Oracle® Argus Safety

BIP Aggregate Reporting User's Guide

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Oracle Argus Safety BIP Aggregate Reporting User's Guide, Release 8.1.1

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Preface

This guide provides documentation on the BI Publisher-based aggregate reporting solution for Argus Safety.

Where to Find More Information

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1 Introduction

This guide is for Argus Safety users who would like to print reports using the BI Publisher. The flexible output format of Argus Safety BI Publisher aggregate reports lets users customize the output format to suit their regulatory interpretations and business needs.

This guide contains the following chapters:

Table 1–1 Components of the Extensibility Guide

Chapter Name	Description
Chapter 1, "Introduction"	Provides a basic overview about the topics that have been covered in this guide.
Chapter 2, "BI Publisher and the Argus Safety Application"	Describes the updates made to the Argus Safety application to support BI Publisher aggregate reports.
Chapter 3, "Aggregate Reporting Data Model"	Describes the Aggregate Reporting Data Model.
Chapter 4, "Reporting Algorithms"	Documents reporting algorithms.
Chapter 5, "Argus Insight Compatibility"	Describes Argus Insight compatibility with the BIP reporting framework.
Chapter 6, "Periodic Benefit Risk Assessment Report"	Details the Periodic Benefit Risk Assessment Report.
Chapter 7, "Development Safety Update Report"	Details the Development Safety Update Report.
Chapter 8, "Post Marketed Aggregate Report"	Details the Post Marketed Aggregate Report.

2

BI Publisher and the Argus Safety Application

This chapter contains the following topics:

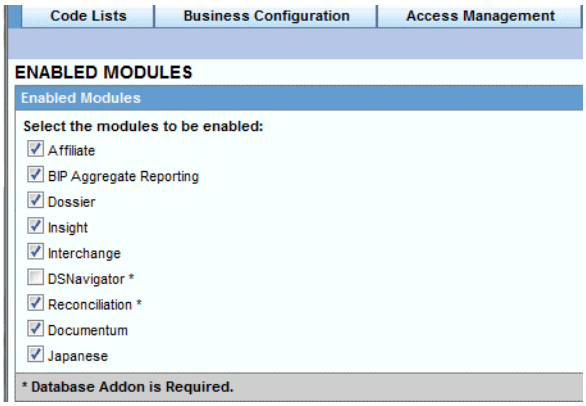
2.1 Enabling BI Publisher Aggregate Reporting

Perform the following steps to enable BI Publisher aggregate reporting:

1. When you log into Argus Safety, click the **Argus Console** tab.
2. Click **System Configuration** on the screen that appears.
3. Click **Enabled Modules**. The Enabled Modules screen appears.
4. Select the checkbox corresponding to BIP Aggregate Reporting to enable Publisher aggregate reporting.

Note: This checkbox is not selected by default. You must enable it.

Figure 2–1 Enabled Modules Screen



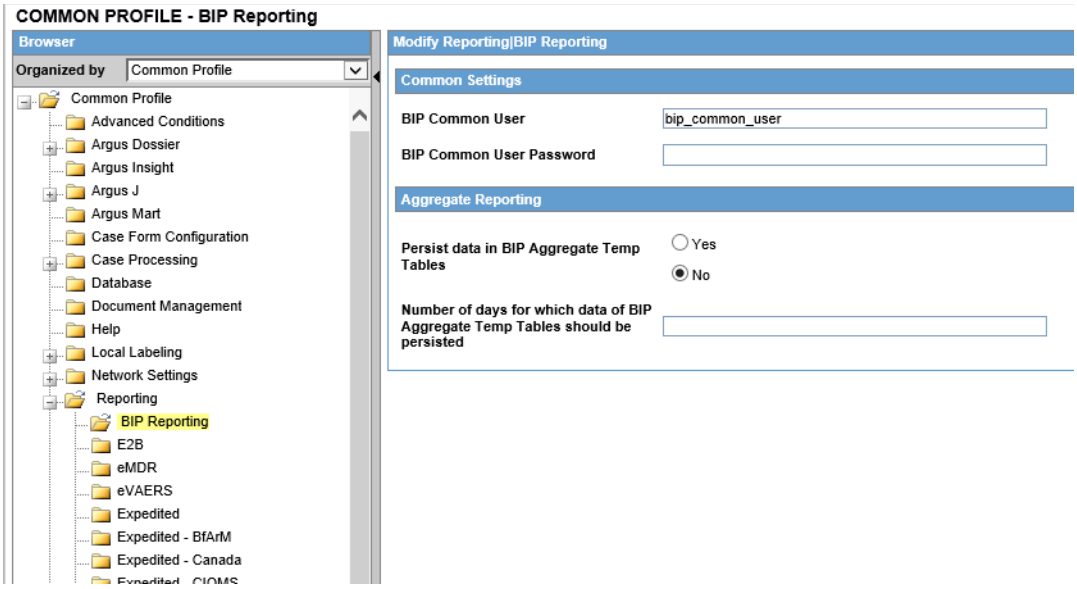
5. Click **Save**.

2.2 Configuring the Argus BIP Integration

Perform the following steps to store your BIP common user and BIP common user password:

1. Under the **System Configuration** tab, click **System Management (Common Profile Switches)**.
2. Under the **Reporting** tree entry, click **BIP Reporting**.

Figure 2–2 BIP Reporting Screen



3. Enter the respective values in the following fields:
   a. BIP Common User
   b. BIP Common User Password

> **Note:** These configuration entries are available at enterprise level in a multi-tenant environment.
>
> You can view the BI Aggregate Reporting tree entry only when you enable the BIP Aggregate Reporting module.

2.3 Report Execution Flow from BI Publisher and Argus Safety

You can execute reports from either Argus Safety or BI Publisher. This section describes the report execution flow from each.

2.3.1 Report Execution Flow from Argus Safety

To execute a report using the Argus Safety user interface:

1. Select a report configuration from Argus Safety Aggregate Reports library.
2. Click **Print** and select the required parameter from the batch print screen.

The report executes as follows. The system:

- Adds an entry into Argus database for status tracking.

- Generates and stores the various case series.
- Sends the request to the BI Publisher server.
- Populates the temp tables based on selected report parameters.
- Before temp tables are populated, verifies the user exits, and updates the temp table data.
- Generates the report output.
- Stores the report output in the Argus Safety database.
- Adds an entry into common regulatory reports table along with a link of the report output.
- Updates the status in Argus database and mark the report as generated.

You can view the report output from Argus Safety.

2.3.2 Report Execution Flow from BI Publisher

To execute a report using the BI Publisher:

1. Select a report template.
2. Select different parameters available in the report or select a report configuration.

If report is scheduled using **BIP**, the system:

- Adds an entry into Argus database for status tracking (executing).
- Assesses report parameters to make any changes in report execution.
- Populates the temp tables based on selected report parameters and case series.
- Before completion of temp tables population, verifies the user exits, and updates the temp table data.
- Generates the report output.
- Stores the report output in Argus database.
- Adds an entry into the common regulatory reports table.
- Updates the status tracking in Argus database to mark the report as generated.

You can view the report outputs from Argus Safety. Final report outputs are available on the Worklist -> Reports screen for submission.

If report is executed using the **BIP Console**, the system:

- Assesses the report parameters to make any changes in report execution.
- Populates temp tables based on selected report parameters.
- Before completion of temp tables population, verifies the user exits, and updates the temp table data.
- Generates the report output.

You can view the report output on the user's browser.

2.4 Periodic Configuration Identification of BIP Parameters

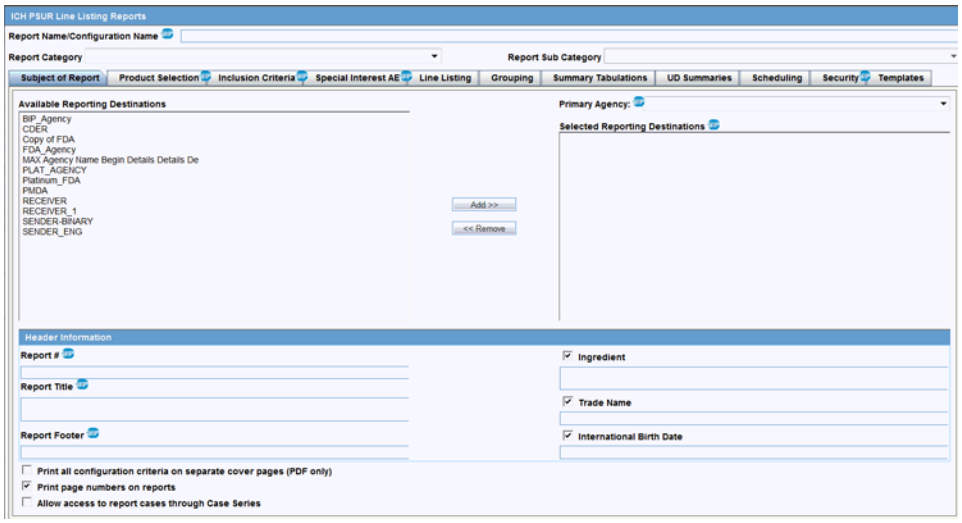
If the report is executed using the Argus Safety user interface:

The ICH PSUR Configuration screen lets you distinguish the configuration options used as parameters in the BIP report only if you have enabled the BI Aggregate Reporting module.

The system marks all configuration parameters passed to BIP reports for data filtering and report formatting with a BIP logo.

The system uses all inclusion criteria available on the ICH configuration screen for query and case series generation in BIP reports.

Figure 2–3 ICH PSUR Configuration Screen



The following configurations are used as report parameters in BIP reports from the ICH PSUR Configuration tab:

2.4.1 Subject of Report Tab

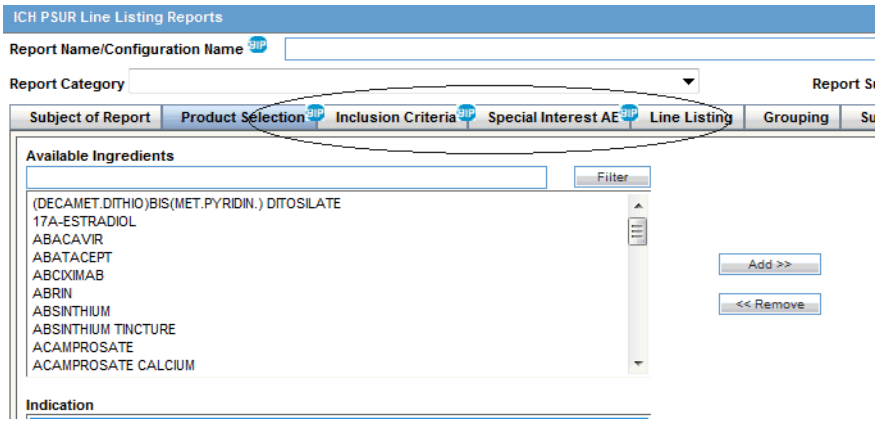
The system uses the following parameters from the **Subject of Report** tab:

- **Report Name/Configuration Name** populates other report parameters from the saved configuration.
- **Report#**, **Report Title**, and **Report Footer**
- **Selected Reporting Destination** and **Primary Agency**.

2.4.2 Product Selection Tab

The system uses all configurations on this tab as query criteria for BI Publisher reports. The BIP logo on the Product Selection tab indicates this.

Figure 2–4 BIP Logo



2.4.3 Inclusion Criteria and Special Interest AE Tabs

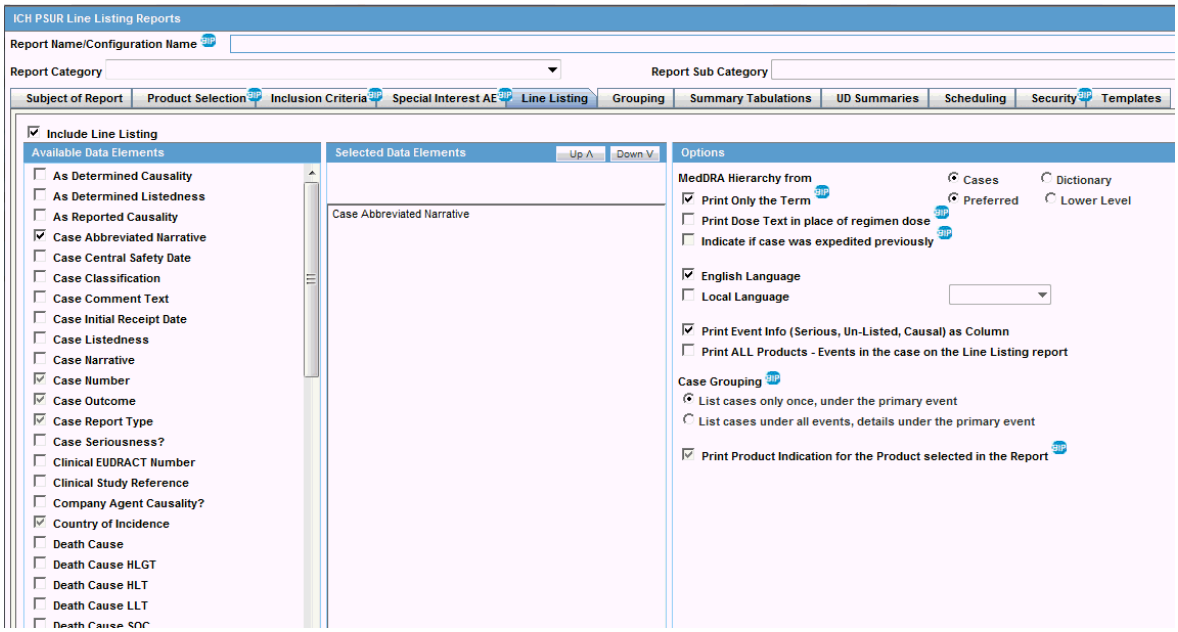
The system uses all configurations on these tabs as query criteria for the Post Marketed Aggregate Report. The BIP logo on these tabs indicates this.

2.4.4 Line Listing Tab

The system uses the following Line Listing tab parameters:

- **Print Only the Term**: Prints event verbatim along with PT or LLT if you uncheck this configuration.
- **Print Dose Text in place of regimen dose**
- **Indicate if case was expedited previously**
- **Case Grouping**
- **Print Product Indication for the Product selected in the Report**.

Figure 2–5 Line Listing Tab



2.4.5 Summary Tabulations Tab

The system uses the following parameters from the **Summary Tabulations** tab:

- **Include Summary of Cases Missing Assessments**
- **Include Summary of Unlocked Cases**
- **Include Section 6.2**: Includes Section 6.2 in the report. Excludes other query criteria under Section 6.2.
- **Include Section 6.3**: Includes Section 6.3 in the report. From the other query criteria available under Section 6.3, the system uses only **Case Classification** and **Observe Study Type** for identifying the non-interventional studies.
- The **Cumulative Start Date**.

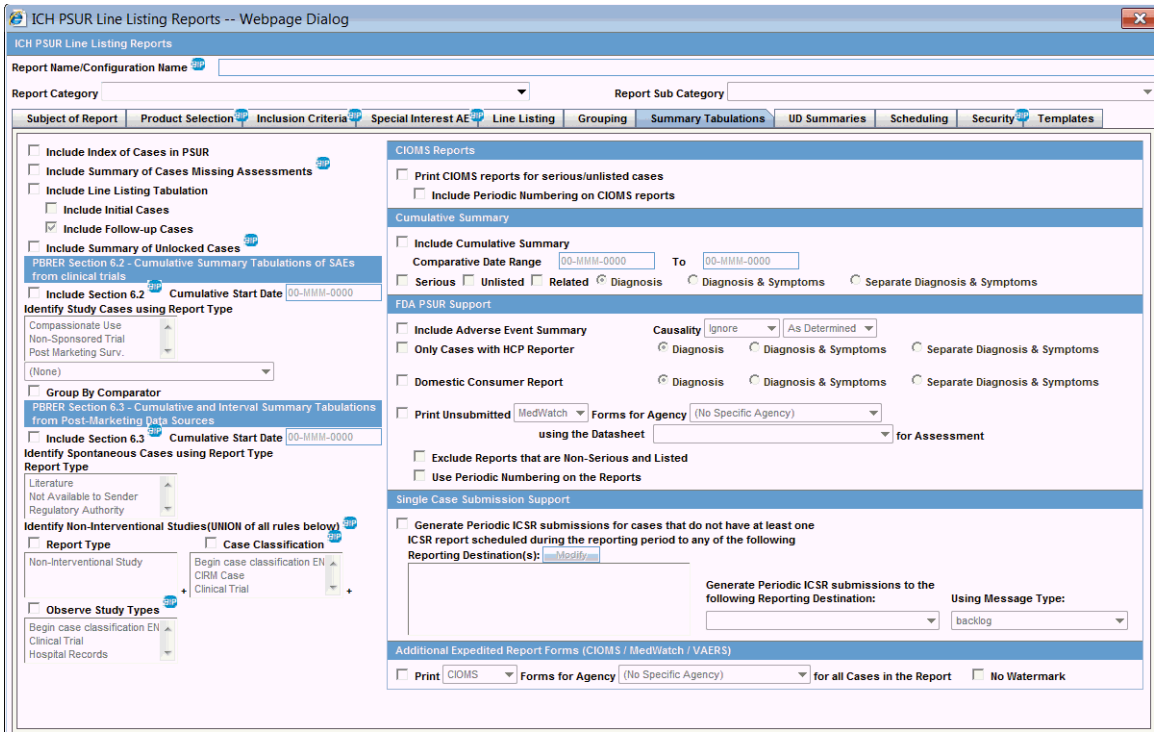
When you select report types in the Main Inclusion Criteria tab, the system automatically selects the same clinical trial report types in the Identify Study Cases using Report Type configuration of PBRER Section 6.2.

This auto selection ensures you can save the configuration without manually selecting any values in Section 6.2. Argus Native report users can deselect any report type if you do not want to use all the selected report types for Section 6.2 case series.

When you select the report types in main inclusion criteria tab, the system automatically selects the same spontaneous report types in Identify Spontaneous Cases using a Report Type configuration of PBRER Section 6.3.

This auto section ensures you can save the configuration without manually selecting any values in Section 6.3. An Argus Native reports user can deselect any report type if you do not want to use all the selected report types for Section 6.3 case series.

Figure 2–6 Summary Tabulations Tab



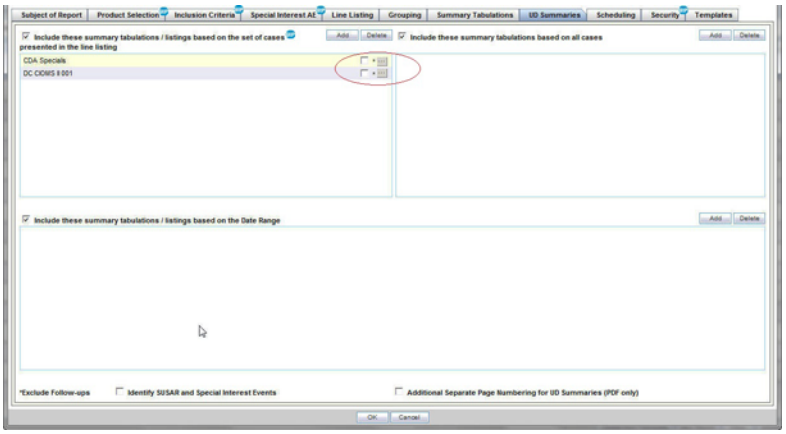
2.4.6 UD Summaries Tab

The system only uses **Include these summary tabulations/listings based on the set of cases presented in the line listing** from this tab.

This configuration is modified, and you have an option to attach selected line listings (memorized line listings) with different ad hoc line listing sections present in the BIP report. A button is provided with each memorized line listing to support this.

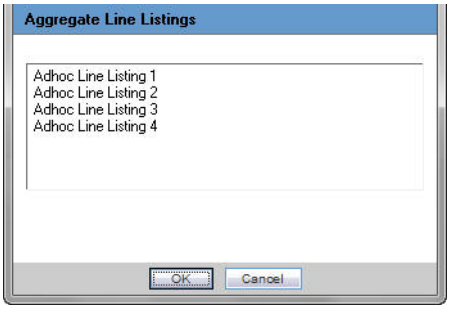
The system does not generate memorized reports for selected configurations along with the aggregate report. It only uses the advanced condition query criteria for generating the case series for these ad hoc line listing sections. Figure 2-7 displays an example of case data line listing query criteria used for ad hoc line listings.

Figure 2–7 Data Line Listing Criteria for Ad hoc Line Listings



When you select the corresponding checkbox, the available ad hoc line listing sections appear in the Aggregate Line Listings dialog box. These are configurable through the Argus Console code list or flex bucketing.

