Instructional Guidance for PV Express II for Licensed Establishments

The PV Express II web-based form is one of two approved methods licensed establishments may use to submit individual adverse event reports (AER) to the Center for Veterinary Biologics (CVB). The PV Express II web-based form can be accessed here. The other approved method licensed establishments may use to submit adverse event reports to the CVB is through the electronic Gateway, which is only for transmissions of AERs created in XML format. For further information on the Gateway, contact the CVB.

The step-by-step instructions provided in this guidance document are to aid your establishment in completing the PV Express II web-based form.

VeDDRA Coding of Clinical Symptoms Reported in an Adverse Event Report

For each of the clinical symptoms described in an individual adverse event report (AER) the licensed establishment submitting the report must assign an acceptable term to each symptom in accordance with the Veterinary Dictionary for Drug Related Affairs (VeDDRA) vocabulary listing. The VeDDRA vocabulary listing is an internationally harmonized list of medical terms used to describe the adverse clinical manifestations identified in an AER and is accepted by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). The most current VeDDRA list can be accessed here: VeDDRA complete list. Guidance Notes for the Use of VeDDRA Terminology for Reporting Adverse Events in Animals' can be accessed here: Guidance notes on the use of VeDDRA terminology. Diagnostic test kit manufacturers reporting an adverse event will only code the VeDDRA term "unclassifiable adverse event" and only code one term per event. Use the event narrative to provide complete details.

Causality Assessment by the Market Authorization Holder (MAH) for an AER Submitted to CVB

In addition to VeDDRA coding, licensed establishments must also assign a 'causality' for each of their products associated with the AER. Each establishment will make a determination as to whether the adverse reaction noted in an individual AER is related to their biological product. For the purposes of reporting adverse events to the CVB under Title 9 Code of Federal Regulations (CFR), the 'ABON system' for assessing causality is the acceptable method to be used.

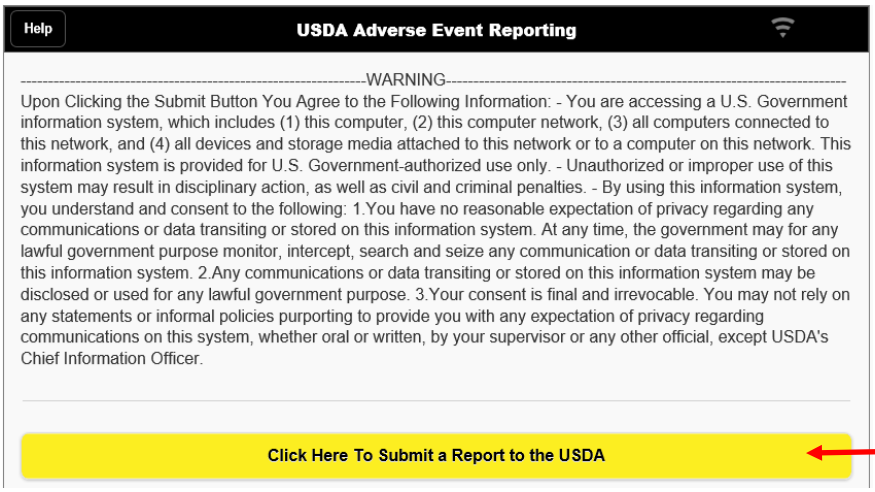
- Category A: **Probable** - *All* of the following minimum criteria should be present:
    - There should be a reasonable association in time between the administration of the biological product and onset and duration of the reported adverse reaction.
    - The description of the clinical event should be consistent with, or at least plausible, given the known ingredients of the biological product described in the adverse event.
    - There should be no other equally plausible explanation(s) of the case reported.
- Category B: **Possible** -The administration and/or use of the biological product is another possible and plausible cause for the reported adverse event where the available data do not meet the criteria for inclusion in Category A.
- Category O: **Unclassifiable/Unassessable** - Applied to cases where reliable data is unavailable or insufficient to make an assessment of causality.
- Category O1: **Inconclusive** – Applied to cases where other associated factors prevented the assessor from drawing a definitive conclusion regarding causality (A or B), but in which association cannot be discounted.
- Category N**: Unlikely -** Sufficient information exists to establish beyond a reasonable doubt that the adverse reaction described in the adverse event report was not likely due to the use of the veterinary biological product.

NOTE: ALL FIELDS on the PV Express II web-based form should be completed if known by your firm. All date fields appear on the form as European dates (DD-MM-YYYY). To delete a case already submitted, contact CVB.

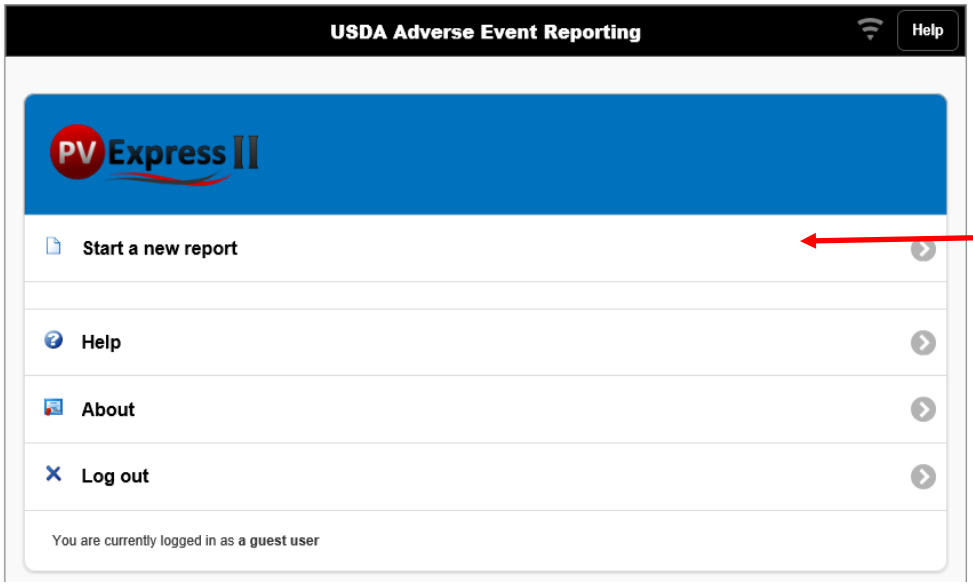
Should you have any questions, need assistance or need to report system problems, please contact Dr. Bill Huls or Dr. John Schiltz at CVB.Pharma@usda.gov or at (515) 337-6100.

https://cvbpv.aphis.usda.gov/PVXClient/index.html

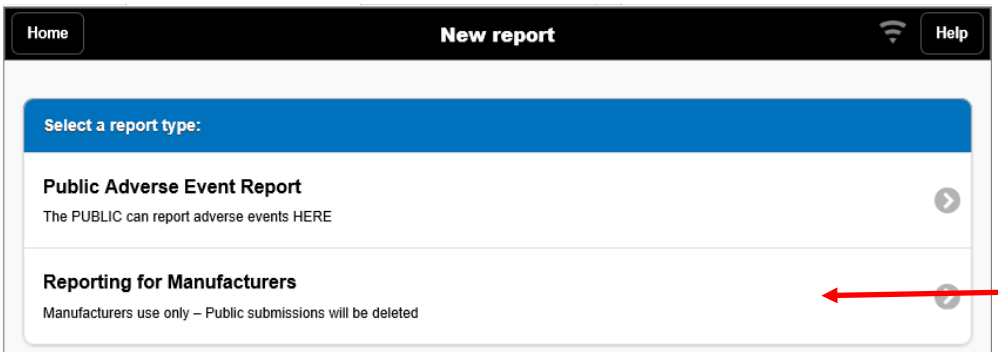
URL to initiate an adverse event report.



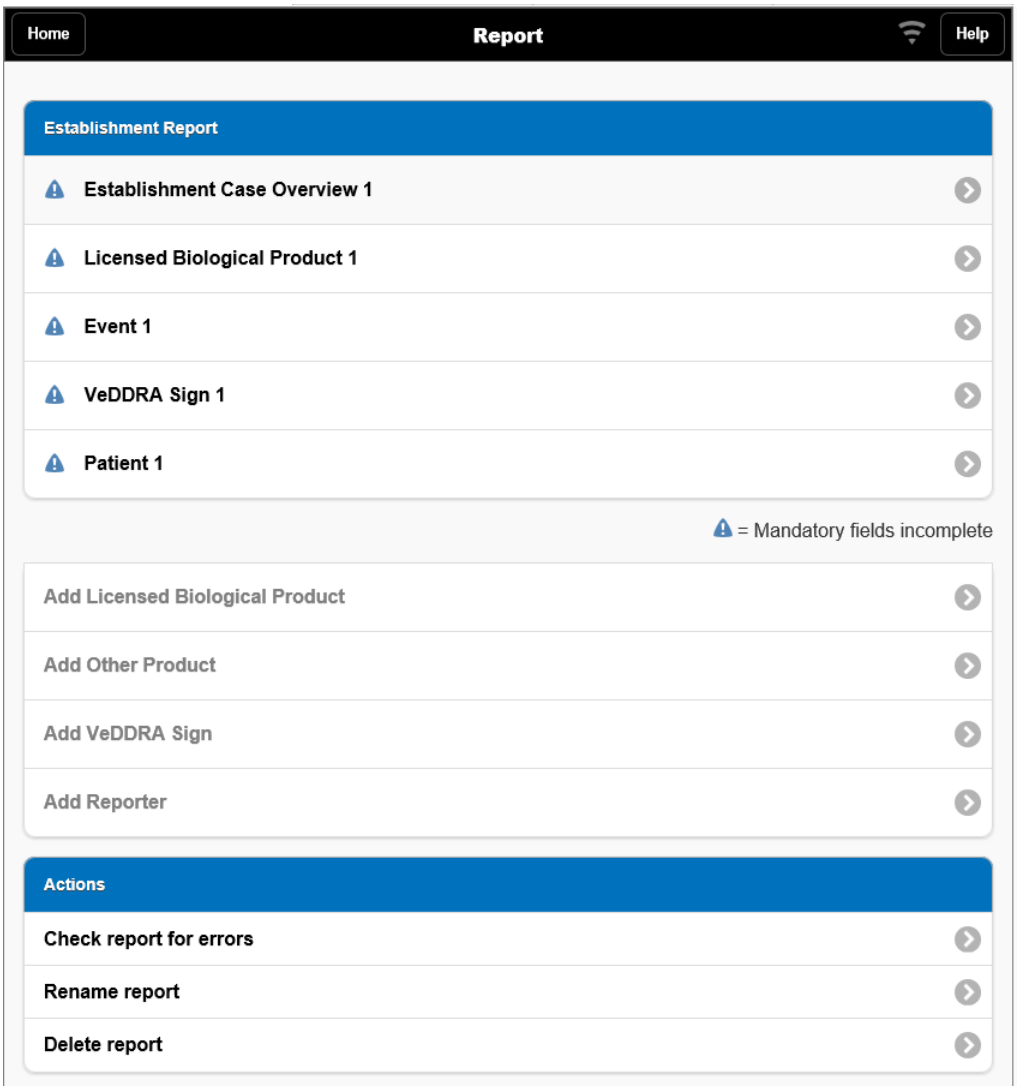
Start the AER by clicking here.



