PV-Works Human User Guide

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1 Overview

1.1 Introduction

The PV-Works application is implemented either:

- locally in a customer's own IT environment.
- hosted Ennov PV / Assured Information Systems Ltd.
- as a hosted pre-configured PV247 system.

This guide applies to all three environments but the reader should be aware that the PV247 implementation is pre-configured and some of the functionality described herein is not available.

1.2 PV-Works: General Description

PV-Works combines workflow functionality with flexible product safety functionality to produce an integrated application that meets both business and regulatory needs for pharmacovigilance. The same software can satisfy the requirements of companies of all sizes ranging from international organisations with distributed databases, through departmental systems, to single users, or in a mixed environment of any combination of system type.

The process management module tracks individual cases through a series of process steps, which may be assigned on a case by case basis. The system supports multiple process templates allowing different processes to be applied to different case types. Individual users only see those cases that require their immediate attention and workload supervisors can review and re-assign the workload for individual users and workgroups. With the process data set, managers are able to measure actual performance against targets, allowing the identification of bottlenecks, over-allocated staff, under-tasked staff and training needs.

(Note: Since the workflow module is optional and an "additional cost" item, not all customers will implement it. Without this module process tracking may be achieved by a combination of queries and the ad-hoc "action board task function").

The design of the pharmacovigilance modules supports:

- international reporting requirements for single case reports and line listings from the key regulatory authorities world-wide.

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- easy to use, intuitive data entry and review screens that may be tailored to meet local business requirements *(not PV247)*.
- multiple assessments by different staff at different times (i.e. reporter, company).
- batch reporting of cases to regulatory authorities, subsidiary offices and partners.
- full compliance with ICH guidelines including a module for data transmission as defined by ICH E2B including medical device reporting in the eMDR format.
- fully integrated proactive workflow (optional module).
- MedDRA coding dictionary.

The system is both flexible and efficient. A separate Systems Administration function allows selected staff to configure PV-Works to an individual customer's requirements (not "PV247"). This includes defining specific code list data values, adding user-defined fields to the database and creating teams of users to be assigned to process tasks.

There is a separate functional specification for the Systems Administration tool.

The PV-Works application and its Systems Administration tools are controlled by strict security functions that allow the administrator to control access to particular functions and to particular cases.

1.3 General Principles for Data Entry & Update

1.3.1 General Principles

PV-Works data entry, update and assessment screens follow the design shown in Figure 1

Figure 1

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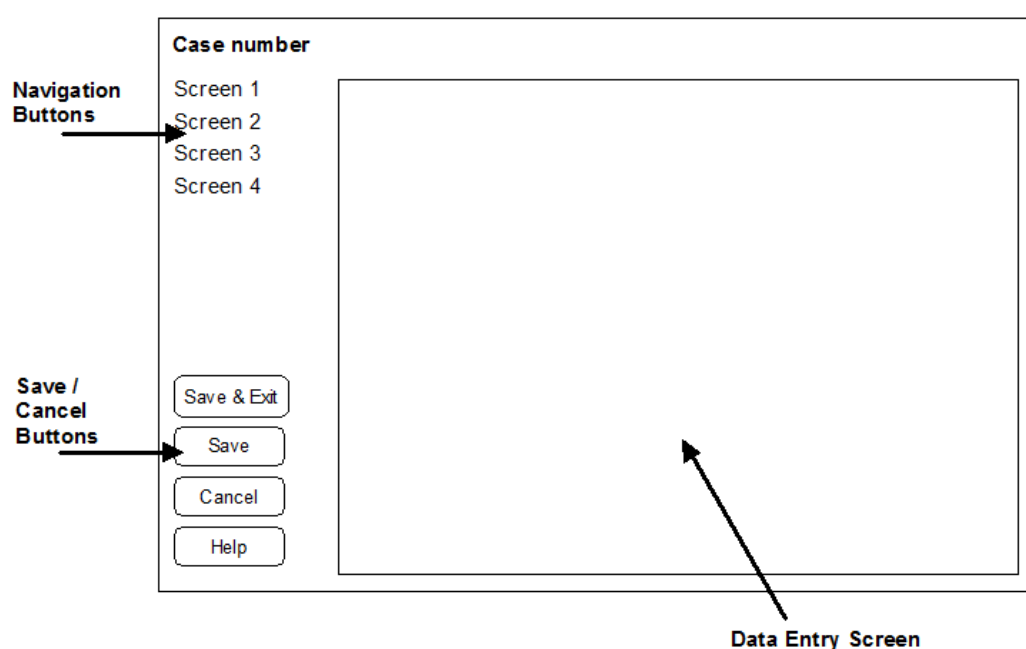
The Navigation Buttons on the top left-hand column of the screen are used to move between individual data entry or review screens in the list.

The 'Save' and 'Save & Exit' buttons are used to save data to the database.

The 'Cancel' button returns to the main menu, discarding any unsaved amendments.

1.3.1.1 How to Move around the system

When the user first starts a Data Entry / Update session the above screen is displayed with the data entry screen window showing 'Screen 1'. The navigation buttons 'Screen1, Screen2' etc. may be clicked using the **left-hand mouse button** to change the display in the Data Entry window.

The user can display individual screens in any order and as many times as required during an editing session. When a screen has been displayed, its title on the navigation area changes colour to indicate to the user that it has previously been visited.

Alternatively, the user may move from page to page in sequence using the **Page Up / Page Down** keys.

The order of the screens displayed in the Data Entry / Update function is controlled by the System Administrator.

1.3.1.2 Read-Only Screens

Screens can be configured with 'read-only' security so that data can be read but not altered; this option may be useful where data needs to be provided to support changes that will be made in other screens, e.g. to support a review. For example the sample screen shown in

Figure 1 - Read Only Screen shows all fields as grey.

Figure 1 - Read Only Screen

1.3.1.3 'Save & Exit', 'Save', 'Cancel' and 'Help'

The four save / cancel buttons at the bottom of the navigation bar have the following functions:

Save & Exit

Saves all the data changes made since the last save (or the editing session began) and then will exit the Data Entry / Update function.

The user is returned to the screen that called the Data Entry / Update screen, typically either the Main Menu or the 'to do' list. The Save & Exit function requires that the user confirms the save operation (see Figure 2).

Figure 2 - Confirm & Save operation

By cancelling the Save command no data is saved to the database and the user is returned to the data entry screen so that further data entry can take place.

Save

Save all the data changes made since the last save (or the editing session began) but remains in the Data Entry / Update function. This Save function can be used during large edit sessions to reduce any risk of data loss due to system failure.

The Save function requires that the user confirm the save operation. See Figure 2 above.

Cancel

Cancels all the data changes made since the last save (or the editing session began) and then exits the Data Update function. The user is returned to the screen that called the Data Update screen. Note that once data changes are saved by either of the two Save options above, they cannot be cancelled.

The Cancel function requires that the user confirms the Cancel operation. See Figure 3 below.

Figure 3 - Cancel operation
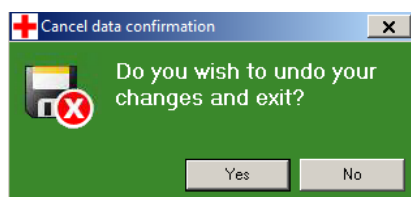
By cancelling the Cancel command no data is saved to the database and the user is returned to the data entry screen so that further entry can take place.