Figure 2–8 Ad hoc Line Listings Screen



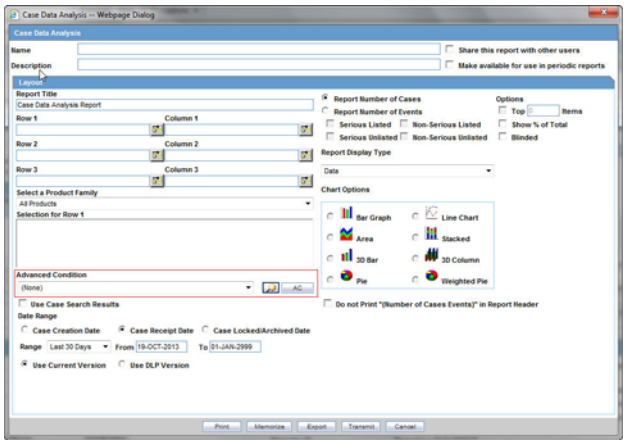
You can associate multiple ad hoc line listing sections with one memorized line listing configuration.

Argus Safety marks the memorized line listing configurations with associated ad hoc line listings with an asterisk. When you hover over the selected memorized line listing configuration, all associated ad hoc line listings appear as a tool tip.

You can attach each ad hoc line listing section to only one memorized line listing configuration. You cannot select ad hoc line listing sections already attached to another memorized line listing configuration.

Figure 2-9 displays an example of query criteria used from the configuration of memorized line listings.

Figure 2–9 Query Criteria from Memorized Configuration



2.4.7 Security Tab

The Security tab shares report configurations with other groups. All case series generated using an aggregate report configuration have the same access privileges as the aggregate report configuration.

> **Note:** The **Scheduling** and **Templates** configurations tabs are not used in BIP reports.

2.5 Generating and Modifying a Case Series

This section documents the process after a periodic report is executed. It also describes the process of creating a case series for analysis and modifying it before use.

The BIP based aggregate report generation process has two parts:

1. Creating the configuration.
2. Running the report within the BIP with that configuration.

All case series can be saved separately (as Argus *hitlists*) for further analysis, addition, or removal of cases. You can also execute the whole process of query criteria execution and report output generation in one step. The native aggregate report generation process is broken into two parts with a provision to review and update all case series.

2.5.1 Generating a Case Series

The **Create Case Series** button on the ICH PSUR and CTPR reports library page is enabled when you select any saved report configuration only if you have enabled the BIP Aggregate Reporting module.

When you click this button, the system generates the following case series by using query criteria available in the selected report configuration:

- **Main Case Series**: This case series is available in the advanced conditions library with the default name Periodic Report Name/Configuration Name and is linked to the respective report configuration.
- **Cumulative Case Series** (for use in tabulations): Based on international birth date of the drug, this case series is available in the advanced condition library with the

default name *Periodic Report Name/Configuration Name (cumulative case series)* and is linked to the respective report configuration.

- **Ad hoc Case Series:** You must ensure that the ad hoc line listings are linked to their respective report configuration. Ad hoc Case Series 1 is used in ad hoc Line Listing 1, ad hoc Case Series 2 in ad hoc Line Listing 2, and so on. You can edit these case series in the advanced condition library.
- **Section 6.2 PBRER Case Series**: When you select Section 6.2 on the ICH PSUR Configuration screen, the system generates an additional case series for Section 6.2 clinical trial cases. This contains all clinical trial cases for the configured product, leaving out any non-interventional study cases (based on report type selection and Section 6.3 case classifications and observer study type configuration).

  This case series is available in the Advanced Conditions Library as a case series with the default name Periodic Report Name/Configuration Name (PBRER Section 6.2) and is linked to the respective report configuration. It is further classified into different categories in the temp tables. There is no additional case series required for Section 6.3. The Main and Cumulative case series generated based on report configuration are classified into different categories in the temp tables.

Note: Case series are associated with a report configuration. At any time, there cannot be more than one case series of each type associated with a report configuration.

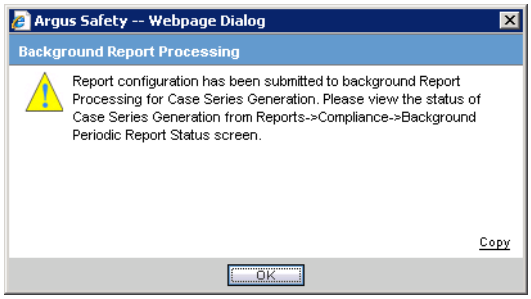
The owner of all aggregate case series is the user creating that case series.

If a case series already exists for a report configuration, the system overwrites the existing case series.

A case series is saved in the system even if there are no cases present in it.

The following message appears after the request for case series generation is pushed to the Argus Safety application when you click **Create Case Series**.

Figure 2–10 Message Displayed



All case series associated with a report configuration are deleted if the associated report configuration is deleted from the system.

2.5.2 Modifying a Case Series

All case series generated using periodic reports configuration are available in the Advanced Condition Library. You can modify these case series by providing a proper justification before the case series are used for report generation.

You can modify a case in the Advanced Condition Library.

2.5.3 Advanced Condition Library

You can view all case series that have been generated in the Advanced Condition Library.

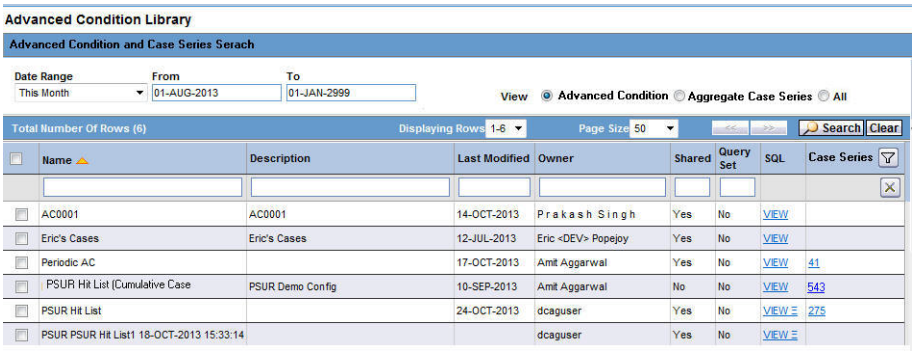
The Advanced Conditions and Case Series Search title bar displays the search options added on this screen.

Table 2–1 Fields and Descriptions

Field	Description
Date Range	An option for searching saved advanced conditions and case series. This date range filters cases based on the last modified date of the Advanced Conditions and Aggregate case series. The system uses the last one year date range by default when the advance condition page is loaded for the first time. The Date Range drop-down list contains the standard date ranges used in other parts of the Argus Safety application.
Advanced Condition Radio button	Clicking this button displays only advanced conditions.
Aggregate Case Series Radio button	Clicking this button displays only aggregate case series.
All Radio button	Clicking this button displays all advanced conditions and aggregate case series.

The Advanced Condition option is selected by default during initial page load.

Figure 2–11 Advanced Condition Library Screen



When you click **Search**, the system filters out the list of Advanced Conditions or Aggregate case series based on the date range selected.

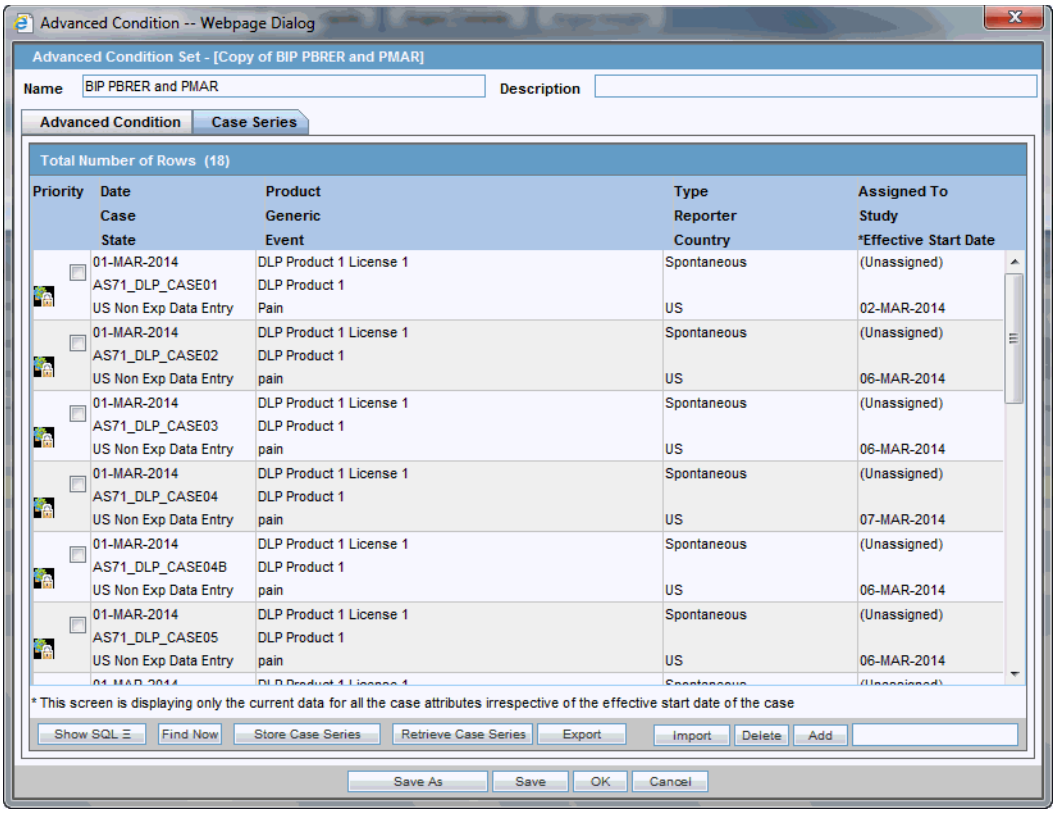
When you click **Case Series**, the Advanced condition dialog box with available cases is displayed.

The **Delete** button on the Advanced Condition Library page is disabled when you select any Aggregate case series.

2.5.4 Deleting a Case Series

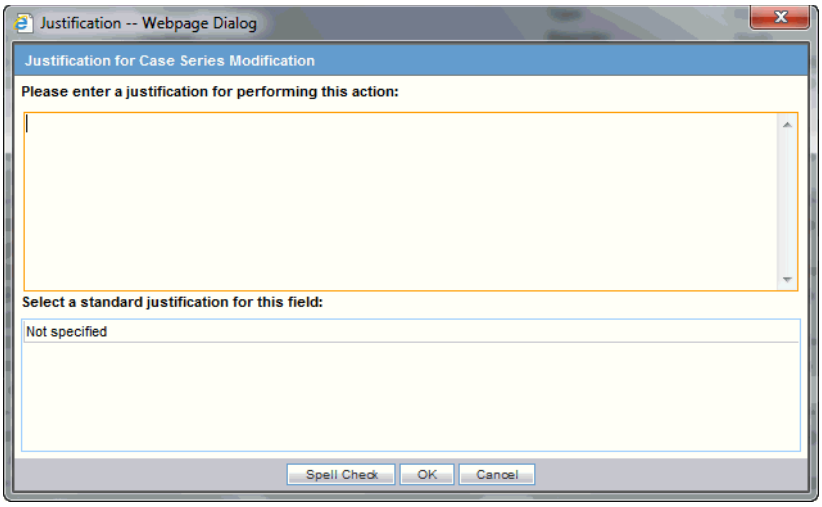
You can delete multiple cases to update the case series. A checkbox corresponding to each case facilitates the deletion of multiple cases.

Figure 2–12 Advanced Condition Set Screen



While you delete or add cases to the case series (single or multiple), the system displays a standard justification dialog requesting the reason for case series modification.

Figure 2–13 Justification Dialog Box



The justification text for case series modification follows the list of case numbers displayed after the report cover page. The system displays all actions performed on a case series separately in the order they were performed. For example, actions performed on a case series are displayed in the following order:

Action Performed: Case Addition

Action Performed By: <User Name>

Justification Text: <These cases were not part of last report submission>

Case Numbers: US2010ABC, US2010XYZ

Date Modified: 12-Oct-2013 12:40:33

Action Performed: Case Deletion

Action Performed By: <User Name> Justification Text: <These cases are already reported to regulatory authorities>

Case Numbers: US2009ABC, US2009XYZ

The Effective Start Date column displays effective start dates corresponding to all cases available in the case series. Values in this column are available only when periodic reports configuration is set to run on the DLP schema instead of current data. The column populates aggregate temporary tables corresponding to a case series during BI Publisher report execution.

Date Modified: 13-Oct-2013 16:22:00

This screen displays only the current data for all available columns, irrespective of whether the case series is being generated on DLP. The system displays an asterisk against the Effective Start Date column and also displays a note as a legend.

This screen displays only the current data for all the case attributes irrespective of the effective start date of the case.

When a case series is being used, you cannot modify it as the system locks the case series. The system disables the **Delete** and **Add** buttons on the advanced conditions case series dialog during the time it is used. It also disbales the **Create Case Series** button on the Periodic Reports page if the case series corresponding to that report configuration is being used.

When a report is being executed, the system disables the Create Case Series for the corresponding report configuration.

When you click the **View** link for an existing case series for selected report configuration, a warning message appears indicating that the case series cannot be modified as it is currently under modification or is being used for a report.

2.6 Running BIP Reports through Argus Safety

You can execute BIP periodic reports as a one-step or two-step process. The Report Batch Print screen provides this option.

The screen provides the following options if you have enabled the BIP Aggregate Reporting module:

- **Run Using**: This drop-down list lets you choose between the BI Publisher and Argus Native options.
- When you select **BI Publisher**, the system provides the following additional options for running the report:

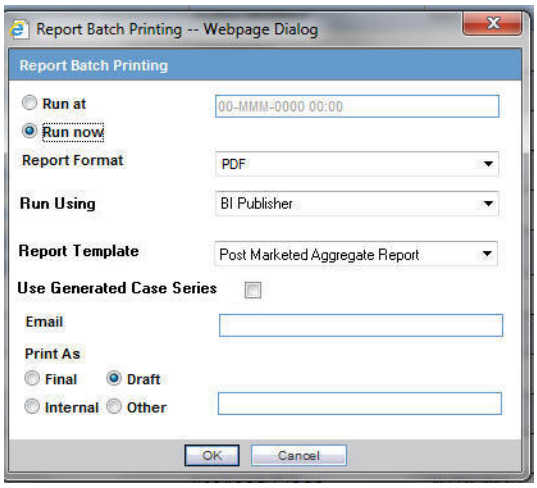
Table 2–2 Options for Running the Report using BI Publisher

Report Template	This drop-down list is populated with all available BIP report templates that can reuse the configuration for the PSUR or other periodic reports.
Use Generated Case Series	This checkbox is enabled only if a case series has been generated using the selected report configuration. It is selected by default if a case series already exists for the selected report configuration. If the Use Generated Case Series checkbox is checked, the system generates the report on already existing case series. The Use Generated Case Series checkbox is checked when a final report that was generated for the selected report configuration is pending submission.

The Print operation works in same way for BIP reports as it works for Argus Native reports.

After a case series is generated for an associated report configuration, any existing case series associated with that report configuration is replaced with that case series. The system keeps only one case series for a report configuration at a time.

Figure 2–14 Report Batch Printing



All reports executed through Argus Safety UI are tracked using the Argus Safety application. The status for all BIP reports is available in the Background Periodic Status screen of Argus Safety.

When you select **Argus Native** from the **Run Using** drop-down list, the system hides the **Report Template** option. Any case series generated as part of Argus Native report execution is not saved in the system by default.

If you select **Run Now**, the system immediately generates a report for the selected configuration. If you specify a date and time in the **Run At** field, Argus Safety schedules it for the provided date and time.

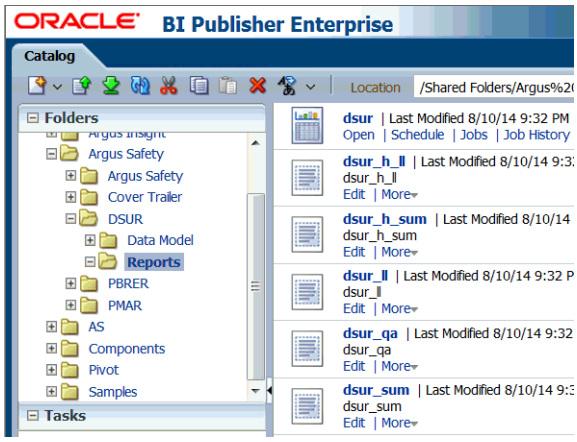
For every BIP report generated from Argus Safety or the BIP scheduler interface, the system adds an entry into the Argus database.

2.7 Running Reports through BIP Console

You can execute all BI publisher reports through the BI Publisher console.

1. When you log into the BI Publisher, click **Catalog**.
2. Select the tree entry for a report, and select **Reports**.

Figure 2–15 Reports Tree Entry Screen



The system displays the available reports on the screen.

3. Click the **Open** link for the report you selected.
4. Select the values for **Enterprise ID** and **Configuration Name** from the drop-down lists.

> **Note:** The Configuration Name drop-down list displays values based on the aggregate reports configuration in Argus Safety to which you have access.
>
> All report configurations that are associated with a report template are available for selection. The system populates any parameters which are NOT associated with Argus report configuration with default values (defined with report parameters).

5. Select the values for all parameters. You can override the default or configured values of all parameters before running a report.

> **Note:** When you select a report configuration, the system uses the parameter values from the selected report configuration if there are no values provided for the corresponding report parameters.

6. You can modify the default case series names associated with a report configuration.

> **Note:** If a report configuration has been executed at least once, all the associated case series values are used by default if there are no overriding values for case series.

7. For overriding case series parameters, you must select all the case series based on their generation source, which is either current data or DLP.

Note: When you select a Main Case Series generated on Current Argus data, the system filters other case series prompts to show only those case series that are generated on current data.

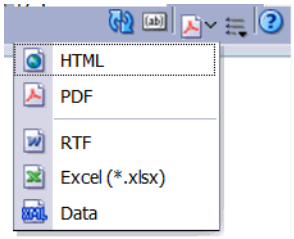
When you select a Main Case Series generated on DLP data, the system filters other case series prompts to show only those case series that are generated on DLP data.

If a report configuration has not been executed even once and you have not selected any overriding case series while running the report, the system executes the report and displays the following information in the *Warning/Error Messages* trailer section of the report.

There is no case series associated with the selected report configuration. Please select a case series or generate a case series and execute the report again.

8. To execute the report, select a report format.

Figure 2–16 Selecting the Report Format

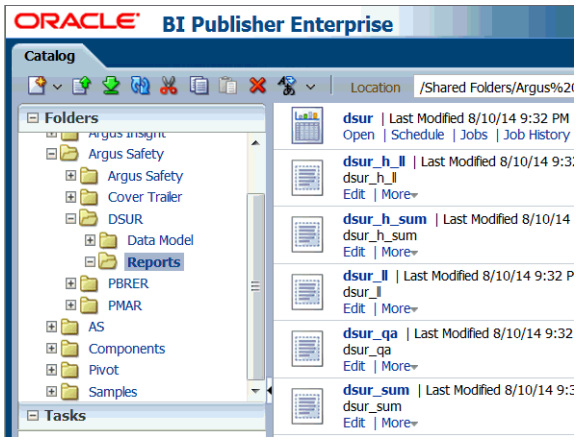


2.8 Running Reports through the BIP Scheduler

You can schedule all BI publisher reports to be run immediately or at a future date using the BI Publisher scheduler.

1. When you log into the BI Publisher, click **Catalog**.
2. Select the tree entry for a report, and select **Reports**.

Figure 2–17 Reports Tree Entry Screen



The system displays the available reports on the screen.

3. Click the **Schedule** link for the report you selected.

   The Schedule Report Job screen appears.

4. Click the **Schedule** tab.

5. Select a value from the **Frequency** drop-down list.

6. Select **Run Now** or enter the date and time details when you select **Start**. Click **Submit**. The Submit screen appears.

7. Enter the details for **Report Job Name** and click **OK**.

You can track reports scheduled through BI Publisher console using Argus Safety.

You can view all report outputs can be viewed from Argus Safety library screens as explained in Section 2.11, "Viewing Aggregate Reports from Argus Safety". The status of all such reports is available in the background periodic status screen of Argus Safety.

For draft reports, you can view only the last version of the generated report output corresponding to a report template from Argus Safety. For Final reports, you can view only the last version of the generated report output corresponding to a report template from the Argus Safety Aggregate Reports library.

2.9 Data Security

The following securities are applied in out-of-the-box BIP reports:

- Product, Study, or Site security
- Blinded Security
- Enterprise security

2.10 Report Output Management

The system saves all reports generated using BI Publisher technology (Argus or BIP Scheduler) in the Argus Safety database. It saves all BIP reports generated through Argus Safety or the BIP scheduler interface in the Argus database and attaches them to

the associated report configuration. For every report configuration and report template combination, you can only view the latest draft and final reports from Argus Safety.

User access rights for accessing a report for a given report configuration are driven using the permissions defined in the security tab in the periodic reports configuration. Any generated report is available to other users if the user's group has been assigned permission to view the report configuration though the Periodic Configuration screen.