Then, clicking here.



Click on the Reporting for Manufacturers Report.

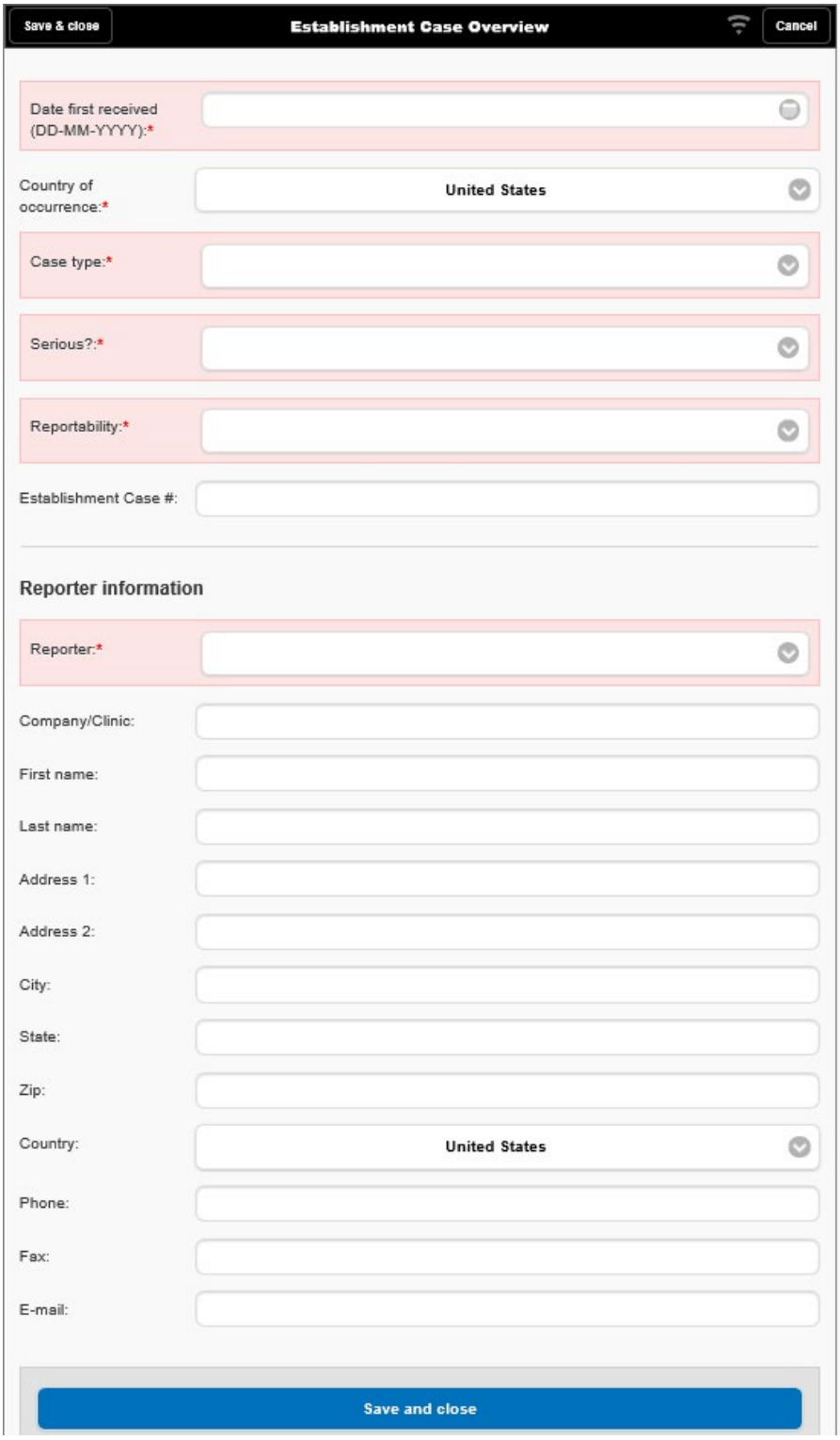


These 5 sections contain mandatory and optional requirements. Once the mandatory items are completed, the icon preceding the section name will change (eg. or). Instructions for completing each section will be covered in this document.

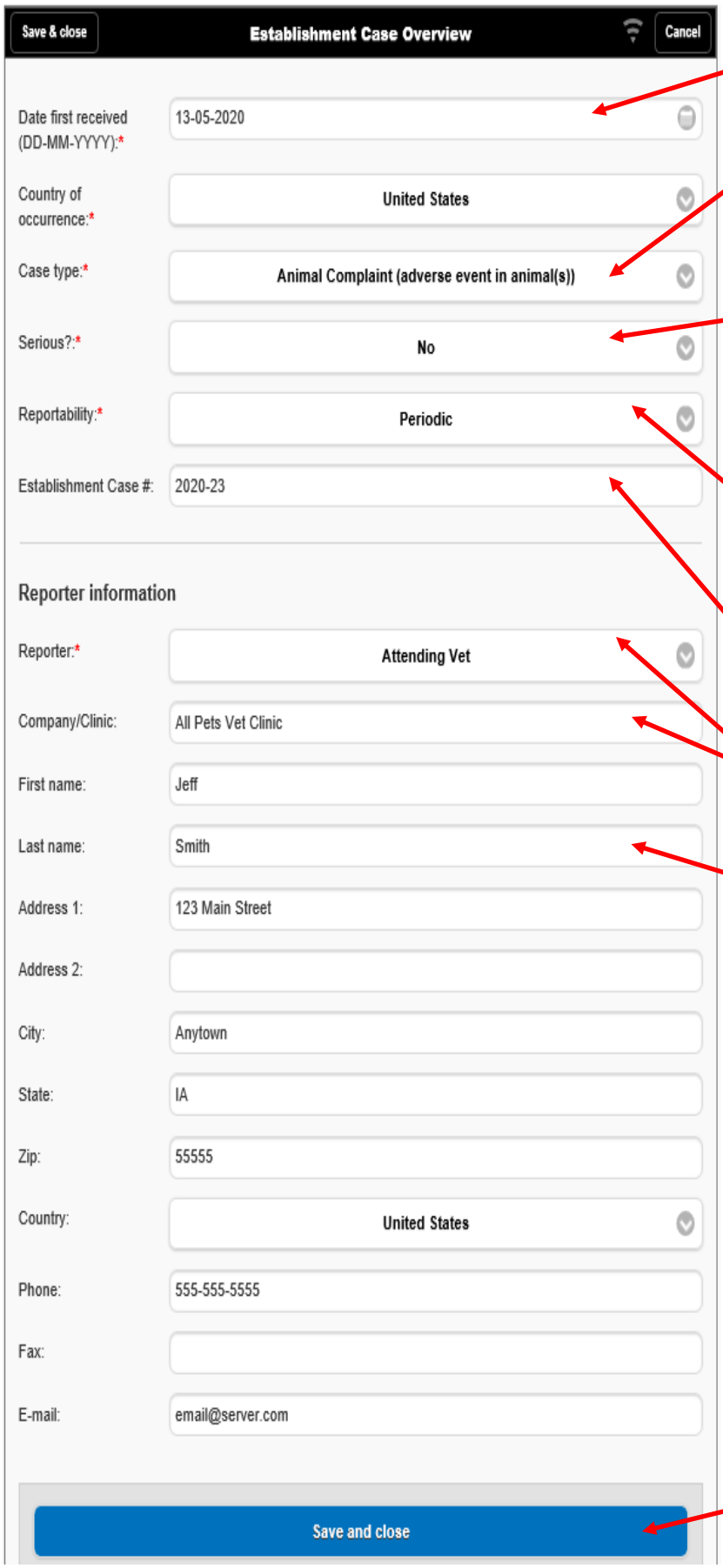
These 4 sections allow for the reporting of additional products, VeDDRA signs, and reporters.

This final grouping allows you to check the report for errors, rename the report, or delete the report.

Establishment Case Overview 1: **This is the screen as it initially appears. Mandatory fields are denoted with red asterisks (*). Remember, fill in ALL fields if they are known to you. Some fields have default values, which can be changed by selecting the down arrow at the right of the field. The down arrows at the right end of each field reveals a drop-down list to choose from.**



The next picture shows the fields completed:



NOTE the date field is in European format (DD-MM-YYYY). Click the calendar icon on the right of the field to select the date the adverse event was reported to your firm.

Two options: Animal Complaint (adverse event in animal(s)) or symptomatic human case.

Is this a serious adverse event? A serious adverse event is any adverse event which results in death, is life-threatening, results in persistent or significant disability/incapacity, or a congenital anomaly or birth defect.

Select the appropriate reportability: 3-day alert for immediate (**serious, unexpected and product related**), periodic for all other initial reports. If a follow-up report, you **must** use the same Establishment Case # as the previous report.

Enter your establishment-assigned AER case number.