Help

View the on-line help text.

1.3.1.4 Data Entry / Update Screen Styles

There are two basic types of data entry screen:

- Simple Style where all data fields are displayed in a single window
- Multiple Record Style where a case has several records holding similar information e.g. Adverse Events

These are described below:

Simple Data Entry Screen Style

Simple data entry screens either display all their data in a single window or in a single window with pop-up windows for additional information.

Figure 4 - Simple Record Data Entry Screen

Above is a typical example. A case has only one patient and therefore only one entry for fields such as gender, initials and weight. Some data is related very closely to the patient but is less commonly entered. This is found on a pop-up window accessed via a button e.g. autopsy details.

Multiple Record Data Entry Screen Style

Some data types may occur several times in a case and the number of occurrences in a case will vary. Examples of this type of record are laboratory tests, adverse events and products. For these types a Multiple Record Data Entry Screen style is used as in the example shown in Figure 6.

Figure 6 – Multiple Record Data Entry Screen

Each event (or product or contact etc.) is displayed in summary form at the foot of the screen. This gives an immediate indication that there are 'n' items of the same data type (e.g. two adverse events in Figure 6). These sections act as navigation bars within the list. Amendment of individual records is achieved via the buttons on the right hand side of the screen:

- Add a new record

Click this button to create a new record. The system will open a new blank record ready for data entry. This is similar in operation to a simple data entry screen. Once data has been entered it is 'saved' to the Multiple Record format and appears as a new record at the bottom of the list.

To Save a new record or changed information to the database you must also use the 'Save' or 'Save and Exit' buttons.

- Delete a record

Click this button to delete the selected record. The system asks you to confirm this action as shown in Figure 7.

Figure 5 - Confirmation of deleting a record
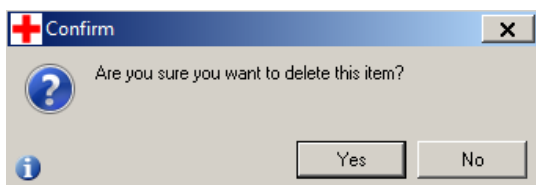
Navigation between the individual records can be achieved in three ways:

1. Using the arrow keys (the 2 outer arrows takes the user to the first / last records while the 2 inner arrows move the user to the adjacent records).

2. Selecting the record to display within a grid

Test Date		Name		Result		Abnormal		Normal range		Self meas
1-Mar-2017		24 Hour Glucose						-		No
1-Mar-2017		Aldosterone						-		No
1-Mar-2017		24 Hour Creatinine						-		No

3. Keyboard shortcuts: CTRL ->, CTRL <-, CTRL ↓ and CTRL +.

1.3.2 Notes on Fields

'Notes on fields' are internal, working comments that may be made against any database field. They can contain additional information about the data item, internal company comments on the significance of the data or any other information that the user feels is pertinent. Such data may be extracted for internal reports if necessary. The notes facility can be tracked using the audit trial facility.

No regulatory information should be stored in notes, i.e. none of the data stored in a field note is reportable. All descriptive text, which is required in a regulatory report (such as a case narrative, PSUR comment), is held in a narrative field, which is part of the main data entry screen.

All notes are displayed on a single screen, the "Call History" screen.

Figure 6 – Notes displayed in a Call History Screen

Any number of notes may be attached to a single data item by one or more users. The author's name and the date and time are automatically saved.

To read a note field browse the 'Call History' screen which is one of the data entry screens listed on the left hand side of the case container.

1.3.3 Dates

Dates entered into PV-Works are of two types:

- User entered – related to the case or its management (e.g. start of treatment, date case received).
- System generated – automated (e.g. date database record created, date of audited change).

Most system-generated dates are not visible to the user.

While system generated dates are always known precisely, user entered dates can be either incomplete (partial) or approximate. For example, the start of treatment may need to be recorded as 'May 2012' or 'around 23 December 2011'.

To achieve this all user-entered dates consists of up to four fields, both in the database and on all PV-Works screens. These are:

Day
Month
Year
Approximation flag

The display of the date on PV-Works screens can be changed to Month, Day, Year by the System Administrator

The approximation flag may not be available for certain fields where it is considered an in appropriate option, e.g. date case received.

Not all dates may be entered as incomplete, partial values. For example, it is not permitted to enter the date of case receipt as a partial date.

Dates can be entered either by typing directly from the keyboard or from a pop-up calendar.

Entering a Date from the Keyboard

1. Select the first field in the date
2. The formats for entering dates are:
    - Day: 01 or 1
    - Month: 01 or JAN or jan or Jan
    - Year: full year 1998 or 2-character year only e.g. 98

    - When a year is typed as two characters the century will default from the century valid for that date:

E.g. today's date 6-APR-00:

a date of birth entered as 12-Jan-57 will become 12-Jan-1957
a date of birth entered as 15-Oct-00 will become 15-Oct-1900

Where the date will accept future dates e.g. batch expiry date
E.g. today's date 6-APR-99

Batch expiry date entered as 12-Jan-99 will become 12-Jan-1999
Batch expiry date entered as 12-Oct-01 will become 12-Oct-2001

Entering a Date using the calendar

The calendar function displays a pop up calendar, which allows the user to select the required date and allows the user to move between years and months via buttons.

Select the Calendar by clicking [icon] , the Calendar will appear as shown in Figure 9 below.

Select the required date and click [checkmark icon]

Figure 7 - Calendar
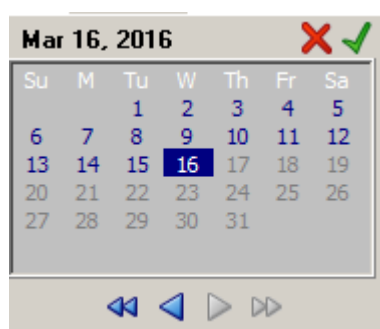
How to erase a Date

Dates can be erased from the screen display using an option available by clicking the right-hand mouse button and selecting 'Clear Date'. This is useful if the date is to be re-entered from the keyboard. See Figure 10Figure 8 au-dessous.

Figure 8 - Deleting a date

Our favourite method of date entry is...

to enter a six-digit number via the keyboard as PV-Works will parse this perfectly. This is the fastest entry method... but remember that the number must be a perfect six-digit number and requires leading zeroes for days and months less than 10. For example, to enter the date 3 May 2012, enter the digits 030512.

2 Starting PV-Works

2.1 How to log on to PV-Works

1. The PV-Works system will have a shortcut icon configured on the desktop or Citrix.
2. Click on this icon to launch PV-Works. The login screen is displayed
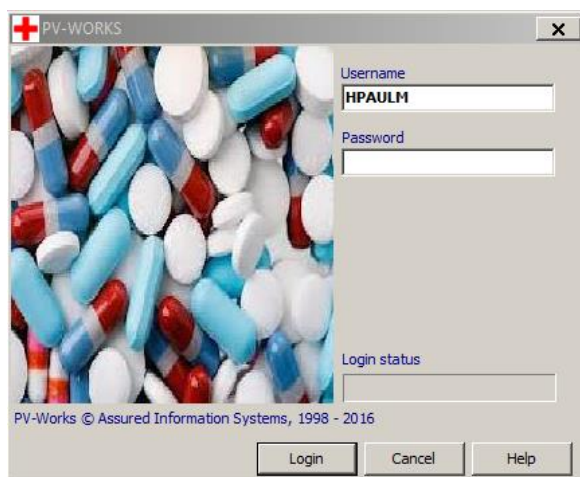
3. Type in your 'Username'.
4. Type in your 'Password'. Note that passwords are case –sensitive.
5. Click 'Login' and upon successful verification of the username and password the user will be logged on and the main screen will be displayed.

