection site pruritus	N/A	N/A	N/A	75	1	1	0	2	2	0	1115	0	0	1	859	1566	184	1%	0%

Return - Analyze - Refresh - Print - Export

Image 36: Detailed view

By clicking over any number, the user will have access to the following functionalities:

- Line listing: A new tab will open with the most detailed table the user has access to, basically with the full information about the cases of the line selected.

Line listing - Overview of AERs

AER ID	Case number	Duplicate report list	Occurrence country	Human or animal	Species	Breed	Min age	Max age	Min weight	Max weight	Date of treatment	Date of onset	Number of animals treated	Number of animals affected	Number of animals died	Reported product	Is use according to label	Is off label indication	Is off label overused	Is off label product expired	Is off label route of admin	Is off label storage	Is off label species target	Is off label treatment	Is off label underdosed	Is off label other issue	Is VedDRA term list	Original received date	Current submission date	Message received date
	388428	USA-PFZRCVMP-2018-US-54479	United States	Animal	Cattle	Cattle (other)	1 years	1 years	0 g	0 g	24/09/2018	24/10/2018	1	1	0	DRA02N - 1:1:R/A:0 Unknown/L/N/A (N/A N/A/s) 24/09/2018-24/09/2018	No	No	No	No	No	No	No	No	No	No	Injection site haemorrhage	24/10/2018	20/11/2018	22/11/2018

Image 37: Line listing view

Narrative description	RA assessment	RA conclusion	MAH conclusion	Organisation	Report link
24Oct2018: A veterinarian reported a suspected Adverse Reaction involving DRA02N in a beef show calf. The calf was described in fair condition prior to	Possible	Assessment Source: Primary information	C33269 - Undeclared/Temporal relationship with injection site lesion could make it related to administration of Drazoxin. However, any product, including Drazoxin	COETIS BELGIUM	Link

Image 38: Line listing view

- List of principal and report duplicates: A new tab will open with a detailed table including the duplicate reports, if any.
- Case listing with VeDDRA terms aligned: The user can see the list of cases with VeDDRA terms aligned and the number of animals affected involved.

Case listing with VedDRA terms aligned - Overview of AERs

VedDRA SOC

			Application site disorders
AER Id	Case number	Number of animals affected	Number of cases
			2
388428	USA-PFZRCVMP-2018-US-54479	1	1
504810	ZAF-MERCKMSD-2019-ZA-00608	35	1

Return - Analyze - Refresh - Print - Export

Image 39: Case listing with VeDDRA terms aligned view

4.2.2 Links to signal detection reports

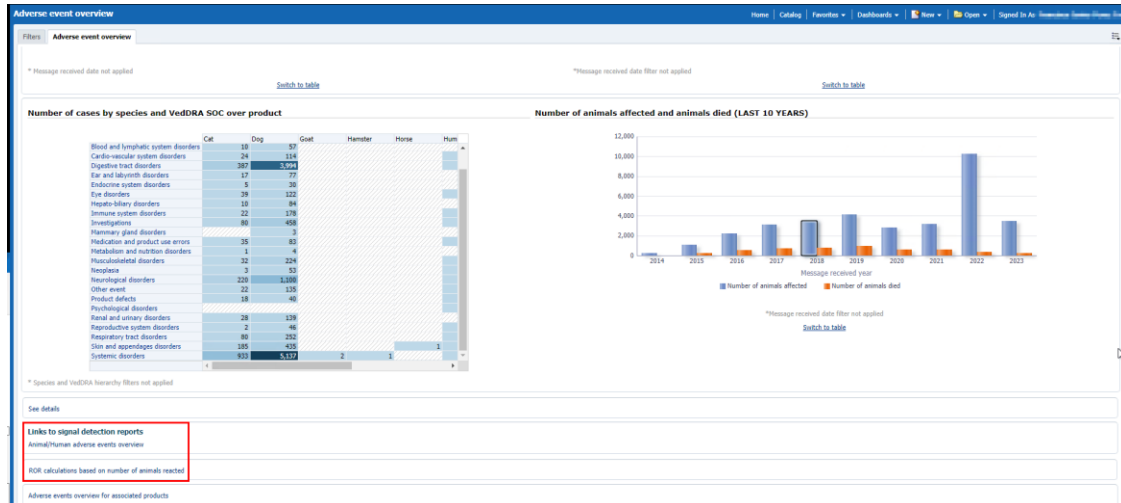


Image 40: Links

4.2.2.1 Animal/Human adverse events overview

This link allows the user to navigate to the Signal Detection and visualize this dashboard applying the same filters selected for the purpose of the current adverse event analysis.

4.2.2.2 ROR calculations based on number of animals reacted

This link allows the user to navigate to the *ROR calculation using animals affected* applying the same filters selected for the purpose of the current adverse event analysis. This table shows a group of ROR metrics related to the animals affected for a preset product and dates.

ROR calculation using animals affected

Species

Medicinal product shorthandname	VedDRA SOC name	Animals affected ROR - A	Animals affected ROR - B	Animals affected ROR - C	Animals affected ROR - D	Animals affected ROR (-)	Animals affected ROR	Animals affected ROR (+)	Message received date
DRAOXIN	Behavioural disorders	1	0	0	15	N/A	N/A	N/A	12/06/2018
	Digestive tract disorders	1	0	12	77	N/A	N/A	N/A	22/11/2019
	Eye disorders	1	0	3	55	N/A	N/A	N/A	07/11/2016
	Investigations	1	0	6	83	N/A	N/A	N/A	22/11/2019
	Neurological disorders	1	0	21	37	N/A	N/A	N/A	07/11/2016
	Neurological disorders	1	0	1	14	N/A	N/A	N/A	12/06/2018
	Respiratory tract disorders	1	0	27	62	N/A	N/A	N/A	22/11/2019
	Systemic disorders	1	0	10	5	N/A	N/A	N/A	12/06/2018
	Systemic disorders	1	0	50	39	N/A	N/A	N/A	22/11/2019

Image 41: ROR calculations based on number of animals reacted table

4.2.3 Link to data stratification report

4.2.3.1 Adverse events overview for associated products

This link allows the user to navigate to the data stratification report, displaying 2 different tables: The first one for the product selected in the filters page, detailing number of cases for the product, VedDRA SOC and the species set in the filter. The table also displays ROR(-), ROR(+) and ROR metrics for the product selected.

The second table shows same information but, in this case, including the associated products (to the one selected in the filters page) and the metrics will be measuring the combination of both products instead of the product selected. The user will also find the reaction count and the number of animals affected columns.

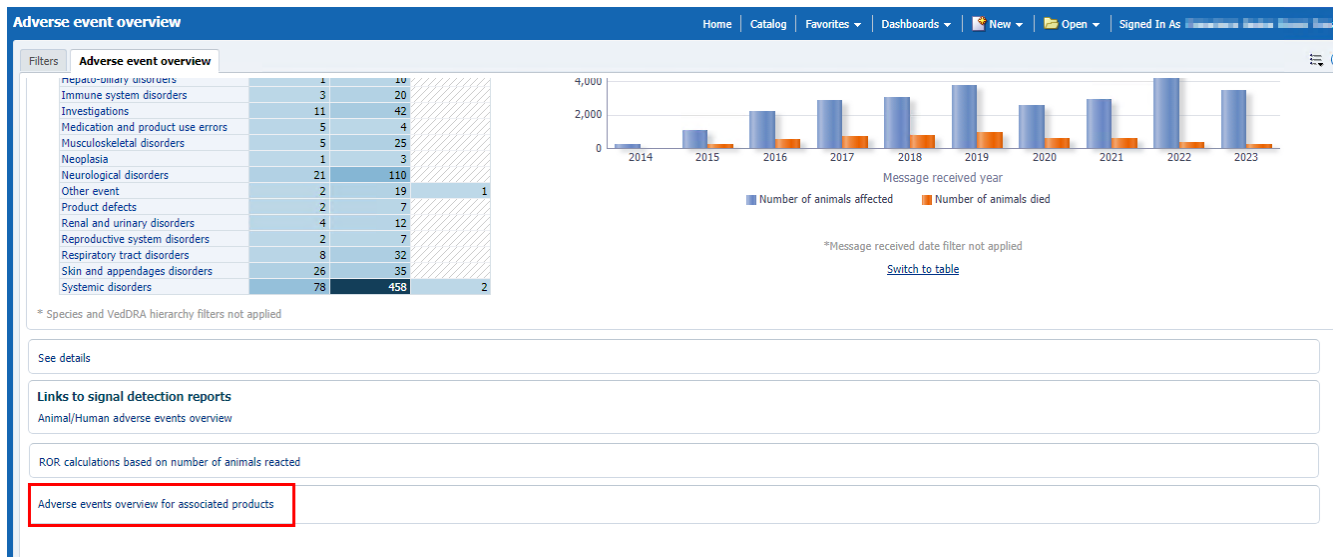


Image 42: Link to data stratification dashboard

Medicinal product shorthandname (DRAOXIN)

Current product

VedDRA SOC name

Species

Medicinal product shorthandname	VedDRA SOC name	Number of cases for the product	ROR (-) for the product	ROR for the product	ROR (+) for the product
DRAOXIN	Behavioural disorders	1	N/A	N/A	N/A
	Digestive tract disorders	1	N/A	N/A	N/A
	Eye disorders	1	N/A	N/A	N/A
	Investigations	1	N/A	N/A	N/A
	Neurological disorders	2	N/A	N/A	N/A
	Respiratory tract disorders	1	N/A	N/A	N/A
	Systemic disorders	2	N/A	N/A	N/A

Associated products

Associated medicinal product shorthandname () VedDRA SOC name ()

Species

Medicinal product shorthandname	Associated medicinal product shorthandname	VedDRA SOC name	Number of cases for the combination	Reaction count	Number of animals affected	Number of cases (Total ALL)	ROR (-) for the combination	ROR for the combination	ROR (+) for the combination
DRAOXIN	BRAVECTO	Digestive tract disorders	1	1	1	1	N/A	N/A	N/A
DRAOXIN	BRAVECTO	Investigations	1	7	1	1	N/A	N/A	N/A
DRAOXIN	BRAVECTO	Respiratory tract disorders	1	2	1	1	N/A	N/A	N/A
DRAOXIN	BRAVECTO	Systemic disorders	1	5	1	1	N/A	N/A	N/A
DRAOXIN	COIVENIA	Digestive tract disorders	1	1	1	1	N/A	N/A	N/A
DRAOXIN	COIVENIA	Investigations	1	7	1	1	N/A	N/A	N/A
DRAOXIN	COIVENIA	Respiratory tract disorders	1	2	1	1	N/A	N/A	N/A
DRAOXIN	COIVENIA	Systemic disorders	1	5	1	1	N/A	N/A	N/A
DRAOXIN	DEXAFORT	Behavioural disorders	1	2	1	1	N/A	N/A	N/A
DRAOXIN	DEXAFORT	Neurological disorders	1	1	1	1	N/A	N/A	N/A
DRAOXIN	DEXAFORT	Systemic disorders	1	1	1	1	N/A	N/A	N/A
DRAOXIN	METACAM	Digestive tract disorders	1	1	1	1	N/A	N/A	N/A
DRAOXIN	METACAM	Investigations	1	7	1	1	N/A	N/A	N/A
DRAOXIN	METACAM	Respiratory tract disorders	1	2	1	1	N/A	N/A	N/A
DRAOXIN	METACAM	Systemic disorders	1	5	1	1	N/A	N/A	N/A
DRAOXIN	UNKNOWIN	Digestive tract disorders	1	1	1	1	N/A	N/A	N/A
DRAOXIN	UNKNOWIN	Investigations	1	7	1	1	N/A	N/A	N/A
DRAOXIN	UNKNOWIN	Respiratory tract disorders	1	2	1	1	N/A	N/A	N/A
DRAOXIN	UNKNOWIN	Systemic disorders	1	5	1	1	N/A	N/A	N/A

Image 43: *Adverse events overview for associated products view*

5. Signal detection dashboard

5.1 Signal detection precalculations

Through the pre-calculations functionality in Signal detection dashboard, it will be possible to get the results faster than using the common Signal detection dashboard, as these have been precalculated for the following predefined time frames (using a single product, active substance or product grouping):

- 1 year
- 6 months
- 3 months
- 1 month

5.1.1. Precalculations at product shortname level in Signal detection dashboard

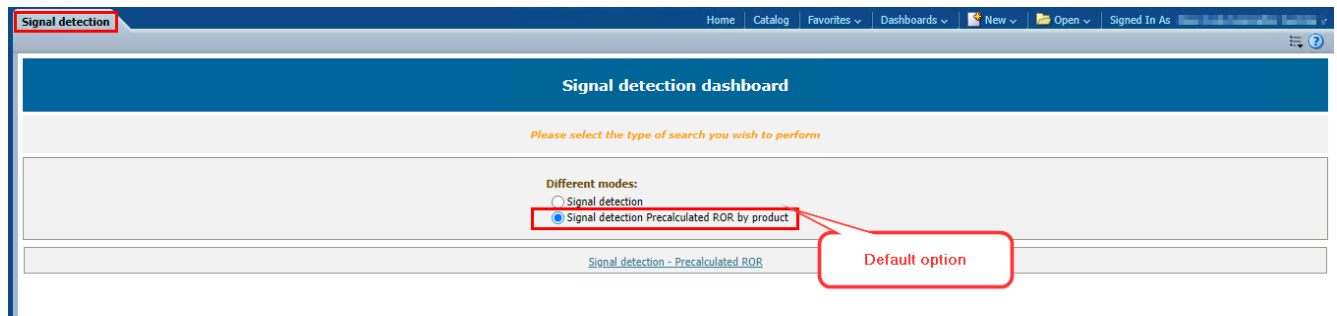


Image 44: Product shortname precalculations in Signal detection dashboard

'Signal detection Precalculated ROR by product' is the default option pre-selected in signal detection dashboard.

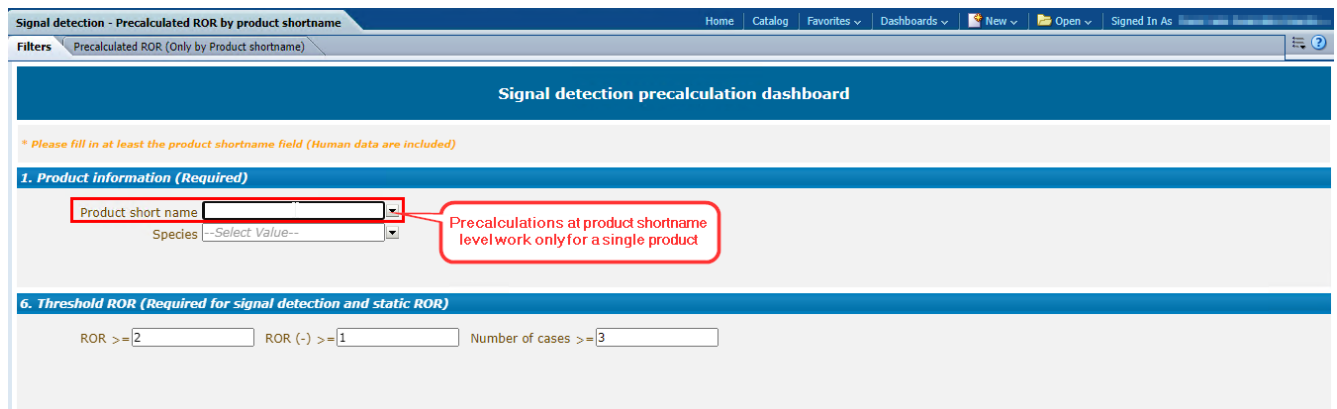


Image 45: Product short name filter in precalculations . Signal detection

When using the precalculations functionality, we should inform a single product as the precalculations cannot be done for more than one product.