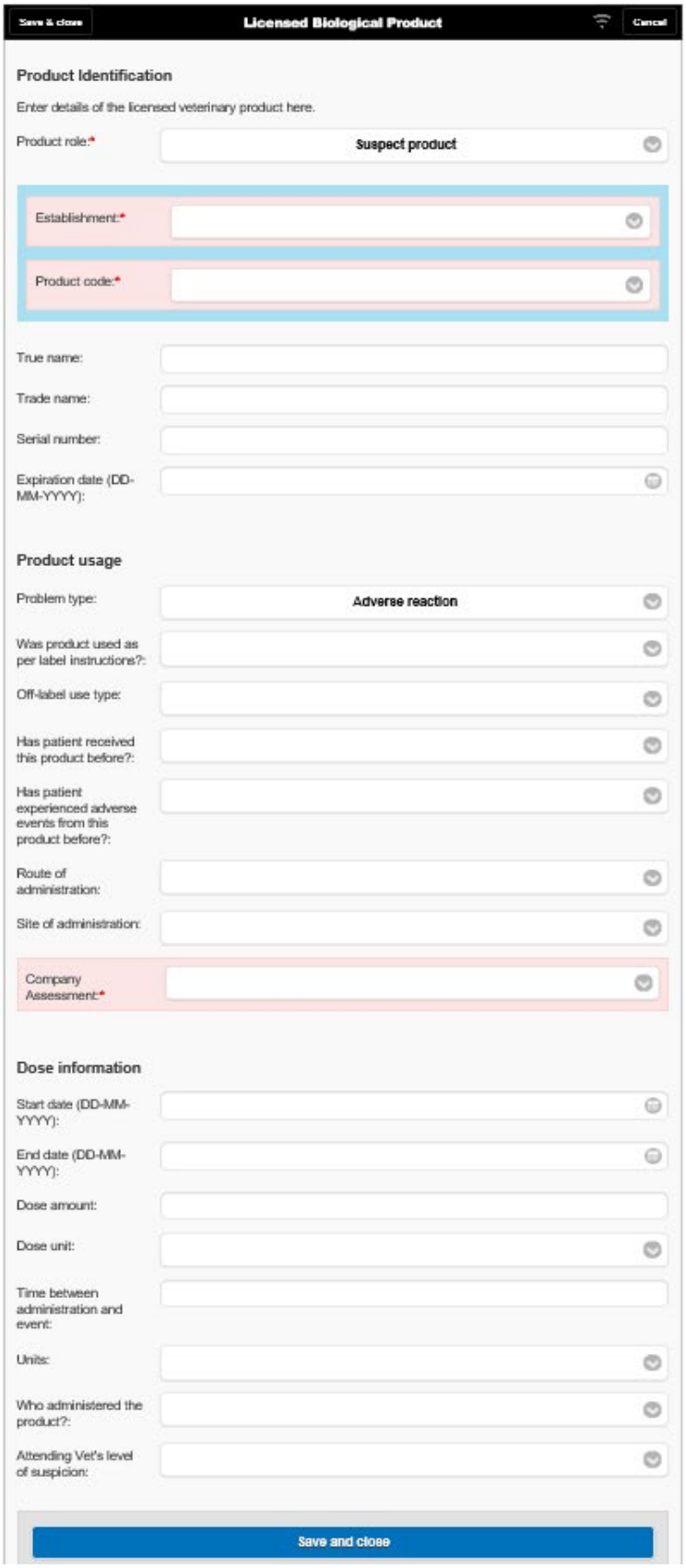
Choose from the drop-down list an appropriate reporter role, and, if known, provide the clinic name

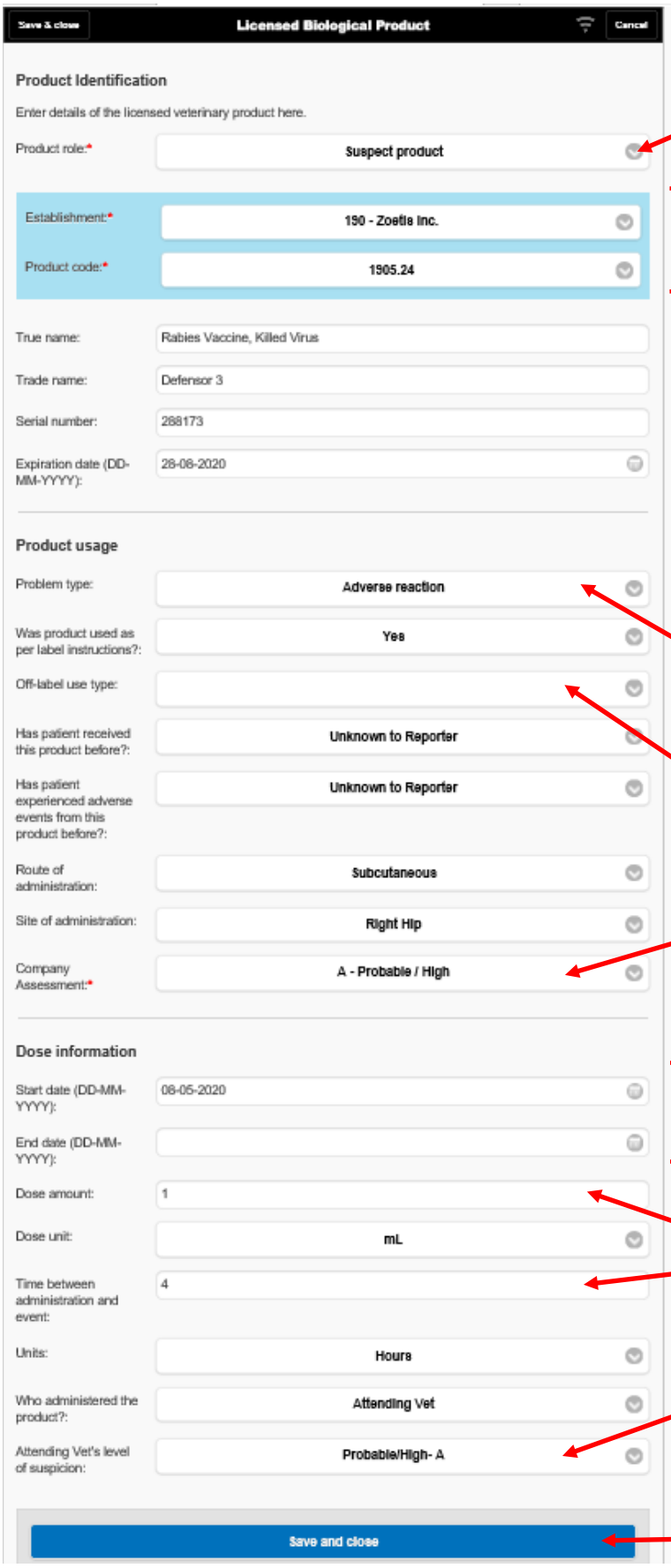
If the reporter requests anonymity, put "Anonymous" in the 'Last name' field.

This section should contain information about the reporter, in this case the Vet Clinic.

Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

<u>Licensed Biological Product 1:</u> This screen is as it initially appears. Enter information on this screen for your Establishment's licensed product involved in this adverse event report. The down arrows at the right end of each field reveals a drop-down list to choose from.





Product role will **always** be "Suspect product" for products prepared by your firm.

Establishment and Product Code for the product involved with this adverse event report. *Combination package* products licensed by APHIS do not receive APHIS release, however AERs involving combination package products are required to be submitted to CVB.

True name, Trade name, Serial number (if known) and expiration date of the product. **NOTE** – serial number is alphanumeric, do not use special characters (-,/, etc.) **NOTE** expiration date is in European format.

3 choices **for this particular product**: Adverse reaction, Human exposure – symptomatic, or Lack of efficacy.

If the product was **NOT** used per label instructions, pick the most appropriate category.

Enter your company assessment of causality.

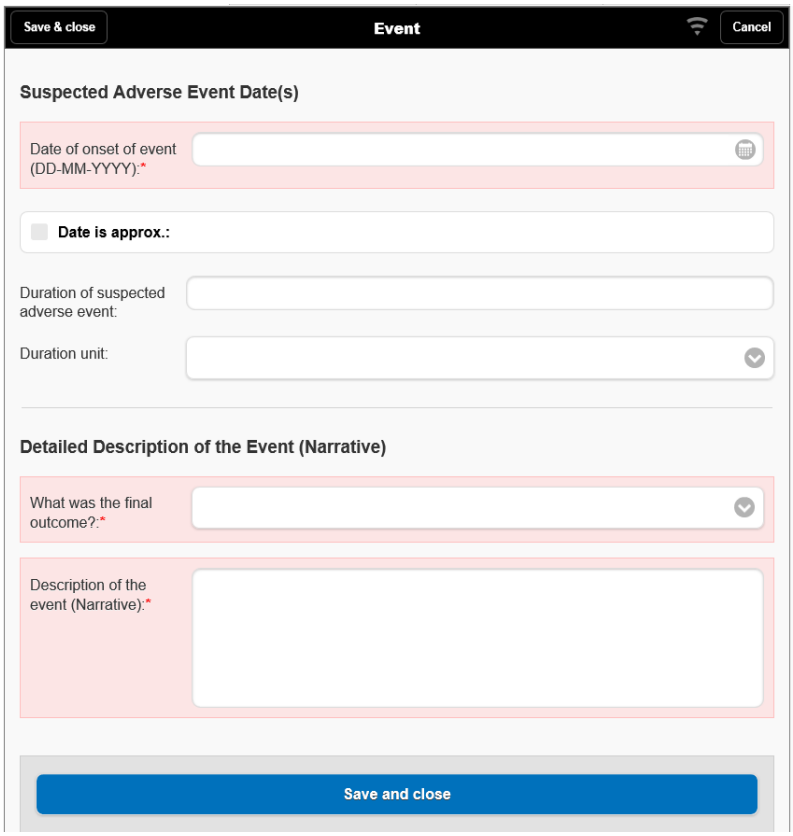
Start date = date of administration. End date is used when vaccination extends over a period of time (vaccinating 500 calves over two days, for example). If part of a series of immunizations for an individual animal, please explain in the case narrative.