> ✎ *If you enter your password incorrectly three times you will be locked out of the system until your System Administrator releases your account lock.*

The System Administrator can force a user to enter a second password where a company wishes to enforce two-factor authentication. The second password could be a pin number, a date or a memorable word.

2.2 Password Expiry.

In some cases, when logging into PV-Works a message may appear after entering your correct password. There are two types of messages that you may be given.

1. Password expiry

   This message is to let you know that your password has expired and must be changed immediately. In order to change your password, you need to select 'OK' on the message displayed.

Figure 9 - Password expired message
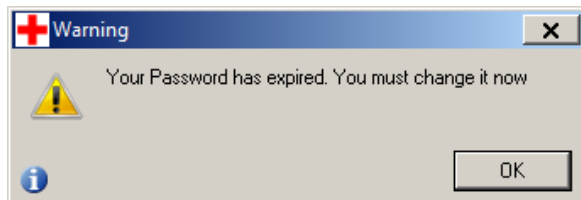
Once your password has expired no access to the PV-Works application will be granted until it has been changed.

2. Password expiry warning
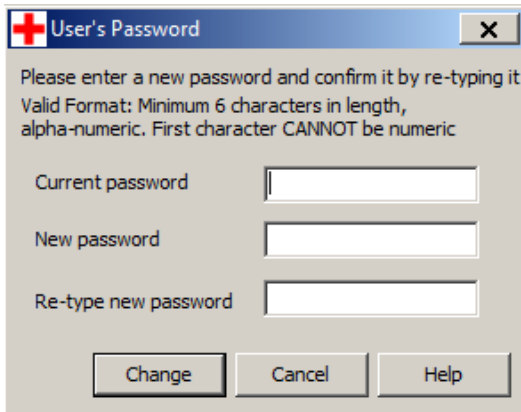
   This message is a warning to let you know that your password is about to expire, and gives you the opportunity to enter a new value now (Figure 13). By pressing 'No' on this message you are taken straight to the main screen with the password unchanged so that you may continue with a more urgent task. Each time you log in you will be warned until the password has been changed.

Figure 10 - Password expires warning message
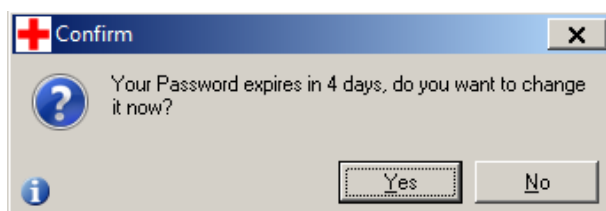
If you decide to change your password (or are forced to change it), another pop-up will appear (see Figure 14). From here you will need to enter your original password then underneath this your new value, then confirm the new value again underneath that.

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Figure 11 - Change User Password Pop-up
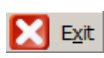
Once you press 'change' a message will appear saying that your new password has been saved.

> 🖉 *In some cases on pressing 'Change' a message may appear saying 'Your new password must be different from your old password'. Re-enter both passwords to ensure that they are identical*

> 🖉 *Alternatively you may see a message saying 'Your new password does not conform to the correct character style'. This means that the new password entered does not comply with business rules, eg is too short, does not include a number etc. The System Administrator can control this pattern.*

> 🖉 *Alternatively you may see a message saying 'Your new password has already been used". This may mean that you are not able to use the new password as it is the same as one of your previous ones. The System Administrator can control the number of distinct passwords you must select.*

2.3 How to log out of PV-Works

PV-Works uses the Windows standards for exiting a system. If you are updating information for example using the Data Entry screen, select the 'Cancel' button to exit back to the main menu or save your data as required. The system will ask you to confirm that you wish to exit this screen.

From the main menu, select the **close window** button on the top right hand side of the screen. ☒ or click the EXIT button ❌ Exit This will return you to the PC desktop. Alternatively, the user can use the menu option 'File' -> 'Exit'.

3 PV-Works Main Screen

The PV-Works main screen is the core screen of PV-Works and is one of the primary methods of changing the current case and of carrying out a task. Its design is a combination of menu items and buttons that lead to the various functions of the application and a query function that finds cases to process or that answer a question.

The Main Screen is broken into four main functional areas:

1. Interactive menu panel offering access to a set of pre-defined queries ("Available queries" in Figure 15)

2. Flexible grid displaying the results of the selected pre-defined case query ("Query Results Grid" in Figure 15)

3. Icon bar and standard Windows menu system offering access to specific case functions ("Function Buttons" and "Drop down menus" in Figure 15)

4. Case number search that allows cases to be found by their reference number. ("Case number entry" in Figure 15)

Figure 12 - PV-Works Main Screen

Figure 12 - PV-Works Main Screen

3.1 Drop Down Menu Options
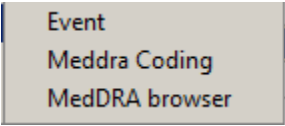
The following menu options and sub-options are available via the drop-down menus at the top of the screen. The precise options available to the current user depend on the user's security rights – this means that YOU may not see all of the options described below:
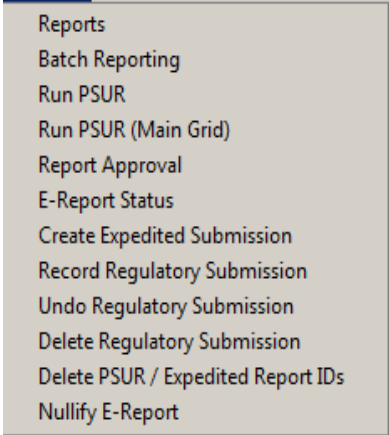
The items marked with an asterisk (*) are those that tend to be available to most users…. But of course as PV-Works is configurable, this is not a hard and fast rule.
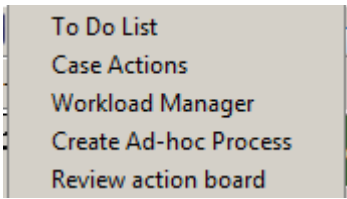
Menu option	Functions	Description
File	Select Version Version Case Copy Case Delete Case Close Case Re-Open Case Case Comparison Lock Case Lock/Close a Clinical Trial Electronic signature questions Change Password Configuration ▶ Exit 1 2016-UK-0144 2 2016-UK-0142 3 2016-UK-0143 4 2016-UK-0139 5 2016-UK-0141 6 2016-UK-0140 7 2016-UK-0137 8 2016-UK-0136 9 2016-UK-0135	• Select a version of a case • Creates a new version of a case • Copy Case to new Case * • Deletes a selected case, once deleted this case cannot be viewed • Closes a case and the case can still be viewed • Re-Open a Case (enabled if a closed case exists) • Case Comparison compares two cases at database level. • Lock case *or* Unlock case * • Lock or close a study • Change Electronic Signature Questions • Change User Password * • Exit from PV-Works* • Select one of the 'most recently used' cases *
Data		• Create a new case * • Link two or more cases together * • Browse the case (read-only mode) * • Edit / update the case *
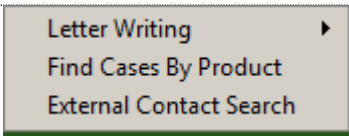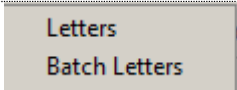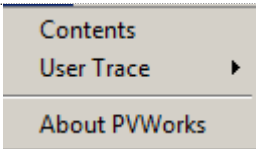
Menu	Options	Description
	New Case Link Case Review Case Entry / Update Review with Audit Trail Equivalent Products Code ▸ Unblind Case Unblind Clinical Trial	• Browse the case - with the changed fields trapped by the Audit Trail indicated in Red * • Selects the equivalent Products screen • Displays a sub menu allowing you to code the case. See Below * • Unblind the current case * • Unblind all cases in a study
Code	Event Meddra Coding MedDRA browser	• Code Events (to Costart / WhoArt) • Code events against MedDRA * • Browse the MedDRA dictionary
Report	Reports Batch Reporting Run PSUR Run PSUR (Main Grid) Report Approval E-Report Status Create Expedited Submission Record Regulatory Submission Undo Regulatory Submission Delete Regulatory Submission Delete PSUR / Expedited Report IDs Nullify E-Report	• Preview, print & export reports (Regulatory & internal) * • Print Multiple Single Case Reports • Selects PSUR Set-up screen * • Run a PSUR from cases on the main screen • Report Approve a case * • View e-report submission status * • Print multiple cases for submission • Record Submission of batch reports • Revoke Submission of batch reports • Delete details of batch report • Submit a nullification e-report *
Tasks	To Do List Case Actions Workload Manager Create Ad-hoc Process Review action board	• Display the 'to do' list * • Display the process for current case • Workload management for the system • Creates an Ad-hoc process for this case

