Oracle Argus Safety

CBER eVAERS Best Practices

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Oracle Argus Safety CBER eVAERS Best Practices, Release 8.4

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Preface

This preface contains the following sections:

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1 Revision History

Argus Version	Description
8.2.2	First release
8.2.3	• Added information to the "Setting up Reporting Rules" table. • Added the Similar Device Case Processing (Single Entity Combination Products) chapter. • Added the Similar Device Case Processing (Co-Packaged Combination Products).
8.4	No changes in this release

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Introduction

This document provides the best practices and recommendations to configure Combination Products and generate PMSR reports for Combination and Non-Combination Products using the eVAERS profile.

As per FDA, Combination Product Applicants should submit PMSRs using the Vaccine Adverse Event Reporting System (VAERS) consistent with the requirements of the combination product with January 31, 2021 as compliance date.

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Configure Co-packaged Combination Products

Two or more separate products packaged together in a single package or as a unit comprising of drug and device products, device and biological products, or biological and drug products, is known as Co-Packaged Combination Products.
Inhaler with filled vaccine cartridge is one of example for co-packaged combination product, as it comprises of 2 components, an inhaler device and vaccine that are within a single package.

In Oracle Argus Safety, vaccines and devices can be added to products belonging to different families to configure a Co-Packaged Combination Product. Follow these steps to configure Single Entity Combination Products:

1. Click **Business Configuration** > **Products and Licenses** > **Add New Family**, for creating family for the vaccine.
2. Enter required mandatory data and save the family.
3. Click **Add New Product**.
4. Enter required mandatory data and save the Product.
5. Create a Primary mode of action product license by clicking **Add New License**.
6. Enter required mandatory data for creating a Vaccine license such as below, and save the license:
    a. Authorization country = UNITED STATES
    b. License Type = Marketed Vaccine
    c. License Number can be entered in either of the following ways:
        i. License # = BLA<License number>
        ii. Application type=BLA
        iii. License # = <License number>
7. To create family for the Device, click **Business Configuration** > **Products and Licenses** > **Add New Family**.

    The N/A value can be added in Ingredient codelist and the same can be selected for the Device family.
8. Enter the required mandatory data and save the family.
9. Click **Add New Product**.
10. Enter required mandatory data and save the Product.

    The N/A value can be added in the Formulation codelist and the same can be selected for the Device Product.
11. Create a Constituent Device License by clicking **Add New License**.
12. Enter the required mandatory data for creating a Drug license as the below, and save the license.

a. Authorization country = UNITED STATES or WORLD
b. License Type = Marketed Device
c. License # = <License number>

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Set up Reporting Destinations

Here are the recommendations for creating the reporting destination to send eVAERS to the FDA.

Agency Information tab

Enter Name and address information as applicable.

CBER Technical specification recommends using CBER_VAERS as Agency Identifier.

Local Company Contact tab

Enter Name and address information of the Local Company Contact that is responsible for eVAERS submission.

The following data are required for eVAERS submission other than mandatory fields shown in UI:

- Sender Type
- Department
- Contact Name information
  - Title
  - First Name
  - Last Name
  - Address
  - City
  - State
  - Postal Code
  - Country
  - Phone
  - Fax
  - Email Address

EDI Tab

- Agency Identifier: CBER_VAERS
- Message Profile: select CBER EVAERS V1.0 MESSAGE TEMPLATE (standard profile).
- ACK Profile: select ICH-ICSR V1.1 ACKNOWLEDGMENT TEMPLATE – FDA
- Transmit ICSR Attachments: Marked
- Attachment Classification: Mark one or more attachment classification that is required to be submitted along with eVAERS

- Allowed attachment file size (in MB): 15
- Allowed report size (in MB): 100
- Outgoing folder: Specify the outgoing folder location such as C:\ESM\CBER\OUT\
- File Name: Include appropriate format such `CBER_##########.xml`
- Method: E2B EDI gateway