Signal detection - Precalculated ROR by product shortname

Filters: Precalculated ROR (Only by Product shortname)

Signal detection (with two RORs, up to Timeframe 1 until today)

Select the corresponding timeframe: One year Six months Three months One month

Signal detection - Precalculated ROR

Species: Dog

Product shortname	Veddra SOC name	VedDRA PT name	Number of cases between date 1 and date 2	Number reacted between date 1 and date 2	ROR (-) until date 2	ROR until date 2	ROR (+) until date 2	Number of cases until date 1	Number reacted until date 1	ROR (-) until date 1	ROR until date 1	ROR (+) until date 1	Total number of cases
	Application site disorders	Application site erythema	0	0	N/A	N/A	N/A	2	4	N/A	N/A	N/A	2
		Application site haemorrhage	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Application site hair change	0	0	N/A	N/A	N/A	2	2	N/A	N/A	N/A	2
		Application site infection	0	0	N/A	N/A	N/A	2	2	N/A	N/A	N/A	2
		Application site inflammation	0	0	N/A	N/A	N/A	1	2	N/A	N/A	N/A	1
		Application site lesion	0	0	N/A	N/A	N/A	2	2	N/A	N/A	N/A	2
		Application site oedema	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Application site pruritus	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Application site skin change	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Injection site hair change	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Injection site mass NOS	0	0	0.12	0.37	1.14	3	3	0.12	0.37	1.14	3
		Injection site oedema	0	0	0.09	0.27	0.85	3	3	0.09	0.27	0.85	3
		Injection site pain	0	0	N/A	N/A	N/A	2	2	N/A	N/A	N/A	2
		Injection site related amputation	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Injection site skin change	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1

Image 46: Predefined time frames for precalculations

NOTE: Precalculations are done considering the last day of the previous month. **Example:** If we run the precalculations during April, all the time frames precalculations will retrieve the data until 31 March.

Signal detection - Precalculated ROR by product shortname

Filters: Precalculated ROR (Only by Product shortname)

Product shortname	Veddra SOC name	VedDRA PT name	Number of cases between date 1 and date 2	Number reacted between date 1 and date 2	ROR (-) until date 2	ROR until date 2	ROR (+) until date 2	Number of cases until date 1	Number reacted until date 1	ROR (-) until date 1	ROR until date 1	ROR (+) until date 1	Total number of cases
	Respiratory tract disorders	Vulvovaginitis	0	0	1.37	2.76	5.56	8	8	1.37	2.76	5.56	8
		Apnoea	0	0	1.15	1.75	2.68	22	22	1.15	1.75	2.68	22
		Atelectasis	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Bradypnoea	0	0	1.17	2.36	4.75	8	9	1.17	2.36	4.75	8
		Bronchitis	0	0	1.29	2.50	4.83	9	9	1.29	2.50	4.83	9
		Bronchopulmonary inflammation	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Cough	0	0	1.66	2.18	2.86	55	58	1.66	2.18	2.86	55
		Dry nose	0	0	1.53	4.85	15.36	3	3	1.53	4.85	15.37	3
		Dysphonia	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Dyspnoea	0	0	1.00	1.25	1.55	84	85	1.00	1.25	1.55	84
		Epistaxis	0	0	1.32	2.33	4.14	12	12	1.32	2.33	4.14	12
		Foam in respiratory tract	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Hydrothorax	0	0	1.55	3.01	5.84	9	9	1.55	3.01	5.84	9
		Hypoplastic trachea	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Hypoxia	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Laryngeal irritation	0	0	N/A	N/A	N/A	2	2	N/A	N/A	N/A	2
		Laryngitis	0	0	N/A	N/A	N/A	2	2	N/A	N/A	N/A	2
		Nasal cavity disorder NOS	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Pneumonia	0	0	1.77	2.90	4.77	16	16	1.77	2.91	4.78	16
		Pneumonitis	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Pulmonary congestion	0	0	0.37	1.15	3.58	3	3	0.37	1.15	3.58	3
		Pulmonary disorder NOS	1	1	0.47	1.26	3.38	3	3	0.30	0.95	2.95	4
		Pulmonary haemorrhage	0	0	0.87	1.96	4.39	6	6	0.88	1.96	4.41	6
		Pulmonary oedema	0	0	0.49	0.94	1.82	9	9	0.49	0.94	1.82	9
		Rale	0	0	1.58	2.53	4.05	18	18	1.59	2.53	4.05	18
		Respiratory tract disorder NOS	0	0	1.77	2.55	3.67	30	30	1.77	2.55	3.68	30
		Respiratory tract infection NOS	0	0	2.11	5.74	15.64	4	5	2.11	5.74	15.65	4
		Rhinitis	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Sinusitis	0	0	N/A	N/A	N/A	1	1	N/A	N/A	N/A	1
		Sneezing	0	0	1.64	2.69	4.42	16	16	1.64	2.69	4.42	16
		Tachypnoea	0	0	1.44	1.74	2.11	117	113	1.44	1.74	2.11	117

Image 47: Line listing functionality in Precalculations

When clicking on the 'Number of cases between date 1 and date 2' values, it's possible to get the line listing for the selected value.

5.2. Signal detection dashboard

This dashboard displays several number of cases and animals affected as well as ROR metrics, so the user is able to get an overview of the data for a product, active substance or group of products for a selected period in order to check for potential signals.

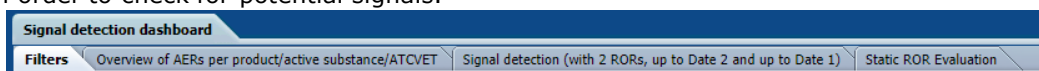


Image 48: Signal detection menu

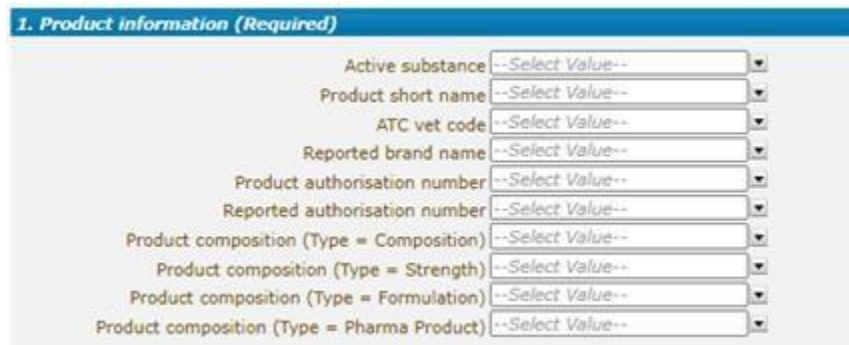
The dashboard is broken down in four tabs: Overview of AERs per product/active substance/ATCVETVET, Signal detection (with 2 RORs, up to Date 2 and up to Date 1) and Static ROR Evaluation as well as the tab for filtering the query (Filters).

1. 5.2.1.Filters Choose from all attributes in the Product Information (Required)

In this prompt you select at what level of the product hierarchy you want to run your query. These

levels are:

- Active substance level: Results will be related to AERs for products that contain the selected active substance(s).
- Product Short name: Results will be related to AERs for selected product(s) grouped by the product short name.
- ATCVET Vet code level: Results will be related to AERs for products that belong to the selected ATCVET Vet Code.
- Reported Brand Name: Results will be related to AERs for a selected Product Brand Name as reported in the AER verbatim, prior to standardisation.
- Product Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number stated in the product dictionary.
- Reported Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number as reported in the AER.
- Product composition level (Composition, Strength, Formulation, Pharma Product): Results will be related to AERs for products that are composed solely of the selected active substance(s), active substance(s) + strength(s), Active substance(s) + Pharmaceutical form(s), Active substance(s) Strength + Pharmaceutical form. This enables users to group products based on their composition, regardless of the trade names of the products.



1. Product information (Required)

Active substance --Select Value--

Product short name --Select Value--

ATC vet code --Select Value--

Reported brand name --Select Value--

Product authorisation number --Select Value--

Reported authorisation number --Select Value--

Product composition (Type = Composition) --Select Value--

Product composition (Type = Strength) --Select Value--

Product composition (Type = Formulation) --Select Value--

Product composition (Type = Pharma Product) --Select Value--

Image 49: Filter options

2. Message received date range (Required)

In this prompt you select a range of dates.

Image 50: Message received date range filter

3. Report filter (Required)

Select whether your result should contain only **Animal** or **Human** AERs by ticking the relevant option, or both by selecting both Animal and Human.

Image 51: Report filter

4. Optional report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

Image 52: Optional report filters

Original Received Date: The date that the MAH or NCA first received the message.

Serious: The system will return only the serious or the non-serious reports.

Information type vs Exclude lack of efficacy: If you want to exclude the lack of efficacy cases and you exclude "Lack of efficacy" within the Information type dropdown (by including all other information types), you will get the reports where LOE has been reported together with other issues/information types. However, if you tick the box "Yes" in "Exclude lack of efficacy", the system will exclude those reports where the VeDDRA term "Lack of efficacy" has been reported.

5. Threshold ROR

This prompt is mandatory but filled by default with ROR \geq 2, ROR(-) \geq 1 and Number of cases \geq 3. The user is able to customize these values for the purpose of the analysis.

Image 53: Threshold ROR

6. Historical data

No answer is required for this prompt. By default, a snapshot of the day will be set. If a different date is selected, the results will reflect the data in EVVET as per the date selecting, excluding data received after the selected date.

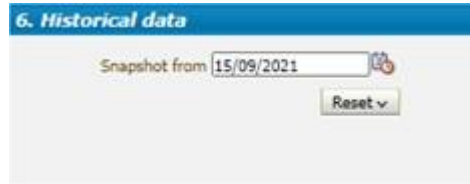


Image 54: Threshold ROR

5.2.1 Overview of AERs per product/active substance/ATCVETVET

Number of cases and number of animals affected can be seen in this first tab, distributed geographically in a map, including a dropdown on top to jump from one metric to the other. The darker the blue, the more cases associated to a specific country.



Image 55: Overview of AERs per product/active substance/ATC vet

Right below the map, the user will find a much more detailed table with the number of cases and number reacted for the product selected, split by occurrence region and country. In addition, Human or Animal and Seriousness flags will be also displayed, as well as the totals for number of cases and number reacted for each country included in the outcome.

Product Hierarchy Level		Medicinal product shortname		Human or animal Seriousness				Number of cases	Number reacted
Human or animal	Seriousness	Animal Yes	Animal No	Animal Yes	Animal No	Animal Yes	Animal No		
Medicinal product shortname	Occurrence region	Occurrence country	Number of cases	Number reacted	Number of cases	Number reacted	Number of cases	Number reacted	
VELACTIS	EEA	Austria	4	8	4	7	8	15	
		Belgium	7	14	2	2	9	16	
		Czech Republic	2	2	1	2	3	4	
		Denmark	41	72	39	61	80	133	
		Estonia			2	27	2	27	
		France	24	27	5	7	29	34	
		Germany	22	29	21	32	43	61	
		Greece	2	4			2	4	
		Italy	7	15	5	25	12	40	
		Luxembourg	1	1			1	1	
		Netherlands	19	24	16	26	35	50	
		Poland			5	6	5	6	
		Spain	7	9	8	17	15	26	
		United Kingdom	4	8	13	18	17	26	
	Non EEA	Brazil	4	4	3	3	7	7	
		Mexico			2	7	2	7	
		Switzerland	1	1			1	1	

Image 56: Number of cases and number reacted for the product selected detail

By the dropdown on top of the table, the user will be able to jump from Medicinal product shortname to Reported brand name, product composition, active substance or ATCvet vet code visualization.

Product Hierarchy Level **Product composition**

Product composition	Occurrence region	Occurrence country	Human or animal		Animal		Number of cases	Number reacted
			Yes	No	Yes	No		
CABERGOLINE	EEA	Austria	4	0	4	0	8	15
CABERGOLINE	EEA	Belgium	7	14	3	2	9	16
CABERGOLINE	EEA	Czech Republic	2	2	1	2	3	4
CABERGOLINE	EEA	Denmark	41	72	39	61	80	133
CABERGOLINE	EEA	Estonia		2	2	27	2	27
CABERGOLINE	EEA	France	24	27	5	7	29	34
CABERGOLINE	EEA	Germany	22	29	21	32	43	61
CABERGOLINE	EEA	Greece	2	4			2	4
CABERGOLINE	EEA	Italy	7	15	5	25	12	40
CABERGOLINE	EEA	Luxembourg	1	1			1	1
CABERGOLINE	EEA	Netherlands	19	24	16	26	35	50
CABERGOLINE	EEA	Poland			5	6	5	6
CABERGOLINE	EEA	Spain	7	9	8	17	15	26
CABERGOLINE	EEA	United Kingdom	4	8	13	18	17	26
CABERGOLINE	Non EEA	Brazil	4	4	3	3	7	7
CABERGOLINE	Non EEA	Mexico			2	7	2	7
CABERGOLINE	Non EEA	Switzerland	1	1			1	1
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Austria	4	8	4	7	8	15
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Belgium	7	14	2	2	9	16
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Czech Republic	2	2	1	2	3	4
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Denmark	41	72	39	61	80	133
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Estonia		2	2	27	2	27
CABERGOLINE - SOLUTION FOR INJECTION	EEA	France	24	27	5	7	29	34
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Germany	22	29	21	32	43	61
CABERGOLINE - SOLUTION FOR INJECTION	EEA	Greece	2	4			2	4

Image 57: Product composition detailed view

What's more, a dropdown for Species is included at the very top of this tab, so the user is able to apply this filter, impacting the data displayed both in the map and the table.

5.2.2. Signal detection (with 2 RORs, up to Date 2 and up to Date 1)

In this tab, the user is able to analyse a diverse set of metrics for the product and the period selected, broken down by VeDDRA SOC and VeDDRA PT levels. Number of cases and number reacted until date 1 and between date 1 and date 2 (period selected), together with ROR calculations are the core of this table.

Moreover, a product hierarchy and species dropdowns have been included at the top, so the user is able to analyse information from different points of view and for any species for which AERs have been received for a particular product/substance.

ROR until Date 2: cumulative ROR

ROR until Date 1: ROR prior to the period selected.

Signal detection dashboard

Filters Overview of AERs per product/active substance/ATCVET **Signal detection (with 2 RORs, up to Date 1 and up to Date 2)** Static ROR Evaluation

NUMBER OF CASES BETWEEN DATE 1 AND DATE 2						NUMBER OF CASES UNTIL DATE 1						TOTAL NUMBER OF CASES					
Product Hierarchy Level [Medicinal product shortname]						Product Hierarchy Level [Medicinal product shortname]						Product Hierarchy Level [Medicinal product shortname]					
Date 1: 09/04/2023 Date 2: 09/05/2023 14:15:30						Date 1: 09/04/2023 Date 2: 09/05/2023 14:15:30						Date 1: 09/04/2023 Date 2: 09/05/2023 14:15:30					
Species [Dog]						Species [Dog]						Species [Dog]					
Medicinal product shortname	VedDRA SOC name	VedDRA PT name	Number of cases between date 1 and date 2	Number reacted between date 1 and date 2	ROR (-) until date 2	ROR (+) until date 2	Medicinal product shortname	VedDRA SOC name	VedDRA PT name	Number of cases until date 1	Number reacted until date 1	ROR (-) until date 1	ROR (+) until date 1	Medicinal product shortname	VedDRA SOC name	VedDRA PT name	Total number of cases
	Application site disorders	blister	0		N/A	N/A		Application site disorders	blister	1	1	N/A	N/A		Application site disorders	blister	1
	Application site burn	blister	0		0.04	0.13	0.40	Application site burn	blister	3	3	0.04	0.13	0.42	Application site burn	blister	26
	Application site erythema	blister	1	1	0.15	0.22	0.32	Application site erythema	blister	25	32	0.15	0.22	0.32	Application site erythema	blister	3
	Application site haemorrhage	blister	0		0.07	0.22	0.67	Application site haemorrhage	blister	3	3	0.07	0.23	0.71	Application site haemorrhage	blister	37
	Application site hair change	blister	5	6	0.23	0.32	0.45	Application site hair change	blister	32	44	0.20	0.29	0.41	Application site hair change	blister	2
	Application site infection	blister	0		N/A	N/A	N/A	Application site infection	blister	2	2	N/A	N/A	N/A	Application site infection	blister	10
	Application site inflammation	blister	0		0.09	0.17	0.32	Application site inflammation	blister	10	11	0.09	0.18	0.33	Application site inflammation	blister	18
	Application site lesion	blister	2	2	0.15	0.24	0.38	Application site lesion	blister	16	16	0.14	0.23	0.37	Application site lesion	blister	2
	Application site mass NOS	blister	0		N/A	N/A	N/A	Application site mass NOS	blister	2	2	N/A	N/A	N/A	Application site mass NOS	blister	2
	Application site mucopurulent discharge	blister	0		N/A	N/A	N/A	Application site mucopurulent discharge	blister	2	2	N/A	N/A	N/A	Application site mucopurulent discharge	blister	2
	Application site	blister	0		N/A	N/A	N/A	Application site	blister	2	2	N/A	N/A	N/A	Application site	blister	5

Image 58: Signal detection view

5.2.2.1 IRIS Line listing – List of signals

From Signal detection dashboard, it is possible to get the List of signals line listing. To get this functionality, we need to access the third tab 'Signal detection (with 2 RORs, up to Date 1 and to Date 2)' and click on the Medicinal Product shortname. Once we click the product, 'List of signals' line listing option will be displayed to be selected.