2.11 Viewing Aggregate Reports from Argus Safety

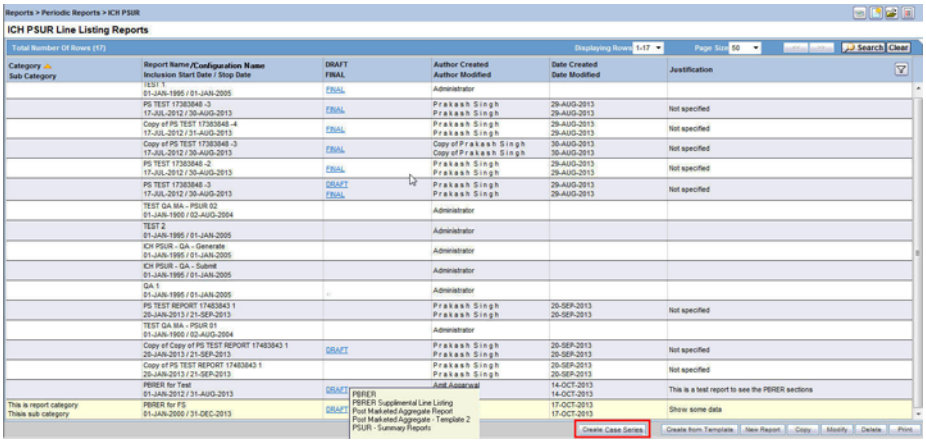
After Draft or Final periodic reports are generated, you can view the generated reports through the Periodic Reports Library screen.

This UI screen shows all reports generated on a report configuration, irrespective of whether the report was generated using Argus Safety UI or BI Publisher scheduler. All reports generated through the BI Publisher console are not available for viewing from Argus Safety.

When you click the **Draft** or **Final** link, a context menu appears with all available report templates that have been generated for a report configuration. When you click a report template, the system opens the selected report in the format that was used to generate the report.

For every report template corresponding to a report configuration, only the last generated draft or final report is available to you.

Figure 2–18 ICH PSUR Line Listing Reports



You can view all BIP aggregate reports generated in final mode on the Worklist -> Reports screen.

2.12 Background Periodic Report Status

You can view the status for all the BIP periodic reports run through Argus Safety or from BIP Scheduler in the Background Periodic Report Status screen.

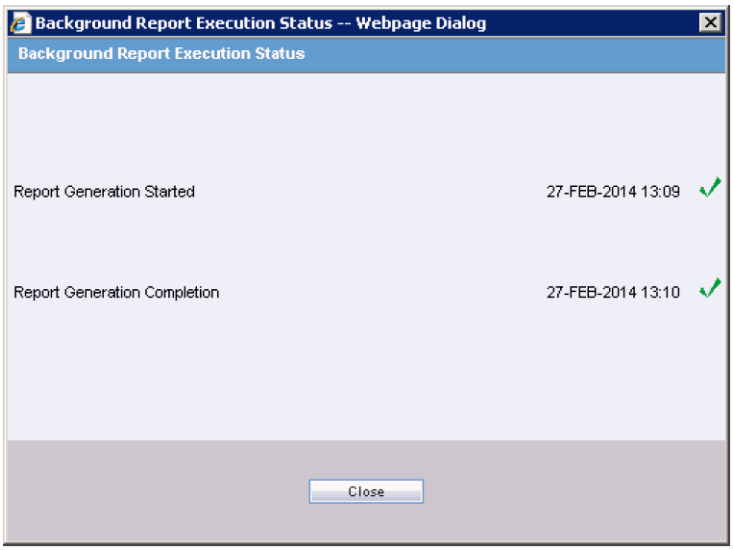
The following are the possible status options for reports scheduled using BIP scheduler:

Table 2–3 Status Options for Reports Scheduled through BIP Scheduler

Status	Description
Executing	When execution for a scheduled BIP report starts, its status is tracked as Executing.
Generated	After a report is generated, the output is stored in the Argus Safety database, and a corresponding entry is made available in Argus database with a report link, the status of the report is marked as Generated.
Error	If an error occurs during the scheduled report execution, the system marks the status of the report as Error.

The system displays the status in the following format when you click the **Generated** link.

Figure 2–19 Background Case Series Execution Status



The following are the possible status options for reports executed using the Argus Safety user interface:

Table 2–4 Status Options for Reports Executed through Argus Safety UI

Status	Description
Pending	When a BIP report is executed from Argus Safety, a corresponding entry is made in the background periodic screen showing the report status as Pending. The report remains in this status until it is picked by AGService or BIP for execution.
Executing	When execution for a BIP report starts, its status is tracked as Executing.
Generated	After a report is generated, the output is stored in the Argus Safety database, and a corresponding entry is made available in Argus database with report link, the status of the report is marked as Generated.
Error	If an error occurs during report execution, the system marks the status of the report as Error.

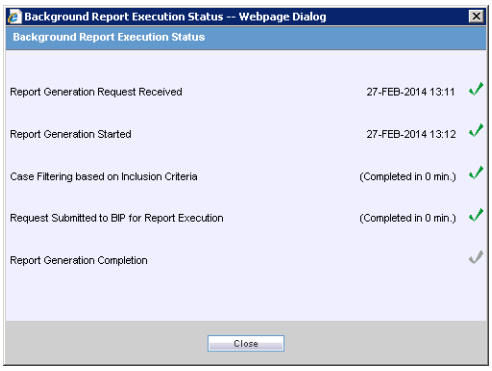
The following are possible status options for a report executed when a user when a user generates a case series by clicking Create Case Series:

Table 2–5 Status Options when User clicks Create Case Series

Status	Description
Pending	When a Case Series is generated from Argus Safety, a corresponding entry is available in the background periodic screen showing the case series status as pending. The case Series remains in this status until it is picked by AGService for execution.
Executing	When execution for a periodic configuration is started for case series creation, its status is tracked as Executing.
Generated	After a case series is generated, the status of background request is marked as Generated.
Error	If an error occurs during case series generation, the system marks the status of the background request as Error.

The system displays the status in the following format when you click on **Generated** link for case series.

Figure 2–20 Report Generation Complete Screen



3

Aggregate Reporting Data Model

This chapter describes the aggregate reporting data model.

3.1 Aggregate Reporting Data Model

The following global temporary tables support the BIP aggregate reporting framework:

- **Case Temp**

  The case temp table contains one row for each unique case ID from all code lists. The system derives data in the same way for all cases. Different flags in the case temp table help to identify the cases that are included in each section or subsection of the various periodic reports.

- **Product Temp**

  The product temp table includes one row for each product configured in the report configuration:

  – The system adds a row to the product temp table for each suspect drug configured in the report configuration (spontaneous or non-company cases).

  – For Clinical cases, the system adds all study drugs that are part of the case into the product temp table.

  – Different flags are available in this table to identify a product as medicinal product, blinded, placebo, or comparator.

- **Event Temp**

  This table contains a row for each event term included in the report. The system uses standard report parameters to remove non-reportable events and symptoms and removes duplicate terms. For example, if the case contains two LLTs for the same PT and you run the report for PT reporting, the system writes only one row to the events temp table. Unless otherwise specified, data for the lower display number term is used in the temp table.

- **Event to Drug Temp**

  This is an intersect table between events and drugs. It contains the causality and unexpectedness at event to drug level. This table contains all assessment information based on event and product.

Refer to the *Argus Safety BI Publisher Periodic Reporting Extensibility Guide* for the Aggregate Reporting Data Model.

4

Reporting Algorithms

This chapter contains the following topics:

4.1 Labeling Algorithm

The system calculates listedness (the expectedness of the undesirable effect experienced in an AE) using an option that you choose when running the Periodic Benefit Risk Assessment Report (PBRER) or Development Safety Update Report (DSUR).

The following options are available:

- Use Assessment in cases from Event Assess table
- Use Assessment in cases from the Event Assess table for the configured License List
- Use Event Assess table with Report type + datasheets
- Re-assess cases against datasheet in effect at the beginning
- Re-assess cases against datasheet in effect at the end

This lets you specify which datasheet to look against for Listedness when running the report.

- When using the Event assessment from the case, the system considers only the *As Determined* listedness of the primary event or the case listedness.
- When you select the *ALL* datasheets Report Type, the system uses the most conservative listedness for the primary event, or the Case Listedness.
- When you select a specific datasheet, the system bases listedness on this datasheet.
- The datasheet for listedness on the Inclusion Criteria is calculated for ALL products within the case and not only for the first suspect drug.

4.1.1 Listedness Determination based on Event Assess Table

When you choose an option that bases listedness on the data in the Event Assess table, listedness is determined as of the time when you run the report.

- **Use Assessment in cases**: Listedness determination is based on the events processed in the Events tab > Event Assessment section of the case form. This means that the system uses the Case Assessment Table to drive the listedness for the periodic report.
- **Use Event Assess Data with License List**: Listedness determination is based on the case event assess table corresponding to the configured license. It ignores others from the case. This option is not available for PBRER and is applicable to DSUR only.

4.1.2 Listedness Determination Based on Event Assess Table and Datasheets

Listedness determination is based on the case event assess table corresponding to the selected report type combined with the datasheet containing the inclusion criteria. The system ignores listedness data for the case in other datasheets.

4.1.3 Listedness Determination based on Datasheets

When you choose an option that bases listedness on datasheets, the date of a datasheet figures in its inclusion in the listedness determination.

- **Re-assess cases against datasheet in effect at beginning**: Listedness determination is based on the earliest datasheet for the product of the PSUR, regardless of the current assessment in the case.

  This option re-assesses all cases in the line listings based on the valid (frozen) datasheets on or before the selected start date of the reporting period.

  – If no datasheet has an active date on or before the start date of the PSUR configuration, an error message appears and the report is not generated.

  – The Report Type selection for **All** datasheets in the Inclusion Criteria overrides the **Re-assess cases against datasheet in effect at beginning** option. When you select All, the system bases listedness on the assessments in cases.

- **Re-assess cases against datasheet in effect at end**: Listedness determination is based on the latest datasheet of the periodic report regardless of the current assessment in the case.

  This option re-assesses all cases in the line listings based on the valid (frozen or active) datasheets on or before the selected end date of the reporting period.

  – If no datasheet has an active date on or before the end date of the PSUR configuration, an error message appears and the report is not generated.

  – The Report Type selection for **All** datasheets in the Inclusion Criteria overrides the **Re-assess cases against datasheet in effect at end** option. When you select All, the system bases listedness on the assessments in cases.

  Note: The system acts on the **Re-assess cases against datasheet in effect at end** or **Re-assess cases against datasheet in effect at the beginning** options only when a specific datasheet is selected. The system does not do a full assessment on all licenses for the product. For example, when you select the **ALL** datasheet option, the system derives the assessment from the cases even if **Re-assess cases against datasheet in effect at end** or **Re-assess cases against datasheet in effect at the beginning** are selected.

4.1.4 Additional Considerations for Determining Listedness

Note the following additional considerations that apply to the determination of listedness for events or cases.

- For the re-assess option, the system does not re-assess case level listedness if the common profile configuration for **Case Inclusion criteria for the ICH PSUR/CTPR report based on Listedness** is set to **Use case level listedness**. However, the system does recalculate event level listedness based on a selected algorithm.
- If the above configuration is set to **Use listedness of the primary event**, the system recalculates case level listedness based on the selected algorithm.
- You must limit a listedness assessment to target products.
- If no datasheet is selected in the inclusion criteria and the re-assess option is based on the datasheets, the system uses the datasheet of all the licenses for the selected product and recalculates the listedness based on the most conservative approach.
- If multiple products are part of the PSUR or CTPR report configuration and these products are also available in a case, the system bases the listedness assessment on the most conservative approach for case level listedness. Consider the following example:
  - Product A and Product B are target products.
  - Both products are available in the case.
  - The case has a primary event of *Pyrexia* and an event of *Fever*.

  For Product A, Pyrexia is a listed event but for Product B, Pyrexia is an unlisted event. The case level listedness is marked as **Unlisted**.

  For event level listedness, the same rules apply when assessing the case for multiple licenses of a product having different datasheets.
- If listedness for a case or event is not listed, it is counted under unlisted. This represents the scenario where event assessment has not been done and is NULL or unknown.

4.2 Choosing a Categorization Algorithm for Compiling PBRER and DSUR

For custom aggregate reports, you can select either of the following case count categorization algorithms:

- The PBRER case count categorization algorithm retrieves cases based on the target drug list.
- The DSUR case count categorization algorithm retrieves cases based on the product type within the study configuration.

The Clinical Drug Role Algorithm report parameter, is available in the PBRER and DSUR template for setting the default algorithm used for OOB reports.

4.3 Initial or Follow-up Algorithm

Aggregate reports generated through the BI Publisher use a different initial or follow-up algorithm from the algorithm for Argus Native reports:

Use the Follow-up Algorithm parameter to select a method for categorizing cases as initial or follow-up in the aggregate reports.

The **Follow-up Algorithm** parameter has the following values:

- Use Submission Tracking: Used as default algorithm for reports executed from Argus Safety UI. This option is selected by default when you run reports from BIP console or BIP scheduler.
- User Initial Receipt Date

4.3.1 Using Submission Tracking

A case is categorized as follow-up if it previously was submitted to the same regulatory agency and report form; otherwise it is categorized as initial. The same logic applies to cases missed in the previous period, and those cases are marked as initial or follow-up based on the submission record:

- Initial: No submission record exists for that case, agency, and report form combination.
- Follow-up: The case has a periodic submission record for the current report form and agency.

4.3.2 Using Initial Receipt Date

A case that is part of the main case series is marked as Initial if the initial receipt date of the case falls in the current reporting period; otherwise it is categorized as follow-up. The same logic applies to cases missed in the previous period, and those cases are assessed for initial receipt date only.

The system uses the existing Argus logic to find cases missed in the previous period. However, to categorize those cases into initial or follow-up, one of two algorithms (Initial of Follow-up) is used.

5

Argus Insight Compatibility

The BIP reporting framework is designed to be compatible with Argus Insight.

- All references to *hitlist* in Argus Safety have been changed to Case Series to keep it in sync with Argus Insight terminology.
- All temporary tables required for data population in the aggregate reports are maintained in a separate schema within the Argus Safety database instance. You can access these tables through the Argus Insight DBLink, with the help of proper database grants and privileges.
- You can use the same BI Publisher server for Argus Safety and Argus Insight reports. For more configuration information required for running both these products on the same BI Publisher server, refer to the *Argus Safety Installation Guide*.
- You can use the same reporting server for Argus Analytics (OBIEE), Argus Safety, and Argus Insight (BIP).

5.1 Configuring Changes for Argus Insight RPD Integration

Argus Insight has introduced an RPD for data analysis of aggregate case series generated using Argus Safety aggregate reports. Argus Insight requires preservation of temp table data so it can be copied into the Argus Insight or Mart database using the ETL process. When aggregate case series data from temp tables is available in the Argus Insight or Mart database, you can use OBIEE RPD to analyze this data using different dimensions and case count measures.

Make the following configuration changes in Argus Console for persisting the BIP temp table data so that the data can be used with OBIEE RPD:

1. Go to System Configuration -> System Management (Common Profile Switches) -> Reporting->BIP Aggregate Reporting.
2. Under the BIP Common User and BIP Common User Password rows, add two common profile entries to the system for defining whether to persist data in BIP temp tables, and the number of days for which data should be persisted in these temp tables.

5.1.1 Common Profile Entries

Profile switches must be added under BIP Common User and BIP Common User Password rows. The following information is available for these profile switches:

Table 5–1 Common Profile Entries

Field Label	Default and Possible Values	Description
Persist data in BIP Aggregate Temp Tables	Default: No Yes No	**Yes**: System persists or stores the data of BIP aggregate temp tables for all the case series generated for aggregate reports generation. **No**: System does not persist data of BIP Aggregate Temp tables.
Number of days for which data of BIP Aggregate Temp Tables should be persisted	Default: NULL Data of BIP Temp tables is persisted for the number of days defined in this configuration. After the configured period (Number of days from the last modified date of case series), a database or system job purges the data that is no longer required (defined separately). You can override the number of days for persisting data of a particular aggregate case series while generating the report through the BIP Console.	-

- If **Persist data in BIP Aggregate Temp Tables** is set to **No**, the system does not persist data of BIP temp tables.
- If **Persist data in BIP Aggregate Temp Tables** is set to **Yes** and **Number of days for which data of BIP Aggregate Temp Tables should be persisted** is not defined, the system throws an error message when you save the value of these configurations. The following message appears:

Please enter the number of days for which data of BIP Temp Tables should be persisted.

- In a multi-tenant environment, you can view these configuration entries on the enterprise level.
- As part of data persistence and purging, two parameters have been added in BIP aggregate reports for overriding the default value. For example, you can choose not to persist data for a draft report run even if the default value is set to persist BIP temp table data. The following parameters have been added in aggregate reports:
  - Persist data of Temp Tables
  - Number of Days for Data Persistence

For more information on these two parameters, refer Appendix A, "Report Parameters and their Definitions".

5.1.2 Data Purging

A data purging is required to remove the data that exceeds the duration specified in the persistence parameters. The purge operation is handled using a database job that is created during the installation of the application.

The data is purged if the current date exceeds report date plus the persistence duration specified while running the report.

After data is purged from the Argus BIP temp tables, the purge is reflected in the Argus Mart database after completion of the ETL process.

6

Periodic Benefit Risk Assessment Report

This chapter contains the following topics:

6.1 Report Objective

The Periodic Benefit Risk Assessment Report (PBRER) is a standard for periodic benefit-risk evaluation reporting on marketed products (including approved drugs that are under further study) among the ICH regions.

When a medicinal product is approved for marketing, demonstration of safety and efficacy are generally based on data from a limited number of patients, with many studied under the controlled conditions of randomized trials. Higher risk subgroups and patients with concomitant illnesses that require use of other drugs are often excluded from clinical trials, and long-term treatment data is limited. Moreover, patients in trials are closely monitored for evidence of adverse events.

In clinical practice, monitoring is less intensive, a broader range of patients are treated (age, co-morbidities, drugs, genetic abnormalities, and so on), and events too rare to occur in clinical trials (such as severe liver injury) may be observed. These factors underlie the need for continuing analysis of relevant safety, efficacy, and effectiveness information throughout the lifecycle of a medicinal product promptly and periodically, for an overall assessment of the accumulating data.

The PSUR provides a comprehensive picture of the safety of approved medicinal products, as the assessment of the risk of a medicinal product is most meaningful when considered in light of its benefits. The PBRER provides greater emphasis on benefits, particularly when risk estimates change, and places greater emphasis on the cumulative knowledge regarding a medicinal product, while retaining a focus on new information.

Oracle Argus Safety customers can use the Periodic Safety Update Report configuration screen for defining the query criteria required for PBRER Section 6.2 - Cumulative Summary Tabulations of Serious Adverse Events from Clinical Trials and

Section 6. 3 - Cumulative and Interval Summary Tabulations from Post-Marketing Data Sources.

The Periodic Benefit Risk Assessment Report contains the following tabulation sections:

- Cumulative Tabulations of Serious Adverse Events from Clinical Trials
- Number of ADR from Post Marketing Sources

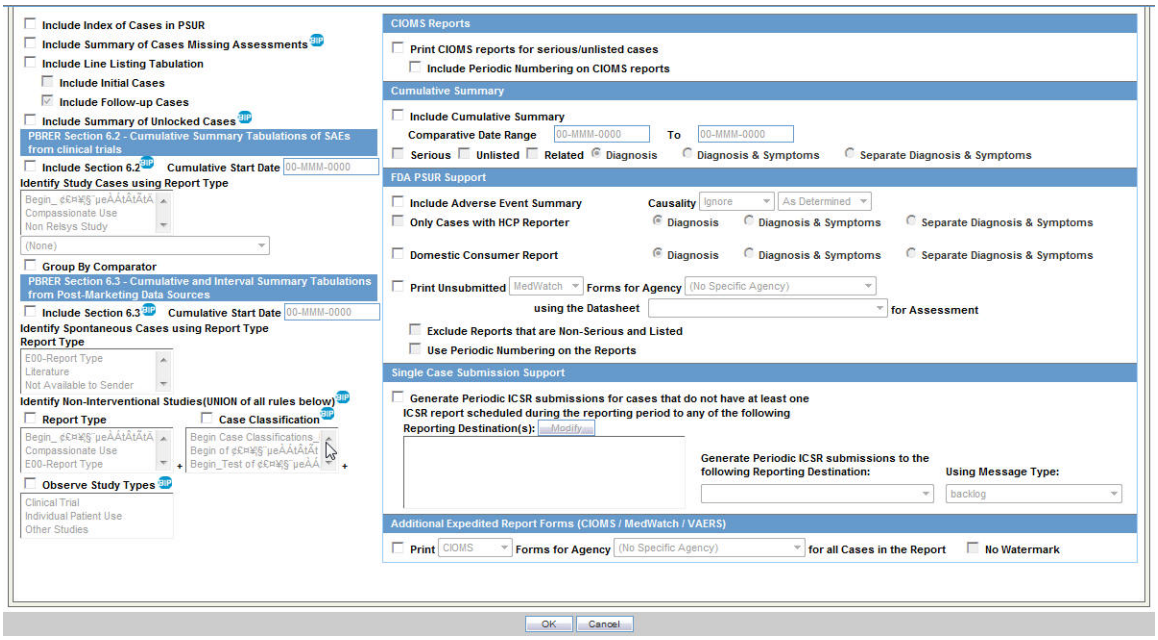
6.2 Configuring Argus Safety for PBRER

To specify the inclusion of PBRER sections:

1. Select the **Summary Tabulation** tab from the Argus Safety ICH PSUR Configuration screen.
2. To include Section 6.2, select the **Include Section 6.2** checkbox. The system does not use other query criteria available under Section 6.2.
3. To include Section 6.3, select the **Include Section 6.3** checkbox. From the other query criteria available, only **Case Classification** and **Observe Study Type** are used for identifying the Non-Interventional studies.
   - The system populates **Case Classification** with values from the Case Classification code list.
   - The system populates **Observe Study Type** with values from the Case Classification code list where E2B code values are not null.
   - The **Cumulative Start Date** in Section 6.2 and Section 6.3 is separate from the Include Section 6.2 and Include Section 6.3 checkboxes.