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Set up Reporting Rules

We recommend you retain the existing expedited reporting rules (#1, #2) for 15-day and periodic report types, and create the other new expedited reporting rules. Below are the suggested reporting rules:

Country	License Type	Agency	Rule Name	Time Frame	Report Form	Condition
United States	Marketed Vaccine	CBER_VAERS	15 day	15	eVAERS	Event Serious = Yes Criteria using Advance conditions: Case Listedness = No Any other condition as per your company's business process
United States	Marketed Vaccine	CBER_VAERS	Periodic	60	eVAERS	Case Serious = No OR Case Serious = Yes Criteria using Advance conditions: Case Listedness = Yes Any other condition as per your company's business process
United States	Marketed Vaccine	CBER_VAERS	5-day	5	eVAERS	Criteria using Advance conditions. • Remedial Action exists • Case Classification = Combination Product Any other condition as per your company's business process

Country	License Type	Agency	Rule Name	Time Frame	Report Form	Condition
United States	Marketed Vaccine	CBER_VAERS	30-day	30	eVAERS	Case Serious = No Criteria using Advance conditions: • Case Classification = Combination Product • Malfunction = Yes Any other condition as per your company's business process
World	Marketed Vaccine	CBER_VAERS	30-day	30	eVAERS	Case Serious = No Criteria using Advance conditions • Classification= Combination • Product Malfunction=Yes • Product type=Treatment • Drug not administered= Yes • Similar Device=Yes Any other condition as per your company's business process

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Configure Combination Product in Flexible Re-categorization Codelists

Flexible re-categorization codelist is enhanced to include a new COMBO_PRODUCT_RELATIONSHIP codelist for maintaining list of Combination Products that are marketed in United States.

1. Click **Codelists** > **Flexible Data re-categorization** > **Flexible re-categorization** > **COMBO_PRODUCT_RELATIONSHIP**.
2. Use the **Add New** button to enter the information for the Combination products.

> **Note:**
>
> Flexible re-categorization codelist does not validate the correctness of the Product Name, License name and Country of authorization, it is required to enter the below information by copying respective data from the Product and License configuration screen.

Column Name	Data Length	Comments
PMOA_PROD_NAME	250	Enter the Primary mode of action product's Product Name (not Trade Name) as Configured in Business Configuration > Product a and Licenses
PMOA_LIC_NUMBER	40	Enter the Primary mode of action product's License number
PMOA_COUNTRY	50	Enter the Primary mode of action product's Authorization Country
CONS_PROD_NAME	250	Enter the Constituent Product's Product Name (not Trade Name) as Configured in Business Configuration > Product a and Licenses
CONS_LIC_NUMBER	40	Enter the Constituent Product's License number
CONS_COUNTRY	50	Enter the Constituent Product's Authorization Country

3. Click on the ✔ icon and then click **Save**.
4. If a Combination Product has multiple Device Constituent Products, then add additional records with the same data for PMOA related fields along with other Constituent Product details.

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Single Entity Combination Product Case Processing

These are the steps for creating/processing cases with Single entity Combination Products:

1. Book-in a Case with information received as per Source documents.

   If the Suspect Product involved is a Combination Product, on product selection from the Product browser, system activates the Vaccine and Device tabs.
2. Enter the Vaccine and Device data in the corresponding tabs.
3. Select **Combination Product** in the **General** > **Case Classification** field.
4. Save the case and ensure that all mandatory data required for the CBER submission is entered.
5. Perform Auto-scheduling and the system schedules an eVAERS report to the CBER agency using the eVAERS Profile.
6. Click the **Draft** link to preview the report in XML view.