NOTE: 'List of signals' line listing is also available in the precalculated Signal detection dashboard.

The screenshot shows the 'Signal detection dashboard' with three main panels. Each panel has a 'Product Hierarchy Level' dropdown set to 'Medical product shortname' and a 'Species' dropdown set to 'Dog'. The panels are:

- NUMBER OF CASES BETWEEN DATE 1 AND DATE 2:** Shows data for BRAVECTO with various application site reactions like 'blister', 'burn', 'erythema', 'haemorrhage', 'hair change', 'infection', 'inflammation', 'lesion', 'mass NOS', and 'mucopurulent discharge'.
- NUMBER OF CASES UNTIL DATE 1:** Shows cumulative data for the same reactions.
- TOTAL NUMBER OF CASES:** Shows the total number of cases for each reaction type.

In all three panels, a red box highlights the 'List of signals' dropdown menu, which is currently open, showing options for 'List of signals' and 'List of signals'.

Image 59: List of signals option from Signal detection dashboard

The screenshot shows a detailed line listing table from the Signal detection dashboard. The table has the following columns:

- Case title
- Process type
- Medicinal product name
- Substance
- Pt veddra term
- Species
- Submitted on
- Date of analysis
- Prioritization
- Proposal for action (MAH)
- Regulatory outcome
- Substatus
- Latest publication date

The table contains data for three process types: 'Annual statements submission', 'Signal management submission', and 'Annual statements submission'. Each entry includes details for the medicinal product (e.g., Bravecto 1000 mg - Chewable tablet), substance (Fluralaner), and regulatory status (e.g., 'Signal is refuted').

Image 60: List of signals line listing from Signal detection dashboard

5.2.3 Static ROR Evaluation

Static ROR is focused on the different inputs for the Reporting Odds Ratio calculation (ROR) as well as the ROR metric itself, including both lower and upper bounds, aka ROR(-) and ROR(+). All the metrics displayed at VeDDRA SOC level, but the user can change the VeDDRA level via the VeDDRA Output Level prompt.

At the top, same filters as in the Signal detection (with 2 RORs, up to Date 2 and up to Date 1) tab have been included, this is:

- Product Hierarchy Level, giving users the chance to visualize the data by medicinal product shortname, reported brand name, active substance, product composition or ATCvet code.
- Species filter so the user can analyze this metrics for every species impacted by the product.
- Reaction filters at the very top, so the user is able to filter at every level.

Lastly, number of animals affected metric is also displayed at VeDDRA SOC level.

VeDDRA SOC name VeDDRA HLT name VeDDRA PT name VeDDRA LLT name

Product Hierarchy Level Medicinal product shortname VeDDRA Output Level VeDDRA SOC name

Species

Medicinal product shortname	VeDDRA SOC name	Number reported	A - Reports with product and reaction	B - Reports with product without reaction	C - Reports without product but with reaction	D - Reports without product and without reaction	ROR (-)	ROR (+)	ROR (±)
VELACTE									
	Behavioural disorders	9	1	264	41		2.97	0.96	1.02
	Blood and lymphatic system disorders	2	1	269	112		2.320	N/A	N/A
	Cardiovascular system disorders	20	23	247	99		2.943	2.28	3.63
	Digestive tract disorders	118	61	269	262		2.28	2.66	1.19
	Eye disorders	1	1	269	67		2.559	N/A	N/A
	Hepato-biliary disorders	8	1	269	27		2.625	N/A	N/A
	Immune system disorders	2	3	267	183		2.489	0.12	0.18
	Invertebrates	34	22	248			1.242	0.62	0.78
	Mammary gland disorders	73	26	244	157		2.481	1.69	2.67
	Metabolism and nutrition disorders	77	48	221	13		2.629	44.84	76.83
	Musculoskeletal disorders	15	11	269	67		1.675	1.63	1.14
	Neurological disorders	41	38	242	244		2.284	0.94	1.13
	Renal and urinary disorders	2	1	269	13		2.629	N/A	N/A
	Reproductive system disorders	60	30	238	278		2.40	1.38	1.62
	Respiratory tract disorders	6	9	265	404		2.228	0.09	0.12
	Skin and appendages disorders	8	9	265	96		2.946	0.39	0.63
	Sustentia disorders	419	244	24	2,242		38	1.29	2.61
	Unlabeled signs	3	3	267	7		1.621	4.33	6.97

Image 61: Static ROR Evaluation

6. Signal evaluation

This dashboard enables the user to evaluate signals using different parameters (age, time to onset, off label use, geographical distribution, pharmaceutical form, other products involved, other VeDDRA terms). It is also focused on finding both associated products and VeDDRAs, so the user is able to visualize the main products and reactions related to ones selected in the filters page.

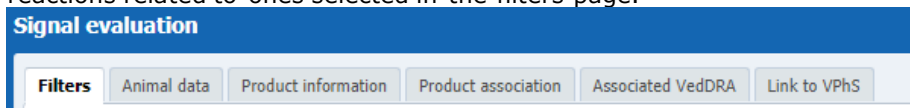


Image 62: Signal evaluation menus

The dashboard is broken down in four tabs: Animal Data, Product Information, Product Association and Associated VeDDRA terms, as well as the tab for filtering the query (Filters) and one last tab with a link to VPhS.

At the top of every tab the user will find a header including the usual key figures, being for this dashboard: Number of cases, Animals affected and Animals died, as follows.

Number of cases 433,280	Animals affected 153,689,856	Animals died 26,903,375
----------------------------	---------------------------------	----------------------------

Image 63: Signal evaluation key figures

6.1 Filters

1. Choose from all attributes in the Product Information (Required)

In this prompt you select at what level of the product hierarchy you want to run your query. These levels are:

- Active substance level: Results will be related to AERs for products that contain the selected active substance(s).
- Product Short name: Results will be related to AERs for selected product(s) grouped by the product short name.
- ATCVET Vet code level: Results will be related to AERs for products that belong to the selected ATCVET Vet Code.
- Reported Brand Name: Results will be related to AERs for a selected Product Brand Name as reported in the AER verbatim, prior to standardisation.
- Product Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number stated in the product dictionary.
- Reported Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number as reported in the AER.
- Product composition level (Composition, Strength, Formulation, Pharma Product): Results will be related to AERs for products that are composed solely of the selected active substance(s), active substance(s) + strength(s), Active substance(s) + Pharmaceutical form(s), Active substance(s) Strength + Pharmaceutical form. This enables users to group products based on their composition, regardless of the trade names of the products.

Image 64: Filter options

2. Message received date range (Required)

In this prompt you select a range of dates.

Image 65: Message received date range

3. Report filter (Required)

Select whether your result should contain only **Animal** or **Human** AERs by ticking the relevant option, or both by selecting both Animal and Human.

Image 66: Report filter

4 VeDDRA hierarchy

In this prompt you select one or multiple VeDDRA terms at different levels. By informing the left column of VeDDRA terms, we can filter by one or multiple terms. When selecting only one term in each level, the query will return all cases where the VeDDRA Terms selected have been reported simultaneously (AND). When using the dropdowns both from the left and the right side, we will get all cases where at least one of the VeDDRA terms informed has been reported (OR). In both sides, if more than one term is selected in the same level, the query will return all cases where at least one of the VeDDRA terms selected has been reported (OR).

*Use the drop down on the left side to filter by one or multiple VeDDRA terms. When selecting only one term in each level, the query will return all cases where the VeDDRA Terms selected have been reported simultaneously (AND).
 *Using the drop downs on both sides will return all cases where at least one of the VeDDRA terms selected has been reported (OR).
 *In both sides, if more than one term is selected in the same level, the query will return all cases where at least one of the VeDDRA terms selected has been reported (OR).

Image 67: VeDDRA hierarchy

5 All cases or new cases (Required)

In this prompt you have to select one of the two options, being "All Cases" selected by default . Selecting "New cases" will return data related only to new reports received in EVVET during the selecting period, and will exclude from the data set follow ups to reports initially received in EVVET prior to the selected period.



Image 68: All cases or new cases

6 Choose from list of optional AE Report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

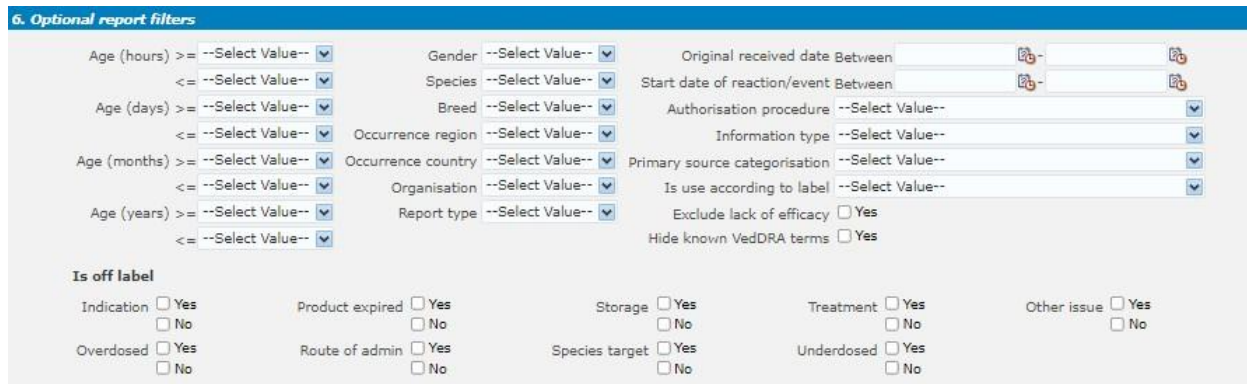


Image 69: Optional AE Report filters

Original Received Date: The date that the MAH or NCA first received the message.

Serious: The system will return only the serious or the non-serious reports.

Information type vs Exclude lack of efficacy: If you want to exclude the lack of efficacy cases and you exclude "Lack of efficacy" within the Information type dropdown (by including all other information types), you will get the reports where LOE has been reported together with other issues/information types. However, if you tick the box "Yes" in "Exclude lack of efficacy", the system will exclude those reports where the VedDRA term "Lack of efficacy" has been reported.

7 Threshold ROR (Required)

This prompt is mandatory but filled by default with ROR >= 2, ROR (-) >= 1 and Number of cases >= 3. The user is able to customize this values for the purpose of the analysis.

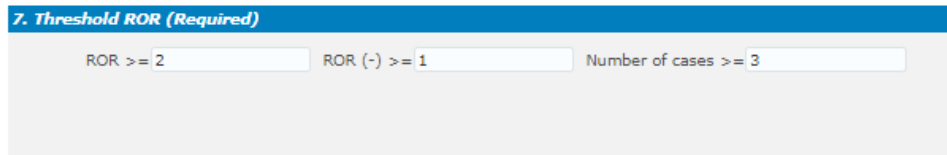


Image 70: Threshold ROR

8 Historical data

No answer is required for this prompt. By default, a snapshot of the day will be set. If a different date is selected, the results will reflect the data in EVVET as per the date selecting, excluding data received after the selected date.



Image 71: Historical data

6.2 Animal data

The charts displayed in the Animal data tab from top to bottom are as follows:

Number of cases time to onset

Pie chart. Shows the number of cases by time to onset for the product and period specified in the filters page. Time to onset goes from ≤ 2 minutes to > 30 days.

Number of animals affected and died over years (LAST 10 YEARS)

Bar chart. Shows the number of animals affected and died over the last 10 years, so it is not limited by the period specified in the filters page. Product selected applies. Red bars show the number of animals died and blue bars the number of animals affected.

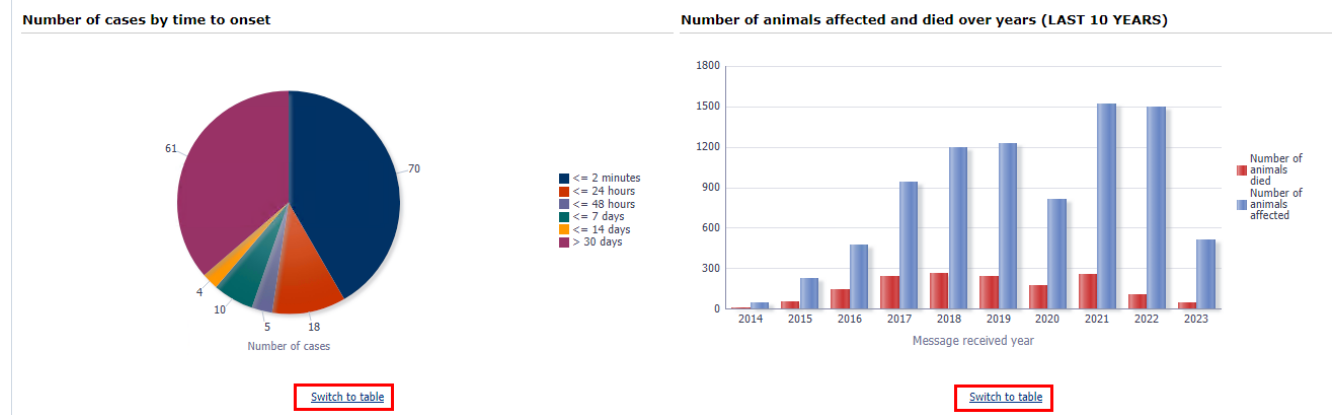


Image 72: Animal data charts

Below this second chart, the user will find a switch to table functionality so the information can be shown both as a chart or a classic table format.

Animal information - Animals affected and died cumulative

Message received year	Number of animals affected	Number of animals died
2016	273	61
2017	11	4
2018	129	38
2019	17	3
2020	5	2

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Image 73: Animal data cumulative view

Number of cases by species

Bar chart. Shows the number of cases by species for the product and period specified in the filters page.

Number of cases by species and off label use

Heat map. Shows the number of cases by species together with the off-label use information, broken down into YES/NO/NO DATA.

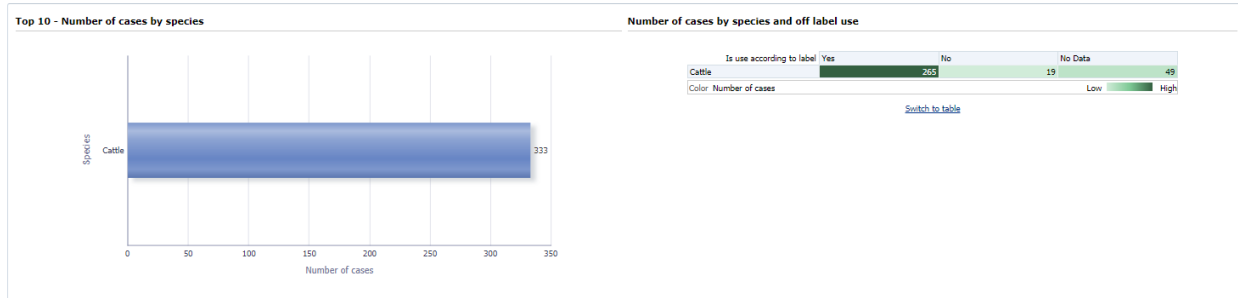


Image 74: Number of cases by species and off label use charts

Below this second chart, the user will find a switch to table functionality so the information can be shown both as a chart or a classic table format.

Number of cases by species and off label use

Is use according to label	Yes	No	No Data	Number of cases
Species	Number of cases	Number of cases	Number of cases	
Cattle	265	19	49	333
Grand Total	265	19	49	333

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Image 75: Number of cases by species and off label use table

6.3 Product information

The charts displayed in the Product information tab from top to bottom are as follows:

Number of animals affected/died by country.

Map. Shows the number of animals affected/died by country for the product and period specified in the filters page. The darker the blue, the more cases associated to a specific country. A dropdown has also been included at the top in order to jump from animals affected to animals died.

In addition, a link has been added at the bottom so the user can visualize in table format the Number of animals affected by pharmaceutical form or active substance.