The system ignores all other configuration parameters on this tab except PBRER configuration, **Include Summary of Cases Missing Assessments,** and **Include Summary of Unlocked Cases**.

Figure 6–1 ICH PSUR Summary Tabulations Tab



6.2.1 Product Types in Study Configuration for Supporting PBRER and DSUR

To support PBRER and DSURs, the Product Type attribute of the Argus Console Study Configuration page displays the following values along with Investigational Product, Comparator, and Placebo:

- **No Study Drug Given**: This value lets you classify an event into the No Study Drug Given category if a serious adverse event occurs even before a patient has started taking any study drug.
- **Additional Study Drug**: These are additional or background drugs that are given as part of a combinational therapy. These drugs are generally given with both investigational products, and comparators. Additional study drugs do not impact the case categorization but are attributes for this configuration in the product temp table.

6.3 PBRER Section 6.2 - Cumulative Summary Tabulations of Serious Adverse Events from Clinical Trials

To support Section 6.2 in PBRER in tabulating based on medicinal product, active comparators, and placebo, the Argus Console Study Configuration is used to identify the a product type as Placebo, Comparator, or an Investigational Medicinal Product. The Argus Console Study Configuration classifies the counts of the various product types.

The system evaluates the list of cases applicable under Section 6.2 using criteria described in the following sections and configuration options from the ICH PSUR Configuration tab -> Summary Tabulations -> PBRER Section 6.2 - Cumulative Summary Tabulations tab for SAEs from clinical trials:

6.3.1 Generating the Case Series for Section 6.2

To generate the case series for Section 6.2, the system:

1. Identifies study cases and serious study cases for the studies that the configured products belong to.
2. Identifies whether a case is serious or not, based on the case level seriousness, primary event seriousness, or a combination of both, as configured in the Argus Console configuration.

   Seriousness is configured using System Management (Common Profile Switches) ->Reporting->Periodic->Case Inclusion criteria for the ICH PSUR or CTPR report based on Seriousness).
3. Excludes the following cases from the Section 6.2 case series:
   - Cases whose value matches the non-interventional rules (if any) configured in Section 6.3, if Include Section 6.3 is selected.
   - Cases from non-interventional studies (where REPTYPECODE =M in flexible report type code list) selected in the main inclusion criteria.

For each case in the Section 6.2 case series identified, the system prints summary tabulation counts broken down by both System Organ Class (SOC) in the internationally agreed order, followed by preferred terms (PTs) in rows, sorted alphabetically. This is based on the following logic and marked clearly in the temporary tables based on the identified product type:

- Company or Configured Study Cases
- Non-Company or Non-Configured Study Cases

6.3.1.1 Company or Configured Study Cases

If the case is being evaluated in a configured study, the system displays all the Section 6.2 case series that are part of study configuration for the product and study being evaluated. Counts are broken down into the following categories:

- **Blinded**:
  - If the study and case are both blinded, the system prints the count under Blinded.
  - If the case is blinded (even if study was unblinded), the system prints the count under Blinded.
  - If the case is unblinded (but the study is blinded) and you do not have the privilege to see unblinded data, the system prints the count under Blinded.
  - If you have access to the unblinded data and case is unblinded (but the study is blinded), or case and study both are unblinded, the system shows the counts under their respective categories if you choose to view the unblinded data; otherwise the system prints it under Blinded.
- **Investigational Medicinal Product (IMP)**: If the target product is of one of the suspect products in the study case, the system counts these cases under Investigational Medicinal Product.
- **Active Comparator**: If the target product is NOT one of the suspect products in the case, and the product type attribute for the suspect product available in the study is either an IMP or Comparator, the system prints it under the Comparator column.
- **Placebo**: If the target product is part of the study but is not one of the suspect products in the case, and the product type attribute for the suspect product available in the case is identified as Placebo in the study configuration, the system counts the case as a Placebo. You can use User Exits to classify different drugs under the Placebo category.
- **No Study Drug Given**: This column allows for retrieval of Serious Adverse Events that occurred from the moment the patient signed the informed consent form to the first administration of study medication, where no actual study medication was given to the patient. The system prints any study drug available in the case having product type defined as No Study Drug Given under No Study Drug Given column.
- **Additional Study Drug OR No product Type Configured**:
  - If the study configuration does not include the product type for that product, or is marked as Additional Study Drug, the system considers the product type as Investigational Medicinal Product if it is one of the target products and is also a suspect product in the case.
  - If the suspect product in the case is not part of the target product list, the system counts it as a Comparator. You can also use the user exits feature for categorizing products under the Investigational Medicinal Product, Comparator, Blinded, or Placebo columns in the temporary tables.

This tabulation also uses the parameter Print Serious Adverse Events or Reactions.

- **Print All Events**: The summary tabulation displays all events present in the cases lying within the reporting period. The in period flag is not used. This is the default value.
- **Print only In Period Events**: This summary tabulation displays only events added within the reporting period. Events in the cases with Follow-up data that does not fall into the reporting period are not considered.

6.3.1.2 Non-Company or Non-Configured Study Cases

If the case being evaluated is a non-company or non-configured study case, the system prints the suspect products with the product type as Investigational Medicinal Product and follows the rules of Investigational Medical Product and Blinded.

- The report prints the count for medicinal products in the first column in the report, followed by the Blinded, Active Comparator, and Placebo columns.
- The report does not suppress the Blinded, Active Comparator, and Placebo columns when there are 0 counts against them. It prints the event count as 0 in each column as long as at least one of the four columns has an event count greater than 0. When PBRER is generated for a product that is a comparator in some studies, and no case qualifies for the report in which that product is a medicinal study drug, the system prints the medical product column with 0 event counts.
- If the event count is 0 in the Medicinal Product, Blinded, Active Comparator and Placebo columns for a given SOC, the system does not print that SOC in the report.

6.3.2 Grand Totals

The system provides the totals and grand totals in out-of-the-box PBRER tabulations as follows:

- Subtotal per System Organ Class (SOC) per study medication category (IMP, Blinded, Active Comparator, Placebo, No Study Drug Given).
- Grand total for all SOCs per study medication category (IMP, Blinded, Active Comparator, Placebo, No Study Drug Given).

6.3.3 Section 6.2 Layout

Figure 6-2 illustrates the layout of PBRER Section 6.2.

Figure 6–2 Section 6.2 Layout

System Organ Class Preferred Term	Investigational Medicinal Product	Blinded	Active comparator	Placebo	No Study Drug Given
Investigations					
Alanine aminotransferase increased	4	0	2	3	0
Aspartate aminotransferase increased	2	3	1	1	0
Subtotal	6	3	3	4	0
Nervous System Disorders					
Syncope	1	6	9	4	0
Headache	3	4	3	5	1
Subtotal	4	10	12	9	1
Grand Total	10	13	15	13	1

6.4 PBRER Section 6.3 - Cumulative and Interval Summary Tabulations from Post-Marketing Data Sources

Section 6.3 is a background for the appendix that provides cumulative and interval summary tabulations of adverse reactions—from the IBD to the data lock point of the current PBRER.

These adverse reactions are derived from non-interventional studies and spontaneous ICSRs, including reports from healthcare professionals, consumers, scientific literature, and regulatory authorities. Serious and non-serious reactions are presented in a single table, with interval and cumulative data presented side-by-side.

6.4.1 Case Selection

The system evaluates the list of cases applicable for section 6.3 using the following criteria and configuration options from ICH PSUR Configuration ->Summary Tabulations screen.

The **Identify Non-interventional Studies** field is mandatory, and you must select at least one of the options if Include Section 6.3 is selected.

If you save the report configuration without selecting a rule or without selecting a Non-Interventional Study report type in the main inclusion criteria, an error message appears.

When you select the Include Section 6.3 option, the system evaluates the list of cases applicable for this section by the following methods and categorizes these cases into the following lists when populating temp tables:

- **Non-Interventional Current cases**: Using the main case list identified from the report inclusion criteria, further restricts it to only the Non-Interventional cases based on all rules that are selected, for the Identify Non-Interventional Studies field. This case list is referred to as Non-Interventional current case list.
  - If the **Case Classification** rule is selected, any case from the main case list qualifies if it has a case classification that matches **Identify Non-Interventional Studies**.
  - If the **Observe Study Type** rule is selected, any case from the main case list that has an Observe Study Type qualifies if it has a case classification that matches **Identify Non- Interventional Studies**.
  - From the main inclusion criteria, any case from the main case list that has a report type that matches a **Non-Interventional Study** as categorized in the report type flexible re-categorization code list qualifies.
- **Non-Interventional Cumulative cases**: Using the report inclusion criteria, identifies cumulative Non-Interventional cases for the report corresponding to the configured product and uses the Non-Interventional selected Non-Interventional rule. This case list is referred to as the Non-Interventional Cumulative case list.
- **Spontaneous Current cases**: Using the main case list identified from the report Inclusion criteria, identifies the Spontaneous Current case list by restricting it to cases that have a spontaneous report type (where report type code list values do not have the **This type includes cases from clinical trials** selected).
- **Spontaneous Cumulative cases**: Using the report Inclusion criteria, first identifies the Cumulative Main case list, corresponding to the configured product. Using this cumulative main case list, it then identifies the Spontaneous Cumulative case list by restricting it to cases that have a report type in which **This type includes cases from clinical trials** is not selected.

After the system identifies the four case lists in the temp tables, it prints the cumulative summary tabulation categorized into the Spontaneous, and Non-interventional columns:

- The Spontaneous column has two sub-columns based on seriousness of the event: Serious, and Non-serious.
- Both the Serious and Non-Serious columns under Spontaneous have two sub-columns: Interval, and Cumulative.
- The Non-interventional column has a sub-column, Serious, based on events that are serious.
- The Serious column under Non-Interventional has two sub-columns: Interval, and Cumulative.

The system prints the summary tabulation counts broken down by both System Organ Class (SOC) sorted in the international order, followed by Preferred Terms (PTs) in rows, sorted alphabetically. The report prints SOCs with zero counts if there are no events reported.

It uses the Spontaneous Current case list for determining the Interval counts under the Spontaneous column (stratified based on Seriousness) and the Spontaneous Cumulative case list for the Cumulative counts under the Spontaneous column (stratified based on Seriousness).

The system uses the Non-Interventional Current case list for the Interval counts under the Non-Interventional column (stratified based on Seriousness) and the Non-Interventional Cumulative case list for the Cumulative counts under the Non-Interventional column (stratified based on Seriousness).

The summary tabulation prints the Total Spontaneous Cumulative all sub totals for Spontaneous column as total of Spontaneous Cumulative Serious plus Spontaneous Cumulative Non-Serious counts.

This tabulation also uses the parameter Print Serious Adverse Events or Reactions.

- **Print All Events**: The summary tabulation displays all events present in the cases lying within the reporting period. The in period flag is not used. This is the default value.
- **Print only In Period Events**: This summary tabulation displays only events added within the reporting period. Events in the cases with Follow-up data that does not fall into the reporting period are not considered.

6.4.2 Section 6.3 Layout

Figure 6-3 displays the number of adverse drug reactions by term from Post-Marketing Sources in Section 6.3.

Figure 6–3 Section 6.3 Layout

System Organ Class / Preferred Term	Spontaneous, including regulatory authority and literature					Non-interventional post-marketing study and reports from other solicited sources	
	Serious		Non-Serious		Total Spontaneous	Seriousness	
	Interval	Cumulative	Interval	Cumulative	Cumulative All	Interval	Cumulative
Investigations							
Alanine aminotransferase increased							
Aspartate aminotransferase increased							
Subtotal							
Nervous System Disorders							
Syncope							
Headache							
Subtotal							
Grand Total							

6.5 Sample Report

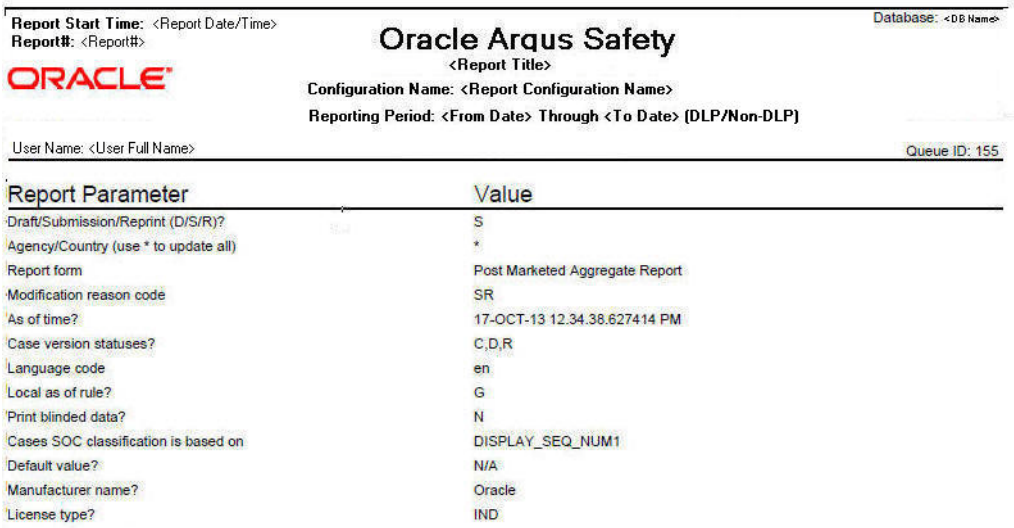
The following sections discuss the parts of the report.

6.5.1 Cover Page

All BI Publisher reports have a cover page with information about all report parameters and their values used in the report.

Figure 6-4 represents a sample PBRER cover page:

Figure 6–4 PBRER Cover Page



6.5.1.1 Information on Drugs and Studies

After the list of report parameters, the cover page provides information about the list of products or study licenses selected in the corresponding Argus Safety Configuration screen for the current report run. The following format is used for this information:

6.5.1.1.1 List of Configured Drugs and Licenses:

- Product Name 1 or License 1
- Product Name 2 or License 2

If you select a study on the CTPR Report Configuration screen, the system displays the list of licenses available in that study for populating this section.

List of Case Numbers

The system also prints all case numbers that are part of current report data. These are displayed after the list of products and licenses.

Figure 6–5 List of Case Numbers

PBRER

Case Numbers			
GOLD07	GOLD 14	GOLD 06	SILVER 04(
CH 1997CH000010	NDA-SCENARIO42	NDA-SCENARIO52	GB TEST E
GB TEST FOLLOWUP	GB TEST FOLOWUP 1	TEST E2B SPONTAEOUS	IMPORT 2
TEST56	087-060809	094-100809	114-170809
124-120908	130-120908	133-120908	134-120908
157-120908	166-120908	182-120908	192-120908
204-120908	219-120908	257-120908	259-120908
270-120908	274-120908	278-120908	PLATINUM_
CSPSR_004	DLP_CASE_03	DLP_CASE_04	DS_ASSES
PLATINUM_CASE_37	PLATINUM_CASE_40	PLATINUM_CASE_8	PLATINUM_

After the list of case numbers, all modifications made to the case series are printed in the reports in the order they were performed.

6.5.2 Labels Configured for Drugs in the Drug List Format

The following format is used for displaying this information in the QA section:

Figure 6–6 Labels Configured for Drugs

Labels configured for drugs in the drug list

Drug Name	Label Name	Label Version	Effective Date
<Product Name>	<Datasheet Name>	<Datasheet Revision Number>	<Datasheet Activation/Effective Date>

Here:

- **Drug Name** prints the name of the product configured for running the report.
- **Label Name** prints the datasheet name for the corresponding product or product family.
- **Label Version** prints the revision number of the corresponding datasheet.
- **Effective Date** prints the activation date of the corresponding datasheet.

If any of the above fields is null, the field is blank.

6.5.3 Cases with Missing Assessments

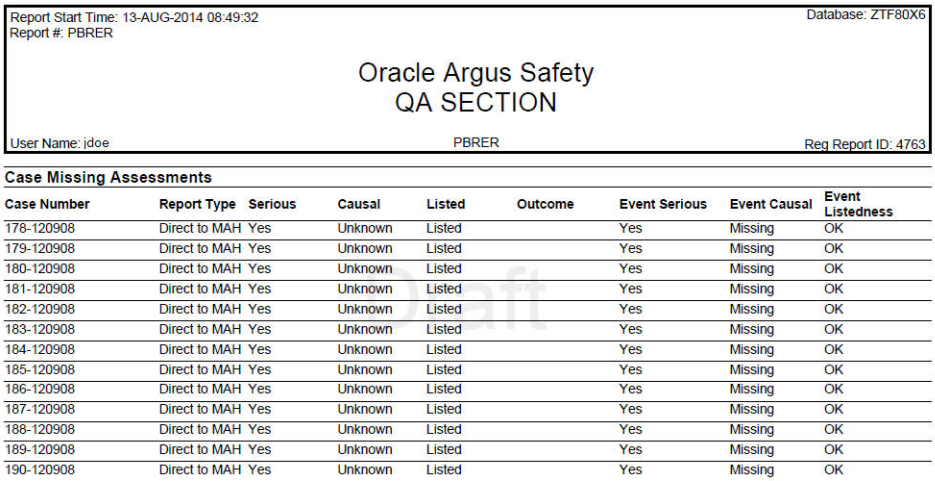
In this sub-report, the system displays cases that are included in the PBRER, but one or more of the following have not been assessed:

- Case Seriousness
- Report Type
- Case Causality
- Case Listedness
- Case Outcome

- Event Seriousness
- Event Causality
- Event Listedness

Case Seriousness, Case Causality, Case Listedness, Case Outcome, and Event Seriousness print their corresponding values, while Event Causality prints *OK* if the information is present and *Missing* if missing. Case seriousness and Event seriousness print values are *Unknown* if seriousness is undefined. The system prints event listedness *OK* if listed or unlisted. Otherwise, it prints it as *Unknown*.

Figure 6–7 Cases Missing Assessments



Report Start Time: 13-AUG-2014 08:49:32
Report #: PBRER

Database: ZTF80X6

Oracle Argus Safety
QA SECTION

User Name: jdoe

PBRER

Reg Report ID: 4763

Case Missing Assessments

Case Number	Report Type	Serious	Causal	Listed	Outcome	Event Serious	Event Causal	Event Listedness
178-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
179-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
180-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
181-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
182-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
183-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
184-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
185-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
186-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
187-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
188-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
189-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK
190-120908	Direct to MAH	Yes	Unknown	Listed		Yes	Missing	OK

6.5.4 Trailer Section

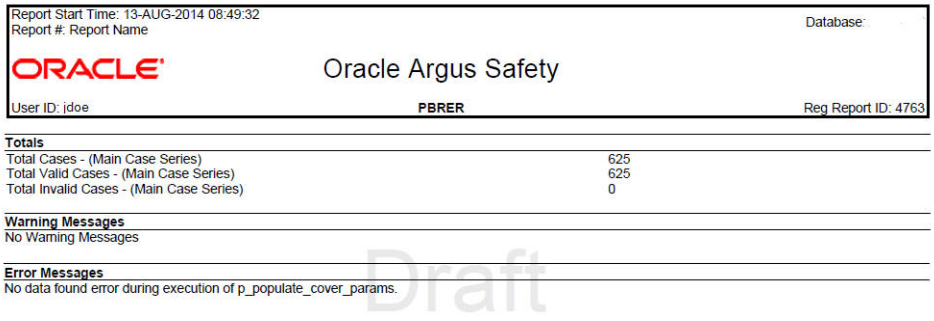
The following information is displayed in the trailer section of PBRER:

Table 6–1 Trailer Section Information

Total Cases-(Main case series)	Count of cases that are part of the main case series.
Total Valid Cases-(Main case series)	Count of cases that are part of the main case series and also fall into the reporting interval. If there are no valid cases, 0 is printed in the count.
Total Invalid Cases -(Main case series)	Report prints the count of cases which are part of the main case series but do not fall into the reporting interval. If there are no invalid cases, 0 is printed in the count.
Warning Messages	All warning messages related to case series and report output. This section prints the exact warning generated during report execution. If there is no warning, the system prints *No Warning Messages*.
Error Messages	All error messages related to case series and report output. This section prints the exact error message generated during report execution. If there is no error, the system prints *No Error Messages*.