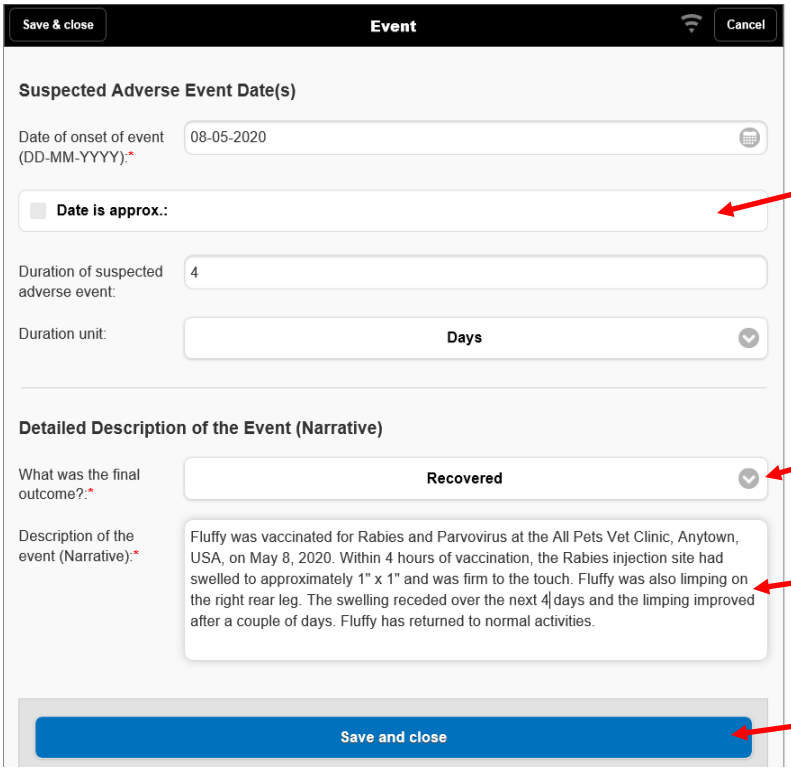
If this value is less than 1 (<1), you must enter a zero followed by the decimal, for example 0.5.

Enter the attending veterinarian's assessment of causality, if known.

Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

Event 1: **This screen is as it initially appears. Enter information on this screen to describe the actual adverse event. Provide a complete, detailed narrative. The down arrows at the right end of a field reveals a drop-down list to choose from.**





If there is uncertainty about the date that the adverse event started, check this box.

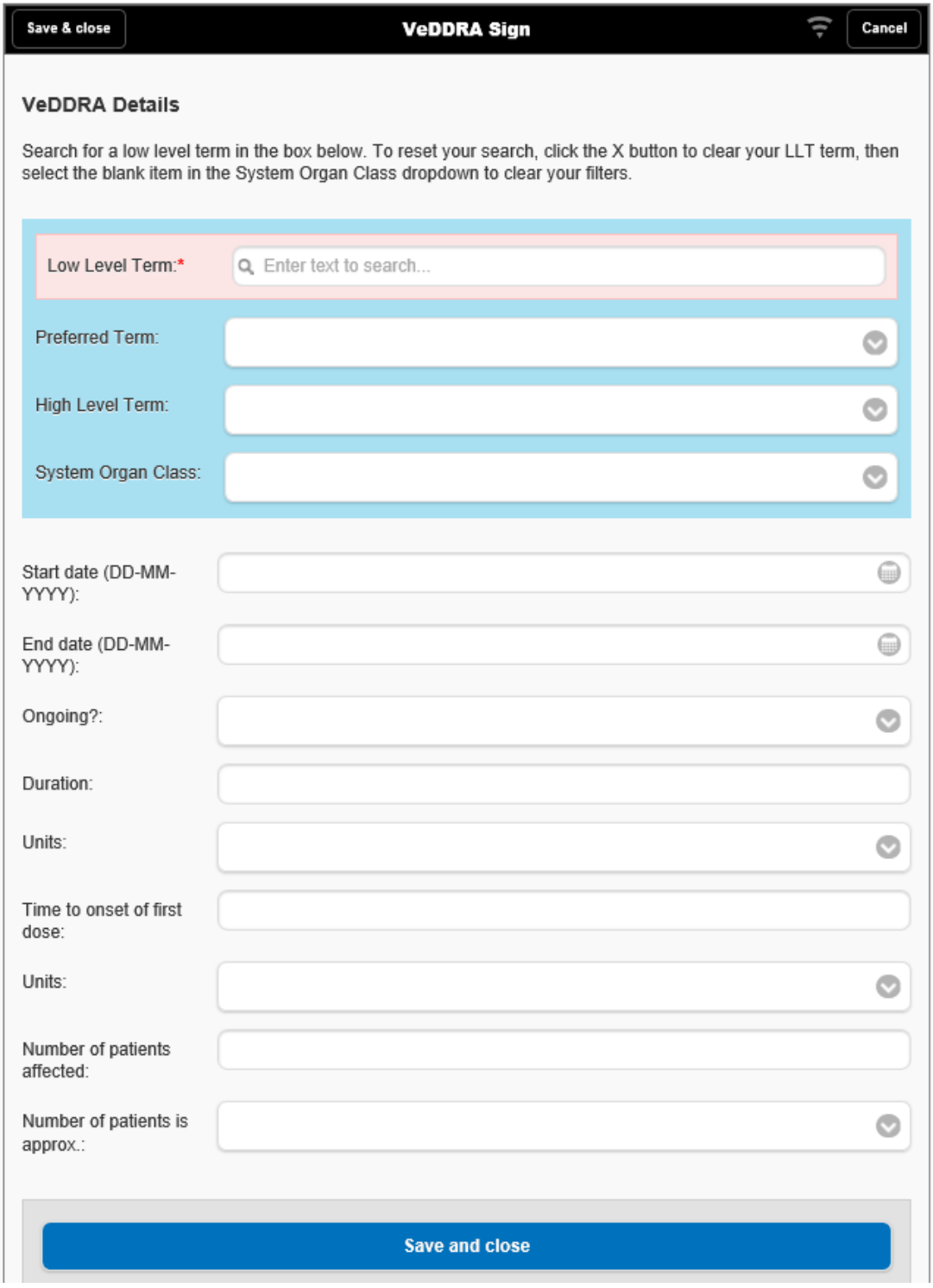
How long did the adverse event last?

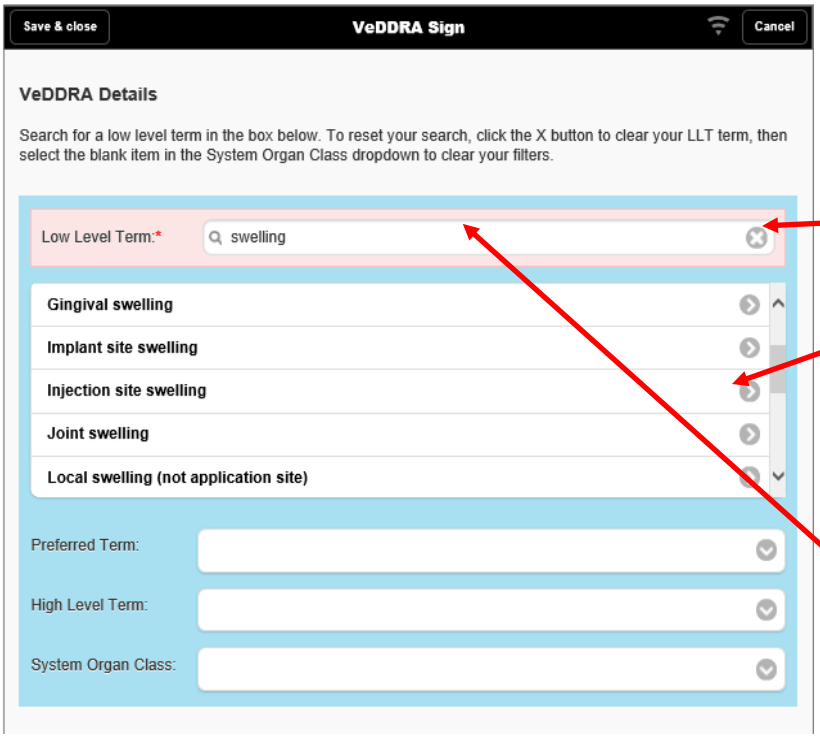
Click the drop-down arrow and select an outcome from the drop-down list.

Provide a **complete, detailed narrative** of the adverse event.

Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

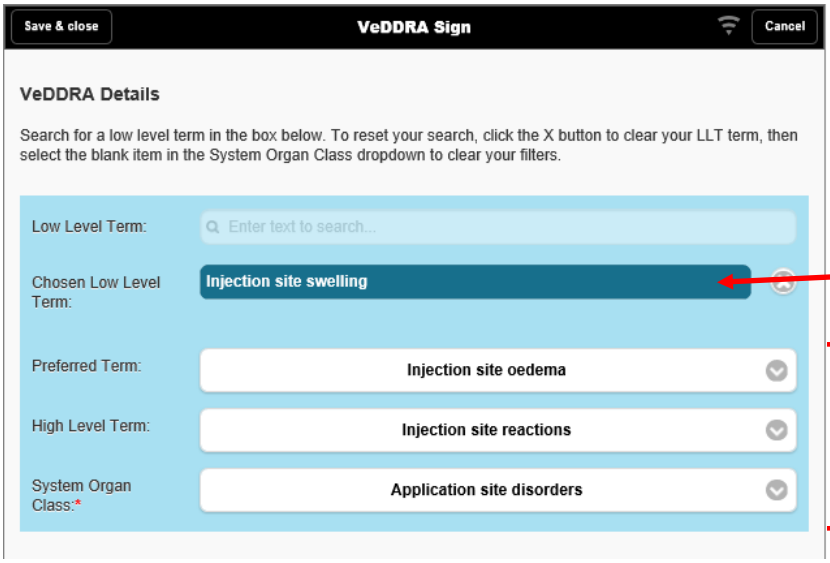
<u>VeDDRA Sign 1:</u> This screen is as it initially appears. Enter a VeDDRA term for one of the clinical signs / symptoms for the actual adverse event. Additional signs will be added at a later screen. The down arrows at the right end of a field reveals a drop-down list to choose from.