		• Review action board tasks initiated by yourself *
External	Letter Writing ▶ Find Cases By Product External Contact Search	• Displays Letter Writing options Menu (see Below) • Find cases by product details • Contact search screen
Letter writing	Letters Batch Letters	• Selects the Letter Writing options • Selects Batch Letter Options
Help	Contents User Trace ▶ About PVWorks	• On-line help system • Run user diagnostic trace – for use when advised by Assured support team • Information about the PV-Works system *

3.2 Toolbar Icons

The following icons are available in a ribbon bar at the top of the screen. The precise icons available to the current user depend on the user's security rights – this means that you may not see all of the icons described below:

The items marked with an asterisk (*) are those that tend to be available to most users…. but of course this is not a hard and fast rule.
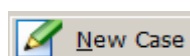
New Case	Creates a new case *
Update	Edits an existing case *
Assess	Assess a case *
Review Case	Review / browse a case *
Duplicate Check	Check for duplicates *
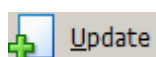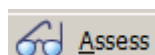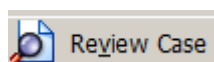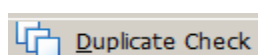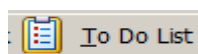
To Do List	Takes you to your To-Do list screen *
E-Report Status	View the status of reports submitted electronically
Action	Create an action board task for the current case *
Reports	Report a case *
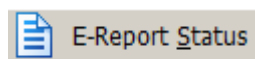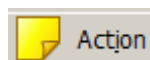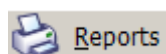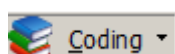
Coding ▾ Gives you a menu of code options (see Below)
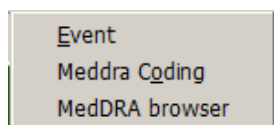
Event
Meddra Coding
MedDRA browser

- Code Events (to Costart / WhoArt)
- Code events against MedDRA *
- Browse the MedDRA dictionary
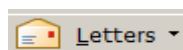
Letters ▾ Write a letter using the current case

Letters
Batch Letters
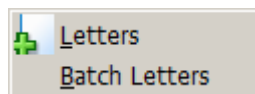
- Letter Templates
- Batch letters
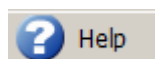
Help Access the On-Line help system *

Find Build a query – note this option is obsolescent as it is replaced by the superior query engine described below (see section 17)
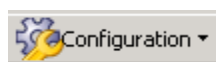
Configuration ▾ Allows for additional configuration of users, products, contacts, codelists, and other system options.

3.3 Case Number Format Box

On the top left hand side of the main screen is the case number format box. This is a quick and easy way to find a case if the case number is already known (Figure 16).

Figure 13 – Case Number Format Box

Once you have entered the case number you need to press the tick button to select the case. The case selected will then be made the currently active case. If, however, the case does not exist a message will be displayed stating this.

4 Case Data Entry

The PV-Works data entry and update functions are designed to:

- Provide easy-to-use screens that are intuitive in operation
- Make extensive use of codelists to promote standardised data entry
- Provide data validation at source so that correction can be made at the earliest opportunity
- Mirror the generic data entry forms as closely as possible.

It is recognised that entry of case data can be a time consuming activity and one that may not be a priority (for example for a case that is non-serious and labelled or the user performs several job roles). If necessary a case may be created with a minimum set of data, giving it a system-generated case number and, if appropriate, initiates a workflow process to control its progress. The user may then return to the case at a later time to complete it.

The above only applies if the case is not received by phone of course. In practice most users will enter the complete case as a single step only returning to it for review or addition of follow up information.

Coding / assessment may be performed during initial data entry or as a subsequent step by the same user or a colleague.

4.1 Creating a new case
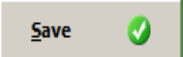
The 'New Case' option registers a new case into the database for the first time.

If the workflow module is implemented, then registering the case allows the user to add a workflow process to the new case thus ensuring management of its handling occurs – even though it contains little or no data.

Figure 14 - New Case Screen

How to create a new case:

1. From the 'Data' menu select 'New Case' or click on the toolbar.
2. The new case screen will be displayed similar to that shown in Figure 17.
3. Enter basic case information on the 'Case Identification' screen:

- Case type – **Mandatory (default value selected by your configuration).**
- Problem type – **Mandatory (product defect cases may be added).**
- Information type – **Mandatory (default value selected by your configuration).**
- Quality complaint associated – A defect is associated with an Adverse Event report.
- References – Hold external case numbers including the ICH E2B world-wide case number.
- Case status – Read-only field that defaults to current case status.
- Date case status set – Read-only field that defaults to the date the case was created.
- Case owner – Read-only field that defaults to the user's location.
- Source – Multiple sources may be added.
- Date first received – **Mandatory (defaults to today's date).**
- Date first valid – **Mandatory field (see below).**
- Date latest follow-up – See below.
- Country where event occurred – **Mandatory (defaults to user's location).**

4. Save the case by clicking _____[Save ✓]_____.

5. A confirmation message will appear and on pressing 'yes' your case will then be assigned a case number, which will appear in the top left hand side of the screen. You are then able to continue on with your case without exiting the data entry screen.

    OR you could click _____[Save and Exit ✓]_____ to save the case information and exit it.

6. The system will ask you to confirm. See Figure 3.

7. Once saved the system will generate the case identification number and return you to the main menu where your new case will be displayed.

Note that it is not a requirement that the case is saved at this point. It is quite acceptable to enter all case information before saving it at a later time.

Notes:

1. If a clinical trial case is selected the user will be prompted to select the appropriate study from a drop down list upon exit from the "Case Type" box. The user may also be able to select the centre at which the study is performed and so add this information to the case automatically (On the "Contacts" screen).