The following format is used for displaying the information:

Figure 6–8 Trailer Section


Report Start Time: 13-AUG-2014 08:49:32
Report #: Report Name
Database:
ORACLE
Oracle Argus Safety
User ID: jdoe
PBRER
Reg Report ID: 4763

Totals

Total Cases - (Main Case Series)	625
Total Valid Cases - (Main Case Series)	625
Total Invalid Cases - (Main Case Series)	0

Warning Messages
No Warning Messages

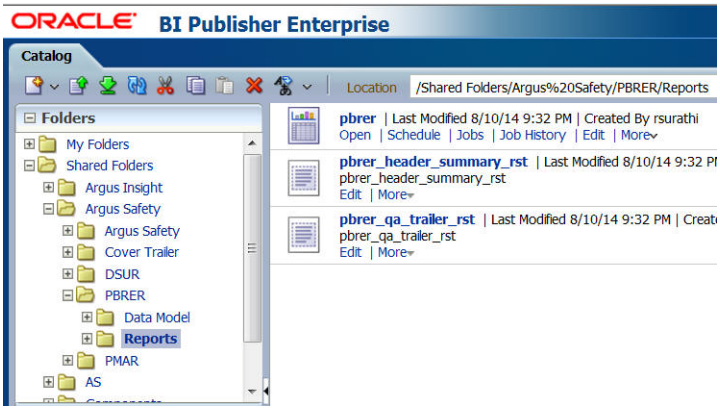
Error Messages
No data found error during execution of p_populate_cover_params.

6.6 Executing the PBRER from BIP

To execute a report from BIP, perform the following steps:

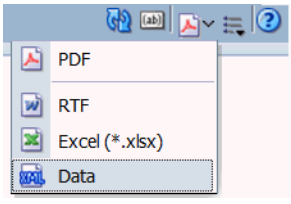
1. Sign in to BI Publisher, and click **Catalog**.
2. Select the tree entry for a report and select **Reports**.

Figure 6–9 The Reports Tree Entry Screen



3. The available reports are displayed on the screen. Click the **Open** link for a report.
4. The report screen appears. Click the **Open** tab.
5. Select the required values from the parameter drop-down lists.
6. Select a format. This executes the report.

Figure 6–10 PBRER Format Selection



7

Development Safety Update Report

This chapter contains the following topics:

7.1 Report Objective

The main objectives of a Development Safety Update Report (DSUR) are to present a comprehensive annual review, and evaluate pertinent safety information collected during the reporting period related to a drug under investigation, whether or not it is marketed, by:

- Examining whether the information obtained by the sponsor during the reporting period is in accord with previous knowledge of the investigational drug's safety.
- Describing new safety issues that could have an impact on the protection of clinical trial subjects.
- Summarizing current understanding and managing identified and potential risks.
- Providing an update on the status of the clinical investigation or development program and study results.

The main focus of the DSUR is data and findings from international clinical trials of drugs under investigation, irrespective of whether they have marketing approval. Because clinical development of a drug frequently continues after the marketing approval, relevant information from post-marketing studies is also included. The report concentrates on the investigational drug, providing information on comparators only where relevant to the safety of trial subjects.

The DSUR provides safety information from all ongoing clinical trials and studies that the sponsor is conducting or has completed during the review period, including:

- Clinical trials using an investigational drug.
- Clinical trials conducted using marketed drugs in approved indications.
- Therapeutic use of an investigational drug (such as expanded access programs, compassionate use programs, or particular patient use).
- Clinical trials conducted to support changes in the manufacturing process of medicinal products

The DSUR presents important clinical safety information through:

- Interval line listings of the SARs that were reported to the sponsor during the period covered by the DSUR.
- Cumulative summary tabulations of serious adverse events that have been reported to the sponsor since the DIBD.

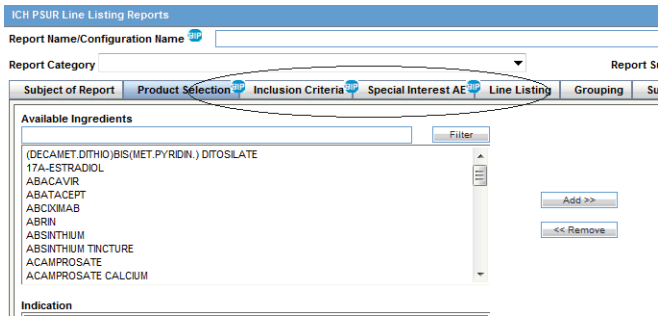
For information on report parameters, refer to Appendix A, "Report Parameters and their Definitions".

7.2 Argus Configuration for DSUR

To clearly distinguish the configuration options used in the BIP report as parameters, you must enable the BIP Aggregate Reporting module.

The system marks all configuration parameters from the CTPR screen that are passed to BIP reports for data filtering and report formatting options with a BIP logo. All inclusion criteria available on the CTPR configuration screen are used for query and case series generation for BIP reports.

Figure 7–1 BIP Logo



- Product Selection
- License or Study
- Inclusion Criteria
- Special Interest AE

7.2.1 Subject of Report Tab

The system uses the following configurations as report parameters in BIP reports:

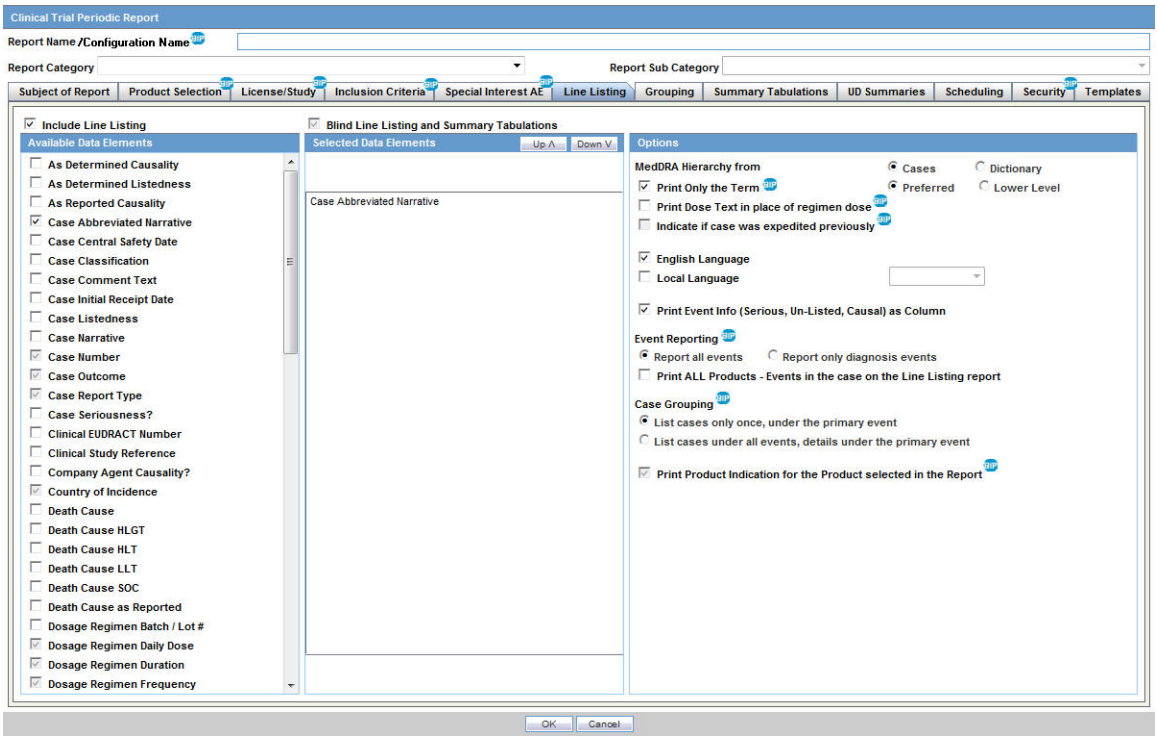
- Report Name is re-labeled to **Report Name or Configuration Name** on the CTPR configuration screen. The system uses this as a Report Configuration Name parameter in the report to populate other report parameters from the saved configuration.
- Selected Reporting Destination and Primary Agency.
- The system passes Report#, Report Title, and Report footer as respective parameters in the BIP report.

7.2.2 Line Listing Tab

The system uses the following configurations as report parameters in BIP reports:

- Print Only the Term (PT, LLT): Prints event verbatim along with PT or LLT if this configuration is unchecked.
- Prints Dose Text in place of regimen dose.
- Indicates if the case was expedited previously.
- Event Reporting.
- Case Grouping.
- Prints Product Indication for the product selected in the report.

Figure 7–2 Line Listing Tab

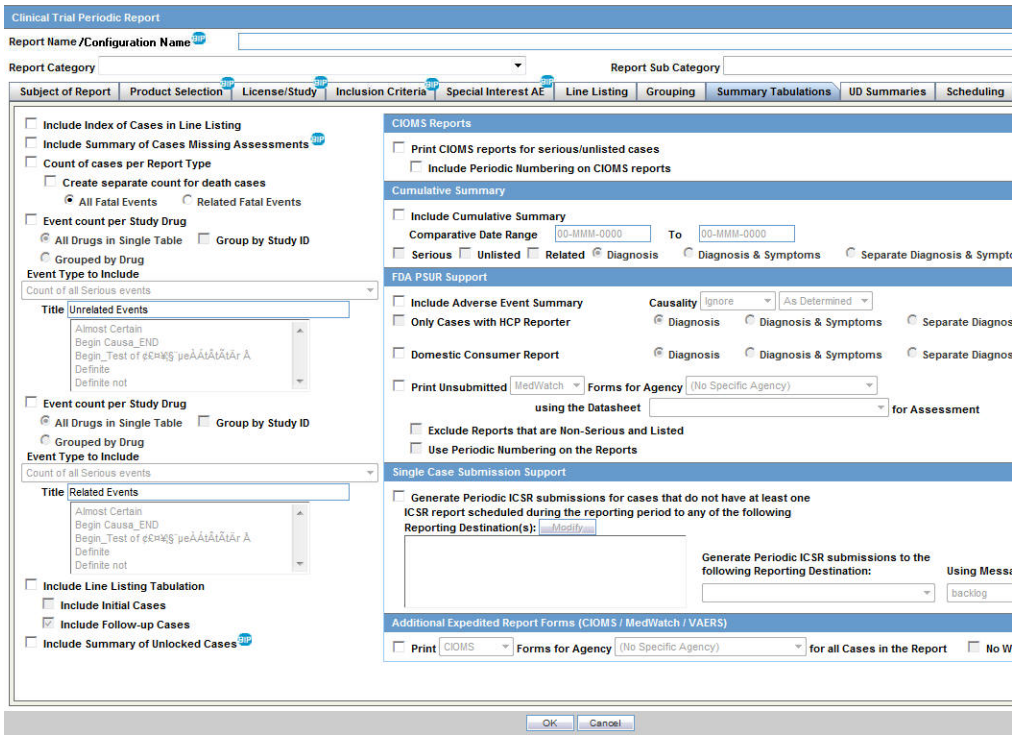


7.2.3 Summary Tabulation Tab

The system uses the following configurations as report parameters in BIP reports:

- **Include Summary of cases Missing Assessments**
- **Include Summary of Unlocked Cases**

Figure 7–3 Summary Tabulation Tab

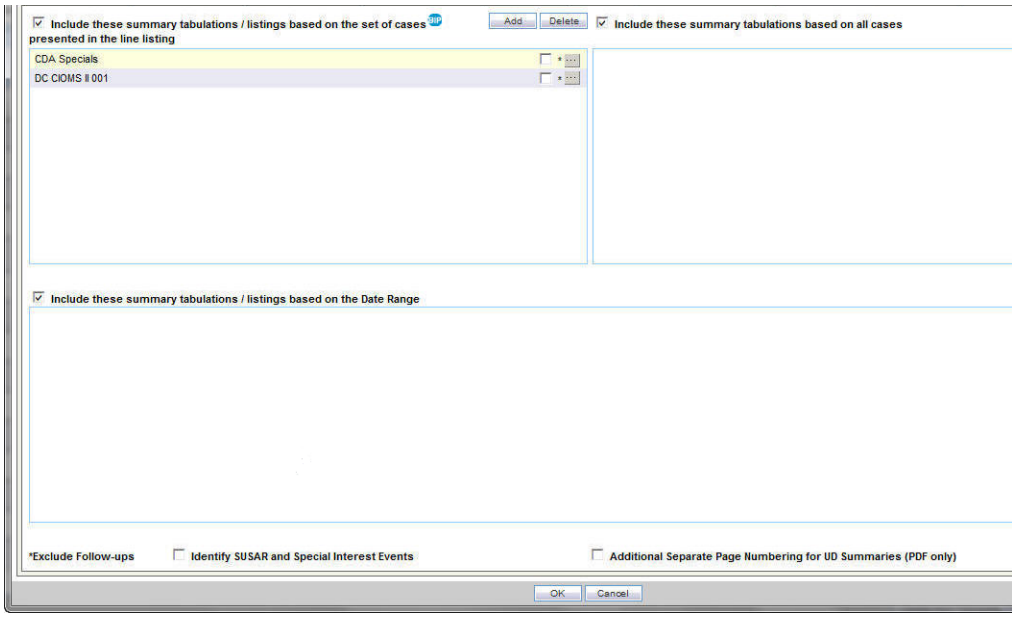


7.2.4 UD Summaries Tab

The system uses only **Include these summary tabulations or listings based on the set of cases presented in the line listing**.

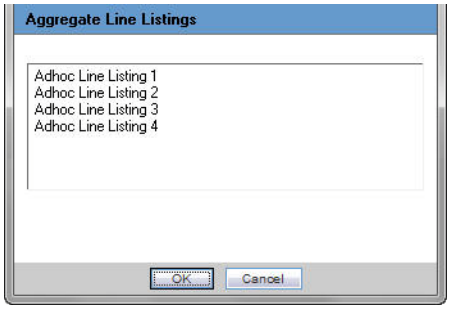
The system does not generate memorized reports for selected configurations are not generated along with the aggregate report. Instead, it only uses advanced condition query criteria used in these configurations to generate the case series for these ad hoc line listing sections. Figure 7-4 is an example of case data line listing query criteria used for ad hoc line listings.

Figure 7–4 Ad Hoc Line Listing Query Criteria



When you select a checkbox in UD Summaries, the available ad hoc line listing sections appear in the Aggregate Line Listings dialog box.

Figure 7–5 Aggregate Line Listings



You can associate multiple ad hoc line listing sections with one memorized line listing configuration. Each ad hoc line listing section can be attached to only one memorized line listing configuration. All ad hoc line listing sections already attached to another memorized line listing configuration are not available for selection again.

The system marks memorized line listing configurations having associated ad hoc line listings with an additional asterisk. The system displays all associated ad hoc line listings as a tooltip when you hover over the selected memorized line listing configuration.

7.2.5 Security Tab

The Security tab shares report configurations with other groups. All case series generated using an aggregate report configuration have the same access privileges available for aggregate report configuration.

7.2.6 Scheduling and Template Tabs

The Scheduling and Templates tabs are not used in BIP reports.

7.3 DSUR Main Line Listings

The system prints all clinical trial cases except non-interventional study cases present in the main case series generated from CTPR report configuration in the DSUR Main line listing.

This report contains a cover page similar to the PBRER. It summarizes how case reports were selected for inclusion in the line listings.

Line listings provide key information on all SARs (blinded and unblinded) reported from the sponsor's studies during the reporting period. The data is organized by trial and then by System Organ Class (SOC).

7.3.1 Grouping

Table 7–1 Grouping Information

Field Name	Description
Initial or Follow-up.	Cases are listed under Initial or Follow-up based on the classification in the temp table. Initial case listing is printed followed by Follow-up cases.
Case Expectedness (Listed or Unlisted)	Case is grouped based on Listed or Unlisted cases. Unlisted case listing is printed followed by Listed cases.
Project Drug (Primary Study Drug)	Cases are grouped based on the primary study drug.
Study ID	After Project Drug, line listing cases are grouped based on the study ID.
EudRactID	Line listing is grouped by EudactID, if available. The Eudract number is the unique identifier for trials authorized in the European Economic Area.
Grouping based on SOC (as per event order specified in the case form event tab)	Cases are grouped by the SOC of the Primary Event. SOC group header is displayed in the internationally agreed order as specified in the code list SOC_DISPLAY_ORDER. If the BIP Report parameter **List cases in the line listing under SOC for each diagnosis** is *Y* and **List Cases under all events, details under the primary event** is selected, cases can appear under multiple SOCs. If the BIP Report parameter **List cases in the line listing under SOC for each diagnosis** is *N* and **List Cases only once, under the primary event** is selected, a case appears under the SOC of the Primary event, and a reference to this information appears under the SOCs of other events.
Country of Incidence	The last level of grouping is based on country of incidence.

7.3.2 Main Line Listing

Table 7–2 Main Line Listing Fields

Field Name	Description
Unique Patient ID	Unique patient identifier based on the format selected by the user while running the report. This value depends upon the *UNIQUE_PATIENT_ID_FORMAT* parameter.
Case Number	▪ Case Number is printed. ▪ If the BIP report parameter **Indicate if case was expedited previously** is *Y*, the symbol specified in the BIP parameter **Symbol for expedited cases** appears with the case number as a superscript. ▪ A footnote appears at the end of the page as follows: *<symbol>: Expedited Case*. Refer to the temp table sheet for the logic of Expedited case. If the BIP report parameter **Indicate if case was expedited previously** is *Y*, the footnote for Expedited Cases appears even though there may not be any cases marked as Expedited.
Report Type	Reporter type is displayed from the flex bucketing code list field **REPTYEPGRP** for the report type entered in the case.
Sex and Age	PATIENTSEXTEXT is populated using global language decode of PATIENTSEXCODE field. If Patient Age is missing, Patient age group appears. If Patient Age or Age group is not entered, text entered for the BIP parameter **Default for NULL Values** appears.
Concomitant Disease and Relevant History	Concatenation of the patient relevant medical history in a table format.
Case Outcome	Case level outcome.
Case Onset Date	Case level event onset date.
Seriousness Criteria	Seriousness Criteria for primary events appears.
Other Medication	List of all suspect drugs and concomitant drugs in the case except the drug for which the report is being run.
Study Product	The logic provided in summary tabulations is used to populate this field.
First or Last Dose to Onset	Duration from the first or last dose until the first onset of the adverse event. It is calculated at the case level using all doses for all drugs in the drug list and the case level onset date.
Action Taken	Action taken appears with the respective company suspect drug. If action taken is not specified in the case, then <> appears.
Indication	Concatenation of reported indications for a product in the case. The report displays a list of indications for products that are configured for current periodic run.
Start and Stop Dates of Reaction	Date of Onset (only from Primary Serious event). Time of Onset (only from Primary Serious event).
Event Outcome	Event outcome for each event present in the case.
Event Reported or Determined Causality	Causality as per reporter and company is printed with the corresponding Product and Events in the format: <Causality as per reporter> or <Causality as per company>.
Event Listedness	Listedness information for the event appears. Listedness appears based on the BIP Report parameter **Labeling Algorithm** if the report is executed from BIP. If this report is executed from Argus Safety, the following report parameters are considered: · Use Assessment in Cases. · Re-assess cases against datasheet in effect at beginning. · Re-assess cases against datasheet in effect at end.

Table 7–2 (Cont.) Main Line Listing Fields

Field Name	Description
Reaction as Reported (PREFERRED TERM)	Reaction as Reported (PT) with diagnosis or signs and symptoms, and company added term behavior.
Dose String	Default format is DoFoRt - Print Dose, Formulation, and Route of administration.
Dates of Treatment	-
Treatment Duration	-
Line listing Comments	-

In DSUR line listings:

• The system displays all Serious and Unexpected Adverse Reactions (SUSAR) events with an asterisk *. The SUSAR event term (PT or LLT) appears with an asterisk to the right of the term. For example, SEPTICEMIA*.

• The system displays all special interest events with a superscript †. For example, OEDEMA†. You configure the list of special interest events for a report using the Argus Safety CTPR configuration screen.

• The system displays primary events in bold and underlines them.

7.3.3 Report Parameters for Printing Reactions or Serious Events

The Print Serious Adverse Events or Reactions parameter prints serious adverse events (SAE) or serious adverse reactions (SAR) based on the value. This parameter can have following possible values:

- Print Serious Adverse Reactions (default)
- Print Serious Adverse Events

Based on the value of this parameter, headings of various line listings or tabulations indicate whether they are for SAEs or SARs. The system displays the following titles for main line listing depending upon parameter values:

Table 7–3 Main Line Listing Titles

Parameter Value	Main Line Listing Title
Print Serious Adverse Reactions	DSUR Main Line Listing for Serious Adverse Reactions
Print Serious Adverse Events	DSUR Main Line Listing for Serious Adverse Events

The system uses the most conservative causality approach for identifying reactions. Most conservative causality means that either reported or company causality is defined for a combination of product and event.