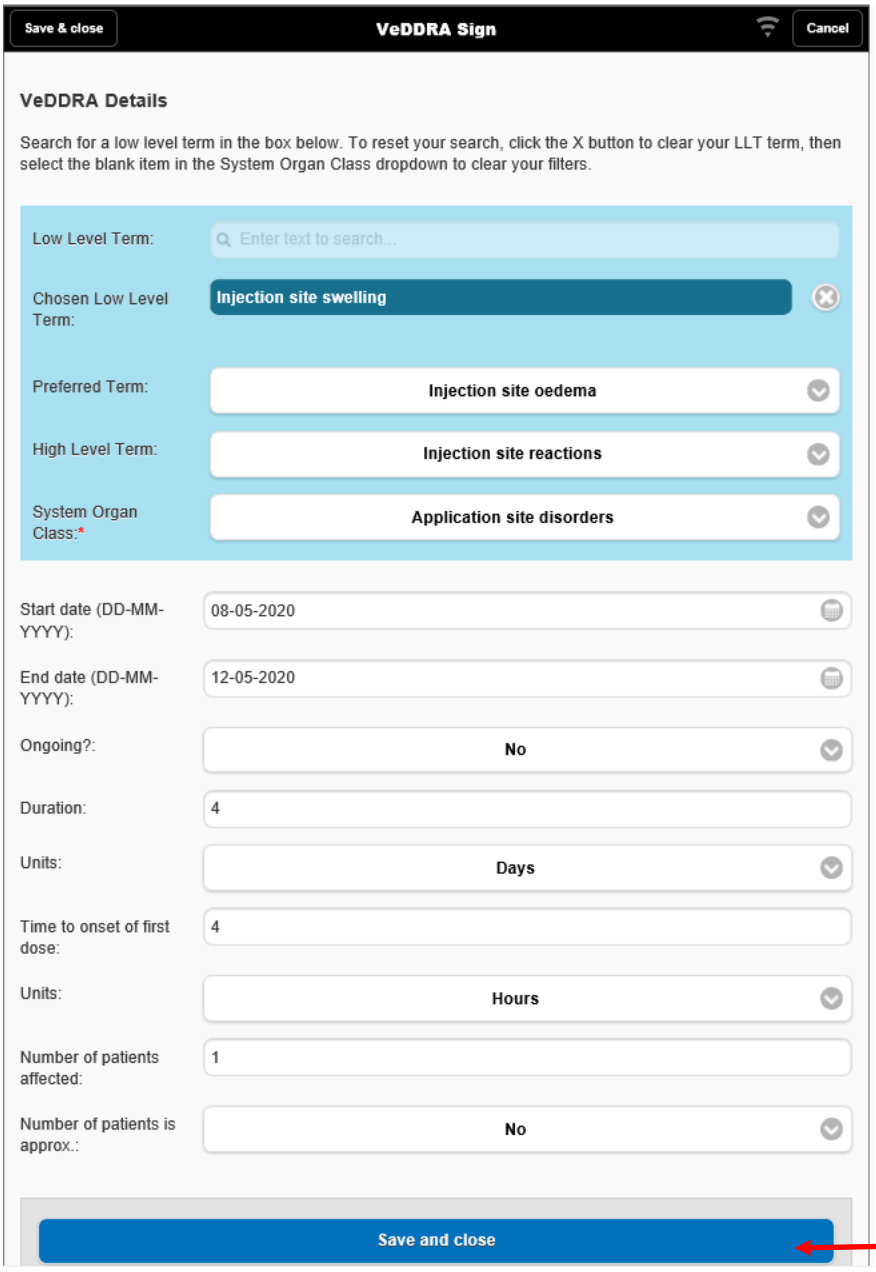
Start by entering a sign / symptom from the event narrative field in the "Low Level Term" field. As you type, possible terms appear in a scrollable box. Select the most appropriate term from the suggested terms (in this example, 'swelling' was noted at the injection site, so select "Injection site swelling").

NOTE: Diagnostic test kit manufacturers reporting an adverse event will only code the VeDDRA term "unclassifiable adverse event" and only code one term per event. Use the event narrative to provide complete details.



Once a term is selected, the remaining fields in the blue box are auto-populated.

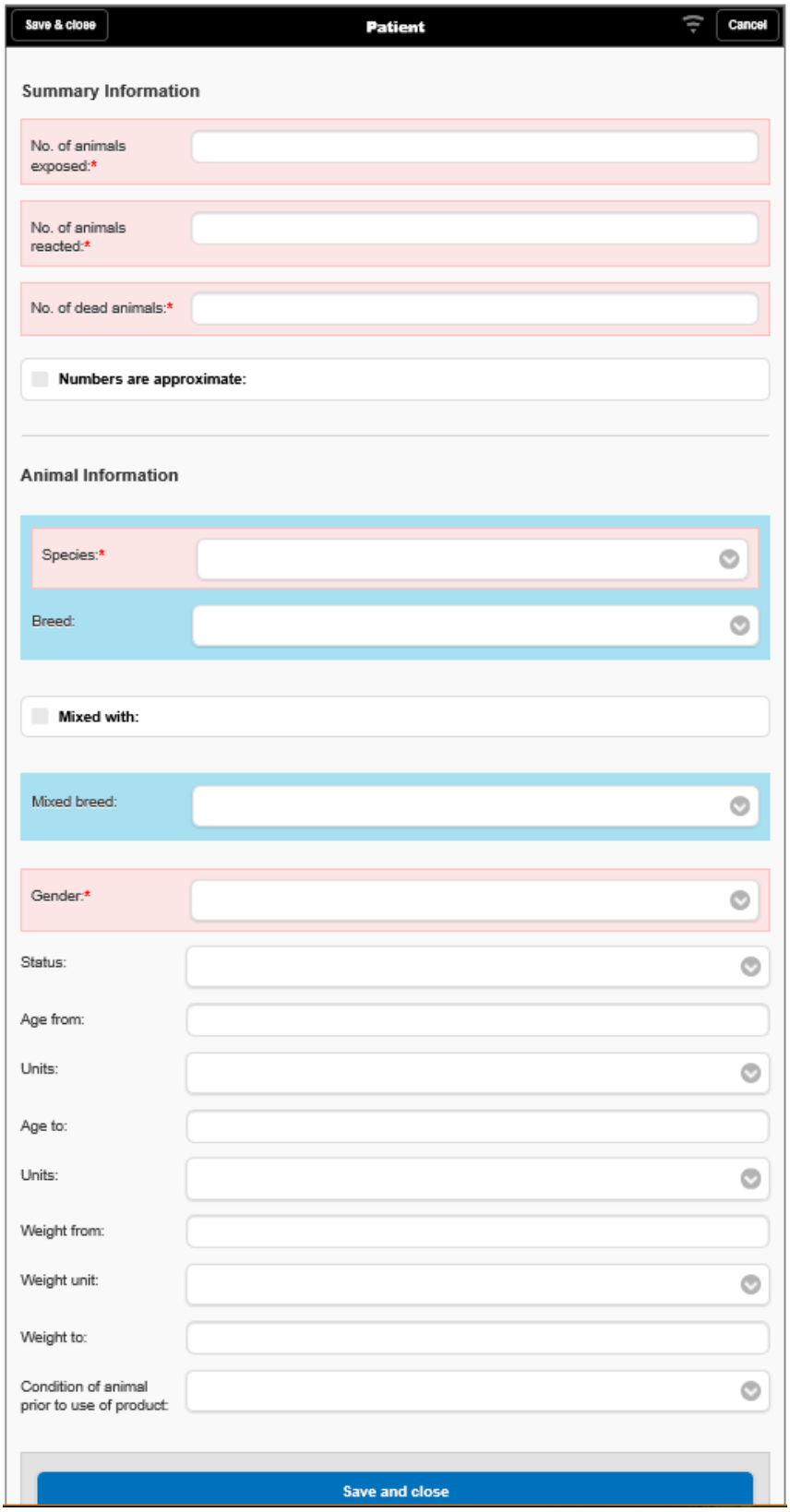
These fields are auto-populated.

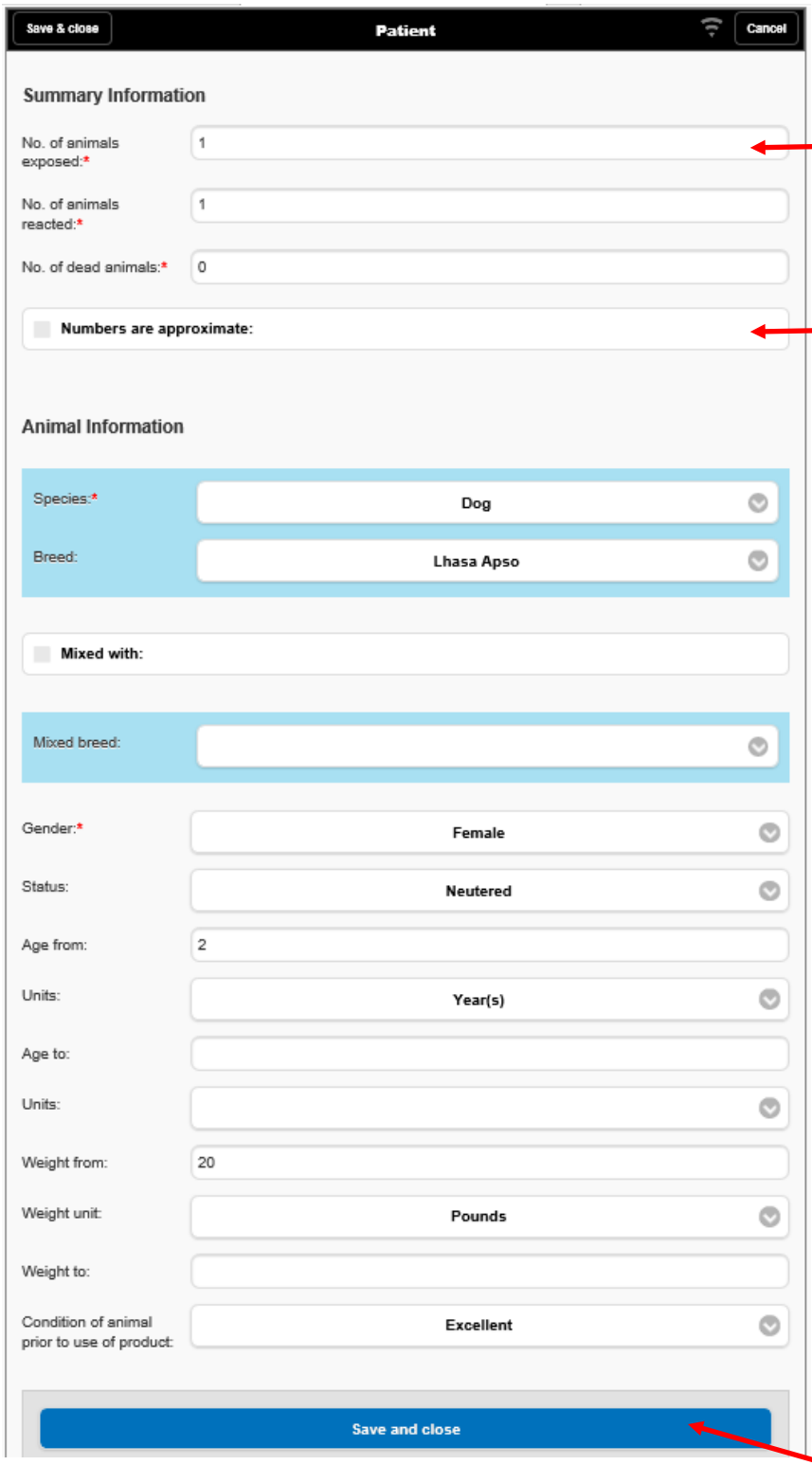


Fill in the remaining fields, based on the narrative. Start date (when symptoms appeared), End date (when symptoms went away), and Duration refer to the particular sign (VeDDRA term). In the example, injection site swelling was noted 4 hours after product administration and lasted 4 days.

Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

Patient 1: **This screen is as it initially appears. Enter patient information. The down arrows at the right end of a field reveals a drop-down list to choose from.**





No. of animals exposed = number of animals vaccinated

If numbers are approximations, check this box.

If a mixed breed, check the box and enter the other breed.

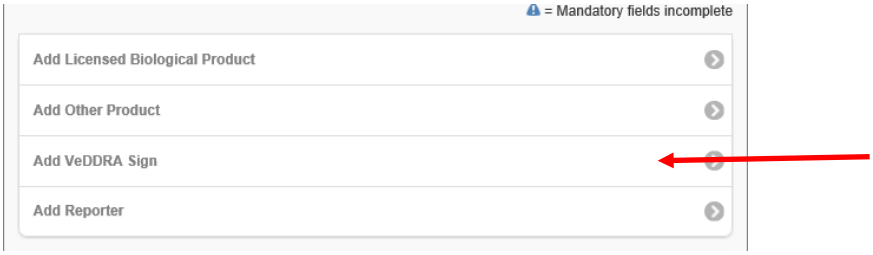
Allows for multiple ages for a group of animals or to provide an approximation of age (eg. 6-8 month old calves). If age is known, only need to enter the "Age from" field and select units.

Allows for weight range for a group of animals or to provide an approximation of weight (eg. 600-800 pound calves). If weight is known, only need to enter the "Weight from" field and select units.

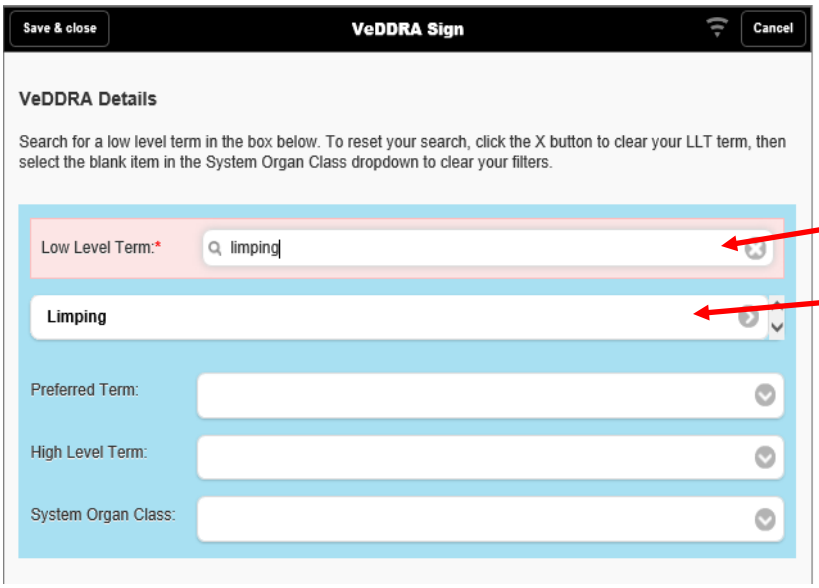
Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

This completes the mandatory sections. However, in this example, there are more VeDDRA terms to be added to the case, and an additional product and reporter needs to be included.

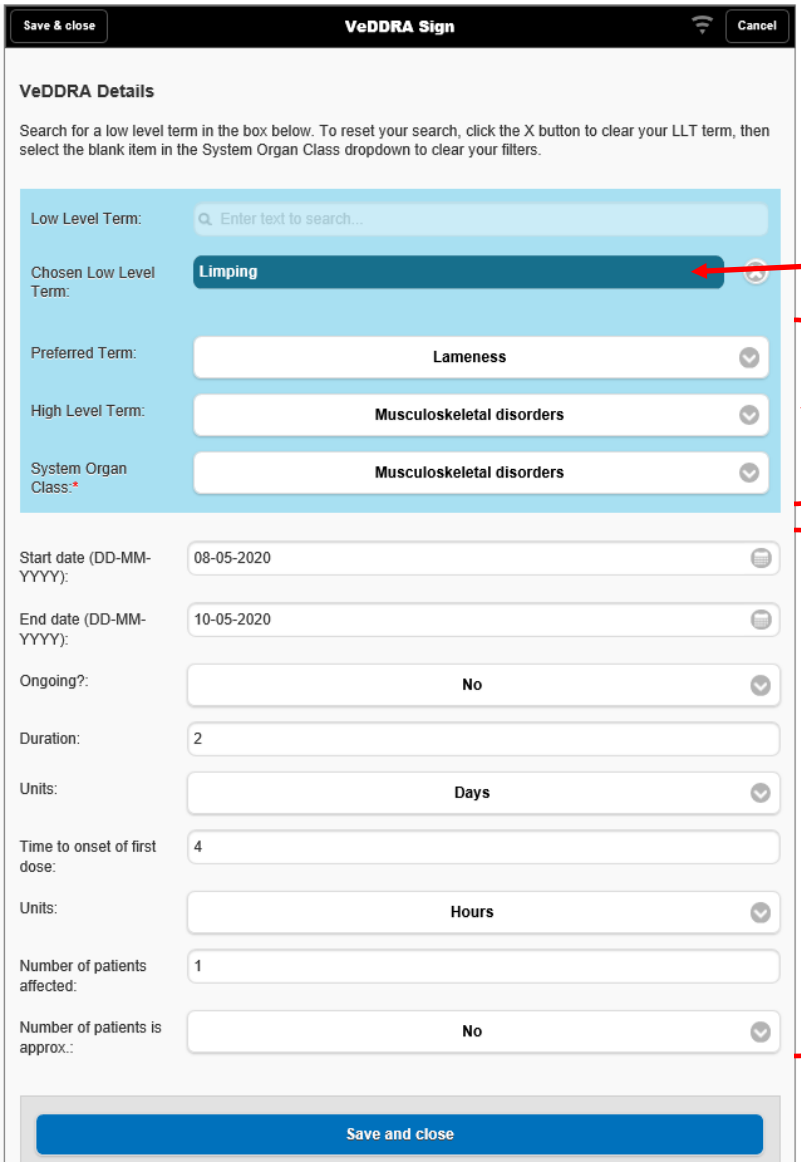
To add additional VeDDRA terms, click on the "Add VeDDRA Sign"



Follow the instructions provided previously for the VeDDRA Sign entry to complete the screens for additional VeDDRA signs. Account for ALL clinical signs/symptoms. In this example, we need to include limping:



Start by entering a sign / symptom in the "Low Level Term" field. As you type, possible terms appear in a scrollable box. Select the most appropriate term from the suggested terms (in this example, select "Limping").



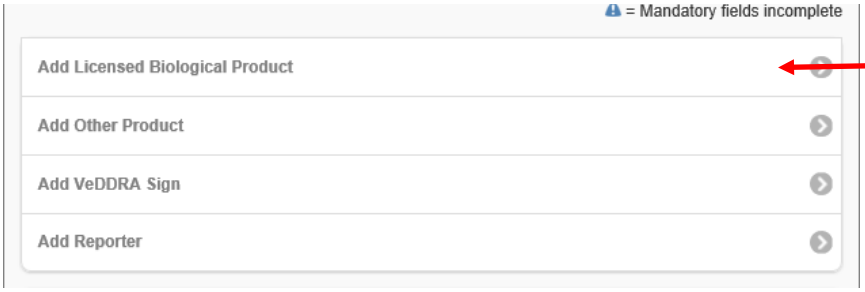
Once a term is selected, the remaining fields in this picture are auto-populated.

These fields are auto-populated.

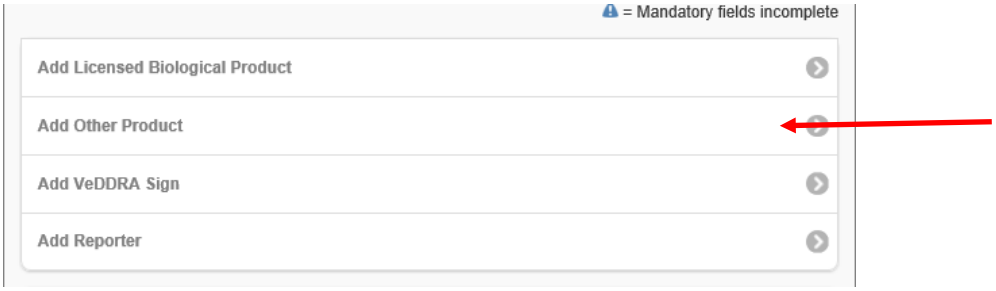
Fill in the remaining fields, based on the narrative. Start date (when symptoms appeared), End date (when symptoms went away), and Duration refer to the particular sign (VeDDRA term). In the example, limping was noted 4 hours after product administration and lasted two days.