This function depends on configuration data added by your System Administrator – or in the case of PV247 customers via PV-Works itself.

Figure 15 – Study Selection Screen

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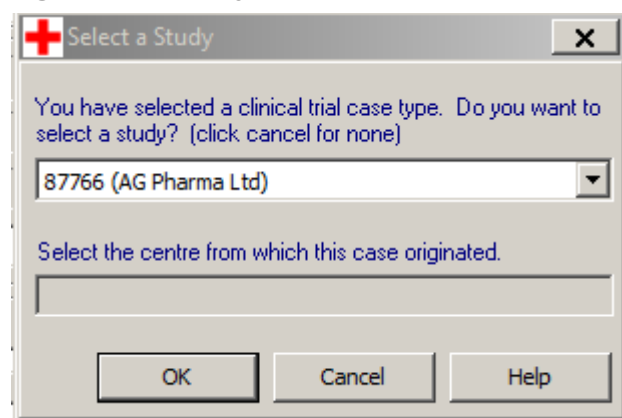
2. Date First Received is the date the information was originally received by the company. The information may be incomplete at this time, e.g. may result in an invalid case. This field is not reported to a regulatory authority and is essentially a "commercial" field

3. Date First Valid is the date that the four key pharmacovigilance items were first received (i.e. patient, reporter, product, event). This is the regulatory clock start date and is used on reports to regulatory authorities. While this date is typically the same as the Date First Received, it can be later. Date First Valid can only be entered if the Information Type is set to "Confirmed AE" – i.e. a valid case.

4. Date Follow Up is the date of latest information received AFTER a report has been submitted to a regulatory authority and is used in regulatory follow up reports. (Information received after initial case entry but before initial report is not recorded here as it is data that will be included in the initial report).

4.2 Assigning a workflow process

If the workflow module is implemented a workflow template is assigned to each new case when it is initialised. The template controls the tasks that are required to evaluate distribute report and archive the case.

Once the workflow process has been assigned to the new case, PV-Works calculates the target dates for each task based upon the date of receipt of the report and the expected duration for each task. The first task (or tasks) is automatically ready to be carried out and will immediately appear in the 'to do' list of the appropriate users.

4.3 Call Notes

Call notes may be captured on the Call History screen. In addition, a separate call notes display side panel (as shown in Figure 19), may also be used to view / edit call notes.

This is made available by the toolbar icon and provides a toggle function (i.e. Show Call Notes / Hide Call Notes). The call notes can be viewed from any data screen. A fresh call note field will be made available for every case editing session and scroll buttons allow the user to review previous entries. The side panel areas may be re-sized and the system will remember the user's previous settings.
The user can configure the call notes to default to being shown or being hidden when

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opening a case by using the system option SHOW_CALL_NOTES.

Figure 16 – Call Notes

5 Data Entry / Update screens

PV-Works is delivered with a complete set of Data Entry / Update screens. These are shown in the following sections. These screens are used both for editing existing cases or entering all new case data directly.

5.1 Case Identification

The case identification screen shown in Figure 6.1.1 summarises the core reference information about the case, such as case type, case source, case status and reference numbers. It is possible to select multiple sources for a case. The initial reporter is displayed in bold text and may be selected via the right mouse button.

Figure 6.1.1: Case Identification screen

The following fields are mandatory:

- Case type
- Problem type
- Date received
- Country where the case occurred

Information type: This field will be used to control whether the reported case is complete / ready for reporting or not. Values will probably include:

- 'Suspect Report' – case is incomplete and not ready for reporting
- 'Confirmed AE Report' – all four elements present (patient, event, product, reporter) and case is reportable
- 'Reported Adverse Health Experience' – all four elements present (patient, event, product, reporter) for a HE product. Case is not reportable
- 'Information only' – not an adverse event or not reportable

Setting this field to 'Confirmed AE Report' will start the regulatory clock (see 'Case Dates' below).

Validation rule

When the case is saved, the system will check the 'Information type' field against the case validity, i.e. whether the case has data in patient, event, product and reporter. If it does and the information type is not set to 'Confirmed report' or 'Reported AHE', the user will be prompted to change the information type (and start the regulatory clock if appropriate).

Case Dates

The field 'Date Received' has been divided into two dates:

- "Date first received" – the date when the company first became aware of the case

- "Date first valid" – the date when the regulatory clock first started for this case, i.e. when it became valid.

Frequently these two dates are coincident.

Basic validation rules are:
- Date first received will default to 'today' when a case is created (i.e. 'New Case' function).
- If information type is set to 'Confirmed report' then 'date case first valid' is set to 'today', otherwise the date is non-enterable.
- Date of latest follow up is greyed out until the case has been approved for reporting
- Date first received is less than or equal to date first valid
- Date first valid is less than or equal to date latest follow up

- Once set the date first received may be edited, but only after the user has clicked the 'edit' button to open this field for editing.
- Once set, the regulatory clock date can be edited.

1. The 'date latest follow up' is set to the date when follow up was received. If the follow up has no regulatory significance, then its date should NOT be entered here as the case will not be re-reported. (The fact that the information was received can be stored in Call Contact History).

2. If the customer has implemented 'report approval', then the 'date latest follow up' will be greyed out until the case has at least one report approval. Then it will be available for edit. The argument is that until report approval all new information is part of the original agency submission.

If the customer has not implemented 'report approval', then the 'date latest follow up' will not be greyed out.

The 'References' section allows the user to enter any number of case reference numbers that pertain to external systems, for example, a licensed partner's case number, a Regulatory Authority's number. The list of available numbers is defined by the System Administrator.

In addition, certain external case numbers are loaded into the database from another system and cannot be edited. Examples include legacy case numbers. The System Administrator may define these so that they can be displayed but cannot be edited and also may limit the case numbers actually displayed 'by location'.

PV-Works will remember the first and last time that a mandatory field is changed after report approval. This may indicate that a report needs to be re-submitted to an agency. The date of first mandatory field change is shown on the Case Identification screen.

When the user selects a case type of 'Clinical trial' the system can prompt for the selection of the study to be used. Section 9.1 gives further details on this feature.

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5.2 Contacts

PV-Works can record details about any number of personnel who are associated with the case. One of the key personnel is the Initial Reporter who is indicated as the 'primary source of information' on the screen shown in Figure 6.2.1. Each contact is shown as a separate record using the multiple records style of the screen.

The screen format allows the searching of existing cases and the contact dictionary for previous callers. The screen will also show any other cases entered for the same reporter, thus increasing the possibility of identifying a duplicate case.

Figure 6.2.1: Contacts Screen

For a new case the Contacts page is opened ready for entry of the caller's details. The clinic search block will be visible so that the user may enter search criteria, typically either the clinic account number or phone number.

Searching Pre-existing Contacts:

For a new call the Contacts page is opened ready for entry of the caller's details. The contact search block will be visible so that the user may enter search criteria, typically either the clinic account number or phone number.

The radio groups above the search criteria allow the user to control the search process:

- to select 'local versus global' names and addresses - default value is 'Local'.

Note: 'Local' will be interpreted as:

a) the country of the case of occurrence if known.
b) else the default country of the user.

If the country of occurrence has not been entered, and the default country of the users is set to blank the default radio button on the contact search selection will be set to Global.