Number of cases by country and species

Bar chart. Shows the number of cases by country and species for the product and period specified in the filters page. Blue bars show the number of cases, orange bars show the number of animals affected and green bars show the number of animals died.

Moreover, a Switch to table link at the bottom has been included so the user is able to display this same information in table format.

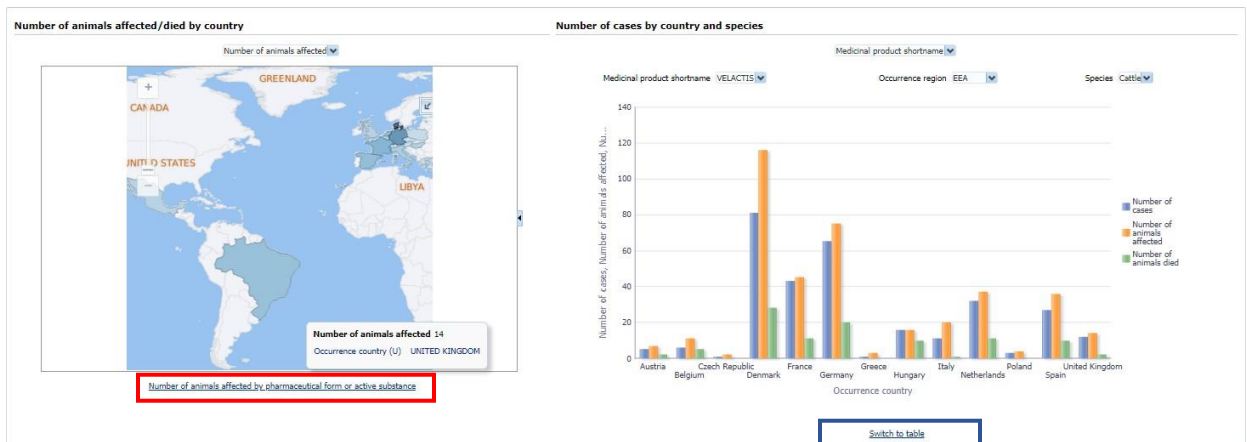


Image 76: Number of animals affected/died by country and by country and species chart

Number of animals affected by pharmaceutical form or active substance

Pharmaceutical product form:

Species:

Information type:

Pharmaceutical product form	Occurrence region	Occurrence country (U)	Animal			Number of AERs	Number of animals affected	Number of animals died
			Number of AERs	Number of animals affected	Number of animals died			
SOLUTION FOR INJECTION	EEA	AUSTRIA	1	3	0	1	3	0
SOLUTION FOR INJECTION	EEA	BELGIUM	1	1	0	1	1	0
SOLUTION FOR INJECTION	EEA	DENMARK	7	21	0	7	21	0
SOLUTION FOR INJECTION	EEA	FRANCE	3	3	1	3	3	1
SOLUTION FOR INJECTION	EEA	GERMANY	3	3	2	3	3	2
SOLUTION FOR INJECTION	EEA	NETHERLANDS	2	2	2	2	2	2
SOLUTION FOR INJECTION	EEA	SPAIN	1	1	0	1	1	0
SOLUTION FOR INJECTION	EEA	UNITED KINGDOM	14	14	0	14	14	0

Image 77: Number of animals affected by pharmaceutical form or active substance

Number of cases by country and species

Medicinal product shortname: VELACTIS | Occurrence region: EEA | Species: Cattle

Occurrence country	Number of cases	Number of animals affected	Number of animals died
Austria	5	7	2
Belgium	6	11	5
Czech Republic	1	2	0
Denmark	81	116	28
France	43	45	11
Germany	65	75	20
Greece	1	3	0
Hungary	16	16	10
Italy	11	20	1
Netherlands	32	37	11
Poland	3	4	0
Spain	27	36	10
United Kingdom	12	14	2

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Image 78: Number of cases by country and species

Number of cases by information type

Pie chart. Shows the number of cases by information type for the product and period specified in the filters page.

A couple of interdependent dropdowns has been included at the top so the user is able to see the information as Medicinal product shortname, Reported brand name, Product composition, Active substance or ATCvet and broken-down consequently.

Number of cases over year (LAST 10 YEAR)

Bar chart. Shows the number of cases over year for the last 10 years span, not applying the message received dates included in the filters page. Blue bars show the number of cases and the orange line shows the cumulative number of cases.

On top of that, two interdependent dropdowns have been included so the user is able to see the information as Medicinal product shortname, Reported brand name, Product composition, Active substance or ATCvet as well as display it by information type.

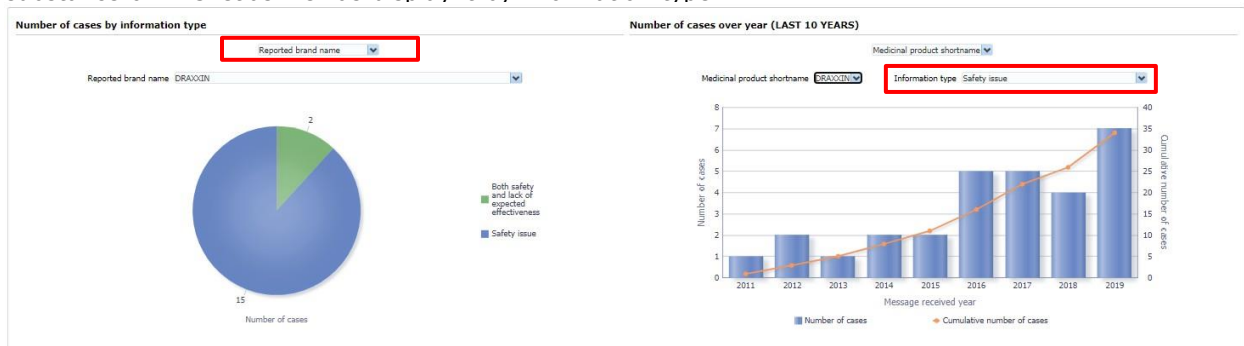


Image 79: Number of cases over year (LAST 10 YEARS) chart

6.4 Product association

The charts displayed in the Product association tab from top to bottom are as follows:

Number of cases by product used in association with others

Treemap. Shows the number of cases by product used in association with others displayed as hierarchical data, so the user is able to see the concomitant products used together with the product selected in the filters page. The darker the blue, the higher the number of cases for the combination of products. Also every rectangle has an area proportional to the number of cases.

Number of cases by species

Horizontal bar chart. Interconnected to the treemap, in this chart the user can see the number of cases by species for the concomitant products to the main product selected in the filters page. These products have to be selected in the dropdown enabled at the top for that purpose.

Number of cases by species

Heat map. Also interconnected to the treemap, in this heatmap the user can see the number of cases by species for the concomitant products related to the main product selected in the filters page, including also the reactions at VedDRA level.

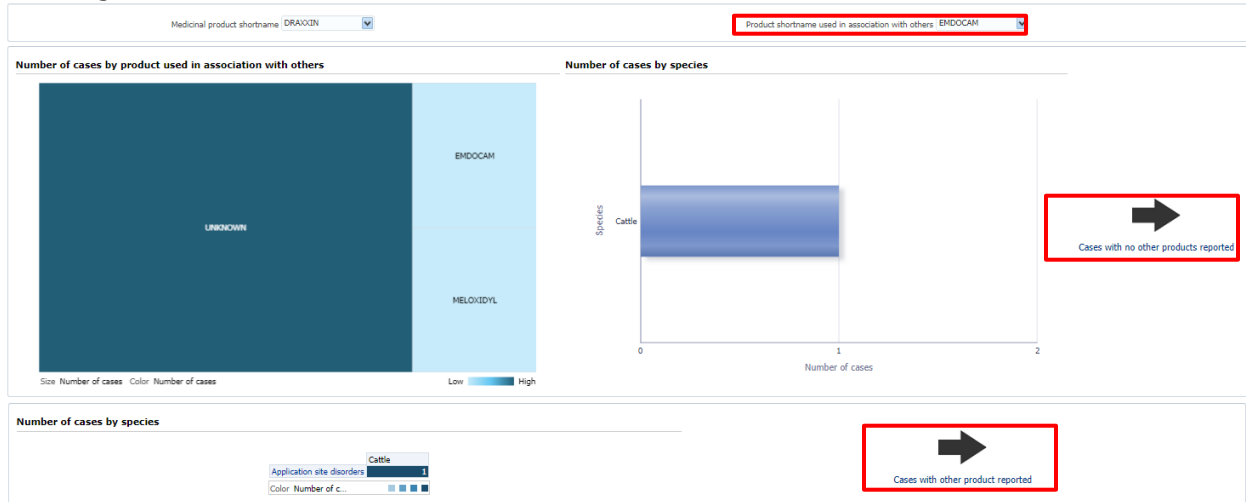


Image 80: Number of cases by species

6.4.1 Cases with no other products reported

Additionally, two links have been enabled at the right side for the user to access to the detailed tables for cases without other products reported...

Non currently used product detail

Species: Cattle

Medicinal product shortname	VedDRA SOC name	VedDRA PT name	Number of cases	Reaction count	ROR (-)	ROR (+)
DRAXXIN	Application site disorders	Injection site hair change	1	1	N/A	N/A
DRAXXIN	Application site disorders	Injection site necrosis	1	1	N/A	N/A
DRAXXIN	Application site disorders	Injection site pain	1	1	N/A	N/A

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Image 81: Cases with no other products reported

6.4.2 Cases with other product reported

And with other products reported.

Medicinal product shortname: DRAXXIN

Current product: VedDRA SOC name

Species: Cattle

Medicinal product shortname	VedDRA SOC name	Number of cases for the product	ROR (-) for the product	ROR for the product	ROR (+) for the product
DRAXXIN	Application site disorders	12	0.16	0.29	0.51

Associated products: Associated medicinal product shortname, VedDRA SOC name

Species: Cattle

Medicinal product shortname	Associated medicinal product shortname	VedDRA SOC name	Number of cases for the combination	Reaction count	Number of animals affected	Number of cases (Total ALL)	ROR (-) for the combination	ROR for the combination	ROR (+) for the combination
DRAXXIN	EMDOCAM	Application site disorders	1	1	11	1	N/A	N/A	N/A
DRAXXIN	UNKNOWN	Application site disorders	5	6	341	12	0.06	0.19	0.59

Image 82: Cases with other product reported

6.5 Associated VeDDRA

The last tab of the Signal Evaluation dashboard is related to the reactions associated to the one selected in the filters page. A table like the one below will show up, displaying the VeDDRA SOC linked to the VeDDRA term(s) previously set.

In addition, a VeDDRA SOC dropdown has been included at the top in case user selects more than one term. Right below, a couple of dropdown allow the user to jump from Medicinal shortname to ATCVET code or active substance based analysis, as well as associated VeDDRA terms displayed at a different level.

VeDDRA SOC name: Application site diso

Associated VeDDRA

Medicinal product shortname: Medicinal product shortname Associated VeDDRA SOC name: Associated VeDDRA SOC name

Species: Cattle

Medicinal product shortname	VeDDRA SOC name	Associated VeDDRA SOC name	Reaction count	Reaction count total for the combination	Number of cases	Total Number of cases (VeDDRA)	ROR (-) for the combination	ROR for the combination	ROR (+) for the combination	Number of animals affected
DRAOXIN	Application site disorders	Behavioural disorders	1	18	18	12	N/A	N/A	N/A	1
DRAOXIN	Application site disorders	Digestive tract disorders	1	18	2	12	N/A	N/A	N/A	2
DRAOXIN	Application site disorders	Investigations	1	18	1	12	N/A	N/A	N/A	1
DRAOXIN	Application site disorders	Musculoskeletal disorders	2	18	1	12	N/A	N/A	N/A	1
DRAOXIN	Application site disorders	Systemic disorders	2	18	4	12	0.10	0.34	1.13	26
DRAOXIN	Application site disorders	Unclassifiable event	1	18	1	12	N/A	N/A	N/A	1

Image 83: Associated VeDDRA

As usual, the Number of cases column includes the access to the second level reports (See [3.2.1. See Details](#)).

6.6 Link to VPhS

Pending to be updated with a link to IRIS.Adverse events comparison between 2 periods

This dashboard allows users to compare data for two time periods based on 3 key dates:

- Message received date
- Original received date
- Date of onset

And 3 performance indicators:

- Number of cases
- ROR
- ROR(-)

Consequently, for the periods selected and date selected, the user will get the number of cases and ROR metrics for both the period 1 and the period 2 in the same chart so it can be quickly compared. The dashboard is broken in 2 tabs: one for the filters and the other for the actual charts:



Image 84: Adverse events comparison between 2 periods menu

7.1 Filters

1. Choose from all attributes in the Product Information (Required)

In this prompt the user selects at what level of the product hierarchy you want to run your query. These levels are:

- Active substance level: Results will be related to AERs for products that contain the selected active substance(s).
- Product Short name: Results will be related to AERs for selected product(s) grouped by the product short name.
- ATCVET Vet code level: Results will be related to AERs for products that belong to the selected ATCVET Vet Code.
- Reported Brand Name: Results will be related to AERs for a selected Product Brand Name as reported in the AER verbatim, prior to standardisation.
- Product Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number stated in the product dictionary.
- Reported Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number as reported in the AER.
- Product composition level (Composition, Strength, Formulation, Pharma Product): Results will be related to AERs for products that are composed solely of the selected active substance(s), active substance(s) + strength(s), Active substance(s) + Pharmaceutical form(s), Active substance(s) Strength + Pharmaceutical form. This enables users to group products based on their composition, regardless of the trade names of the products.

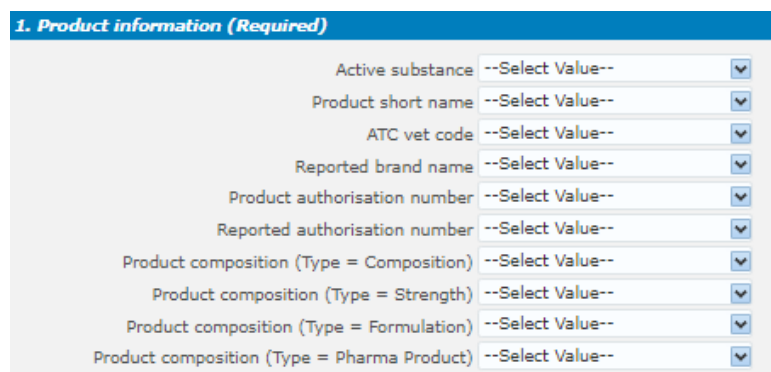
The image shows a screenshot of a web form titled '1. Product information (Required)'. The form contains ten rows, each with a label and a dropdown menu. The labels are: 'Active substance', 'Product short name', 'ATC vet code', 'Reported brand name', 'Product authorisation number', 'Reported authorisation number', 'Product composition (Type = Composition)', 'Product composition (Type = Strength)', 'Product composition (Type = Formulation)', and 'Product composition (Type = Pharma Product)'. Each dropdown menu currently displays '--Select Value--' and has a downward-pointing arrow on the right side.

Image 85: Filter options

2. Time periods (Required)

In this prompt the user sets the different time periods likely to be compared for the 3 indicators included in the dashboard: Message received date, Original received date and Date of onset.



Image 86: Time periods

3. Report filter (Required)

Select whether your result should contain only **Animal** or **Human** AERs by ticking the relevant option, or both by selecting both Animal and Human.

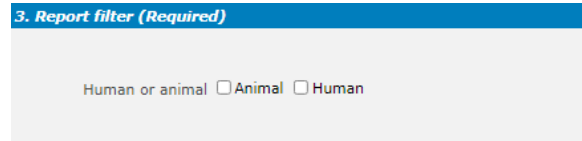


Image 87: Report filter

4. All cases or new cases (Required)

In this prompt you have to select one of the two options, being "All Cases" selected by default. Selecting "New cases" will return data related only to **new** reports received in EVVET during the selecting period, and will exclude from the data set follow ups to reports initially received in EVVET prior to the selected period.