7.3.4 Summary Columns

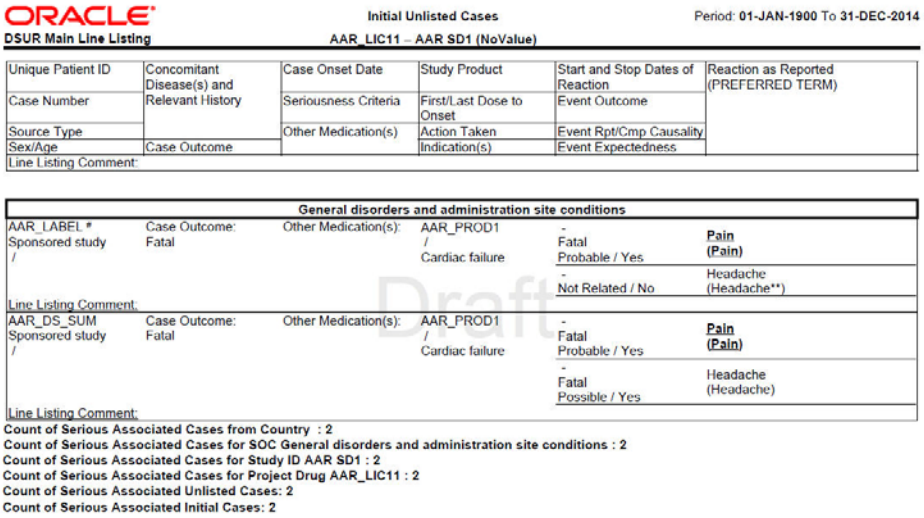
The following counts are available for Main line listings:

- Count of Serious Associated Cases from Country: <Count>
- Count of Serious Associated Cases for SOC: <Count>
- Count of Serious Associated Cases for Study ID: <Count>

- Count of Serious Associated Cases for Project Drug (Actual drug for which trial is going on or to say investigational drug of study): <Count>
- Count of Serious Associated Unexpected Cases: <Count>
- Count of Serious Associated Initial Cases: <Count>

7.3.5 DSUR Main Line Listing Format

Figure 7–6 DSUR Main Line Listing



ORACLE

Initial Unlisted Cases — Period: **01-JAN-1900** To **31-DEC-2014**

DSUR Main Line Listing — **AAR_LIC11 – AAR SD1 (NoValue)**

Unique Patient ID	Concomitant Disease(s) and Relevant History	Case Onset Date	Study Product	Start and Stop Dates of Reaction	Reaction as Reported (PREFERRED TERM)
Case Number		Seriousness Criteria	First/Last Dose to Onset	Event Outcome	
Source Type		Other Medication(s)	Action Taken	Event Rpt/Cmp Causality	
Sex/Age	Case Outcome		Indication(s)	Event Expectedness	
Line Listing Comment:					

General disorders and administration site conditions

AAR_LABEL * Sponsored study /	Case Outcome: Fatal	Other Medication(s):	AAR_PROD1 / Cardiac failure	- Fatal Probable / Yes	**Pain (Pain)**
				- Not Related / No	Headache (Headache**)
Line Listing Comment:					
AAR_DS_SUM Sponsored study /	Case Outcome: Fatal	Other Medication(s):	AAR_PROD1 / Cardiac failure	- Fatal Probable / Yes	**Pain (Pain)**
				- Fatal Possible / Yes	Headache (Headache)
Line Listing Comment:					

Count of Serious Associated Cases from Country : 2
Count of Serious Associated Cases for SOC General disorders and administration site conditions : 2
Count of Serious Associated Cases for Study ID AAR SD1 : 2
Count of Serious Associated Cases for Project Drug AAR_LIC11 : 2
Count of Serious Associated Unlisted Cases: 2
Count of Serious Associated Initial Cases: 2

7.3.6 DSUR Fatal Line Listing

From the cases present in the main case series generated from the CTPR report configuration, the system prints only fatal cases (event seriousness=death) in the DSUR Fatal line listing. This line listing does not restrict cases based on reaction terms. That is, Print Serious Adverse Events or Reactions parameters are not used for Fatal line listing.

The following additional fields have been added to Fatal line listing over the Main line listing fields:

Table 7–4 Fatal Line Listing Fields

Field Name	Description
Death Date and Cause of Death	Patient death date along with cause of patient death.
Verified	**Y** if the patient cause of death has been verified. If CASE_DEATH_DETAILS.TERM_TYPE=2, cause of death came from autopsy results, which means cause of death verified=Y; otherwise N.

7.4 Summary Tabulations of Serious Adverse Events

This section in the DSUR provides the main and cumulative summary tabulation of SAEs reported in the sponsor's clinical trials from the DIBD to the data lock point of the current DSUR.The report displays only serious events in this tabulation. You cannot display any non-serious events of special interest in this section as filtering is based on the seriousness of an event.

The tabulation is organized by Study and SOC for the investigational drug and for the comparator arm (active comparators, placebo, and treatment unknown due to blinding) used in the program.

The Development Safety Update Report provides the following tabulations:

- **DSUR Main Summary Tabulation of Serious Adverse Events**: This tabulation contains all serious cases from the main case series (interval period). For each case, the system prints a summary tabulation count SOC in the internationally agreed order, followed by PTs in rows.
- **DSUR Fatal Cases Summary Tabulation**: This tabulation is similar to the Main Summary tabulation, except that the report only prints cases where event seriousness criterion is death.
- **DSUR Cumulative Summary Tabulation of Serious Adverse Events or DSUR Cumulative Summary Tabulation of Serious Adverse Reactions**: This tabulation contains all serious cases from the cumulative case series. For each case in the cumulative case series, the system prints summary tabulation counts broken down by SOC in the internationally agreed order, followed by PTs in rows. This tabulation prints either the serious adverse events or serious adverse reactions based on the value of the report parameter **Print Serious Adverse Events or Reactions**.

  Based on the value of the above parameter, the heading of the cumulative tabulation indicates whether it is for a serious adverse reaction or a serious adverse event.
- **DSUR Fatal Cases Cumulative Summary Tabulation of Serious Adverse Events or DSUR Fatal Cases Cumulative Summary Tabulation of Serious Adverse Reactions**: This tabulation contains those serious cases from the cumulative case series where the event seriousness criterion is death. For each case, the system prints summary tabulation counts broken down by SOC in the internationally agreed order, followed by PTs in rows.

  This tabulation also uses the parameter **Print Serious Adverse Events or Reactions**.
- **Print All Events**: The summary tabulation displays all events present in the cases lying within the reporting period. The in period flag is not used. This is the default value.
- **Print only In Period Events**: This summary tabulation displays only events added within the reporting period. Events in the cases with Follow-up data that does not fall into the reporting period are not considered.

7.4.1 Groupings

Main and Cumulative DSUR Tabulations are grouped in the following order:

1. Initial or Follow-up
2. Study ID

3. SOC

Fatal or Death Cases and Fatal Cumulative DSUR Tabulations are grouped in the following order:

1. Initial or Follow-up
2. Study ID
3. SOC

7.4.2 Count Breakdown in Tabulations based on IMP, Comparator, Placebo, and Blinded

All DSUR tabulations provide serious events counts broken down by SOC and PT. To tabulate based on medicinal product, active comparators and placebo, the Argus Console Study Configuration identifies a product type as placebo, comparator, or an investigational medicinal product.

Note: You must configure all studies with the Product Type attribute to get the correct data.

The Argus Console study configuration classifies the different product type counts.

The system evaluates the list of cases applicable for the DSUR based on the main inclusion criteria present on the CTPR configuration screen to generate a main case series and all cases corresponding to configured licenses or studies for generating the cumulative case series. If multiple licenses or studies are configured on the CTPR configuration screen, the system retrieves the cases of all configured licenses or studies.

Serious study cases are identified from the main and cumulative case series generated using the CTPR configuration.

For each case in the main cumulative case series, the system prints a summary tabulation count broken down by SOC in the internationally agreed order, followed by PTs in rows.

After classifying counts into Medicinal Product, Blinded, Comparator and Placebo, the system breaks the counts down by the actual treatment received by the patient.

For each case, the system counts only serious events under the following categories:

For each Company or Configured Study case, the system counts:

- **No Study Drug Given**: This column lets you retrieve Serious Adverse Events that occurred from the moment the patient signed the informed consent form to the first administration of study medication where no actual study medication was given to the patient.
- **Additional Study Drug**: Also known as background therapy drugs, these are given with IMPs or comparators of a study and do not impact the categorization logic of a case into different categories. All drugs marked as Additional Study Drugs in Argus Console do not impact the case categorization. The system displays these drugs in the reports as part of the treatment field without affecting categorization logic.

Using the configuration of the study to which each case belongs, the system classifies the cases into the following categories based on the product type attribute of the study configuration and print counts for each category:

- **Blinded**:
  - If the study and the case are both blinded, the system prints the count under Blinded.
  - If the case is blinded (even if study is unblinded), it appears under Blinded.
  - If the case is unblinded (but the study is blinded) and you do not have access to unblinded data, the count appears under Blinded.
  - If you do not have access to unblinded data, the count appears under Blinded.
  - For a blinded case having blinded and open label therapy drugs, the case is counted under Blinded category.
- **Investigational Medicinal Product or Study Drug**: A case falls into the Investigational Product category if the case and study are not blinded and the product type in the study configuration is identified as Investigational Product.

  If the case is unblinded (but the study is blinded) and you have access to unblinded data, and the product is identified as an Investigational Product, then the system prints the count under the medicinal product. The medicinal product count is broken down into the actual treatments given to patients for the corresponding case.

  A suspect product that is also an Investigational Product as identified by the study configuration appears under the Investigational Product Name column, and the count of all serious events cases where the same product is used as a treatment is added under this column.

  When there are multiple suspect drugs in a case and they are classified as IMP in the study configuration, the system prints the count under the combined product treatment. All such cases are counted under the combined products that are part of the study.

  The product combination for counts is unique in a report. Based on the number of licenses and studies selected, there may be many combinations. There could be the following scenario for investigational products:

- **Investigational Product (Including Combinational Therapy)**:

  Only study drugs are part of the DSUR treatment list. The following combinations of treatments can appear:

  Drug A + Drug B: Both Drug A and Drug B are identified as suspect study products in the case and are identified as Investigational Product in the corresponding study configuration.

  Drug A or Drug B: Only one of the drugs from the case is identified as a suspect study and this drug is identified as an Investigational Product in the study configuration.

  Drug A + Placebo: When multiple drugs are identified as suspect product in the case, and these are part of the study, and some drugs are identified as Investigational Products in the study configuration and others as Placebo, the system prints the count of such scenarios under Drug A or Drug A + Drug B only, without adding the placebo drug name.

  Drug A + Drug B: Drug A is identified as a suspect study product in the case and as an Investigational Product, and Drug B is identified as a suspect study product in the case and as an Additional Study Drug in the corresponding study configuration.

Investigational Drug + Comparator: When multiple drugs are identified as suspect products in the case, and these are part of the study, and some drugs are identified as Investigational Products in the study configuration and others as Comparators, the system prints the count of such scenarios under the Investigational Product count only.

- **Active Comparator**: There may be cases where multiple suspect drugs are part of the case and two or more of those drugs are classified as comparators in the study configuration. Serious events of all such cases are counted under the combined products that are part of the study.

  A case falls into the Active Comparator category if the study configuration identifies the suspect product as type Comparator in the study configuration.

  If the case is unblinded (but the study is blinded) and you have access to unblinded data, the system prints the count under Comparator. This column has sub columns based on the actual treatments that were given to patients and were identified as Comparators in the corresponding study.

- **Comparator (Combinational Therapy)**:

  The following combinations can appear under the Comparator counts:

  Drug X + Drug Y: Both Drug X and Drug Y are identified as suspect study products in the case and are identified as Comparator Products in the corresponding study configuration.

  Drug X or Drug Y: Only one of the drugs from the case is identified as a suspect study drug, and this drug is identified as a Comparator Product in the study configuration.

  Drug X + Placebo: When some drugs that are part of the study are identified as Suspect Products in the case, some as Comparator Products and others as Placebos in the study configuration, the system prints the count of such scenarios under Drug X OR Drug X + Drug Y only, without adding the placebo drug name.

  Drug X + Drug Y: Drug X is identified as a suspect study product in this case and is identified as a Comparator Product, and Drug Y is identified as a suspect study product and as an Additional Study Drug in the corresponding study configuration.

- **Placebo**: For a drug identified as the Placebo type, the system prints the count under Placebo. If multiple placebos are part of the case, they are shown under the heading of Placebo only without showing multiple Placebos in the summary tabulation.

- **No Study Drug Given**: For a drug identified as the No Study Drug Given type, the report prints the count under this category without printing the name of configured drug. This column lets you retrieve Serious Adverse Events that occurred from the moment the patient signed the informed consent to first administration of study medication, where no actual study medication was given to the patient.

7.4.3 DSUR Tabulation Format

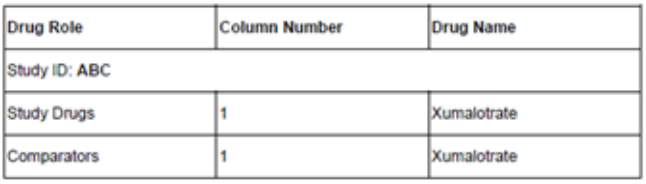
The report prints the count for medicinal products in the first column, followed by Blinded, Active Comparator, Placebo, and No Study Drug Given.

If the event count is 0 for Medicinal Product, Blinded, Active Comparator and Placebo columns for a given SOC, the system does not print that SOC in the report.

The DSUR tabulation prints the short name for investigation drugs and comparator drugs. For investigational drugs, the system prints SD1, SD2, SD3, and so on, based on the number of study drugs that are part of the investigational product column count. For comparator drugs, the system prints the short name as Comp1, Comp2, and so on, based on the number of comparator drugs that are part of the Active Comparator column count.

The system provides a table of information for all tabulations for detailing the study drugs and comparator drugs names used in the tabulation corresponding to each short name. This table has the following format and contains the following fields:

Figure 7–7 Table Format



Drug Role	Column Number	Drug Name
Study ID: ABC		
Study Drugs	1	Xumalotrate
Comparators	1	Xumalotrate

Table 7–5 Drug Roles and their Descriptions

Drug Role	Description
Study ID	Name of the study ID used in the tabulation grouping.
Study Drugs	The system prints the column number of the study drugs used in the tabulation and its actual name in the Drug Name Column.
Comparators	The system prints the column number of each comparator drug used in the tabulation and its actual name in the Drug Name Column.

Note: The system displays all SUSAR events with an asterisk *. The SUSAR event term (PT or LLT) appears with an asterisk to the right of the term. For example, SEPTICEMIA*.

The system displays all special interest events with a superscript †. For example, OEDEMA†. You can configure the list of special interest events for a report by using the Argus Safety CTPR configuration screen.

Drugs configured as Placebo or No Study Drug Given are not part of the summary table.

Figure 7–8 Drug Roles

Drug Role	Column Number	Drug Name
Study ID: **Combo Study**		
IMP Treatment	1	Drug A + Drug B
IMP Treatment	2	Drug A
Comparator Treatment	1	Drug X + Drug B
Comparator Treatment	2	Drug X

Preferred Term	IMP1	IMP2	Blinded	Comp 1	Comp 2	Placebo	No Study Drug Given	Total
Alanine aminotransferas increased	1	2	1	0	0	0	0	4
Total	**1**	**2**	**1**	**0**	**0**	**0**	**0**	**4**

Nervous System Disorders

Preferred Term	IMP1	IMP2	Blinded	Comp 1	Comp 2	Placebo	No Study Drug Given	
Syncope	1	3	1	1	0	1	1	5
Headache	0	1	0	0	1	1	0	2
Total	**1**	**4**	**1**	**1**	**1**	**2**	**1**	**11**

Data Example

In the example above (Figure 7-8), the product types configured for this study are:

Drug A – IMP

Drug B – Additional Study Drug

Drug X – Comparator

Drugs configured as Placebo or No Study Drug Given are not part of summary table.

7.4.4 Totals

The system provides the following totals and subtotals for each tabulation:

- Subtotal per System Organ Class (SOC) per study medication category (IMP, Blinded, Active Comparator, Placebo, No Study Drug Given).
- Row-level totals for Total event counts for a preferred term including investigational, blinded, comparator, placebo and No Study Drug Given (Total).

7.4.5 Summary Counts

The **Total Counts for All Cases (Initial + Follow-up) and Studies** summary count table displays various counts for all cases (Initial + Follow-up) from all studies. It appears once for each tabulation, that is, once for the Main Summary tabulation, once for Fatal Summary Tabulation, and so on.

This count table has fixed columns that print the total of all event terms, cases and patients for IMP treatments, Comparator treatments, Blinded, Placebo and No Study Drug Given columns from the DSUR tabulation.

The system uses the following labels for these counts:

- **Total Number of Events**: Displays the sum of all events terms corresponding to IMP Treatment, Comparator Treatment, Blinded, Placebo and No Study Drug Given for each column. These totals are based on Main, Fatal, and Cumulative tabulations.
- **Total Number of Distinct Cases**: Displays the count of distinct cases for all summary columns.

- **Total Number of Distinct Patient IDs**: Displays the count of distinct patient IDs configured for cases that are part of the respective tabulation. Any case where patient ID is not configured is not counted in this column, that is, only those patients are counted where patient ID is configured. If the same patient ID is configured in multiple cases or the same patient is part of multiple cases from this tabulation, that patient ID is counted only once.

Figure 7–9 Summary Count Table

Total Counts for All Cases (Initial + Follow-up) and Studies

	IMP Treatments	Blinded	Comp Treatments	Placebo	No Study Drug Given	Total
Total Number of Events	6	8	1	0	2	17
Total Number of Distinct Cases	5	6	1	0	1	13
Total Number of Distinct Patient IDs	4	5	1	0	1	11

7.5 Executing a DSUR from BIP

For information about how to execute a DSUR from BIP, refer Section 6.6, "Executing the PBRER from BIP".

8

Post Marketed Aggregate Report

This chapter contains the following topics:

8.1 Report Objective and Sections

The Post-Marketing Aggregate Report (PMAR) includes OOB line listings and summary tabulations that can be used to meet supplemental line listings for PBRERs.

The Post Marketed Aggregate Report includes the following line listing sections:

- Main line listing
- Ad hoc 1 line listing
- Ad hoc 2 line listing
- Ad hoc 3 line listing
- Ad hoc 4 line listing

8.2 PMAR Sections

The PMAR includes the following Summary tabulations:

- Summary Tabulation for HCP
- Summary Tabulation for Consumer
- Summary Tabulation for Clinical Trials

- Cumulative Summary Tabulation for Serious Unlisted Events

The following Information is part of the PMAR Trailer Section:

- Case IDs without any qualifying drugs
- Case IDs without any qualifying events
- Labels configured for drugs in the drug list
- Cases with Missing Assessment

The PMAR considers parameters as per the sheet available in the PBRER specifications section for the column **Required in PMAR?** marked as **Yes**.

- PSUR Configuration: as per the attached sheet **Related Argus Configuration**.
- BIP report parameters: as per attached sheet **Parameter Display**.
- To support PMAR, a main case series and cumulative case series is generated based on the inclusion criteria defined in the PSUR configuration of Argus Safety. The system evaluates the list of cases from the main and cumulative case series to categorize them.
- Name

8.3 Argus Configuration (PSUR) for PMAR

The PSUR configuration screen lets you distinguish the configuration options used in the BIP report as parameters only if the BIP Aggregate Reporting module is enabled.

Refer to the section Section 2.4, "Periodic Configuration Identification of BIP Parameters," for the report parameters used in PMAR.

8.4 Main Line Listing

Cases printed in the Main line listing are based on the Main case series if specified; otherwise they use the Inclusion Criteria and Product Selection parameters of the PSUR configuration.

8.4.1 Grouping

The Main Line Listing provides grouping based on the following groups of cases:

Table 8–1 Main Line Listing Grouping

Sl	Temp table reference
Grouping based on HCP or Consumer	Cases having Primary reporter marked as Health care Professional are considered as HCP cases. Cases having Primary reporter not marked as Health care Professional are considered as Consumer cases.
Grouping based on Initial or Follow-up	Cases are listed under **Initial** or **Follow-up** based on temp table logic. Initial case listing is printed followed by Follow-up cases.
Grouping based on Products	Cases with company suspect products matching those in the Products selected are grouped. If there are no cases for a product specified in the product selection specified in Report Configuration, this product name does not appear as a header. If a case has multiple company suspect products that are in the product selection specified in report configuration, the case is presented in each product's section; that is, the case appears multiple times in the report.