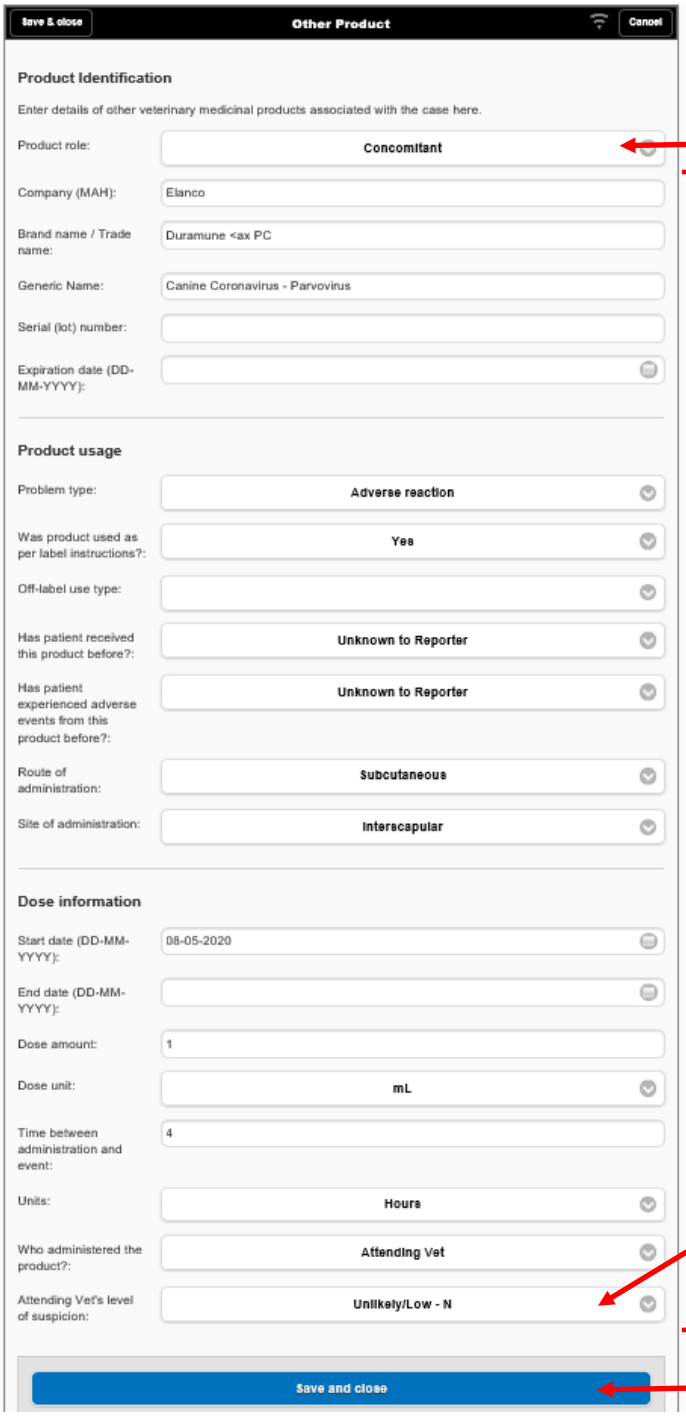
For the additional biological products that were administered:

- **If the product(s) are produced or distributed by the firm filing this report, select "Add Licensed Biological Product" and follow the instructions for Licensed Biological Product. Remember to select "Suspect product" for the Product role field. All products produced or distributed by the firm filing the report are considered suspect products.**



- **If the product(s) were produced by a different firm, select "Add Other Product." See example below.**





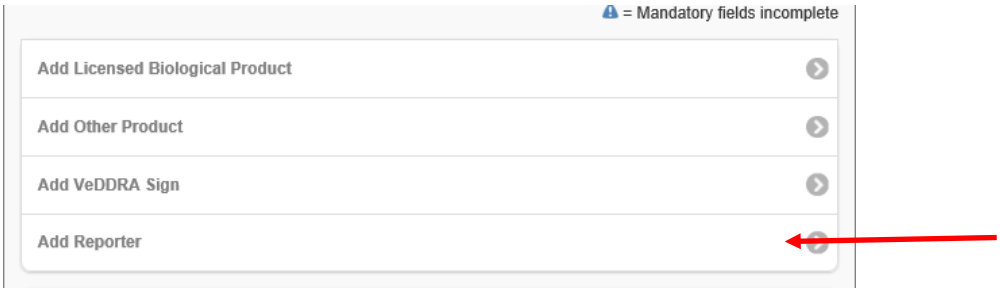
For products produced by a different firm, **always** select "Concomitant".

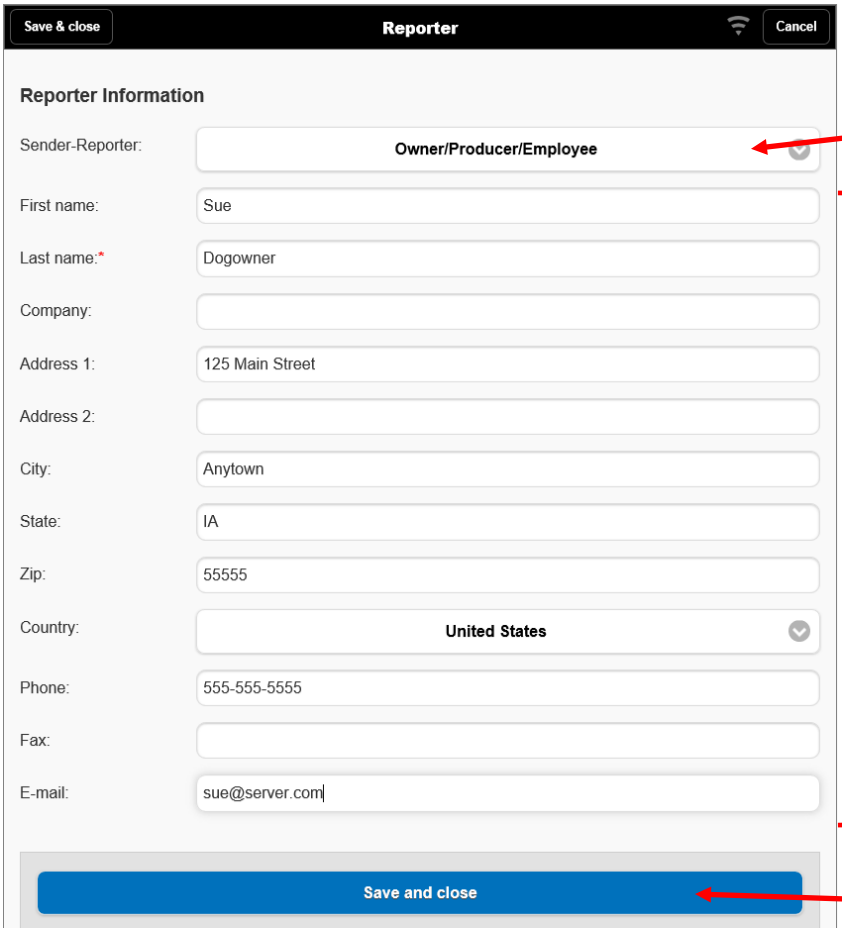
Fill out all the fields as completely and accurately as possible.

In this example, the attending vet felt that this product was "unlikely" to have contributed to the adverse event.

Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

To add additional reporters (owner, vet clinic), select "Add Reporter." See example below.



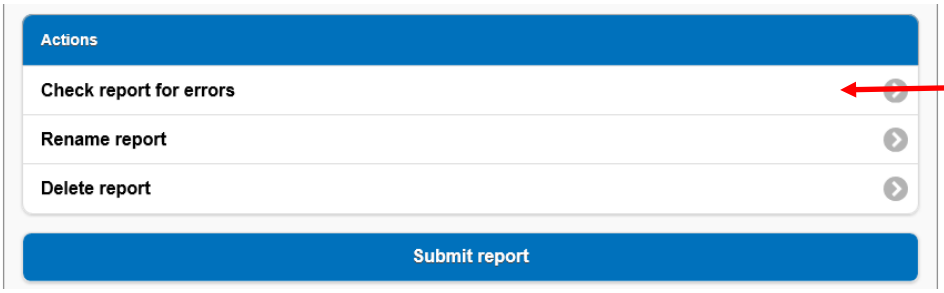


Select additional reporters from the drop-down list.

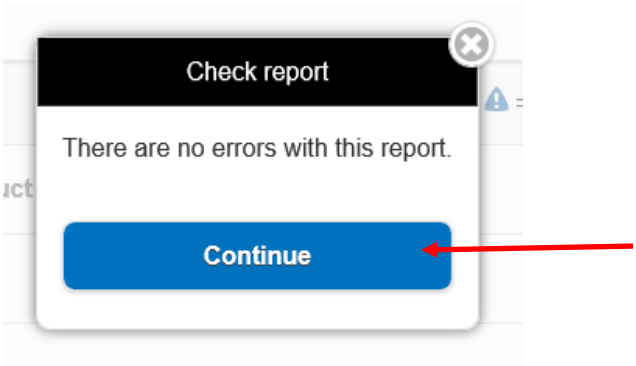
Fill out all the fields as completely and accurately as possible.

Once all information is entered, click "Save and close." Note you can click here or on the top left corner of the screen.

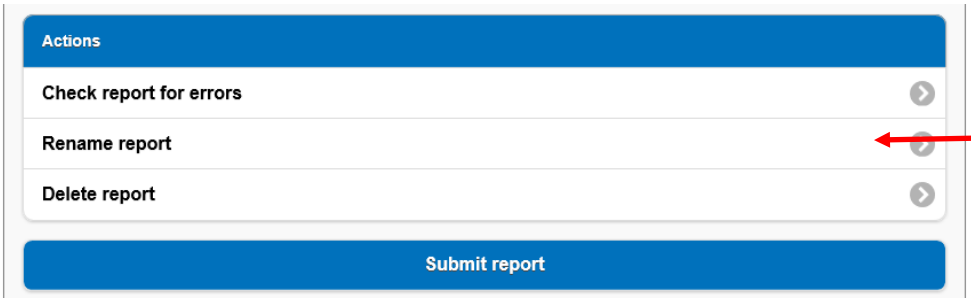
The final step involves checking the report for errors. If an error is found, you will be directed to correct the error and then allowed to submit the report.