The <combinationproductreport> element is populated with the true value indicating ICSR contains Combination Product.
The <localcriteriareportype> element is populated with one of these values below indicating the report type:

- 1 = 15-day
- 2 = Non-Expedited
- 4 = 5-day
- 5 = Malfunction Only (No AE)

The Device data is embedded within the <drug> block pertaining to the Primary mode of action product as below:

```
<drug>
<drugcharacterization>1</drugcharacterization>
<medicinalproduct>Tetanus</medicinalproduct>
<obtaindrugcountry>US</obtaindrugcountry>
<deviceinfo>
<malfunction>true</malfunction>
<brandname>Tetanus</brandname>
<commondevicename>Piston Syringe </commondevicename>
<typeoffollowup>
<followuptype>1</followuptype>
</typeoffollowup>
<deviceproblem>
<deviceproblemcode>1095</deviceproblemcode>
</deviceproblem>
<manufacturer>
<manufacturername>Aster Inc</manufacturername>
<manufacturercity>Bridgewater</manufacturercity>
```

```
<manufacturerstate>NJ</manufacturerstate>
<manufacturercountry>US</manufacturercountry>
</manufacturer>
<remedialaction>
<remedialactioninitiated>5</remedialactioninitiated>
</remedialaction>
</deviceinfo>
</drug>
```

8

Similar Device Case Processing (Single Entity Combination Products)

The following stept are required to create and process cases that have a Non-US marketed device which involves reportable malfunction with similar devices that are marketed in the US. These devices are part of Single entity Combination Product.

1. Book-in a Case with information received as per Source documents.
2. If the Suspect Device had caused a reportable malfunction, then check for the Product Portfolio for Similar devices marketed in US as Combination Product.
3. If a US Marketed similar device product, that is part of Single entity combination product already exists, add the Product from the Product browser and enter the following data in the **Vaccine** tab:
   a. **Product type = Treatment**
   b. **Drug not administered =Ticked**
4. Enter the following data in the **Device** tab:
   a. **Similar Device= Ticked**
   b. **Malfunction = Yes**
   c. Specify the Device problem information by selecting appropriate FDA codes using the lookup.
5. Select **Combination Product** in the General Tab > Case Classification field.
6. Save the case and ensure all the mandatory data is entered that is required for CBER submission.
7. Perform Auto-scheduling and system schedules for an eVAERS report for the suspected vaccine which caused malfunction to the CBER agency.
8. Click the **Draft** link to preview the report in XML view:
   a. The element `<fulfillexpeditedcriteria>` is populated with value false indicating Non-expedited report.
   b. The element `<localcriteriareporttype>` is populated with the value 5 indicating ICSR is a Malfunction.
   c. The element `<drugcharacterization>` is populated with value 4 indicating that the drug was not administered.
   d. The element `<otherdrugcharacterization>` is populated with value 1 indicating Similar Device.
9. The Similar Device data is populated in the XML view of ICSR viewer as shown in the example below.

```
<drug>
          <drugcharacterization>4</
drugcharacterization>
          <otherdrugcharacterization>1</
```

```
otherdrugcharacterization>
          <medicinalproduct>BCG-Vaccine</medicinalproduct>
       <deviceinfo>
          <malfunction>true</malfunction>
          <brandname>BCG-Vaccine Needle</
brandname>
          <commondevicename>Needle</commondevicename>
       </deviceinfo>
</drug>
```

9

Configure Single Entity Combination Products

A product comprised of two or more regulated components (e.g. drug/device, biologic/device, drug/biologic, or drug/device/biologic) that are physically, chemically, or otherwise combined and produced as a single entity is known as a Single Entity Combination Product.
The Tetanus Pen is one of example for single entity combination product, as the product comprises of Tetanus (vaccine) and an injector pen (device).