Table 8–1 (Cont.) Main Line Listing Grouping

Sl	Temp table reference
Grouping based on SOC (as per event order specified in the case form event tab)	Cases are grouped by the SOC of the Event. The system displays the SOC group header in the internationally agreed order as specified in the codelist SOC_DISPLAY_ORDER. Case appears under the SOC of the Primary event and the system prints a reference of this information for SOCs of other events if the BIP Report parameter **List cases in the line listing under SOC for each diagnosis** is **Y** and **List Cases under all events, details under the primary event** is selected. Case appears under the SOC of the Primary event and not under other SOCs if the BIP Report parameter **List cases in the line listing under SOC for each diagnosis** is **N** and **List Cases only once, under the primary event** is selected.
Grouping based on Case Seriousness	Cases with Serious case level seriousness are printed under the group header **Serious**. Cases with Non-Serious case level seriousness are printed under the group header **Non-Serious**. Cases with case level seriousness as blank are printed under **Seriousness not defined**. The order of printing these group headers is **Serious**, **Non-Serious** and **Seriousness not defined**.
Sorting based on Case Numbers	Cases are displayed in the ascending order of the Case Numbers in the Main line listing.

8.5 Line Listing Columns

Table 8–2 Main Line Listing Columns

Column Name	Field Description
Case Number	If the BIP report parameter **Indicate if case was expedited previously** is **Y**, the symbol specified in the BIP parameter **Symbol for Expedited cases** appears as a superscript. A footnote appears at the end of the page as: *<symbol>: Expedited Case*. If the BIP report parameter **Indicate if case was expedited previously** is **Y**, the footnote for Expedited Cases appears even though there may not be any cases marked as Expedited.
Country	Country of Occurrence.
Report Type	Report type is displayed from the flex bucketing codelist field **RPTTYEPGRP** for the report type entered in the case.
Unique PatientID	Unique Patient ID as per the BIP report configuration parameter UNIQUE_PATIENT_ID_ FORMAT, which has the following options: Pt - Patient ID CePt - Center ID, Patient ID InPt - Investigator Name, Patient ID StCeInPt - Study ID, Center ID, Investigator Name, Patient ID StCePt - Study ID, Center ID, Patient ID StCnCeInPt - Study ID, Country name, Center ID, Investigator Name, Patient ID StCnCePt - Study ID, Country name, Center ID, Patient ID StCoCeInPt - Study ID, Country ISO Code, Center ID, Investigator Name, Patient ID StCoCePt - Study ID, Country ISO code, Center ID, Patient ID StInPt - Study ID, Investigator Name, Patient ID
Sex	Patient Sex. **PATIENTSEXTEXT** is populated using the decode context GL of the **PATIENTSEXCODE** field.
Age	Patient Age; if this data is missing, the Patient age group is printed.
Company Suspect Products	Company suspect products that match the Product specified in the Report configuration. If the BIP report parameter **Print Unblinded Data** is **Y**, the system prints the Unblinded Study Product. If the BIP report parameter **Print Unblinded Data** is **N**, the system prints the Blinded Study name instead of the actual study product.
Strength	Strength and Strength units.

Table 8–2 (Cont.) Main Line Listing Columns

Column Name	Field Description
Dosing Regime	If the Report parameter **Print Dose Text in place of Regimen Dose** is checked, then Regimen Dose data is printed. Otherwise, Daily dose and Route data are printed with the respective company suspect drug based on the BIP report parameter **Dosage String Format** with the options: Do - Print Dose Only. DoFo - Print Dose, and Formulation. DoFoFr - Print Dose, Formulation, and Frequency. DoFoFrRt - Print Dose, Formulation, Frequency, and Route of administration. DoFoRt - Print Dose, Formulation, and Route of administration. DoFr - Print Dose, and Frequency. DoRt - Print Dose, and Route of administration. Multiple components are separated by semicolons. If a suspect drug has multiple dosage regimens, the dosage information for each record is printed in a separate line.
Action Taken	Action taken is printed for the company suspect drug.
Treatment Date	Dates of the First and Last dose are printed in **DD-MON-YYYY** format.
Treatment Duration	Dosage duration is printed with units. If duration is not available, the text entered for the BIP parameter **Default for NULL Values** is printed.
Event Start and Stop Date	Event Onset and Stop dates are printed for the corresponding Reactions in the **DD-MON-YYYY** format.
First Dose to Onset	Onset Latency data is printed for the corresponding suspect product and events.
Outcome	Event Outcome is printed for the corresponding events. If Event Outcome is not entered, nothing is printed.
Event as Reported (Preferred term)	Description as Reported and LLT or PT of Event is printed in the format: <Desc. As reported> (<LLT or PT>). If Description as Reported is not entered, LLT or PT is printed with brackets. LLT or PT are based on the BIP report parameter **Print LLT instead of PT**. If the BIP Report Parameter **Print only the Term (LLT or PT)** is **Y**, only the LLT or PT is displayed. Description as reported is not printed. The system prints the Diagnosis if the BIP report parameter **Use Only Diagnosis Events** is **Y**. If this parameter is **N**, the **Diagnosis** and **Symptoms** are printed. The system prints diagnosis and symptoms separately and marks them clearly using symbols provided in the BIP parameter **Symbol for Diagnosis Symptoms**, if the BIP report parameter **Print Diagnosis Symptoms Separately** is **Y**. If this parameter is **N**, then they are printed without any identification symbol. For Unlisted events, the system prints the text specified in the BIP parameter **Symbol for Unlisted Events**. For SUSAR events, the system prints the text specified in the BIP parameter **Symbol for SUSAR Events**. For events marked as Special Interest Events in the Report parameter, the system prints the text specified in the BIP parameter **Symbol for Special Interest Events**.
Causality Rpt/Cmp	Causality as per reporter and Company are printed for the corresponding Product and Events in the format: <Causality as per reporter> / <Causality as per company>.
Seriousness	Event seriousness is printed against each event. Serious, Non-Serious, and Seriousness not determined are printed based on the data in CASE_EVENT.SERIOUSNESS.
Listedness	Listedness information of the event. Listedness is printed based on the BIP Report parameter **Labeling Algorithm** if the PMAR is executed from BIP. If the PMAR is executed from Argus Safety, the following report parameters are considered: Use Assessment in Cases. Re-assess cases against datasheet in effect at beginning. Re-assess cases against datasheet in effect at end.

Table 8–2 (Cont.) Main Line Listing Columns

Column Name	Field Description
Line listing Comments	Text from the Company comment fields.
Other Medications	The list of all suspect products and concomitant products in the case, except the drug for which the report is being run, is printed in the following format: Other suspect Products: <Other suspect Products> Concomitant Medication: <Concomitant Products>
Death date and cause of death (Verified ? Y/N):	Patient Death date and Cause of death are printed in the following format only for **Death** cases: Death date and cause of death (Verified? Y/N): DD-MON-YYYY <Cause of death > (<Y/N>) *For example, Death date and cause of death (Verified? Y/N): 01-JAN-2014 cholera(Y).* If cause of death is populated from autopsy results, then cause of death verified is Y; otherwise it is N.

8.6 Summary Columns for Count

The following counts are provided in the Main line listings at the end of various groupings:

Count of Cases for Initial or Follow-up based on HCP or Consumer and Drug appear in the following order:

1. Count of Cases for Initial / Follow-up based on HCP /Consumer and <Drug>
2. Count of Cases for Initial based on HCP and <Drug>
3. Count of Cases for Follow-up based on HCP and <Drug>
4. Count of Cases for Initial based on Consumer and <Drug>
5. Count of Cases for Follow-up based on Consumer and <Drug>

Count of Cases for Initial or Follow-up HCP appear in the following order:

1. Count of Cases for Initial HCP
2. Count of Cases for Follow-up HCP

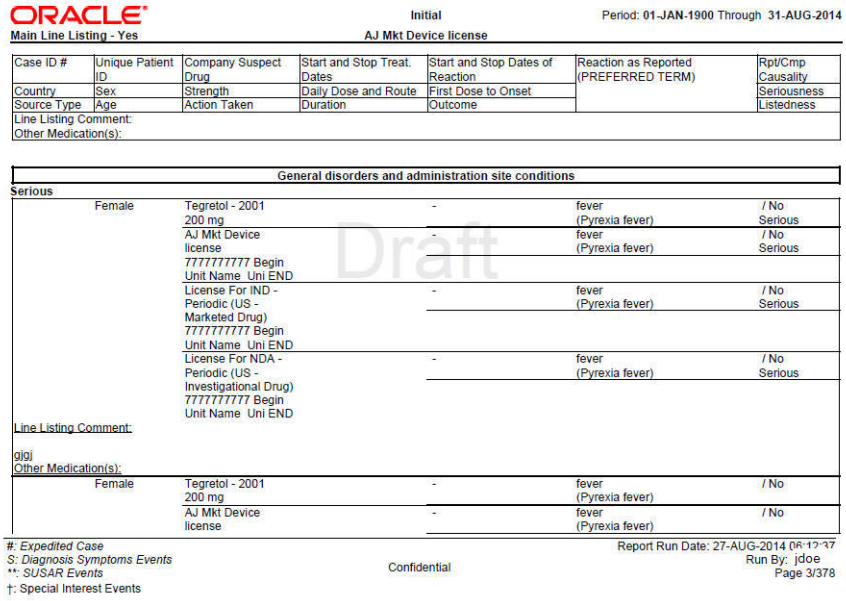
Count of HCP or Consumer Cases appear in the following order:

1. Count of HCP Cases
2. Count of Consumer Cases

8.7 Report Format

The following is the PMAR Report format:

Figure 8–1 Report Format



ORACLE

Initial — Period: 01-JAN-1900 Through 31-AUG-2014

Main Line Listing - Yes — AJ Mkt Device license

Case ID #	Unique Patient ID	Company Suspect Drug	Start and Stop Treat. Dates	Start and Stop Dates of Reaction	Reaction as Reported (PREFERRED TERM)	Rpt/Cmp Causality
Country	Sex	Strength	Daily Dose and Route	First Dose to Onset		Seriousness
Source Type	Age	Action Taken	Duration	Outcome		Listedness
Line Listing Comment:						
Other Medication(s):						

General disorders and administration site conditions

Serious

Female	Tegretol - 2001 200 mg	-	fever (Pyrexia fever)	/ No Serious
	AJ Mkt Device license 7777777777 Begin Unit Name Uni END	-	fever (Pyrexia fever)	/ No Serious
	License For IND - Periodic (US - Marketed Drug) 7777777777 Begin Unit Name Uni END	-	fever (Pyrexia fever)	/ No Serious
	License For NDA - Periodic (US - Investigational Drug) 7777777777 Begin Unit Name Uni END	-	fever (Pyrexia fever)	/ No Serious
Line Listing Comment: gjgj				
Other Medication(s):				
Female	Tegretol - 2001 200 mg	-	fever (Pyrexia fever)	/ No
	AJ Mkt Device license	-	fever (Pyrexia fever)	/ No

Draft

#: Expedited Case
S: Diagnosis Symptoms Events
**: SUSAR Events
†: Special Interest Events

Confidential

Report Run Date: 27-AUG-2014 06:12:37
Run By: jdoe
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8.7.1 Ad Hoc Line Listing Sections

Ad hoc section has the same line listing format and fields as the Main line listing section.

- Ad hoc 1 line listing is based on cases from ad hoc Case List 1.
- Ad hoc2 line listing is based on cases from ad hoc Case List 2.
- Ad hoc3 line listing is based on cases from ad hoc Case List 3.
- Ad hoc4 line listing is based on cases from ad hoc Case List 4.
- Counts that are displayed in the ad hoc section are the same as those in Main line listing.

8.7.2 Summary Tabulations

Cases considered for Summary Tabulations section are based on the Main case series.

The PMAR supports the following tabulation sections:

- PMAR Summary Tabulation
- Summary Tabulation for Consumer Cases
- Summary Tabulation for Clinical Cases
- Cumulative Summary Tabulation for serious unlisted events

8.7.3 PMAR Summary Tabulation

- HCP and Non-HCP cases are tabulated in this section of the report. The table is organized first by Initial or Follow-up, Product and SOC, then by Solicited or Non Solicited, Seriousness, Study Type (Sponsored versus Unsponsored Study).

- Only related events (related to company drug that is specified in product selection) are considered for this tabulation for solicited cases. Relatedness information is not considered for Non-Solicited cases.
- If the report parameter **Exclude non serious cases from summary tabulations** is set to **Y**, the system still prints the Grouping and Counts based on Non-Serious events which are part of serious cases. Only Non-serious cases and corresponding events are ignored based on parameter value of Y.

8.7.4 Grouping

Summary Tabulations for HCP cases report are grouped on the following options:

Table 8–3 HCP Case Grouping

Sl	Temp Table Reference
Grouping based on Initial or Follow-up	Cases are listed under **Initial** or **Follow-up** based on temp table logic. If the report parameter **Include Follow-up cases from Summary Tabulation** is set to **N**, then summary tabulations are not printed for follow-up cases.
Grouping based on Products within Product Selection	Cases with the company suspect products matching with the products selected in the report configuration are grouped. Drug names that appear in the group header are arranged in ascending order. If there are no cases for a drug that is specified in the drug list, then this drug name does not appear as a header. If a case includes multiple company suspect drugs that are in the drug list, the case is presented in each drug's section; the case appears multiple times in the report.
Grouping based on SOC	Cases are grouped by the SOC of the Primary Event. SOC group headers are displayed in the Internationally agreed order as specified in the codelist SOC_DISPLAY_ORDER. If the Report parameter **List cases in the Line Listing under SOC for each diagnosis** is **Y**, the case is listed multiple times under different SOCs. If this parameter is set to **N**, the case is printed under the SOC of the primary event, and a reference to this information is printed for the SOCs of other events.

8.8 HCP Summary Tabulation Columns

Table 8–4 HCP Summary Tabulation Columns

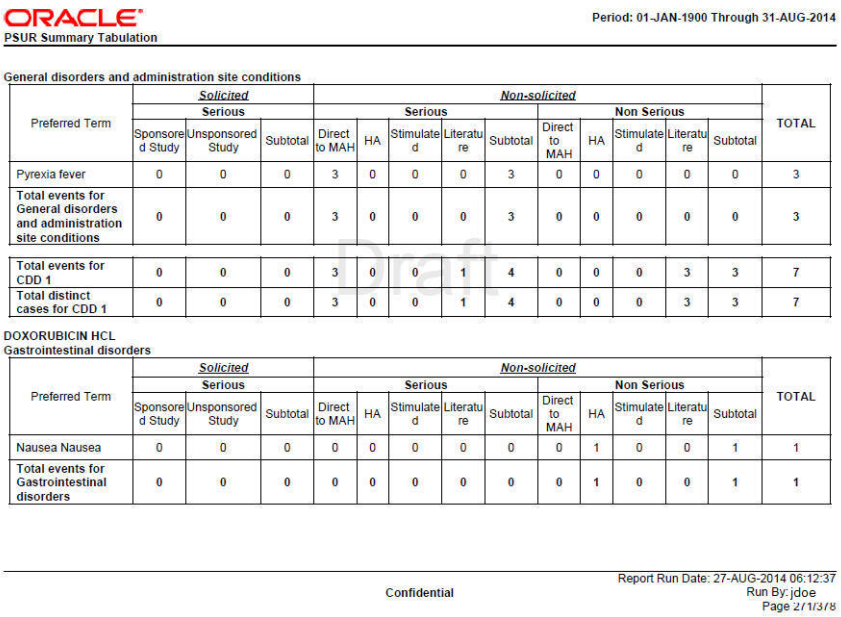
Sl	Temp table reference
Preferred Term	LLT or PT is printed based on the report parameter **Print LLT instead of PT**. System prints diagnosis if the report parameter **Use Only Diagnosis Events** is **Y**. If this parameter is **N**, then diagnosis as well as symptoms are printed. LLT or PT is arranged in alphabetical order within a SOC.
Solicited	Solicited cases are clinical trial cases having atleast one event related to the drug. Either the company or reporter causality flag is Y.
Serious-Sponsored	The count of Serious Events with report type group as **Sponsored Study**, and case type text as **Solicited** is printed in this column.
Serious-Non-Sponsored	The count of Serious Events with report type group as **Non-Sponsored Study**, and case type text as **Solicited** is printed in this column.
Sub-total	The sub-total is computed by summing-up Serious sponsored and unsponsored events from Solicited cases.
Non-Solicited	Non-Solicited cases are Non-Clinical trial cases having atleast one event related to the drug. Either the company or reporter causality flag is **Y**.

Table 8–4 (Cont.) HCP Summary Tabulation Columns

SI	Temp table reference
Serious-Direct to MAH	The count of Serious Events with report type group as **Direct to MAH**, and case type text as **Non-solicited** is printed in this column.
Serious-HA	The count of Serious Events with report type group as **HA**, and case type text as **Non-solicited** is printed in this column.
Serious-Stimulated	The count of Serious Events with report type group as **Stimulated**, and case type text as **Non-solicited** is printed in this column.
Serious-Literature	The count of Serious Events with report type group as **Literature**, and case type text as **Non-solicited** is printed in this column.
Sub-total	The sub-total is computed by summing-up Serious events from Non-Solicited cases.
Non-Serious -Direct to MAH	The count of Non-Serious Events with report type group as **Direct to MAH**, and case type text as **Non-solicited** is printed in this column.
Non-Serious-HA	The count of Non-Serious Events with report type group as **HA**, and case type text as **Non-solicited** is printed in this column.
Non-Serious-Stimulated	The count of Non-Serious Events with report type group as **Stimulated**, and case type text as **Non-solicited** is printed in this column.
Non-Serious-Literature	The count of Non-Serious Events with report type group as **Literature**, and case type text as **Non-solicited** is printed in this column.
Sub-total	The sub-total is computed by summing-up Non-Serious events from Non-Solicited cases.
Total	The total is computed by summing-up the sub-totals of Solicited and Non-solicited columns.
Total events for <SOC>	The count of Events is printed against respective column at the end of SOC grouping.
Total events for <Drug>	The count of Events is printed against respective column at the end of Drug grouping.
Total of distinct cases for <Drug>	The count of Distinct Cases is printed against respective column at the end of Drug grouping.

8.8.1 Format for HCP Summary Tabulations

Figure 8–2 Format for HCP Summary Tabulations



ORACLE
PSUR Summary Tabulation

Period: 01-JAN-1900 Through 31-AUG-2014

General disorders and administration site conditions

Preferred Term	Solicited			Non-solicited									TOTAL
	Serious			Serious					Non Serious				
	Sponsored Study	Unsponsored Study	Subtotal	Direct to MAH	HA	Stimulated	Literature	Subtotal	Direct to MAH	HA	Stimulated	Literature	Subtotal	
Pyrexia fever	0	0	0	3	0	0	0	3	0	0	0	0	0	3
Total events for General disorders and administration site conditions	0	0	0	3	0	0	0	3	0	0	0	0	0	3
Total events for CDD 1	0	0	0	3	0	0	1	4	0	0	0	3	3	7
Total distinct cases for CDD 1	0	0	0	3	0	0	1	4	0	0	0	3	3	7

DOXORUBICIN HCL
Gastrointestinal disorders

Preferred Term	Solicited			Non-solicited									TOTAL
	Serious			Serious					Non Serious				
	Sponsored Study	Unsponsored Study	Subtotal	Direct to MAH	HA	Stimulated	Literature	Subtotal	Direct to MAH	HA	Stimulated	Literature	Subtotal	
Nausea Nausea	0	0	0	0	0	0	0	0	0	1	0	0	1	1
Total events for Gastrointestinal disorders	0	0	0	0	0	0	0	0	0	1	0	0	1	1

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8.9 Summary Tabulation for Consumer Cases

Format for HCP Summary Tabulations

Consumer cases are tabulated in this section of the report. The table is organized first by Initial or Follow-up, Product and SOC, then by Seriousness.

Cases with GTT_RPT_AGG_CASE.CASEMEDICALLYCONFIRMTEXT = Consumer are considered for this section, that is, consumer cases are those cases where the primary reporter has **Health Care Professional** set to **No**.

This section is not printed if **Include only HCP cases if Summary Tabulation** is set to **N**.

Grouping

Summary Tabulations for Consumer cases reports are grouped on the following options:

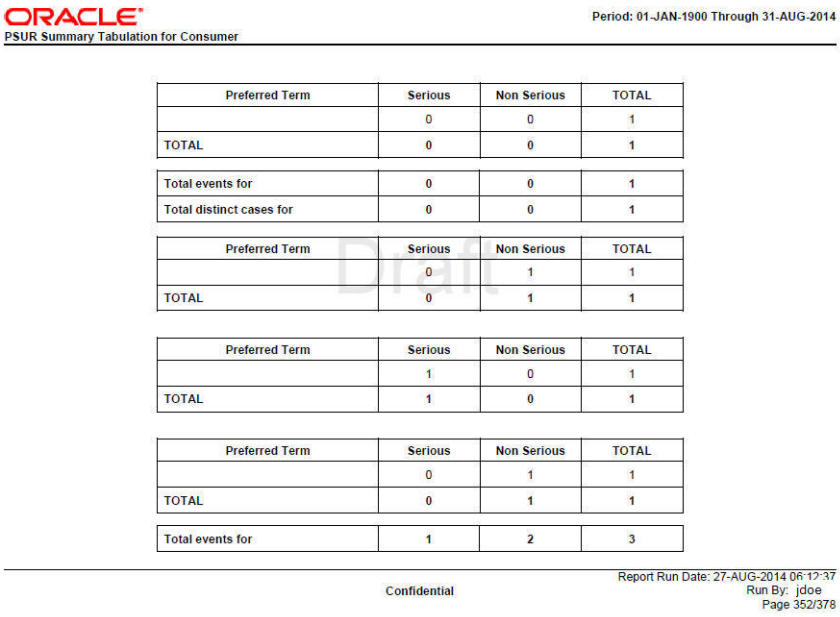
- Grouping based on Initial or Follow-up
- Grouping based on Products within Product Selection
- Grouping based on SOC
- Grouping logic is as per requirements defined in Summary Tabulation for HCP Cases.