- to switch from searching the dictionary of customers only to searching all previous cases (only) or both

The dictionary of customers is typically set from an external source, e.g. a CRM system, a Sales system. Users are not permitted to edit this data.

Two methods of searching are available:

Most of the search criteria fields include a 'search binoculars' button to the right of the field. If this is clicked, the contact dictionary and / or cases are searched for matches based on the individual field only e.g. for the contact's last name only.

The following criteria in the Search box have been given individual 'find' buttons:
- Account no
- Phone no
- Mobile / cell no
- Last name
- City
- Zip/Post Code
- Company

By clicking any of these fields the user will be able to search on the dictionary and / or cases using this individual field only. The 'Find' button to the right of the screen offers multi-field searching. The matching cases screen shown after a search and its functionality (and described below) is the same regardless of which find button is used.

If the 'Find' button to the right of the screen is clicked, the search criteria are considered in combination with an 'AND' join between each e.g. 'Last name AND City'

The system will automatically search the contact database and/or previous cases for matches when search criteria data are added to either the 'account no' or 'phone no' fields and the user hits the <<enter>> key. If the user tabs from these fields (or moves using the mouse) and no search criteria have been given, then no search is performed and the user will initiate the search using the 'search' button (binoculars).

The search criteria can be extended by entering data into any of the six search fields. If these fields are used, the user will initiate the search using the 'search' button (binoculars).

All search fields may be partially entered. PV-Works will add wild card characters automatically prior to searching.

1. The same principles apply to the other five search fields (company/clinic name, surname (i.e. last name), city, zip code and country). If criteria are added to these it will be used in combination with the other fields. For each of these fields (except country) a wild character will be added automatically to both the front and the end of the user's search characters.

2. A search criteria field left blank infers that this criterion has no filtering effect.

3. The drop down list allows the user to search for other types of contact, e.g. patient owners, or 'all types'. By default, this will be set to 'clinic'.

4. If a search yields just one "hit" (and this will be a common occurrence when account numbers are entered), the details of the clinic are copied to the Contacts page in Figure without user confirmation. The user may be asked to select the name of the caller from previous contacts made with the selected clinic (see below).

5. If the search yields no hits, a suitable warning message is displayed and the user is left on the Contacts page. The user may click the 'Fill' button to copy the search parameters into the data entry fields to save data entry time.

6. If the search yields more than one "hit" a pop-up display is presented showing the clinics found in the database that match the criteria. See Figure 6.2.2.

Figure 6.2.2: Clinics matching search criteria

From this screen the user may:

1. Select a clinic as the required one. To select a clinic, click any part of the row containing its details and click 'select' or (preferably) double-click the clinic's details. The user will be returned to the Contacts page with the details of the selected clinic pre-loaded. The user may be asked to select the name of the caller from previous contacts made with the selected clinic (see below).

2. Modify the search criteria and re-search as described above.

3. Determine that the clinic details are not in the database and return to the main Contacts page. The user will now enter clinic details manually.

Selecting the caller's name:

When a clinic is selected, PV-Works will provide a list of names known to be associated with this clinic. These will be taken from all calls received from this clinic in the last 12 months together with names of personnel registered in the PV-Works contact database for the clinic. If only one name is retrieved, this will be copied automatically to the contact screen and the user will be returned to 6.2.1.

If more than one name is found, the user will be presented a choice via a re-display of the pop-up window shown in Figure 6.2.2.

The user may select one of the names listed by double-clicking the name or highlighting it and clicking 'select' (in which case it is copied to the contact screen). Alternatively, the user may click 'new caller' in which case the name on the contacts screen is left blank. After clicking either button the user is returned to Figure 6.2.1.

Note that the 'search' criteria fields in Figure 6.2.1 will only be enabled when a new contact is being added, (i.e. via 'add' or initial entry). At all other times these fields will not be available so that the user cannot accidentally overwrite existing data.

Enter Consumer / patient details

If the caller is not a clinic, their contact details are added manually to the screen shown in Figure 6.2.1 Data items may be entered in any order.

Mandatory fields are:

- Case role
- Country (this will default to the country where the event occurred (if known), otherwise to the country of the user).

It is possible to enter an account number manually. While this information is normally supplied from the contact database it is occasionally necessary to enter this data manually, for example in the situation where a new customer raises a complaint or inquiry before their account number is allocated.

To make certain that any changes to the account number are deliberate:

- It will not be possible to tab in to the 'account number' field. Editing will only be possible after the user has 'clicked' the edit box with the mouse.

- When a user leaves the 'account number' field (e.g. via tab or mouse click) and the account number has been changed, a confirmation message will be shown, e.g. 'Are you sure you want to change the Account number?'.

Enter Clinic Name and Address

If the clinic is not in the database, their contact details are added manually to the screen shown in Figure 6.2.1 Data items may be entered in any order.

"Case role" is a mandatory field.

"Country" will default to the country where the event occurred (if known).

It is possible to enter an account number manually

The actual territory and sales representative name(s) are not stored as part of a PV-Works case. This data is derived dynamically when required so that the current information is always displayed and not the historical data at the time when the case was received.

Regulatory reporting and Data Privacy

A flag on the contact screen allows the user to restrict which reporter's details are included in a regulatory report:

If this box is checked, the reporter will be included in a regulatory report; if unchecked it will not.

State and Zip Codes:

It is possible for the System Administrator to create a drop down list of states such that the user may select these rather than type them. Typically this may be set up for USA, Canada and Australia.

Once established, if the country is, say, USA the entry of a valid zip code will populate the state and city fields or will validate them if they are already entered. If a discrepancy is found the user may choose to overwrite the current data with the computer suggested city and state.

5.3 Patient

Patient details are entered on a screen similar to that in Figure 6.3.1 Entry of patient initials needs to be managed according to local data privacy legislation and guidelines. Note that it is possible to make this field 'read only' if necessary.

Some fields are not available until certain criteria has been met. For example, pregnancy details are 'greyed out' and cannot be entered unless the patient's sex is female. Similarly, 'Cause(s) of death' is greyed out until 'Patient died?' is set to 'Yes'.

Figure 6.3.1: Patient Details screen

Entry of weight data is possible using either pounds or kg as units with automated conversion from one to the other. As soon as a value is entered in one of these weight fields, the other is made 'read-only' so that the integrity of the weight value conversion is maintained. Range checks will be added with a warning given if the weight is outside of the range 2 – 150 kg.

In exactly the same manner, height may be entered as:

- Centimetres
- Feet and inches
- Inches only

When an 'inches value' greater than 12 is entered it will be converted to feet and inches. A warning will be given if the height is outside of the range 60 – 225 cm.
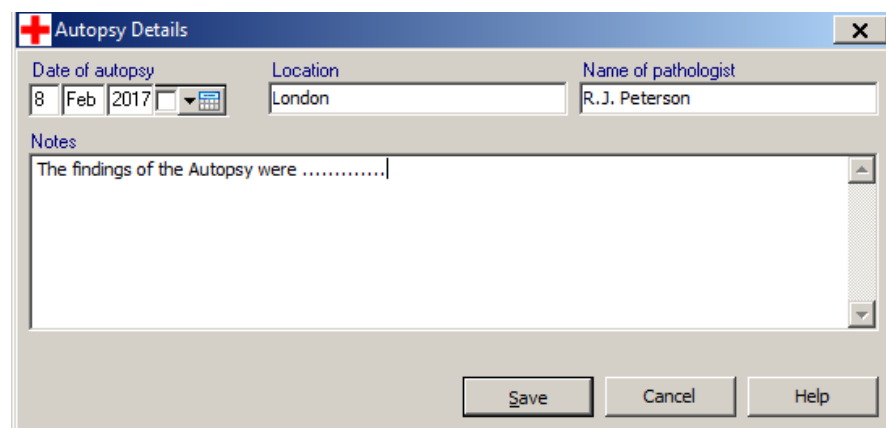
The maximum permitted height is 300 cm (3m) and the maximum permitted weight is 600kg. Attempt to enter values above these limits are rejected. Body mass index is calculated automatically from the given height and weight values. Body Surface area is also calculated from patient height and weight and is presented to two decimal places.