In Oracle Argus Safety, vaccine and device components can be within the same product to configure Single Entity Combination Products. Follow these steps to configure Single Entity Combination Products:

1. Click **Business Configuration** > **Products and Licenses** > **Add New Family**.
2. Enter required mandatory data and save the family.
3. Click **Add New Product**.
4. Enter required mandatory data and save the Product.
5. Create a Primary mode of action product license by clicking **Add New License**.
6. Enter the required mandatory data for creating a Vaccine license as below, and save the license:
    a. Authorization country = UNITED STATES
    b. License Type = Marketed Vaccine
    c. License Number can be entered in either of the following ways:
        i. License # = BLA<License number>
        ii. Application type = BLA
        iii. License # = <License number>
7. Create a Constituent Device License by clicking **Add New License**.
8. Enter required mandatory data for creating a vaccine license as below, and save the License:
    a. Authorization country = UNITED STATES or WORLD
    b. License Type = Marketed Device
    c. License # = <License number>

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Co-packaged Combination Product Case Processing

Use the following steps for creating/processing cases with Co-packaged Combination Products:

1. Book-in a Case with information received as per Source documents.
2. Enter the text of the second step here.
3. If the Suspect Product involved is a Combination Product, ensure the Primary mode of action (PMOA) product is selected first using product browser, and the vaccine data is entered.
4. Add the Constituent Device Product using Product browser.
5. Enter Device data in the **Constituent Product**.
6. Select **Combination Product** in the **General** > **Case Classification** field.
7. Save the case and ensure all the mandatory data required for the CBER submission is entered.
8. Perform Auto-scheduling and system schedules an eVAERS report for the PMOA Product to CBER_VAERS agency.
9. Click the **Draft** link to preview the report in the XML view.

> **Note:**
>
> The element <combinationproductreport> is populated with the true value indicating ICSR contains Combination Product.

> **Note:**
>
> The Device data is embedded within the <drug> block pertaining to the Primary mode of action product as in the example provided in the Single Entity Combination Product section.

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Similar Device Case Processing (Co-Packaged Combination Products)

The following steps are required to create and process cases that have a Non-US marketed device which involves reportable malfunction with similar devices that are marketed in the US. These devices are part of Co-packaged Combination Product.

1. Book-in a Case with information received as per Source documents.
2. If the Suspect Device had caused a reportable malfunction, then check for the Product Portfolio for Similar devices marketed in US as Combination Product.
3. If a US Marketed similar device product, that is part of Single entity combination product already exists, add the PMOA Product from the **Product** browser and enter the following data:
    a. **Product type = Treatment**
    b. **Drug not administered =Ticked**
4. Add the **Constituent Device Product** from **Product** browser and enter the following data:
    a. **Product type = Treatment**
    b. **Drug not administered =Ticked**
    c. **Similar Device= Ticked**
    d. **Malfunction = Yes**
    e. Specify the Device problem information by selecting appropriate FDA codes using the lookup.
5. Select **Combination Product** in the General Tab > Case Classification field.
6. Save the case and ensure all the mandatory data is entered that is required for CBER submission.
7. Perform Auto-scheduling and system schedules for an eVAERS report for the suspected vaccine which caused malfunction to the CBER agency.
8. Click the **Draft** link to preview the report in XML view:
    a. The element `<fulfillexpeditedcriteria>` is populated with value false indicating Non-expedited report.
    b. The element `<localcriteriareporttype>` is populated with the value 5 indicating ICSR is a Malfunction.
    c. The element `<combinationproductreport>` is populated with value 5 indicating ICSR contains Combination Product.
    d. The element `<drugcharacterization>` is populated with value 4 indicating that the drug was not administered.
    e. The element `<otherdrugcharacterization>` is populated with value 1 indicating Similar Device.