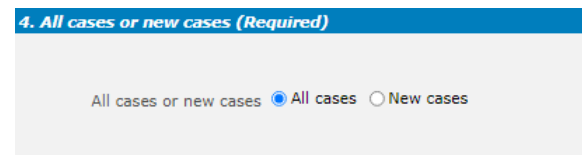


Image 88: all cases or new cases

5. Choose from list of optional AE Report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

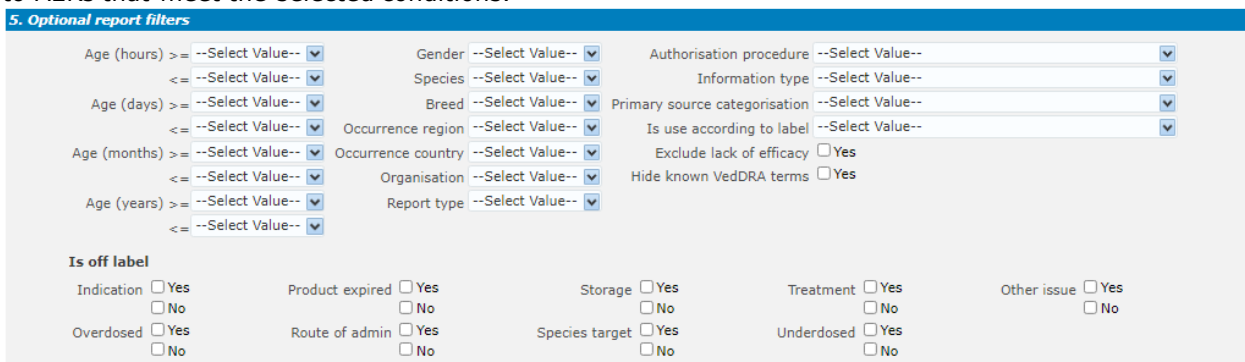


Image 89: Optional AE Report filters

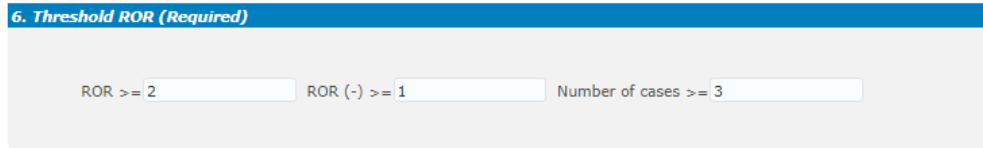
Original Received Date: The date that the MAH or NCA first received the message.

Serious: The system will return only the serious or the non-serious reports.

Information type vs Exclude lack of efficacy: If you want to exclude the lack of efficacy cases and you exclude "Lack of efficacy" within the Information type dropdown (by including all other information types), you will get the reports where LOE has been reported together with other issues/information types. However, if you tick the box "Yes" in "Exclude lack of efficacy", the system will exclude those reports where the VedDRA term "Lack of efficacy" has been reported.

6. Threshold ROR (Required)

This prompt is mandatory but filled by default with ROR \geq 2, ROR(-) \geq 1 and Number of cases \geq 3. The user is able to customize this values for the purpose of the analysis.



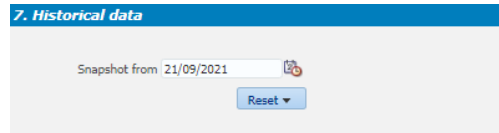
6. Threshold ROR (Required)

ROR \geq 2 ROR (-) \geq 1 Number of cases \geq 3

Image 90: Threshold ROR

7. Historical data

No answer is required for this prompt. By default, a snapshot of the day will be set. If a different date is selected, the results will reflect the data in EVVET as per the date selecting, excluding data received after the selected date.



7. Historical data

Snapshot from: 21/09/2021

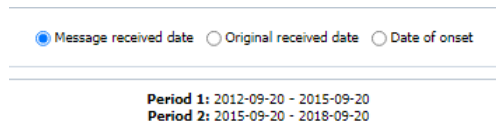
Reset

Image 91: Historical data

7.2 Adverse events comparison between 2 periods

After setting the time periods and the rest of required fields within the filters page, the user clicks on the "Adverse events comparison between 2 periods" tab to visualize the dashboard.

First functionality the user is going to see is the radio buttons, at the very top. Using those, the user will be able to jump from one indicator to the others for the selected time period, which will be always stated right below



Message received date Original received date Date of onset

Period 1: 2012-09-20 - 2015-09-20
Period 2: 2015-09-20 - 2018-09-20

Image 92: Adverse events comparison between 2 periods date criteria

Apart from that, the user will visualize the 3 main elements included in the dashboard: the horizontal bar charts representing the following KPIs: Number of cases, ROR and ROR (-).

On top of everyone of them, several dropdowns have been included in order to:

- Visualize the charts by product, reported brand name, product composition, active substance or ATCvet.
- Jump from one VeDDRA level to the others.
- Select all the species involved with this product and time periods.
- Jump between the products selected in the filters page.

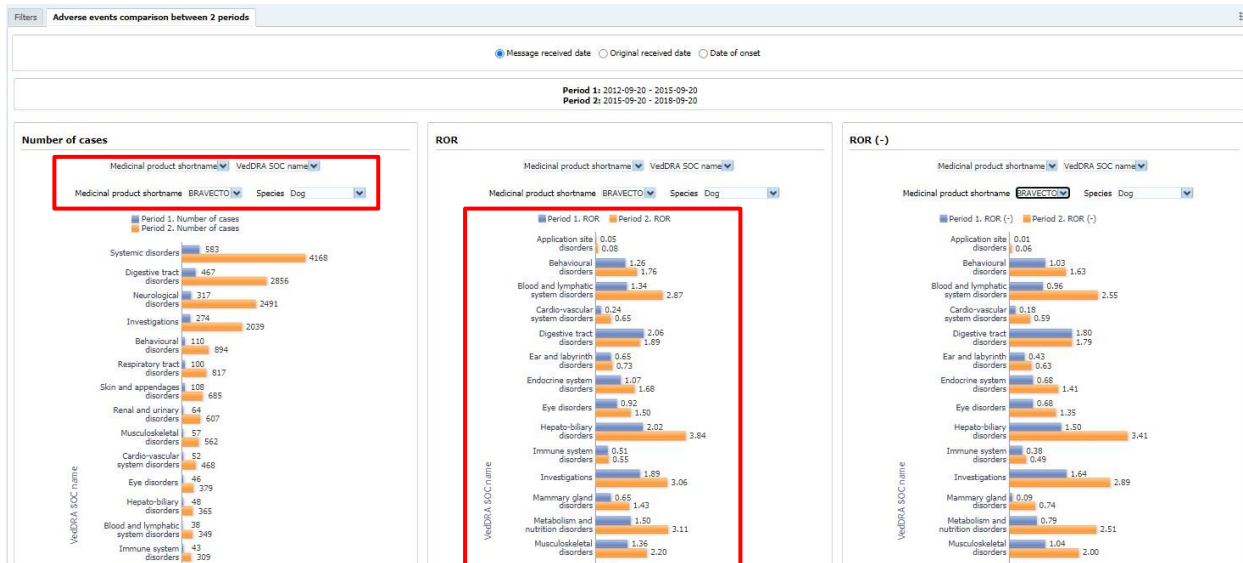


Image 93: Adverse events comparison between 2 periods dashboard

In addition, two heatmaps in the bottom display the number of cases for the product and period selected, one for the Period 1 and another for the Period 2, optional filter for species not applicable.

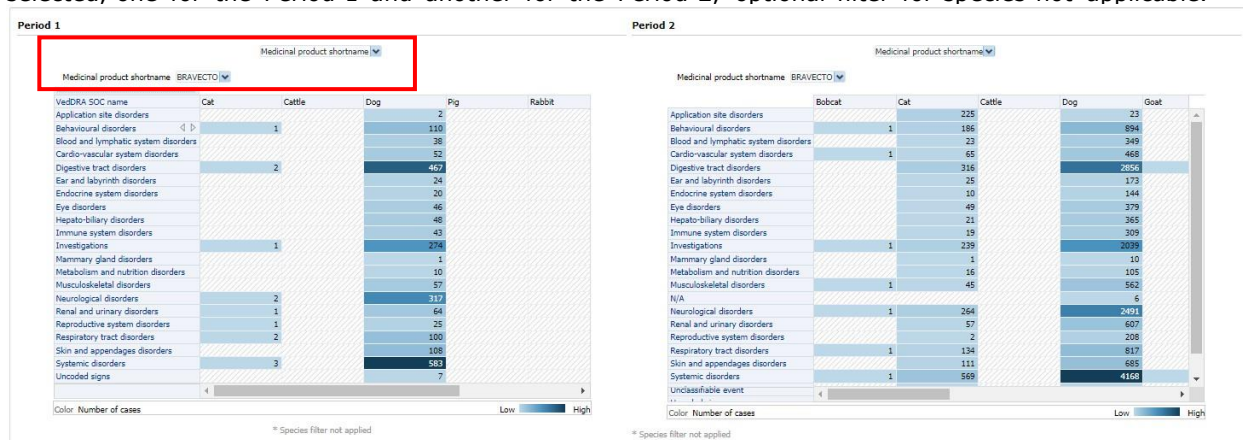


Image 94: Period by period view

The heatmap can be visualized by product, reported brand name, product composition, active substance or ATCvet using the dropdown on top. After selecting the type of visualization, the dropdown set right below will display a list accordingly.

7.2.1 Message received date – See details

At the very bottom of the dashboard, a link has been enabled for the user to navigate to the See details tables, and depending on the radio button selected this will display on date or the others.

[Message received date - See details](#)

Image 95: Message received date – See details

By clicking in this link, the user will open the table in a different tab, with the following information:

7.2.2 Original received date – See details

Same for the Original received date.

Original received date detail

Medical product shortname

Species Alpaca

Medical product shortname	VedDRA SOC name	Period 1. Number of cases	Period 1. Animals affected	Period 1. ROR (-)	Period 1. ROR (+)	Period 1. ROR (-)	Period 1. ROR (+)	Period 2. Number of cases	Period 2. Animals affected	Period 2. ROR (-)	Period 2. ROR (+)	Period 2. ROR (-)	Period 2. ROR (+)	Number of cases
DRAXXIN	Neurological disorders	0	0	N/A	N/A	N/A	N/A	0	0	N/A	N/A	N/A	N/A	1
	Systemic disorders	0	0	N/A	N/A	N/A	N/A	0	0	N/A	N/A	N/A	N/A	1

Return - Analyze - Print - Export

Image 96: Original received date – See details

7.2.3 Date of onset – See details

Same for the Date of onset. Data stratification

This dashboard allows user to find products involved in a particular reaction or group of reactions by displaying the number of cases for that pre-set conditions (**Adverse events by VeDDRA terms**). Additionally, using the second tab (**Product stratification**) the user can check the ROR for the product or group of products at all VeDDRA levels, including or excluding a second product from the equation, as well as the Number of animals affected divided by species at VeDDRA SOC level. On all other dashboards, the ROR is calculated by comparing the number of cases for the selected product/substance to “all other products” in the EVVET database. This dashboard aims to allow the user to exclude outliers or simply narrow the ROR for comparison purposes.

The data stratification dashboard is divided in 3 tabs:

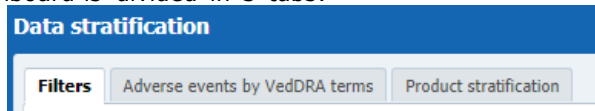


Image 97: Data stratification menu

8.1 Filters

1. Product information (Required for product stratification)

The first prompt is product-oriented and the user must fill it to get an overview of the Product stratification tab. For that purpose and depending on the analysis, the user will check “Compared to” or “Compared to all except”.

The user should select the product/substance subject to their evaluation on the left side.

For instance, selecting “Compared to” and an ATCvet code on the filter on the right side will restrict the denominator of the ROR to products belonging to the selected ATCvet.

Selecting “Compared to all except”, and a product or substance on the left side will exclude the selected product/substance from the denominator of the ROR.

1. Product information (Required for product stratification)

Active substance: --Select Value--	<input type="checkbox"/> Compared To	Active substance: --Select Value--
Product short name: --Select Value--	<input type="checkbox"/> Compared To All Except	Product short name: --Select Value--
ATC vet code: --Select Value--		ATC vet code: --Select Value--
Reported brand name: --Select Value--		Reported brand name: --Select Value--
Product authorisation number: --Select Value--		Product authorisation number: --Select Value--
Reported authorisation number: --Select Value--		Reported authorisation number: --Select Value--
Product composition (Type = Composition): --Select Value--		Product composition (Type = Composition): --Select Value--
Product composition (Type = Strength): --Select Value--		Product composition (Type = Strength): --Select Value--
Product composition (Type = Formulation): --Select Value--		Product composition (Type = Formulation): --Select Value--
Product composition (Type = Pharma Product): --Select Value--		Product composition (Type = Pharma Product): --Select Value--

Image 98: Product information filters

2. VeDDRA terms (Required for adverse events by VeDDRA terms)

The second prompt is related to AE reactions and the user must fill it to get an overview of the Adverse events by VeDDRA terms tab. For that purpose and depending on the analysis, the user will check “AND” or “AND NOT”.

2. VeDDRA terms (Required for adverse events by VeDDRA terms)

VedDRA Term SOC: --Select Value--	<input type="radio"/> AND	VedDRA Term SOC: --Select Value--
VedDRA Term HLT: --Select Value--	<input type="radio"/> AND NOT	VedDRA Term HLT: --Select Value--
VedDRA Term PT: --Select Value--		VedDRA Term PT: --Select Value--
VedDRA Term LLT: --Select Value--		VedDRA Term LLT: --Select Value--

Image 99: VeDDRA terms filter

3. Animal information (Required)

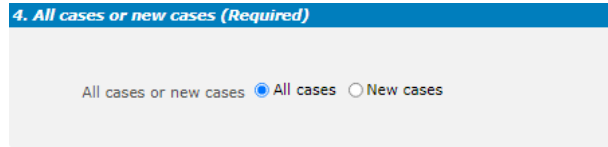
3. Animal information (Required)

Human or animal Animal Human

Image 100: Animal information filter

4. All cases or new cases (Required)

In this prompt you have to select one of the two options, being "All Cases" selected by default . Selecting "New cases" will return data related only to **new** reports received in EVVET during the selecting period, and will exclude from the data set follow ups to reports initially received in EVVET prior to the selected period.



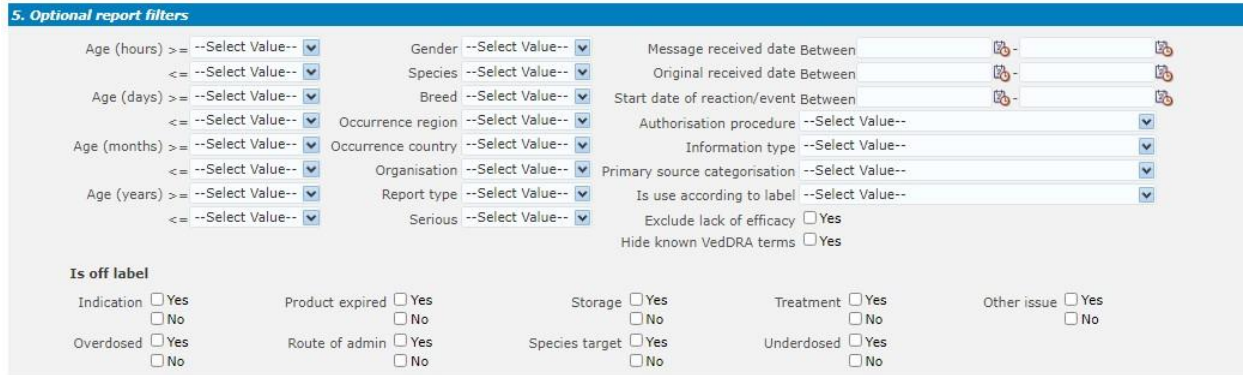
4. All cases or new cases (Required)

All cases or new cases All cases New cases

Image 101: All cases or new cases filter

5. Choose from list of optional AE Report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.



5. Optional report filters

Age (hours) >= --Select Value-- Gender --Select Value-- Message received date Between --Select Value--
<= --Select Value-- Species --Select Value-- Original received date Between --Select Value--
Age (days) >= --Select Value-- Breed --Select Value-- Start date of reaction/event Between --Select Value--
<= --Select Value-- Occurrence region --Select Value-- Authorisation procedure --Select Value--
Age (months) >= --Select Value-- Occurrence country --Select Value-- Information type --Select Value--
<= --Select Value-- Organisation --Select Value-- Primary source categorisation --Select Value--
Age (years) >= --Select Value-- Report type --Select Value-- Is use according to label --Select Value--
<= --Select Value-- Serious --Select Value-- Exclude lack of efficacy Yes
Hide known VedDRA terms Yes

Is off label

Indication Yes No Product expired Yes No Storage Yes No Treatment Yes No Other issue Yes No
Overdosed Yes No Route of admin Yes No Species target Yes No Underdosed Yes No

Image 102: Optional AE Report filters

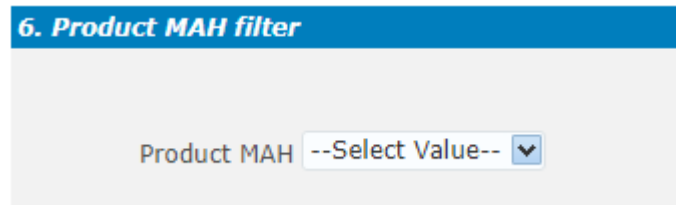
Original Received Date: The date that the MAH or NCA first received the message.

