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EVVET – Data Warehouse User Manual
Version 1.0
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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 the *Product grouping dashboard*
- **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 behaviour.
2. EVVET3 DWH

2.1 DWH Login

EVVET3 Data Warehouse is accessible by clicking on the production URL: [https://bi.ema.europa.eu](https://bi.ema.europa.eu) by using any modern browser:

![Image 1: Login to DWH application](image)

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

![Image 2: Enter credentials](image)

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):
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:

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.
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

Image 7: AER received

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.

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.

![Correctness and Classification dropdowns](image9)

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.

![Correctness and Classification charts](image10)

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:

![Filters set](image11)

### 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.

![Received date to original and most recent charts](image12)
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:

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:

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.
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.

2. Message received date range (Required)
   In this prompt you select a range of dates.

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

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.

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.

**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 23: ROR threshold](image)

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](image)

### 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](image)

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.
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:

**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.

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:

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

**Image 27: detailed chart view at country level**

**Image 28: number of fatal cases and average chart**

**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 died charts**

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.
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 32: Animal affected over died chart](image)

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.

![Image 33: detailed view](image)

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
- 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:

Image 35: 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.

  Image 36: Line listing view

  Image 37: 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.

  Image 38: Case listing with VeDDRA terms aligned view

### 4.2.2 Links to signal detection reports

#### 4.2.2.1 Animal/Human adverse events overview

This links 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 links 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.
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.
5. 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.

The dashboard is broken down in four tabs: Overview of AERs per product/active substance/ATCVET/VET, 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).

5.1 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.

2. Message received date range (Required)
In this prompt you select a range of dates.
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.

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.

   **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>=2, ROR(-)>=1 and Number of cases>=3. The user is able to customize these values for the purpose of the analysis.

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.
5.2 Overview of AERs per product/active substance/ATCvet

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.

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.
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.

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.

5.3 **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.

5.4 **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.

*Image 52: 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 VeDDRA, so the user is able to visualize the main products and reactions related to ones selected in the filters page.

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.

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**: 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.
2. **Message received date range (Required)**
In this prompt you select a range of dates.

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

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.

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.
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.

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.

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.
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 \( \leq 2 \) 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.

![Animal data charts](Image 63)

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**

<table>
<thead>
<tr>
<th>Message received year</th>
<th>Number of animals affected</th>
<th>Number of animals died</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>273</td>
<td>61</td>
</tr>
<tr>
<td>2017</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>2018</td>
<td>129</td>
<td>28</td>
</tr>
<tr>
<td>2019</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>2020</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

![Animal data cumulative view](Image 64)

**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.

![Number of cases by species and off label use charts](Image 65)

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.
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.
Number of cases by country and species

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

Number of cases by information type

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 YEARS)

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.

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 71: 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...

<table>
<thead>
<tr>
<th>Non currently used product detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medicinal product shortname</th>
<th>VeDDRA SOC name</th>
<th>VeDDRA FT name</th>
<th>Number of cases</th>
<th>Reaction count</th>
<th>ROR (−)</th>
<th>ROR (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRAKXIN</td>
<td>Application site disorders</td>
<td>Injection site hair change</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DRAKXIN</td>
<td>Application site disorders</td>
<td>Injection site necrosis</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DRAKXIN</td>
<td>Application site disorders</td>
<td>Injection site pain</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Image 72: Cases with no other products reported

6.4.2 Cases with other product reported
And with other products reported.

Image 73: 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 SOCs 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.

![Image](image74.png)

**Image 74: 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.
7. 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 75: 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.

Image 76: 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 77: 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 78: 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 79: 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 80: 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>=2, ROR(-)>=1 and Number of cases>=3. The user is able to customize this values for the purpose of the analysis.

![Threshold ROR](image)

Image 81: 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.

![Historical data](image)

Image 82: 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

![Adverse events comparison between 2 periods date criteria](image)

Image 83: 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.
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.

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.

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.
### 7.2.3 Date of onset – See details

Same for the Date of onset.

<table>
<thead>
<tr>
<th>Medical product surname</th>
<th>Medical product ID (if applicable)</th>
<th>Period 1: Number of cases</th>
<th>Period 2: Number of cases</th>
<th>Period 1: ROR (1)</th>
<th>Period 1: ROR (2)</th>
<th>Period 1: ROR (&gt;=)</th>
<th>Period 2: Number of cases</th>
<th>Period 2: ROR (1)</th>
<th>Period 2: ROR (2)</th>
<th>Period 2: ROR (&gt;=)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological disorders</td>
<td>3</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
8. 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:

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.

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".

3. Animal information (Required)

The user should select the product subject to their evaluation on the left side. 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.
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 92: 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.

![Image 93: 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>=2, ROR(-)>=1 and Number of cases>=3. The user is able to customize this values for the purpose of the analysis.

![Image 94: 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.
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:

<table>
<thead>
<tr>
<th>Key figure</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>12,852</td>
</tr>
<tr>
<td>Product count</td>
<td>796</td>
</tr>
<tr>
<td>Animals affected</td>
<td>253,317</td>
</tr>
</tbody>
</table>

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”.

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.
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.

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 an 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.

![Image 100: Output level]

2. Message received date range (Required)
In this prompt you select a range of dates.

![Image 101: 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 102: 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.

![Image 103: 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.
6. Threshold ROR
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.

9.2 Signaling for reactions linked to a product or ingredient

In this dashboard the user can see the Top 15 products/active substances/ATCvet codes by number of cases between date 1 and date 2. ROR and ROR(-) are also included in the visualization.

At the top the user will be able to jump between the species and reactions (at PT level) for the period and product information selected in the filters page.

9.2.1 See details

Link included at the bottom (See 3.2.1. See Details).
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.

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.

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

4. **Country filter (Required)**
The user is required to select either the occurrence region of country.

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.

### 10.2 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.
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.
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 115: Product Information filters](image)

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 116: Optional report filters](image)

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 117: List of products key figures](image)
The first set of charts shows 2 pie charts with the number of cases by active substance and by medicinal product shortname:

![Image 118: Number of cases by active substance and by medicinal product shortname](Image 118)

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

![Image 119: Number of cases by ATCvet, pharmaceutical form and authorization procedure](Image 119)

Third set includes a map representing the number of cases by authorization country, a treemap for 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 120: number of cases by authorization country, number of cases by product and authorisation number and Top 15 number of cases by medicinal product](Image 120)

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 121: Number of cases by MAH and by Species](Image 121)

**11.2.1 See details**

(See 3.2.1. See Details).
12. Product grouping

12.1 Introduction to product grouping

For contextual purposes, this product 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.

Image 122: Static ROR Dashboard for 2 medicinal products

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

![Image 123: Static ROR with VeDDRA SOC filter applied](image123)

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

![Image 124: Menu option where user can exclude column from table](image124)

![Image 125: Recalculation from ROR after removing column split with of medicinal products](image125)

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

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.
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 Evalution” 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 pharmacovigilance 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 pharmacovigilance profile within an active substance class |
| Investigate and advise on future approaches for improving pharmacovigilance 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:
  o Global (all substances/products)
  o Tablets versus spot-on
  o Per active substance
  o Per product

Relate the number of adverse event reports for a particular product or group of products:
  o To the sales volumes of this product/group of products = INCIDENCE
  o 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
  o All the products included in the subgroup analysis
  o Only the products with the same route of administration within the subgroup analysis
  o 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
- Number of cases without the product

**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

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 13.2.1 ROR Calculation](#)) and potentially changing the outcome.