9. The Similar Device data is populated in the XMLview of ICSR viewer as shown in the example below:

```
<drug>
          <drugcharacterization>4</
drugcharacterization>
          <otherdrugcharacterization>1</
otherdrugcharacterization>
          <medicinalproduct>TETANUS</medicinalproduct>
       <deviceinfo>
          <malfunction>true</malfunction>
          <brandname>SYRINGE</brandname>
          <commondevicename>Syringe Piston</commondevicename>
       </deviceinfo>
</drug>
```

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Other Considerations

For submitting a Malfunction Only (No AE) report to CBER, these are the data entry recommendations:

1. Patient tab:
   - No data required to be entered in the Patient Information, Patient Details, Race Information, Other Relevant History sections. Export mappings populates most of the Patient elements as None, as per regulations.
   - Click on the **Patient Notes** icon in the Patient Information section, either enter the text None in the text area or select any Null flavor using the NF button.
2. Product Tab: Set the **Malfunction** field to **Yes** and select one or more Device Problem codes in the **Device** tab of the Constituent Device Product.
3. Event tab:
   - Enter **No Adverse Event as Reported** term to get the properly coded corresponding MedDRA term.
   - Set **Null Flavor NASK** for the following fields:
     - Onset date/time
     - Stop date/time
   - Outcome of Event: Unknown
4. Analysis tab:
   - Case Serious is set to No.

13 FAQ

What type of product configuration is recommended for Combination Products?

If the PMOA Product is a single device constituent, then the product can be configured as per the steps suggested in the single entity combination products.

However, if there is a requirement to perform assessment of vaccine and devices separately in the case then it is recommended to configure the PMOA and device constituents under different products.

If the PMOA Product has a multiple device constituents, then the product can be configured as per steps suggested in the co-packaged combination products.

In the flexible COMBO_PRODUCT_RELATI ONSHIP codelist, is it required to enter Product Name or Trade Name for PMOA and Constituent Products?

It is required to specify the Product Name and not the Trade Name.

Does the Combination Product solution provided byOracle Argus Safety allow configuration of Combination Product that comprises for multiple device constituents?

Yes, if the Combination Product comprises of multiple device constituents, then it is required to create separate entries for each of the device constituent in COMBO_PRODUCT_RELATI ONSHIP codelist with the same PMOA Product.

For which type of Combination Products is the flexible codelist configuration required?

You can use the flexible re-categorization codelist to specify combination products that belong to the following categories:

- Company Drug / Biologic (PMOA Product) and Company Device (Constituent Product)
- Company Vaccine (PMOA Product) and Company Device (Constituent Product)

If the Device is a PMOA Product, is it required to configure the combination products in the flexible codelist?

For the products having device as a PMOA Product, eMDRs must be submitted. eMDRs do not require configuration of flexible recategorization codelists for combination products, as eMDR does not embed the constituent product data within the PMOA product block.

Is MAH required to report cases that contain combination products that include a non-company product as PMOA?

MAH is not required to report to the FDA on cases that contain combination products that include a non-company product as PMOA.

Do the entries populated in the CASE_PMOA_CONS_RELATI ON table for a case get copied on performing Case Copy?

No, Case Copy does not copy the data from the CASE_PMOA_CONS_RELATI ON table. The data present in this table is neither printed in Case Form Print, nor is it audit logged.

If a Case having drug and device data was submitted as eVAERS to FDA in prior versions of Oracle Argus Safety and now if there is a follow-up data is received and requires to be processed as Combination Product, what needs to be done from the data entry perspective?

Follow these steps to ensure the case is treated as Combination Product ICSR:

- Case Classification needs to be set to Combination Product.
- Ensure that the appropriate device information is entered for the device constituents.
- Generate the eVAERS report draft to the CBER_VAERS agency to check if case qualifies to be Combination Product Case.

If a PMOA Product has multiple device constituents associated, is it required to enter all the device constituents in the case in order to recognize the product as Combination Product?

If the case has PMOA Product along with at least one device constituent present, then it is considered as a Combination Product. The system does not expect all device constituents to be entered in the case.

If a foreign case (Non-US) has a combination product having equivalent US licensed combination products, will the system be able to determine that the case qualifies for combination product reporting in US?

Yes, the system evaluates the products within the case and compares all licenses associated with the product with the entries in the flexible codelist and determines if it is a combination product or not.