Serious: The system will return only the serious or the non-serious reports.

Information type vs Exclude lack of efficacy: If you want to exclude the lack of efficacy cases and you exclude "Lack of efficacy" within the Information type dropdown (by including all other information types), you will get the reports where LOE has been reported together with other issues/information types. However, if you tick the box "Yes" in "Exclude lack of efficacy", the system will exclude those reports where the VedDRA term "Lack of efficacy" has been reported.

6. Product MAH filter

By using 'Product MAH filter', it is possible to filter by one specific MAH, so the output of the query will only be data related to the informed MAH (its products)



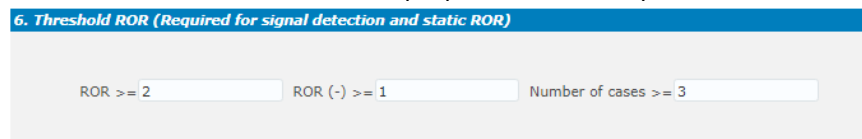
6. Product MAH filter

Product MAH --Select Value--

Image 103: Product MAH filter

7. Threshold ROR (Required)

This prompt is mandatory but filled by default with ROR>=2, ROR(-)>=1 and Number of cases>=3. The user is able to customize this values for the purpose of the analysis.



7. Threshold ROR (Required for signal detection and static ROR)

ROR >= 2 ROR (-) >= 1 Number of cases >= 3

Image 104: Threshold ROR

8. Historical data

No answer is required for this prompt. By default, a snapshot of the day will be set. If a different date is selected, the results will reflect the data in EVVET as per the date selecting, excluding data received

after the selected date.

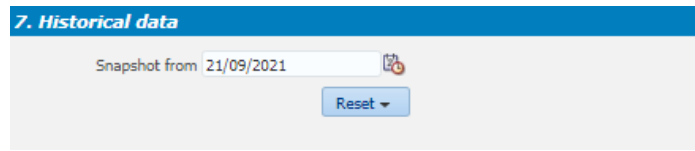


Image 105: Historical data

8.2 Adverse events by VeDDRA terms

Filling prompt number 2 is required to visualize this tab.

At the top of every tab the user will find a header including the usual key figures, being for this dashboard: Number of cases, Product count and Animals affected, as follows:



Image 106: Adverse events by VeDDRA terms key figures

Right below the header, 2 charts will display with the Top 15 (15 products or less will be listed) of the products associated with the reactions set at the filters page. First chart shows products associated with the first product and second chart will show:

- Products associated with the combination of VeDDRAs if the user selects "AND".
- Products associated with the first VeDDRA selected and excluding the second from the equation if the user selects "AND NOT".

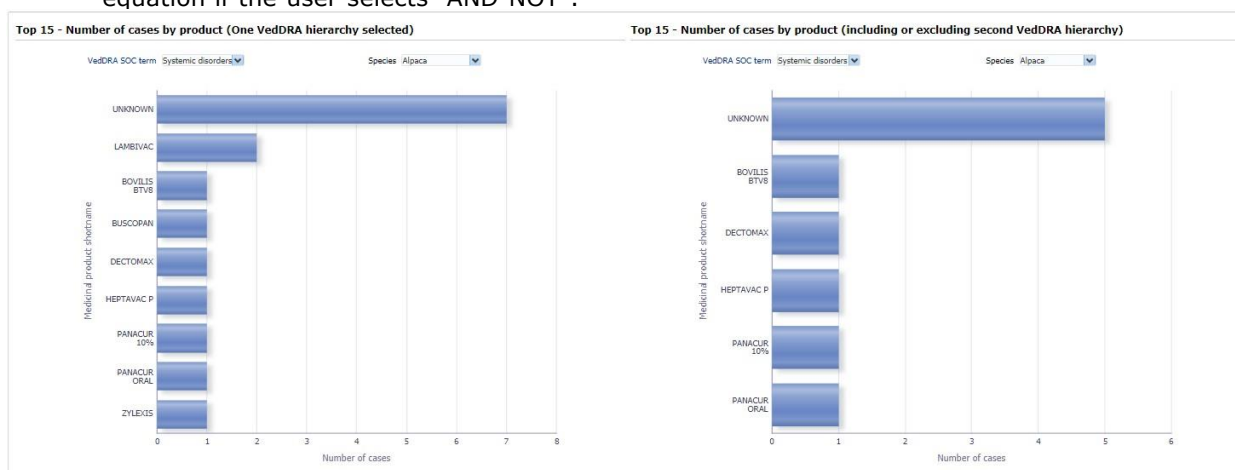


Image 107: Adverse events by VeDDRA terms top 15

Product filters do not apply on this report.

Above the charts, 2 dropdowns have been included, one for selecting the different VeDDRA terms at SOC level (in case the user selects more than one) and the other for changing from one species to the others.

8.3 Product stratification

Filling prompt number 1 is required to visualize this tab.

Right below the header ([see 7.2 Adverse events by VeDDRA terms](#)) 2 charts will display with the Top 15 (15 products or less will be listed) of reactions at VeDDRA SOC level by ROR.

First chart shows the ROR for the reactions (at SOC level) related with the first product selected and second chart will show:

- ROR for the reactions (at SOC level) related to the product selected in the left prompt compared to other products **but** the product selected in the right prompt if "compared to all except" was selected. **Or** ROR for the reactions (at SOC level) related to the product selected in the left prompt compared all other products belonging to the selected ATCvet code if "Compared to" was selected.

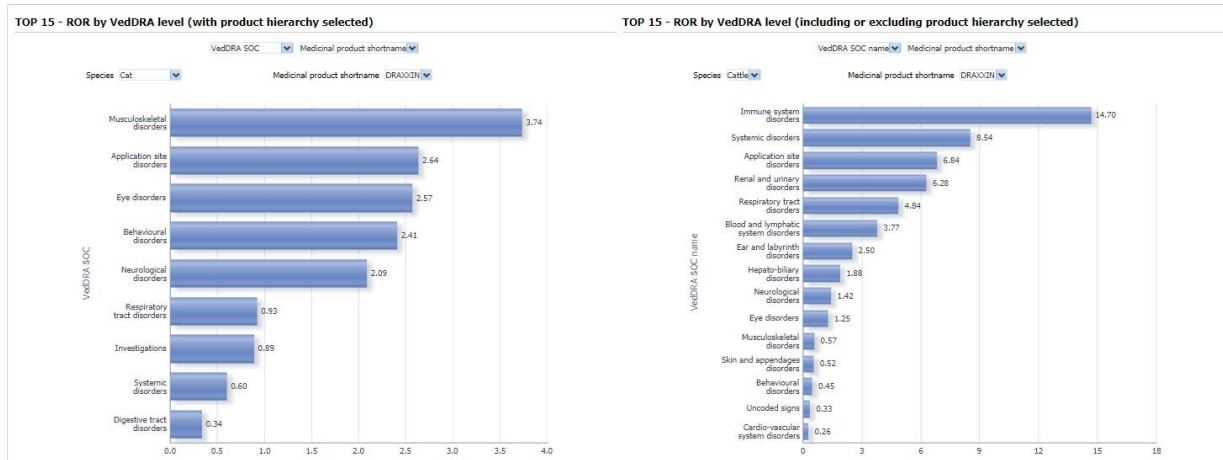


Image 108: Product stratification top 15

Above the charts, 4 dropdowns have been included:

- For jumping between VeDDRA levels.
- For jumping between Species.
- A product hierarchy level so the user will be able to display the chart by medicinal product shortname, reported brand name, product composition, active substance or ATCvet.
- A dropdown interconnected with the previous, displaying the selected product or active substance depending on the level selected on the product hierarchy above.

Another chart is included in this tab, a heatmap, showing the Number of animals affected by VeDDRA SOC terms and ATCvet code. The different blues indicate if that Species- SOC combination belongs to the first, second, third or fourth quartile.



Image 109: Number of animals affected by VeDDRA SOC and ATCvet code

On top of this the user will see a couple of dropdown, one for jumping between products (in case more than one is selected) and the other enabled to pick between the ATCvets involved.

8.3.1 See details

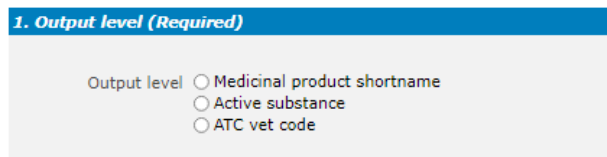
The "see details" table is only relevant and becomes enabled when the user has selected a n ATCvet code for the "Compared to" option on the filters page. .
(See [3.2.1. See Details](#)).

9. Signaling for reactions linked to a product or ingredient

9.1 Filters

1. Output level (Required)

The user must select one of the output levels.



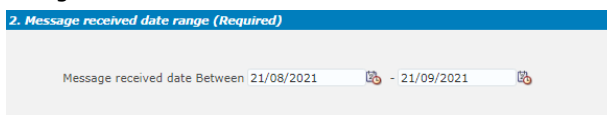
1. Output level (Required)

Output level Medicinal product shortname
 Active substance
 ATC vet code

Image 110: Output level

2. Message received date range (Required)

In this prompt you select a range of dates.



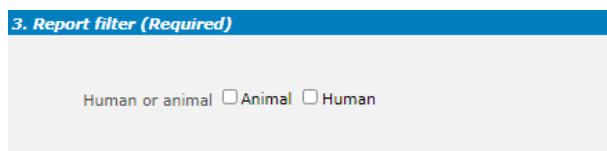
2. Message received date range (Required)

Message received date Between 21/08/2021 - 21/09/2021

Image 111: Message received date range

3. Report filter (Required)

Select whether your result should contain only **Animal** or **Human** AERs by ticking the relevant option, or both by selecting both Animal and Human.



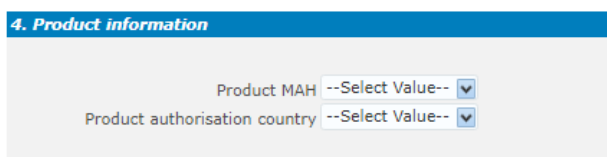
3. Report filter (Required)

Human or animal Animal Human

Image 112: Report filter (human or animal)

4. Product information

The user is required to select either the Product MAH or the Product authorization country to enabled the signalling for reactions tab.



4. Product information

Product MAH --Select Value--
Product authorisation country --Select Value--

Image 113: Product information

5. Optional report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

10. Line listing

The line listing dashboard is actually a two tabs line listing, first tab being focused on the medicinal hierarchy, second tab on the occurrence country/occurrence region.

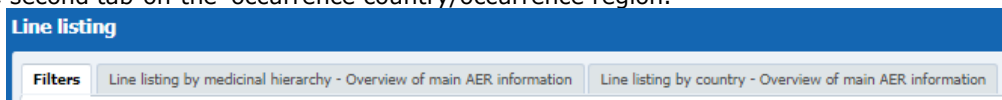


Image 117: Line listing menu

10.1 Filters

1. Choose from all attributes in the Product Information (Required)

In this prompt the user selects at what level of the product hierarchy you want to run your query. These levels are:

- Active substance level: Results will be related to AERs for products that contain the selected active substance(s).
- Product Short name: Results will be related to AERs for selected product(s) grouped by the product short name.
- ATCVET Vet code level: Results will be related to AERs for products that belong to the selected ATCVET Vet Code.
- Reported Brand Name: Results will be related to AERs for a selected Product Brand Name as reported in the AER verbatim, prior to standardisation.
- Product Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number stated in the product dictionary.
- Reported Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number as reported in the AER.
- Product composition level (Composition, Strength, Formulation, Pharma Product): Results will be related to AERs for products that are composed solely of the selected active substance(s), active substance(s) + strength(s), Active substance(s) + Pharmaceutical form(s), Active substance(s) Strength + Pharmaceutical form. This enables users to group products based on their composition, regardless of the trade names of the products.

* At least one required field is mandatory in form

1. Product information (Required)

Active substance	--Select Value--	▼
Product short name	DRAXXIN	▼
ATC vet code	--Select Value--	▼
Reported brand name	--Select Value--	▼
Product authorisation number	--Select Value--	▼
Reported authorisation number	--Select Value--	▼
Product composition (Type = Composition)	--Select Value--	▼
Product composition (Type = Strength)	--Select Value--	▼
Product composition (Type = Formulation)	--Select Value--	▼
Product composition (Type = Pharma Product)	--Select Value--	▼

Image 118: Product information filters

2. Report filter (Required)

Select whether your result should contain only **Animal** or **Human** AERs by ticking the relevant option, or both by selecting both Animal and Human.

Image 119: Report filter (animal or human)

3. Product MAH filter

The user is required to select either the Product MAH or the Product authorization country.

Image 120: Product MAH filter

4. Country filter (Required)

The user is required to select either the occurrence region of country.

Image 121: Country filter

5. Optional report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

Image 122: Optional report filters

10.2 Line listing by medicinal hierarchy – Overview of main AER information

After filling the mandatory fields, the user clicks on the first tab and navigates to the line listing dashboard, with the usual second level's line listing report structure.

The line listing is the most detailed table the user has access to, basically with the full information about a case.

In the dashboard, though, a couple of dropdowns have been included at the top. In regards of this first tab, the user will be able to select a product hierarchy (Medicinal product shortname, reported brand name, product composition, active substance, ATCVET) and then another interconnected dropdown to jump from one product, substance, etc. to the others.

Medicinal product shortname														Medicinal product shortname													
Medicinal product shortname DRAXOIN																											
AER Id	Case number	Duplicate report list	Occurrence country	Human or animal	Species	Breed	Min age	Max age	Min weight	Max weight	Date of treatment	Date of onset	Number of animals treated	Number of animals affected	Number of animals died	Reported product list	Is use according to label	Is off label indication	Is off label overdosed	Is off label product expired	Is off label route of admin	Is off label storage	Is off label species target				
185	2004-34-51	185	Ireland	Animal	Cattle	Holstein-Friesian also known as Holstein	-1 sec	-1 sec	120 kg	120 kg	01/01/1900	01/07/2004	4	4	1	Draxoin - O/N/A/O Unknown/N/A/N/A (N/A N/A) (N/A N/A)	No Data	No	No	No	No	No	No	No			

Is off label treatment	Is off label underdosed	Is off label other issue	VedDRA term list	Original received date	Current submission date	Message received date	Narrative description	RA assessment	RA conclusion	MAH conclusion	Organisation	Report link
No	No	No	Lack of efficacy	20/07/2004	20/07/2004	19/01/2005	The product was used in four cattle for the treatment of suspected pneumonic pasteurellosis. All four failed to respond to Draxoin and had to receive alternative treatment. One of the four died. Animal Laboratory Test: No Information Animal	Unknown	Assessment Source: Competent authority: No Information	-	HEALTH PRODUCTS REGULATORY AUTHORITY Ireland	link



Image 123: Line listing by medicinal hierarchy – Overview of main AER information

10.3 Line listing by country – Overview of main AER information

In regards of the second tab, the user will be able to select between occurrence region or country, and then another interconnected dropdown to jump from one region or country to the others.