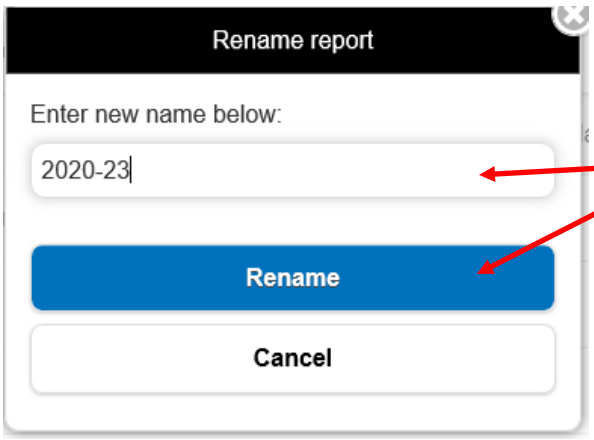


If there are no errors, select continue:



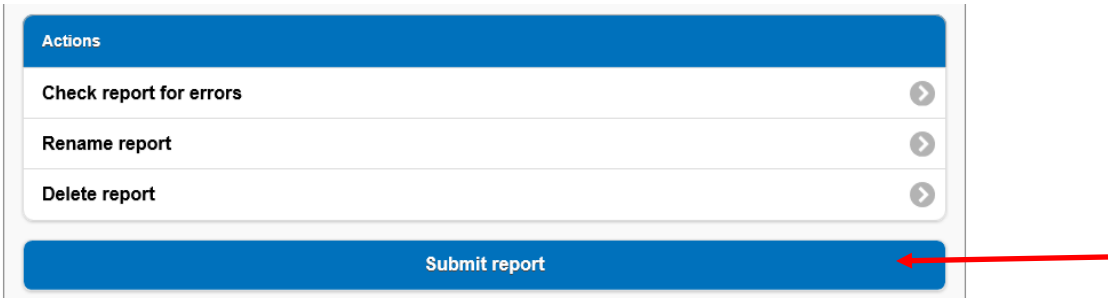
You can rename the report.

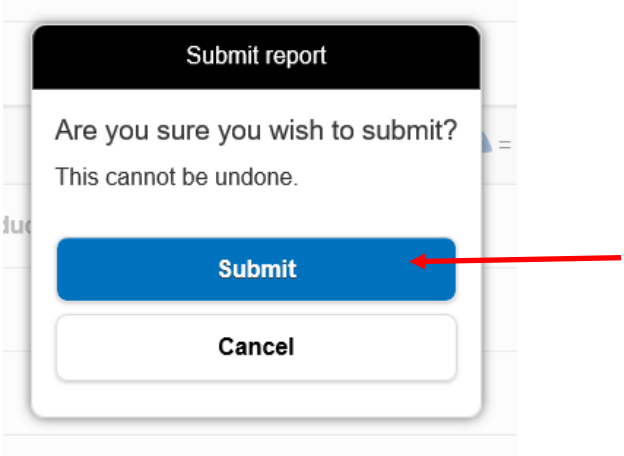




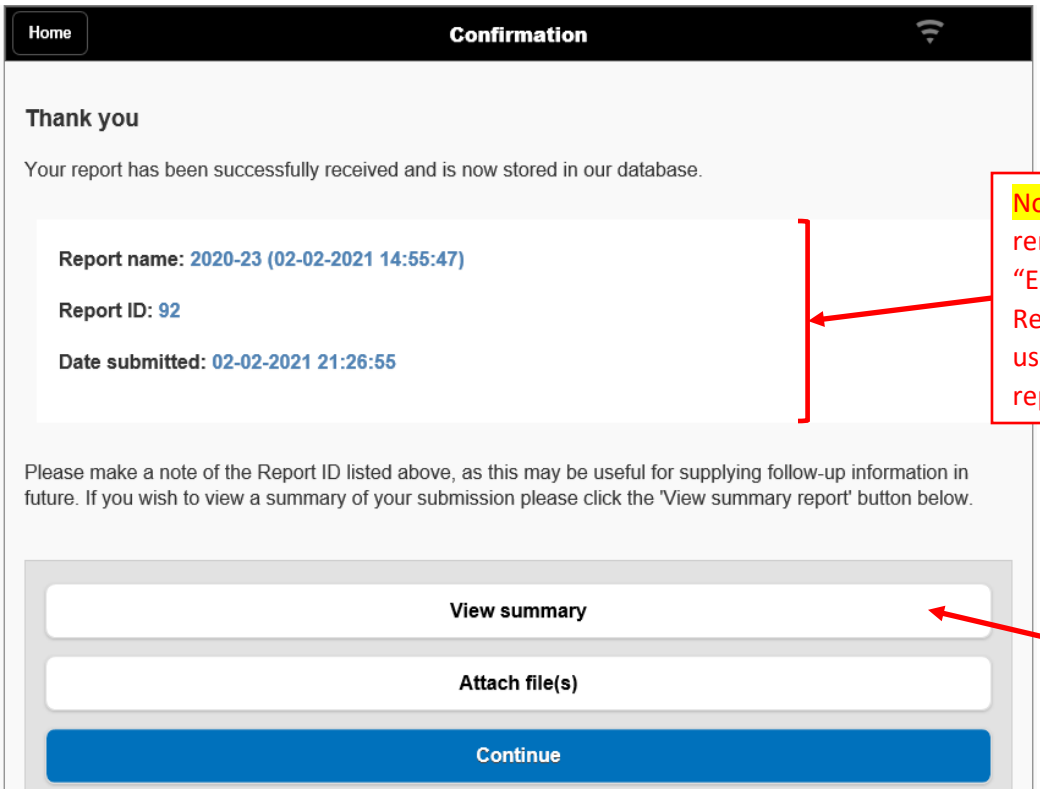
Enter a new name and then select "Rename."

Select "Submit report."



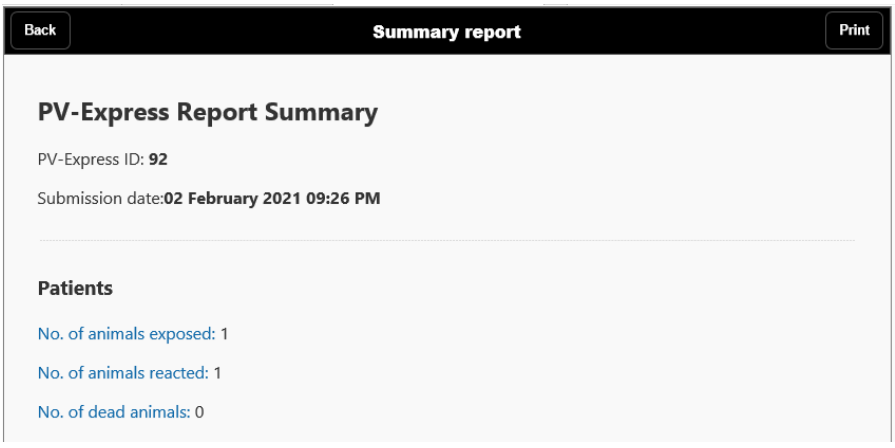


You will get a "confirmation" screen:



Note the Report name (you renamed it; default name is "Establishment report.") and the Report ID. The Report ID is a useful field for CVB to find your report.

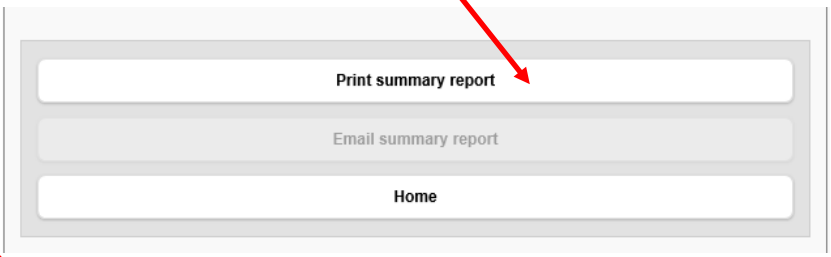
Select View summary. This will allow you to see, save, and print the report. This provides documentation of the report.



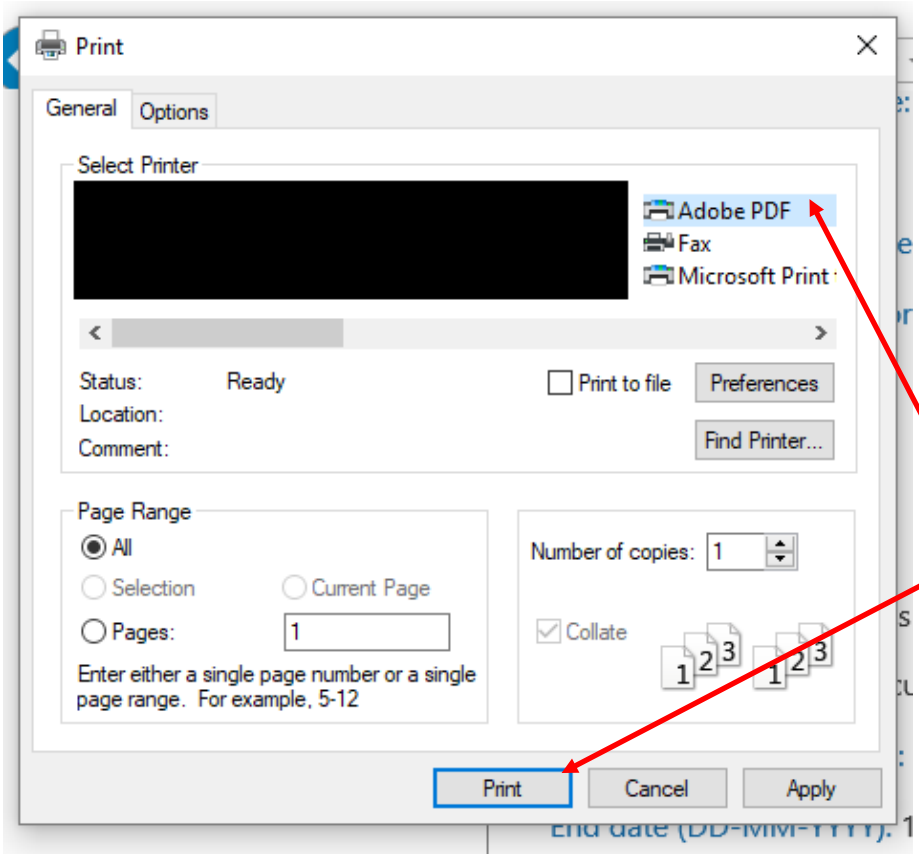
Enlarged view of beginning of report.

While too small to read in this picture, the summary contains all of the data you entered into the report.

TO SAVE A COPY OF THE REPORT, select Print Summary Report.



Enlarged view of bottom of report.



From the print screen, select "Adobe PDF" as the printer, and then select Print. You will be asked where to store the PDF file that is generated on your computer / network. Consider naming the file in a manner that facilitates organizing and retrieval of the adverse events you are reporting. Firms are required to maintain Adverse Event Report records for 3 years.

Finally, select "Home" to start a new report or exit the AER web-based reporting application.