Consumer Summary Tabulation Columns

Table 8–5 Consumer Summary Tabulation Columns

Sl	Temp table reference
Preferred Term	LLT or PT is printed based on the report parameter **Print LLT instead of PT**. System prints diagnosis if the report parameter **Use Only Diagnosis Events** is **Y**. If this parameter is **N**, the **Diagnosis** and **Symptoms** are printed. LLT or PT is arranged in the alphabetical order within a SOC.
Serious	The count of Serious Events from Consumer cases grouped by Initial or Follow-up, Product SOC, is printed in this column.
Non-Serious	The count of Non-Serious Events from Consumer cases grouped by Initial or Follow-up, Product SOC, is printed in this column.
Total (Column)	The total is computed by summing-up Serious and Non-Serious events against individual LLT or PT.
Total (Row)	The total is computed by summing-up Serious and Non-Serious events; Grand total of all events is computed by summing-up all serious and non-serious events.

Figure 8–3 Consumer Summary Tabulation Screen


ORACLE
PSUR Summary Tabulation for Consumer
Period: 01-JAN-1900 Through 31-AUG-2014

Preferred Term	Serious	Non Serious	TOTAL
	0	0	1
TOTAL	0	0	1

Total events for	0	0	1
Total distinct cases for	0	0	1

Preferred Term	Serious	Non Serious	TOTAL
	0	1	1
TOTAL	0	1	1

Preferred Term	Serious	Non Serious	TOTAL
	1	0	1
TOTAL	1	0	1

Preferred Term	Serious	Non Serious	TOTAL
	0	1	1
TOTAL	0	1	1

Total events for	1	2	3

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8.10 Format for Clinical Trial Summary Tabulations

8.10.1 Cumulative Summary Tabulation for Serious Unlisted Events

The Cumulative Summary Tabulations section is derived based on the Cumulative case series for Cumulative period event counts and Main case series for Current period event counts.

This tabulation includes only the S or UL Diagnosis events (relatedness of an event is not considered for this tabulation).

This table is organized first by HCP or Consumer, Product, and SOC, then by a comparison of events from current reporting with the cumulative reporting report.

Grouping

Cumulative Tabulations for Serious Unlisted (S or UL) cases report are grouped on the following options:

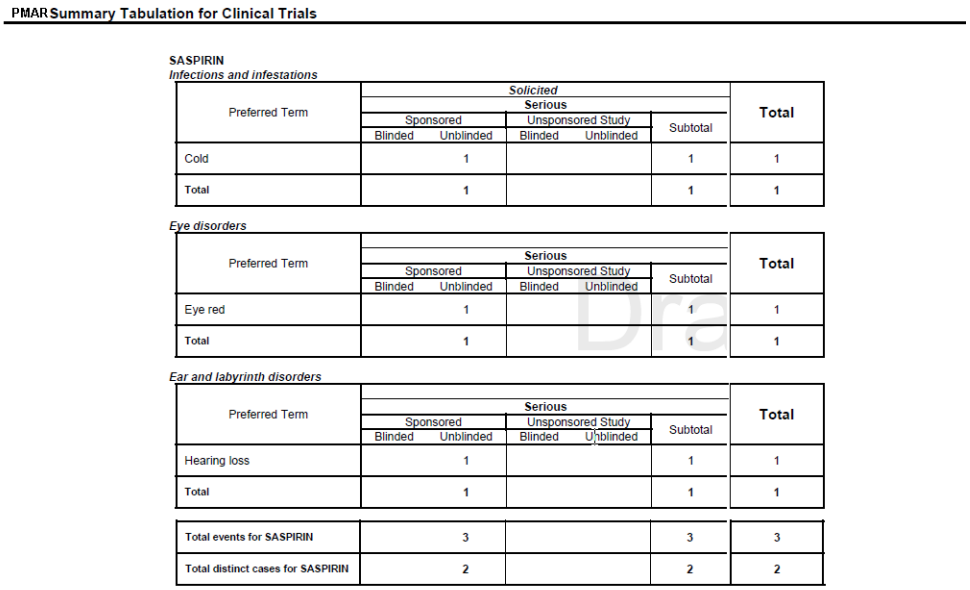
- Grouping based on HCP or Consumer
- Grouping based on Products within Product Selection
- Grouping based on SOC
- Grouping logic is as per requirements defined in Summary Tabulation for HCP Cases.

Clinical Trial Summary Tabulations

Table 8–6 Clinical Trial Summary Tabulations

Sl	Temp table reference
Preferred Term	LLT or PT from S or UL diagnosis events is printed based on the report parameter Print LLT instead of PT. LLT or PT is arranged in the alphabetical order within an SOC.
Current Period	The count of S or UL diagnosis events from the Main case series is computed against LLT or PT. Follow-up events from the Main case list are not considered for the Current Period.
Cumulative Period	The count of S or UL diagnosis events from the Cumulative case series is computed against LLT or PT.
Total	Summation of count of diagnosis event within SOC is printed under Current Period and Cumulative Period respectively.
Overall total diagnosis for <Product>	The count of diagnosis is printed against respective column at the end of Product grouping.
Overall total of distinct cases for <Product>	The count of Distinct Cases is printed against respective column at the end of Product grouping.

Figure 8–4 Summary Tabulation for Clinical Trials Screen



PMAR Summary Tabulation for Clinical Trials

SASPIRIN

Infections and infestations

Preferred Term	Solicited / Serious					Total
	Sponsored		Unsponsored Study		Subtotal	
	Blinded	Unblinded	Blinded	Unblinded		
Cold		1			1	1
Total		**1**			**1**	**1**

Eye disorders

Preferred Term	Serious					Total
	Sponsored		Unsponsored Study		Subtotal	
	Blinded	Unblinded	Blinded	Unblinded		
Eye red		1			1	1
Total		**1**			**1**	**1**

Ear and labyrinth disorders

Preferred Term	Serious					Total
	Sponsored		Unsponsored Study		Subtotal	
	Blinded	Unblinded	Blinded	Unblinded		
Hearing loss		1			1	1
Total		**1**			**1**	**1**

Total events for SASPIRIN	3		3	3
Total distinct cases for SASPIRIN	**2**		**2**	**2**

Format for Summary Tabulations for Serious Unlisted Events

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8.11 Executing a PMAR from BIP

Refer to Section 6.6, "Executing the PBRER from BIP" to execute a PMAR from BIP.

A

Report Parameters and their Definitions

The following is a list of parameters required for PBRER, PMAR, and DSUR.

Table A–1 Parameter List

Parameter Display Name	Related Argus Configuration	Possible Values	Parameter Description
Enterprise ID	-	All enterprises to which the user has access.	This parameter displays the values of all enterprises to which the user has access. Depending upon the enterprise value, the system filters the other parameter values and shows values corresponding to the selected enterprise only.
Report Configuration Name	Selected Periodic Configuration Name	All the aggregate report configurations to which the user has access.	The configuration name executes the associated inclusion criteria for case series generation. If **Case Series Name** is not selected, use this parameter by default for fetching the case series name for report generation.
Print As	Report Batch Printing-> Print As	Draft, Final, Internal, or Other.	Defines the mode of printing for the report. Selected value is printed as a watermark , except the *Final* mode. The possible values are Draft, Final, Interval, and Other. For the *Final* mode, a submission record is created in the Argus database. The value of 'Other' supported by Argus Safety application is not supported through BIP user interface. When running a report through the Argus Safety interface, you can still choose the Other option and provide a different watermark to print in the report.
Main Case Series Name	-	All main case series generated using aggregate report configurations.The user can view these case series.	Selects a case series for report generation. The system only displays the main case series that are available for report generation and to which the user has access.
Cumulative Case Series Name	-	All cumulative case series generated using aggregate report configurations. The user can view these case series.	Selects a case series for cumulative counts during report generation. The system displays cumulative case series that are available for aggregate report generation and to which the user has access. For correct results, you must only select related main case series and cumulative case series.
PBRER 6.2 Case Series Name	-	-	All PBRER 6.2 Case Series to which user has access that are generated in the system are available for selection.

Table A–1 (Cont.) Parameter List

Parameter Display Name	Related Argus Configuration	Possible Values	Parameter Description
Ad hoc Case List 1	Line Listing Query Criteria	-	If a case series has already been generated through Argus, auto populate through the selected Configuration Name and provide an option to override the auto populated values. If case series has NOT been generated through Argus, use the configuration name to associate the attached line listing queries and generate the case series at run time. If Line Listing queries are not attached to any ad hoc section, that section is printed without any case data.
Ad hoc Case List 2	Line Listing Query Criteria	-	If a case series has already been generated through Argus, auto populate through the selected Configuration Name and provide an option to override the auto populated values. If case series has NOT been generated through Argus, use the configuration name to associate the attached line listing queries and generate the case series at run time. If Line Listing queries are not attached to any ad hoc section, that section is printed without any case data.
Ad hoc Case List 3	Line Listing Query Criteria	-	If a case series has already been generated through Argus, auto populate through the selected Configuration Name and provide an option to override the auto populated values. If case series has NOT been generated through Argus, use the configuration name to associate the attached line listing queries and generate the case series at run time. If Line Listing queries are not attached to any ad hoc section, that section is printed without any case data.
Ad hoc Case List 4	Line Listing Query Criteria	-	If a case series has already been generated through Argus, auto populate through the selected Configuration Name and provide an option to override the auto populated values. If case series has NOT been generated through Argus, use the configuration name to associate the attached line listing queries and generate the case series at run time. If Line Listing queries are not attached to any ad hoc section, that section is printed without any case data.
Primary Reporting Destination	Selected Reporting Destinations	List of all the available reporting destinations from LM_ REGULATORY_ CONTACT.AGENCY_NAME where deleted is NULL.	The submission record is added to the Argus database corresponding to the primary reporting destination. The system looks at primary destinations for a list of cases that were submitted during the previous reporting cycle. Note: When a report is marked as submitted for the primary reporting destination, the system provides an option to add the submission record for other configured destinations. This does not affect the BIP report. Only one destination can be selected as the primary destination while running the report.
Print Unblinded Data	-	Y/N	This parameter is applicable only if you can view unblinded data; otherwise blinded data is printed irrespective of the value of this parameter.
Default for NULL Values	-	-	This default value is populated in temp tables corresponding to any NULL values for specific set of fields.

Table A–1 (Cont.) Parameter List

Parameter Display Name	Related Argus Configuration	Possible Values	Parameter Description
Labeling Algorithm	-	1. Use Case Assessment from Event Assess	The system provides five options for this parameter while running the report through BIP:
		2. Re-assess using datasheet at start date	Use Event Assess table with License List Use Case Assessment from Event Assess Re-assess using datasheet at start date Re-assess using datasheet at end date Use Event Assess table with Report type + datasheets: Lets you specify which Datasheet to look against for Listedness when running the report.
		3. Re-assess using datasheet at end date	
		4. Use Event Assess table with License List	
		5. Use Event Assess table with Report type + datasheets	When using the Event assessment from the case, the system considers only the **As Determined** listedness of the primary event or the case listedness from the case.
			When the **ALL** datasheet is selected, the system uses the most conservative listedness for the primary event, or the Case Listedness, for the report.
			When a datasheet is selected, the system uses the listedness against this datasheet for the report.
			The system calculates the Datasheet for Listedness on the Inclusion Criteria for ALL products within the case and not only for the first suspect drug.
Indicate if case was expedited previously	-	Y/N	Y: The system identifies expedited cases in the report and marks them with a symbol provided.
			N: No action required.
Symbol for expedited cases	-	-	A symbol to mark expedited cases in main line listing and tabulation summary reports.
Print only the Term (LLT or PT)	Line Listing-> Print Only the Term	Y/N	If N: Print verbatim along with PT or LLT as selected in other parameter.
			If Y: Print only PT or LLT as selected.
Print LLT instead of PT	Line Listing-> Print Only the Term (PT or LLT)	Yes/No	If No, print PT.
			If Yes, print LLT
Use Only Diagnosis Events	Line Listing->Event Reporting (CTPR)	Y/N	If Y Only Diagnosis events are populated in the temp table. If any value other than 1 or 0 is present in database, the system considers the event as diagnosis event.
Print Diagnosis Symptoms Separately	-	Y/N	If Y, the system prints the diagnosis and symptoms separately and marks them clearly using the symbol provided.
			If N, the system prints the diagnosis and symptoms without any identification symbol. Only applicable to summary tabulations.
Symbol for Symptoms	-	Symbol for identifying symptom	Identifies symptoms. If above parameter is N, nothing is printed for symbol.
Dosage String Format	-	Dose	Based on the value of combination of values selected, the system displays the dosage information in the report.
		Dose,Formulation	
		Dose,Formulation,Frequency	
		Dose,Formulation,Frequency,Route	
		Dose, Formulation,Route	
		Dose,Frequency	
		Dose, Route	

Table A–1 (Cont.) Parameter List

Parameter Display Name	Related Argus Configuration	Possible Values	Parameter Description
Include only HCP cases in summary tabulation	-	Y/N	If Y, the system includes only HCP cases in summary tabulation. If N, the system includes HCP and Non-HCP cases in summary tabulations.
Include follow-up cases from summary tabulations	-	Yes/No	If Yes, the system includes the follow-up cases also. If No, the system includes only initial cases in summary tabulations.
Exclude non-serious cases from summary tabulations	-	Y/N	Filter Criteria for Summary tabulation to exclude non-serious cases.
List cases in the line listing under SOC for each diagnosis	Line Listing-> List Cases only once, under the primary event, and List Cases under all events, details under the primary event	Y/N	If Y, the system prints other SOC as a reference. Otherwise, the system prints the details each time.
Log debugging messages	-	Y/N	-
Print identical events in line listing(Y/N)?	-	Y/N	The system compare PT code to identify matching events. If Y, the system prints all identical events. If N, the system prints the primary event. It prints the primary event or compare seq number or the event which appears first on Argus case form if primary event is not identical.
Print Dose Text in Place of regimen dose	Line Listing-> Print Dose Text in place of regimen dose	Y/N	-
Include Summary of Cases Missing Assessments	Summary Tabulations	Y/N	If this parameter is set to Y, the system displays the summary of cases missing assessment in report QA section.
Include Summary of Unlocked Cases	Summary Tabulations->Include Summary of Unlocked Cases	Y/N	If this parameter is set to Y, the system displays the summary of unlocked cases in report QA.
Report Title	Subject of Report-> Report Title	-	If this parameter is set to Y, the system displays the Report Title in the report. If this parameter is NULL, the system uses the report template Name.
Report #	Subject of Report-> Report #	-	If this parameter is set to Y, the system displays the Report # in the report cover page. If this parameter is NULL, the Report # is blank.
Report Footer	Subject of Report-> Report Footer	-	If this parameter is set to Y, the system displays the Report footer in the report. If this parameter is NULL, the system uses the default text.

Table A–1 (Cont.) Parameter List

Parameter Display Name	Related Argus Configuration	Possible Values	Parameter Description
UNIQUE_ PATIENT_ID_ FORMAT	-	Center, Patient Investigator, Patient Patient Study, Center, Investigator, Patient Study, Center, Patient Study, Country name ,Center, Investigator, Patient Study, Country name, Center, Patient Study, Country ISO Code, Center, Investigator, Patient Study, Country ISO code, Center, Patient Study, Investigator, Patient	Prints unique patient identifier based on following selections: Patient ID Center, Patient Investigator, Patient Study, Center, Investigator, Patient Study, Center, Patient Study, Country name, Center, Investigator, Patient Study, Country name, Center, Patient Study, Country ISO Code, Center, Investigator, Patient Study, Country ISO code, Center, Patient Study, Investigator, Patient.
Symbol for SUSAR Events	-	-	A hidden parameter with a default value of SUSAR that is printed with any SUSAR events in the case. You can update the report parameter list with another default value.
Symbol for Special Interest Events	-	-	A hidden parameter with the default value of **†.** The list of special Interest events can be configured on the periodic configuration screen on the **Special Intereset AE** tab.You can update the report parameter list with another default value.
Print As Other Text	Report Batch Printing-> Print As	-	When the **Other** Option is selected in **Print As** parameter, you can use this text box to enter the water mark text.
Clinical Drug Role Alogorithm	-	1. Categorize based on Target Drug List 2. Categorize based on Product Type within the Study Configuration	For Algorithm 1: Use product list or target product list for categorization of case. For Algorithm 2: Use Study Configuration for categorization of case Based on the selected algorithm population logic of ClinicalDrugRole column of GTT_RPT_AGG_CASE is determined. This column is used in PBRER and DSUR report for categorizing a case under IMP, Blinded, Comparator and Placebo columns.
Print Serious Adverse Events or Reactions	-	1. Print Serious Adverse Reactions 2. Print Serious Adverse Events	DSUR Cumulative tabulation, DSUR Main Listings and PBRER 6.3 section either print the serious adverse reactions (SAR) or serious adverse events (SAE) based on the value of this report parameter and the default value for the parameter is SAR.

Table A–1 (Cont.) Parameter List

Parameter Display Name	Related Argus Configuration	Possible Values	Parameter Description
Follow-up Algorithm	-	1. Use Submission Tracking 2. User Timeframe (Initial Receipt Date)	Algorithm#1: 1. A case is categorized as follow-up if it has previously been submitted to the same regulatory agency and report form; otherwise it is categorized as initial. For cases that have been missed in the previous period, the same logic applies and those cases are marked as initial or follow-up based on the submission record. Algorithm#2: 1. A case that is a part of the case series is marked as Initial if the initial receipt date of that case falls into current reporting period; otherwise it is marked as follow-up. For cases that have been missed in the previous period, the same logic applies and those cases are assessed for initial receipt date only.
Persist data of Temp Tables	Argus Console->System Configuration->System Management (Common Profile Switches) -> Reporting->BIP Aggregate Reporting-> Persist data in BIP Aggregate Temp Tables	Yes/No	Yes: System persists or stores the data of BIP aggregate temp tables for selected case series used for aggregate reports generation. No: Data of BIP Aggregate Temp tables are not persisted for selected case series.
Number of Days for Data Persistence	Argus Console->System Configuration->System Management (Common Profile Switches) -> Reporting->BIP Aggregate Reporting-> Number of days for which data of BIP Aggregate Temp Tables are persisted.	-	Data of BIP Temp tables for selected case series is persisted for the number of days defined in this parameter. On completion of configured period (Number of days from the last modified date of selected case series), database/system job purges the data of this case series fro temp tables.

Glossary

compassionate use

In certain situations, the Food and Drug Administration (FDA) allows companies to provide their experimental drugs to people outside of clinical trials. This is referred to as compassionate use. Basically, *compassionate use* to the treatment of a seriously ill patient using an unapproved drug (investigational drug) when no other treatments are available.

development international birth date (dibd)

The date of first authorization for the conduct of an interventional clinical trial in any country.

international birth date (idb)

The date of the first marketing authorization for any product containing the active substance granted to any company in any country in the world.

investigational drug

The term investigational drug indicates only the experimental product under study or development. This term is more specific than *investigational medicinal product*, which includes comparators and placebos.

medicinal product

Medicinal product is a product containing a substance or a combination of substances produced and intended for the treatment or prevention of diseases in humans or in animals, for diagnostic purposes, improvement or modification of physiological functions or for achieving other medically justified objectives.

non-interventional trials

Non-interventional trials are not within the scope of the regulations, that is, those where the medicinal product is prescribed in the usual manner in accordance with the terms of the marketing authorization. In these cases the assignment of a patient to a particular therapeutic strategy is not decided in advance by a trial protocol, but falls within current practice, and the prescription of the medicine is clearly separated from the decision to include the patient in the study. Also, no additional diagnostic or monitoring procedure related to the therapeutic strategy is applied to the patients and epidemiological methods that are to be used for the analysis of data.

ongoing clinical trial

Trial where enrolment has begun, whether a hold is in place or analysis is complete, but for which a final clinical study report is not available.

solicited reports

Solicited reports are those derived from organized data collection systems, which include clinical trials, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare providers, or information gathering on efficacy or patient compliance.

spontaneous report or spontaneous notification

An unsolicited communication to a company, regulatory authority, or other organization that describes an *adr* in a patient given one or more medicinal products and which does not derive from a study or any organized data collection scheme.