Occurrence country Australia														Occurrence country													
AER Id	Case number	Duplicate report list	Human or animal	Species	Breed	Min age	Max age	Min weight	Max weight	Date of treatment	Date of onset	Number of animals treated	Number of animals affected	Number of animals died	Reported product list	Is use according to label	Is off label indication	Is off label overdosed	Is off label product expired	Is off label route of admin	Is off label storage	Is off label species target					
79172	AL-UKPEIZAH-2011-AU-00200	79172	Animal	Cattle	Holstein-Friesian also known as Holstein	2 months	2 months	100 kg	100 kg	03/10/2011	03/10/2011	1	1	1	DRAXOIN INJECTABLE ANTIBIOTIC SOLUTION - O/N/A/O Unknown/N/A/N/A (N/A N/A) (N/A N/A) 03/10/2011-03/10/2011	No	No	No	No	No	No	No	No				

Is off label treatment	Is off label underdosed	Is off label other issue	VedDRA term list	Original received date	Current submission date	Message received date	Narrative description	RA assessment	RA conclusion	MAH conclusion	Organisation	Report link
No	No	No	Secure NOS. Unexplained death	05/10/2011	05/10/2011	13/10/2011	This farm has been having severe problems with pneumonia in calves over the last few weeks. The vet has performed several cultures but has not grown any bacteria and so has diagnosed the problem as most likely to be viral.	Unknown	No data	-No temporal association to time of injection. No diagnostic work performed on the calf pre or post mortem. Off label use as this cannot be used in dairy cattle. Insufficient information.	COETIS BELGIUM Belgium	link



Image 124: Line listing by country – Overview of main AER information

11. List of products

11.1 Filters

1. Choose from all attributes in the Product Information (Required)

In this prompt the user selects at what level of the product hierarchy you want to run your query. These levels are:

- Active substance level: Results will be related to AERs for products that contain the selected active substance(s).
- Product Short name: Results will be related to AERs for selected product(s) grouped by the product short name.
- ATCVET Vet code level: Results will be related to AERs for products that belong to the selected ATCVET Vet Code.
- Reported Brand Name: Results will be related to AERs for a selected Product Brand Name as reported in the AER verbatim, prior to standardisation.
- Product Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number stated in the product dictionary.
- Reported Authorisation Number: Results will be related to AERs for selected product(s) grouped by the product authorisation number as reported in the AER.
- Product composition level (Composition, Strength, Formulation, Pharma Product): Results will be related to AERs for products that are composed solely of the selected active substance(s), active substance(s) + strength(s), Active substance(s) + Pharmaceutical form(s), Active substance(s) Strength + Pharmaceutical form. This enables users to group products based on their composition, regardless of the trade names of the products.

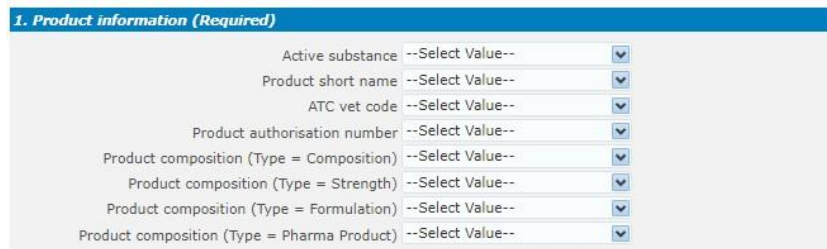


Image 125: Product Information filters

2. Optional report filters

No answer is required for this prompt. By applying any of these filters the results dataset will be restricted to AERs that meet the selected conditions.

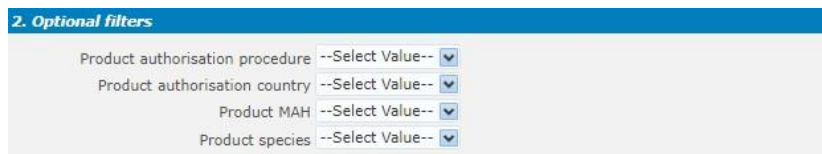


Image 126: Optional report filters

11.2 List of products

This dashboard displays several charts representing Number of cases metrics for the product or products selected in the filters page.

At the top the user will find a header including the usual key figures, being for this dashboard: Number of cases, Number of AERs and Fatal cases, as follows:



Image 127: List of products key figures

The first set of charts shows 2 pie charts with the number of cases by active substance and by medicinal product shortname:



Image 128: Number of cases by active substance and by medicinal product shortname

Second set of charts includes 3 pie charts with number of cases by ATCvet, pharmaceutical form and authorization procedure:

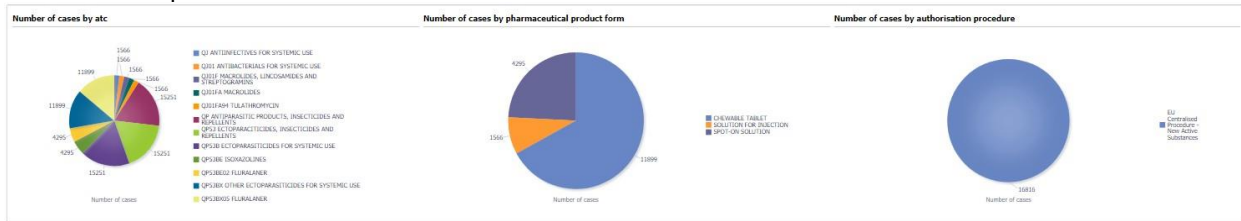


Image 129: Number of cases by ATCvet, pharmaceutical form and authorization procedure

Third set includes a map representing the number of cases by authorization country, a treemap of the number of cases by medicinal product authorisation number and finally a bar chart with the Top 15 number of cases by medicinal product:



Image 130: number of cases by authorization country, number of cases by product and authorisation number and Top 15 number of cases by medicinal product

Lastly, 2 extra pie charts show the number of cases by MAH and by Species for the product or products selected in the filters page:

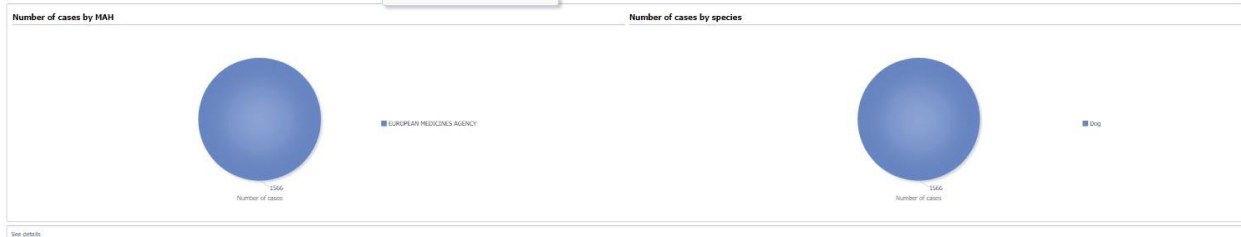


Image 131: Number of cases by MAH and by Species

11.2.1 See details

(See [4.2.1. See Details](#)).

11.3 List of products and substances without AERs associated

The second tab in 'list of products' dashboard will retrieve those products and substances that do not have any report associated. It means they were not reported in any AER.

Medicinal product code	Medicinal product	Medicinal product shortname	Active substance code	Active substance
600000000084	Aftovaxpur DOE (60) O1 BFS + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000075987	HUMAN MEASLES IMMUNOGLOBULIN
600000000085	Aftovaxpur DOE (61) O Taiwan 3/97 + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000075988	HUMAN PLASMA FOR FRACTIONATION
600000000086	Aftovaxpur DOE (62) A22 Iraq + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000075989	HYDROCHLORIC ACID, CONCENTRATED
600000000094	Aftovaxpur DOE (41) O1 Manisa + A Turkey 14/98 + Asia1 Shamir	AFTOVAXPUR DOE	100000075990	DILUTED HYDROCHLORIC ACID
600000000097	Aftovaxpur DOE (32) O1 Manisa + O1 BFS + Asia1 Shamir	AFTOVAXPUR DOE	100000075991	HYDROGEN PEROXIDE SOLUTION (3 PER CENT)
600000000098	Aftovaxpur DOE (33) O1 Manisa + O Taiwan 3/97 + A22 Iraq	AFTOVAXPUR DOE	100000075992	HYDROGEN PEROXIDE SOLUTION (30 PER CENT)
600000000122	Aftovaxpur DOE (34) O1 Manisa + O Taiwan 3/97 + A24 Cruzeiro	AFTOVAXPUR DOE	100000076067	Mevalonic acid
600000000142	Aftovaxpur DOE (63) A24 Cruzeiro + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076068	Midazolam maleate
600000000232	Aftovaxpur DOE (54) O Taiwan 3/97 + A24 Cruzeiro + Asia1 Shamir	AFTOVAXPUR DOE	100000076070	MILLET
600000000312	Aftovaxpur DOE (74) O1 BFS + A24 Cruzeiro + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076071	Minaprine dihydrochloride
600000000313	Aftovaxpur DOE (75) O1 BFS + A Turkey 14/98 + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076074	COD-LIVER OIL (TYPE B)
600000000314	Aftovaxpur DOE (77) O Taiwan 3/97 + A22 Iraq + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076075	COLA
600000000315	Aftovaxpur DOE (78) O Taiwan 3/97 + A24 Cruzeiro + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076077	Copovidone
600000000321	Aftovaxpur DOE (17) O1 BFS + A Turkey 14/98	AFTOVAXPUR DOE	100000076081	COUCH GRASS RHIZOME
600000000322	Aftovaxpur DOE (20) O Taiwan 3/97 + A24 Cruzeiro	AFTOVAXPUR DOE	100000076085	Decyl oleate
600000000327	Aftovaxpur DOE (23) A22 Iraq + A24 Cruzeiro	AFTOVAXPUR DOE	100000076087	DEVIL'S CLAW ROOT
600000000328	Aftovaxpur DOE (31) O1 Manisa + O1 BFS + A Turkey 14/98	AFTOVAXPUR DOE	100000076088	DEXTRAN 1 FOR INJECTION
600000000332	Aftovaxpur DOE (49) O1 BFS + A24 Cruzeiro + Asia1 Shamir	AFTOVAXPUR DOE	100000076089	DEXTRAN 40 FOR INJECTION
600000000459	Aftovaxpur DOE (58) SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076090	DEXTRAN 60 FOR INJECTION
600000000472	Suvaxyn CSF Marker (--) - Lyophilisate and solvent for suspension for injection	SUVAXYN CSF MARKER	100000076091	DEXTRAN 70 FOR INJECTION
600000000480	Aftovaxpur DOE (59) O1 Manisa + SAT2 Saudi Arabia	AFTOVAXPUR DOE	100000076093	Dibutyl phthalate
600000000481	Aftovaxpur DOE (24) A22 Iraq + Asia1 Shamir	AFTOVAXPUR DOE	100000076095	Diethyl phthalate
600000000482	Aftovaxpur DOE (25) A24 Cruzeiro + A Turkey 14/98	AFTOVAXPUR DOE	100000076098	DIGITALIS LEAF
600000000483	Aftovaxpur DOE (26) A24 Cruzeiro + Asia1 Shamir	AFTOVAXPUR DOE	100000076099	DIHYDRALAZINE SULPHATE, HYDRATED
600000000484	Aftovaxpur DOE (27) A Turkey 14/98 + Asia1 Shamir	AFTOVAXPUR DOE	100000076101	DIPHThERIA, TETANUS AND PERTUSSIS VACCINE (ADSORBED)

Image 132: List of products and substances without AERs associated

12. How to group data for different products

12.1 Introduction to product grouping

For contextual purposes, this grouping is related to 3 main scenarios:

- Grouping products with different names but referring to the same Medicinal Product.
- Grouping data based on the composition by selecting Scientific Product or Active Substance
- Ad-hoc aggregations for random analysis purposes

We will focus mainly on the first scenario and 2 specific medicinal products, analyzing in detail how to group them as well as how this grouping impacts in the metrics recalculation

As mentioned, the analysis will consider:

- Active substance **ENROFLOXACIN**
- Products **PRODUCTX & PRODUCTX OTIC**
- MAH **BAYER B.V. HEALTHCARE ANIMAL HEALTH & BAYER S.P.A.**

12.2 Demo

- Active substance ENROFLOXACIN
- Products **PRODUCTX & PRODUCTX OTIC**
- MAH **BAYER B.V. HEALTHCARE ANIMAL HEALTH & BAYER S.P.A.**
- MAH **BAYER B.V. HEALTHCARE ANIMAL HEALTH & BAYER S.P.A.**

Static ROR evaluation

VedDRA SOC name VedDRA HLT name VedDRA PT name VedDRA LLT name

Product Hierarchy Level Medicinal product shortname VedDRA Output Level VedDRA SOC name

Species

Medicinal product shortname	VedDRA SOC name	Number reacted	A - Reports with product and reaction	B - Reports with product without reaction	C - Reports without product but with reaction	D - Reports without product and without reaction	ROR (-)	ROR	ROR (+)
	Application site disorders	5	5	186	6,015	164,311	0.03	0.79	0.85
	Behavioural disorders	23	23	13,474	154,452	1,591	1.59	1.86	1.86
	Blood and lymphatic system disorders	27	27	164	2,853	167,479	0.99	10.93	10.93
	Cardio-vascular system disorders	34	34	157	11,451	158,975	3.01	3.52	3.52
	Digestive tract disorders	99	99	92	49,265	121,161	2.65	3.25	3.25
	Ear and labyrinth disorders	20	20	171	5,161	165,265	3.75	4.36	4.36
	Endocrine system disorders	10	10	181	2,028	168,398	4.59	5.34	5.34
	Eye disorders	23	23	168	6,118	164,308	3.68	4.29	4.29
	Hepato-biliary disorders	26	26	165	2,464	167,962	10.74	12.58	12.58
	Immune system disorders	15	15	176	13,807	156,619	0.83	0.97	1.12
	Investigations	124	124	67	21,020	149,406	13.15	16.72	16.72
	Mammary gland disorders	1	1	190	186	170,240	N/A	N/A	N/A
	Metabolism and nutrition disorders	6	6	185	580	169,846	9.50	11.21	11.21
	Musculoskeletal disorders	23	23	168	6,483	163,943	3.46	4.04	4.04
	N/A	2	2	189	201	170,225	N/A	N/A	N/A
	Neurological disorders	62	61	130	34,263	136,163	1.86	2.22	2.22
	Renal and urinary disorders	31	31	160	6,462	163,964	4.92	5.75	5.75
	Reproductive system disorders	8	8	183	1,266	169,160	5.94	6.82	6.82
	Respiratory tract disorders	52	52	139	13,131	157,295	4.48	5.30	5.30
	Skin and appendages disorders	20	20	171	16,591	153,835	0.93	1.08	1.26
	Systemic disorders	162	162	29	113,111	57,318	2.83	4.07	4.07
	Unclassifiable event	1	1	190	797	169,829	N/A	N/A	N/A
	Uncoded signs	3	3	188	1,895	168,531	1.42	1.65	1.65
	Application site disorders	2	2	29	6,018	164,566	N/A	N/A	N/A
	Behavioural disorders	4	4	27	13,493	157,093	1.72	2.52	2.52
	Digestive tract disorders	2	2	29	49,362	121,221	N/A	N/A	N/A
	Ear and labyrinth disorders	28	28	3	5,153	165,433	299.64	929.39	929.39
	Eye disorders	3	3	28	6,138	164,448	2.87	4.16	4.16
	Investigations	5	5	26	21,139	149,447	0.93	1.36	2.00
	Neurological disorders	4	4	27	34,320	136,266	0.40	0.59	0.86
	Renal and urinary disorders	2	2	29	6,491	164,095	N/A	N/A	N/A
	Skin and appendages disorders	4	4	27	16,607	153,979	0.94	1.37	2.00
	Systemic disorders	6	6	25	113,267	57,319	0.08	0.12	0.18

Image 133: Static ROR Dashboard for 2 medicinal products

We can see highlighted the ROR(-), ROR and ROR(+) for the VedDRA SOC Behavioural disorders:

Behavioural disorders	4	4	27	13,493	157,093	1.72	2.52	2.52
Behavioural disorders	23	23	168	13,474	156,952	1.59	1.86	1.86

We filter by VeDDRA SOC up in the dashboard so we only see the 2 products under analysis, PRODUCTX and PRODUCTX OTIC and their respective metrics:

Static ROR evaluation

VedDRA SOC name Behavioural disorders | VedDRA HLT name --Select Value-- | VedDRA PT name --Select Value-- | VedDRA LLT name --Select Value--

Product Hierarchy Level Medicinal product shortname | VedDRA Output Level VedDRA SOC name

Species Dog

Medicinal product shortname	VedDRA SOC name	Number reacted	A - Reports with product and reaction	B - Reports with product without reaction	C - Reports without product but with reaction	D - Reports without product and without reaction	Reaction	ROR (-)	ROR (+)
	Behavioural disorders	23	23	168	13,474	156,925		1.59	1.86
	Behavioural disorders	4	4	27	13,493	157,093		1.72	2.52

Image 134: Static ROR with VeDDRA SOC filter applied

After removing the product (by clicking on the column header and then on “exclude column”) the system delete the Medicinal Product column and recalculates the RORs :

Product Hierarchy Level Medicinal product shortname | VedDRA Output Level VedDRA SOC name

Species Alpaca

Medicinal product shortname	VedDRA SOC name	Number reacted	A - Reports with product and reaction	B - Reports with product without reaction	C - Reports without product but with reaction	D - Reports without product and without reaction	Reaction	ROR (-)	ROR (+)
Draxoin	Behavioural disorders								
	System disorders								
	Disorders								

Image 135: Menu option where user can exclude column from table

Product Hierarchy Level Medicinal product shortname | VedDRA Output Level VedDRA SOC name

Species Dog

VedDRA SOC name	Number reacted	A - Reports with product and reaction	B - Reports with product without reaction	C - Reports without product but with reaction	D - Reports without product and without reaction	Reaction	ROR (-)	ROR (+)
Behavioural disorders	27	27	195	13,470	156,925		1.61	1.86

Image 136: Recalculation from ROR after removing column split with of medicinal products

$$\text{ROR} = \frac{27/195}{13.470/156.925} = 1.61$$

13. Dashboard walkthrough

The purpose of this dashboard walkthrough is to make an itinerary through the different dashboards implemented, focusing the analysis on its diverse functionalities depending on the potential business scenarios.