There are several algorithms for this calculation. The one to be implemented by PV-Works is that of Mosteller (reference www.ajdesigner.com/fl_bsa/bsa.php) and the calculation is:

BSA = SQRT (height in cm * weight in kg / 3600)
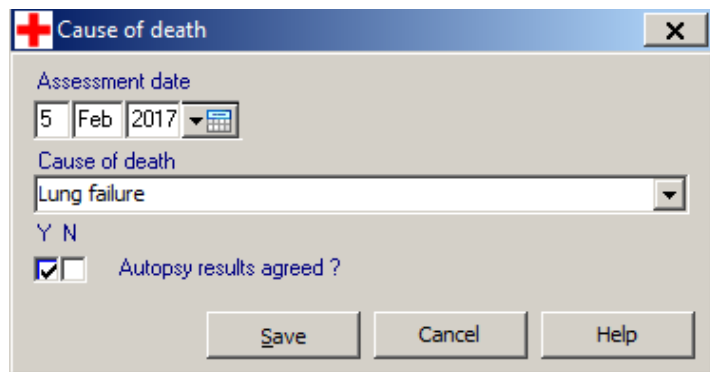
Autopsy details are entered on a pop-up screen (see Figure 6.3.2) that is accessed from a button; this is only possible if the patient is marked as 'dead' and 'autopsy performed' is set to 'yes'.

Figure 6.3.2: Autopsy Details

Similarly, a record of the cause of death may be entered by clicking [Add] in the 'Cause(s) of death' field. This is only available if 'Patient died?' is 'Y'. The cause of death is entered using the popup shown below. Multiple causes may be entered and these may be ranked in order of importance.

Figure 6.3.3: Cause of Death

Medical history data may be entered at the foot of the patient screen, or on a separate Medical History screen that is described in section 6.4.

5.4 Medical History

Medical History data is entered in two sections:

- Medical history, i.e. previous reactions or experiences, in this screen
- Previous treatment, entered as part of the Product record (see section 6.7).

Medical history data (as previous reactions) may be entered in two styles:

- Up to 999 Medical History experiences may be entered using the standard 'multiple record' style of screen.

- As a single block of narrative text.

It is possible to mix both styles in a single case.

Figure 6.4.1 shows a sample Medical History screen for entry as multiple clinical signs and shows a sample Medical History screen for narrative text. Moving from screen type to screen type requires the use to click the record tab title.

Medical History details (of either style) cannot be entered until the user has noted that this data is available. The drop down box at the top allows the user to record the fact that the caller refused to give this information.

Both styles of Medical History will be reported on regulatory reports such as CIOMS and MedWatch with the clinical sign style being presented before the narrative.

Figure .4.1: Medical History as clinical signs

Medical History verbatim terms may be coded against MedDRA from this screen as an alternative to coding from the Coding function described in section 8.2.

Multiple MedDRA coded terms may be entered against a narrative description of Medical History.

Figure 6.4.2: Medical History as narrative

5.5 Adverse Events

Up to 999 Adverse Events may be entered for each case using the multiple record style of screen and is illustrated in figure 6.5.1.

Dates and durations

A quick entry method has been provided to calculate the event start date – by populating the 'event started… ago' field with a value and unit the start date will be automatically filled. The start date can be manually changed if desirable.

From the dates entered for the event start and event end, the system will calculate the duration. The units for the duration are chosen according to the calculated value with limits defined by the System Administrator. This means that durations are displayed in units that are more meaningful to the user, e.g. '6 months' rather than '189 days'.

If the start date / end date / duration fields become inconsistent due to data edits, the system will warn that this has occurred and will offer to correct the duration field.

Duration values may also be entered as 'free text', e.g. 'a few days'. Where a free text duration is entered, this will be used in preference to the calculated value on reports.

Copy event data

The button 'Copy event data' can be used on events subsequent to the first one entered in order to duplicate data. (This is particularly useful when several events are reported in the same episode). Clicking this button will copy the following fields from the PREVIOUS event (i.e. if the user is looking at the 5th event the data is copied from the 4th event):

- Start date
- End date
- Ongoing
- Duration – value and units
- Duration text
- ICH serious reasons
- Action taken
- Outcome

This is just a 'copy to screen' function; the user may edit the data after copying it.

Figure 6.5.1: Adverse Events Screen

Actions and Outcomes

The user may record the action taken and the outcome of the event from a drop down list of possible options. This list is defined by the System Administrator. The actions and outcomes are divided into three lists:

- Outcomes and actions that define a case as 'serious' – as per ICH
- Other actions
- Other outcomes

In each of these lists all actions are displayed in blue text and all outcomes are displayed in black text.

Once one or more actions or outcomes are defined, only these values are displayed.

Clicking ![icon] will display the full list of options again. Both are shown in Figure 6.5.2

Figure 6.5.2: Full display and Short display of actions / outcomes
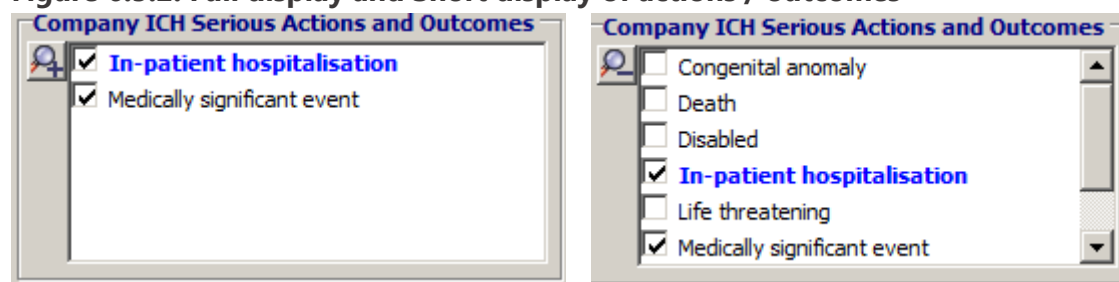
The user may set one of the outcomes to be defined as the "most important outcome". To do this, select the outcome, right click its name and select "Set as most important". The most important outcome is shown in bold text. If only one outcome is entered, then this is the most important one by default.

It is possible to deselect the current most important outcome, by selecting the outcome, right click its name and select "unset most important outcome" or by selecting a different outcome as "most important".

Coding

Events may be coded either during data entry or as a separate step in the pharmacovigilance process. A single event may be coded against any number of available dictionaries (e.g. Costart and MedDRA). Coding events during data entry will display the same screens and functions as described in section 8.