The itinerary will cover the user’s decision-making process, depending on a series of factors which will determine using one dashboard or group of dashboards to conduct a specific analysis.

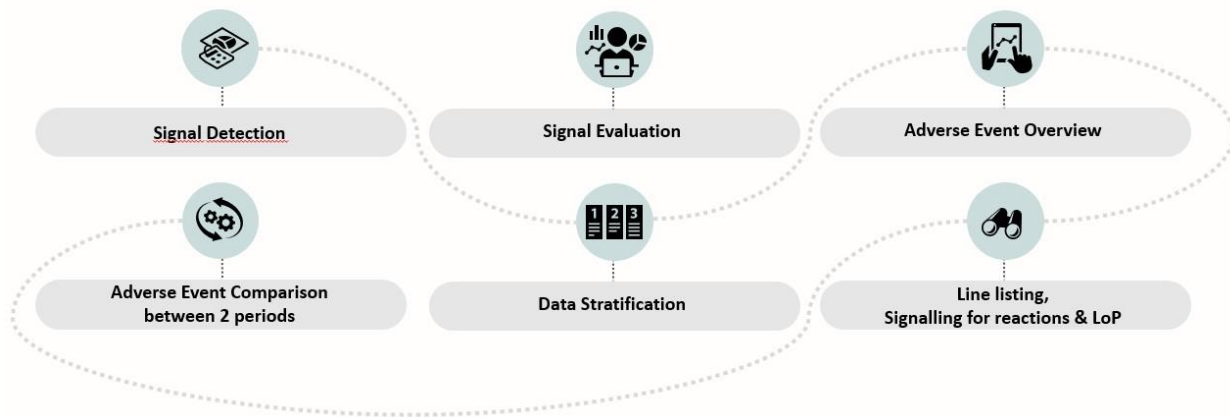


Image 137: Dashboard walkthrough

As a general rule, here's a schema of which dashboard is the most appropriate depending on the purpose of the query and what kind of information the user is trying to obtain:

- **Adverse Event Overview:** To get a simple overview of the data for a product, substance, group of products
- **Signal Detection:** To view data for product, active substance, group of products in order to check for potential signals
- **Signal Evaluation:** To evaluate signals (age, time to onset, off label use, geographical distribution, pharmaceutical form, other products involved, other VeDDRA terms)
- **Data Stratification:** To exclude outliers or simply narrow a query for comparison purposes
- **Adverse Event Between 2 Periods of Time:** To compare data for 2 time periods
- **Line Listing:** To list the cases for a product, substance, group of products, MAH, country
- **Signalling for Reactions:** To monitor data for MAH/NCA products or substances (weekly, monthly)
- **List of Products:** To monitor number of cases (by active substance, product, pharmaceutical form, ATCVET, authorization country, number, MAH, species)

In terms of searching for concrete metrics or products, some useful tips for the user would be:

- **Number of Cases:** When the question is about number of cases for a product, the user should use the Adverse Event Overview dashboard.
- **Statistical measure of signals:** In order to know about the type of reaction with relative frequency at a specific level, the user should go either through the Adverse Event or the Signal Detection Dashboards.
- **Products involved:** In regards of the products involved in a specific group of cases, the user should either go to the Data Stratification Dashboard or jump to it from the Adverse Event Overview query by using the link at the bottom.
- **Number of fatalities:** To see the number of animals treated with a product and died or euthanized as a consequence of this, the user should go to the Signal Evaluation and selecting a concrete period and VeDDRA terms (death, death by euthanasia).
- **Period analysis:** If the user wants to see the number of cases within a period or from a specific date onwards, Adverse Event Overview is the way to go.

In this sense, we will divide those potential business scenarios in 3 different paths, depending on the profile of the user and/or the purpose of the analysis, just as follows:

1. Standard data exploring query for both NCA and MAH users
2. MAH users monitoring their own products or ingredients on a weekly/monthly basis
3. NCA users conducting an active substance class-based analysis

1. Standard path

In the case of what we have named "standard path", we will go through a set of practical questions for a concrete product and reaction, in this case a signal has been found for **Product A** for the VeDDRA

term recumbency, so the following concerns emerge in a standard analysis process:

- ❑ How many cases for Product A have occurred?
 - ✓ The user goes to dashboard Adverse Event Overview and selects Product A in the first prompt in the filter Product Shortname
 - ✓ Enter the Message Received Date range as required. i.e. 1 year
 - ✓ Select VeDDRA Hierarchy, VeDDRA PT name = Recumbency and tick the box for "Animal" and then run the query
- ❑ Which signs have been reported on the cases of Product A at PT level? Which PT VeDDRA terms have the highest number of reports?
 - ✓ In the same dashboard (Adverse Event Overview) the user can see a table with all the VeDDRA terms reported in the cases for the product at SOC level
 - ✓ Go to "See details" and a table will appear with the cases at PT level, or...
 - ✓ Click the link to Signal Detection and go to the tab "Signal detection with 2 RORs"
- ❑ Where have the majority of the cases occurred? How many animals have been affected?
 - ✓ In the Adverse Event Overview, the user clicks on Animal/Human adverse events overview which is a link to the Signal Detection dashboard
 - ✓ It will automatically navigate to the Overview of human/animal AERs per product/active substance/ATCvet code tab
- ❑ Are other products involved?
 - ✓ Go to the "Signal evaluation" dashboard and select Product A in the first prompt in the filter "Product short name".
 - ✓ Enter the "Message received date range" as required i.e. last 5 years
 - ✓ Select "VeDDRA Hierarchy, VeDDRA PT name = Recumbency". Tick the box for "animal" in the 4th prompt and then run the query. Go to the "Product association" tab
- ❑ How many animals treated with Product A, have died? How many of those have been euthanised?
 - ✓ "Adverse event overview" query gives you the number of animals died (Select Product A, click the animal box and make sure to select the dates that include the whole period when Product A has been on the market)
 - ✓ To see the number of animals euthanised, select the VeDDRA term LLT "Death by euthanasia".
- ❑ How many cases have been reported between 01/03/2016 and 31/05/2016 and how many cases in total?
 - ✓ "Adverse event overview" select Product A, and select the dates.
 - ✓ In the column "Number of cases (Period specified)", you have the n. of cases for specified period. To see the total n. of cases, either remove the date filters, or go to "see details". In the column "N. of cases (Total ALL)" you have the n. of total cases in the database per VeDDRA term
 - ✓ In the column "N. of cases (Case count (filter not applied))" you have the n. of total cases for the product.
- ❑ Which other products are associated with recumbency? Which product has the highest number of cases of recumbency after Product A?
 - ✓ Go to the "Data stratification" dashboard and select "VeDDRA terms, VeDDRA PT name = Recumbency"
 - ✓ Then click on "and", then select "VeDDRA term PT = Death"
 - ✓ Tick the box for "Animal" then run the query by clicking on "Adverse events by VeDDRA terms. The first graph will give you the answer
- ❑ Which other signs have been reported together with recumbency? Which pair has the highest count?
 - ✓ Go to the dashboard "Signal Evaluation" and select Product A in the first prompt in the filter "Product short name"
 - ✓ Enter the "Message received date range" as required e.g. last 5 years
 - ✓ Tick the box for "animal" in the 3rd prompt.
 - ✓ Select "VeDDRA Hierarchy, VeDDRA PT name = Recumbency" and go to "Associated VeDDRA"





2. MAHs path

In the case of MAH users, we will follow 2 different potential scenarios:

- ❑ The continuous monitoring scenario, with two alternatives:
 - List of Products:
 - Use "Product MAH" filter to get an overview of data for all products owned by MAH, with or without "Product authorization procedure" and/or "Product authorization country"
 - Select specific product(s), active substance(s) or ATCVET codes to focus the analysis on a specific area
 - Signalling for reactions linked to a product or ingredient:
 - Run signalling for reactions linked to a product or ingredient to find potential new signals.
 - Frequency: Weekly, monthly...
- ❑ The product-based analysis scenario, with four different alternatives:
 - Adverse Event Overview: To obtain baseline data: Number of AERs per product and species, Number of animals affected, Number of fatalities
 - Signal Detection: To view the type of Adverse Events reported for a selected product or group of products (at SOC and PT) and to compare the frequency to the number of reports involving other products and other clinical signs = ROR / ROR(-)
 - Signal Evaluation: To analyse the profile of affected animals (i.e. breed, age) for adverse reactions of interest (potential signs) and identify potential risk factors, effects of co-medication, geographical distribution or pharmaceutical form
 - Data Stratification: To compare a product to products of the same class, or to identify and exclude certain products from the comparison (products with a disproportionate number of reports for a specific AE)

3. NCAs path

To conduct an active substance class-based analysis for a class of products (e.g. antiparasitics), some guidelines should be taken into account, such as:

	Investigate and identify the nature of adverse events that can be attributed to the active substance class
	Investigate and identify similarities and differences in the <u>pharmacovigilance</u> profile between products within a particular substance class
	Investigate how additional factors of the active substances within a class may contribute to the differences of a <u>pharmacovigilance</u> profile within an active substance class
	Investigate and advise on future approaches for improving <u>pharmacovigilance</u> surveillance of for instance, new products containing an active substance from a similar class already on the market

In the case of NCA users, this active substance class-based analysis is therefore based on the following generic 2 steps methodology and the dashboards associated to do so:

Define baseline: Identify the products and their active substances, target species, pharma forms, any combination products:

- ✓ Collect sales data
- ✓ Run queries to get overview of the number of reports in the database (per active substance / pharma form / species)

This defining baseline procedure would be achieved using the Adverse Event Overview dashboard.

AEs profile in target species (including human reactions): What is the clinical profile of adverse reactions in each target species: is there a "class effect", a disproportion of reporting of a given sign for a particular product/active substance/pharma form, or for the entire group:

- ✓ Profile of affected animals (e.g. breed, age) for all adverse reactions
- ✓ Effect of co-medication

- ✓ Incidence calculation
- ✓ ROR with/without stratification (antiparasitics)

This profiling step would be achieved on the other hand by using Signal Detection, Signal Evaluation and Data Stratification dashboards.

Summing up:

Define baseline: Number of AEs for all the products per species, Number of AEs per product and species, Number of affected animals/Number of fatalities

Clinical profile and comparison with the current SPCs: To capture the clinical profile of adverse reactions focusing on medically important events, obtain the number of reports per VeDDRA term at SOC and PT level. To identify similarities and differences in this profile based on the species, pharmaceutical form, therapeutic class:

- Global (all substances/products)
- Tablets versus spot-on
- Per active substance
- Per product

Relate the number of adverse event reports for a particular product or group of products:

- To the sales volumes of this product/group of products = INCIDENCE
- To the number of reports involving other products and other clinical signs= ROR

ROR analysis: For selected PTs, in each species, calculate a ROR for each product in comparison to

- All the products included in the subgroup analysis
- Only the products with the same route of administration withing the subgroup analysis
- Exclude potential overrepresented products based on the VeDDRA term of interest

14. Annex

14.1 *KPIs explanation*

Number of cases: Number of cases with the same Case number within the adverse event report.

Number of animals affected: Animals affected within the adverse event report which will also include indirectly exposed animals, e.g. treated during pregnancy or lactation, co-mingled, infectious spread, etc.

The total number of animals affected includes: Recovered/Normal, Recovered with Sequela, Died, Euthanized, Unknown.

Number of animals reacted: Animals experimenting reactions to VMPs within the adverse event report.

Number of animals died: Animals died as a consequence of an adverse reaction to VMPs within the adverse event report.

The total number of animals died includes: Died, Euthanized.

14.2 *ROR*

14.2.1 ROR calculation

The Reporting Odds Ratio (ROR) calculates the odds of a certain event occurring with your medicinal product, compared to the odds of the same event occurring with all other medicinal products in the database.

A signal is considered when the lower limit of the 95% confidence interval of the ROR is greater than one. The 95% confidence interval gives an indication of the precision of the estimate of the ROR. For instance, if the ROR is 3, the odds of reports of this event with the medicinal product are x3 times higher than the odds of reports of this event among all other reports in the database.

The ROR formula is $ROR = \frac{a/b}{c/d}$ where

	Number of cases with the VedDRA term	Number of cases without the VedDRA term
Number of cases with the product	a	b
Number of cases without the product	c	d

Image 138: ROR Calculation formula

14.2.2 ROR calculation for data stratification

ROR calculation for data stratification follows the same logic as the regular ROR calculation does. Same 4 variables apply, this is:

- Number of cases with the VeDDRA term and without the VeDDRA term
- Number of cases with the Product and without the Product

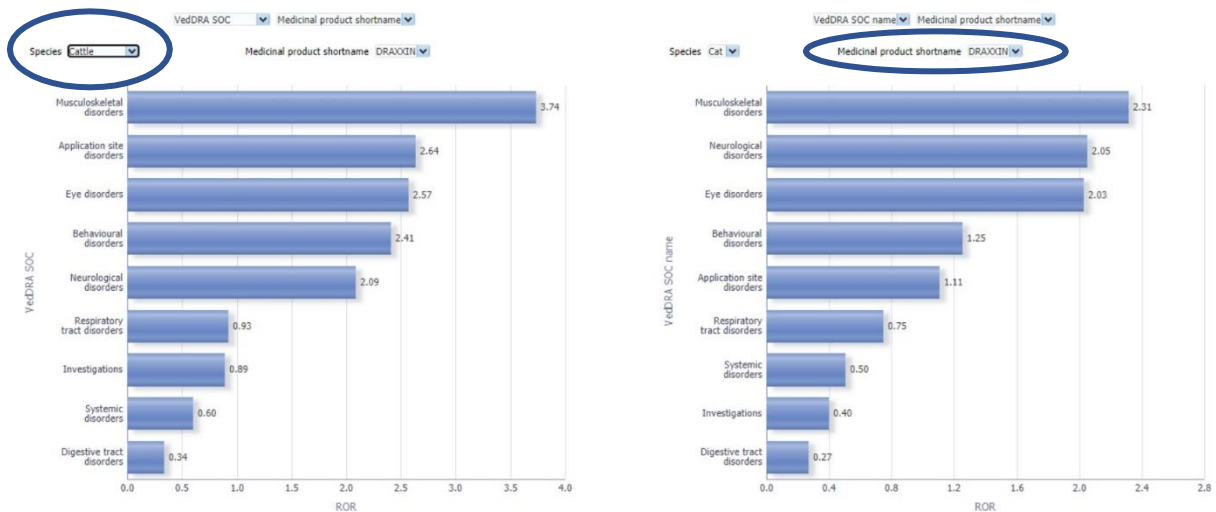


Image 139: ROR calculation for data stratification

It is important to state that changes in the scope (Products or Species involved in the calculation) will impact in the ROR metrics since this modifications have a direct impact in the variables of the formula explained in the ROR Calculation ([See 14.2.1 ROR Calculation](#)) and potentially changing the outcome.