Coded events are shown on this screen as a summary. Where the MedDRA dictionary has been used the version of the MedDRA dictionary used at the time of coding is displayed. The System Administrator may set a system option to control whether the code displayed is the low level term or the preferred term.

An automated coding function can be set up for the most commonly entered verbatim terms. This is described in section 8.3

Adverse Events screen - Additional Tab

An additional record tab (named "Additional Event Information") is available to display further data fields related to clinical trials. Since this tab is not required by all customers, it is possible to configure the system to determine whether or not to display it.

Note that if this tab is not displayed, then the record tabs 'Event' and 'Additional Information' are not displayed in Figure 6.5.1.

The additional information screen is shown in Figure 6.5.3:

Figure 6.5.3: Adverse Event Screen: Additional information record tab

Note that these additional data items can be specified 'per event'.

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5.6 Laboratory Tests

Laboratory Test data may be entered in three ways:

1. In a structured form where each data item is held in a separate database field
2. As a free-text narrative
3. Or a combination of both styles. Both structured and free-text laboratory data will be used in reports.

Structured laboratory tests may be pre-set with defined units of measurement. If the unit of measurement is defined as 'ALL' then all units of measurement are available for user selection. (Note it is also possible to define a test with a pseudo test unit of 'NONE'. This means that the test takes no units e.g. pH).

Structured laboratory tests may also be coded in advance against MedDRA and these terms are loaded with the selection of each test. Figure 6.6.1 shows the Laboratory Test data entry form. Each structured test result is displayed in the standard multiple record style with summary grid and navigation bar.

Additional functionality is built into the laboratory data summary grid so that the user may:

- 'filter' the tests displayed so that a particular test may be traced, or results on a particular date, or all abnormal results.

- 'group' and 'sort' results by any column to aid review

Free-text laboratory data may be up to 200,000 characters long.

Figure 6.6.1: Laboratory Tests Screen

MedDRA codes are shown for each laboratory test if these have been set up by the System Administrator. Alternatively coding may be added from the Main Screen (see section 8.2). The 'Duplicate tests' button allows the user to copy selected laboratory tests to create a set of skeleton entries for another date. This allows repetition of the same set of tests on another date without the need to re-define the set. If this button is selected the following screen is displayed:

Figure 6.6.2: Laboratory Tests Duplication

The tests to be duplicated are copied into the right hand side and then the user clicks
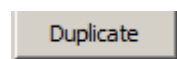
[Duplicate] . The duplicated tests should appear in the grid of the 'Laboratory Tests' screen. Test result values are not duplicated but the test units and normal range values are.

5.7 Products

All non-device products are entered on the same screen regardless of their role in the case. This includes suspect products, concomitant medications, previous treatments and products used to treat the adverse experience. A system option can be set to define the default role for product entry. For medical devices the user may select the device name on this screen but all other details are entered as described in section 6.8.

A maximum of 999 products may be entered for each case. The dosing history of each product is kept as a separate data item so that multiple dosing episodes of the same product may be recorded. Each product may have up to 999 associated dosing episodes.

Due to the number of data fields that may be entered about each product, PV-Works displays product information at three levels (see Figure 6.7.1):

Main details

The first screen displayed (Figure 6.7.1) shows the key data for each product in a multiple record format. Additional products may be added and products may be deleted. In the display area the main details may be added for each product, including details of its first or only dosing episode and the primary indication (reason for use).

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Figure 6.7.1: Product Screen

It is possible to suppress the display of fields such as 'was the product used correctly?' via a system option. If this option is taken the product screen appears as in Figure 6.7.2

Figure 6.7.2: Product Screen - alternative display style

The product may be entered either via its Brand Name or by searching the product dictionary (see below). Using the 'Find' button allows a user to select a product from previously defined data. The appropriate dictionary is chosen according to the 'Company Product' check box:

- Company product check box marked leads to the Company Product Dictionary
- Company product check box not marked leads to the WhoDrug Dictionary or a customer-defined third-party dictionary

These dictionaries help product selection when the marketed range is less familiar to the user but also help reduce the data entry effort and improve spelling accuracy.

These searches share the same screens. If the Company product check box is not ticked and the user clicks **Find** then the user is shown the pop up screen to select the third party dictionary to be used (see Figure 6.7.3). This allows the user to select a commercial dictionary such as WhoDrug (subject to a separate licence agreement) or a customer-defined dictionary.

Figure 6.7.3: Third Party Product Dictionary Selection
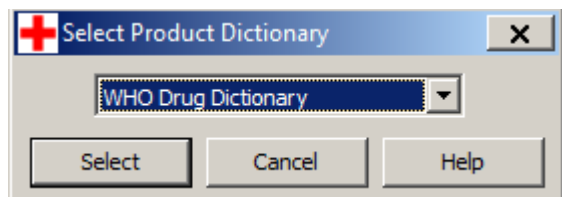
Regardless of the dictionary selected (company, commercial, or customer defined), the search screen in Figure 6.7.4 is shown.

Figure 6.7.4: Product Dictionary Search screen

The user may search the selected dictionary specifying various search criteria either as full or partial values. A list of matching products will be displayed in the grid. Highlight the required product and double-click its name (or highlight and click 'save') to return the product details to the product screen. Note that inactive products are displayed on the above grid in blue text. This is the only method to select an inactive product as by default they do not appear in the drop down list on the main product screen. This is intended to emphasise their discontinued nature.

If the brand or generic name is not recognised or differs from the dictionary entries, the 'reported name' may also be recorded.

A quick entry mechanism has been provided to calculate the product start date – by populating the 'product given… ago' field with a value and unit the start date will be automatically filled. The start date can be manually changed if desirable.

From the dates entered for the dose start and dose end, the system will calculate the duration of product use. The units for the duration are chosen according to the calculated value with limits defined by the System Administrator. This means that durations are displayed in units that are more meaningful to the user, e.g. '6 months' rather than '189 days'.

Duration values may also be entered as 'free text', e.g. 'a few days'. Where a free text duration is entered, this will be used in preference to the calculated value on reports. Time to onset may also be calculated automatically.

One suspect product may be marked as 'primary', i.e. the main product believed to lead to the adverse experience. If the user changes the product to be marked as primary, a warning will be given before the change is effected.

It is possible to access a link to additional product information (say, a product datasheet for example) via an icon which appears next to the product name. This functionality must be configured on a product by product basis if required.

A batch number may be entered by typing the value or by selecting an existing batch number for the selected product. The list is populated with batch numbers from previous cases that were received in the last 'x' months for the same product, where 'x' is set by the Customer's Systems Administrator via a system option.

When a Batch Number is entered PV-Works may perform two checks:

1. Test the entered batch number to confirm that it is valid (i.e. this number has been manufactured for this brand)
2. Determine whether any other cases (or complaints) have been entered for the same batch number.

Both checks are controlled via system options such that customers may execute one, both or neither check.
For the 'valid batch number' check, the Customer must provide a list of batch numbers from manufacturing for each product. These are imported regularly to PV-Works, typically using a bespoke program written for each Customer. A batch number that fails this check should raise a warning rather than an error, i.e. the user will be able to save a batch number that could be invalid.

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The 'other cases from this batch' will match the entered batch number against other cases, warning the user if other cases or complaints already exist for the same batch of product (see Figure 6.7.5). If other cases exist the user is given some brief details of them and may print a report of matching cases.

Figure 6.7.5: Product Batch Number Check
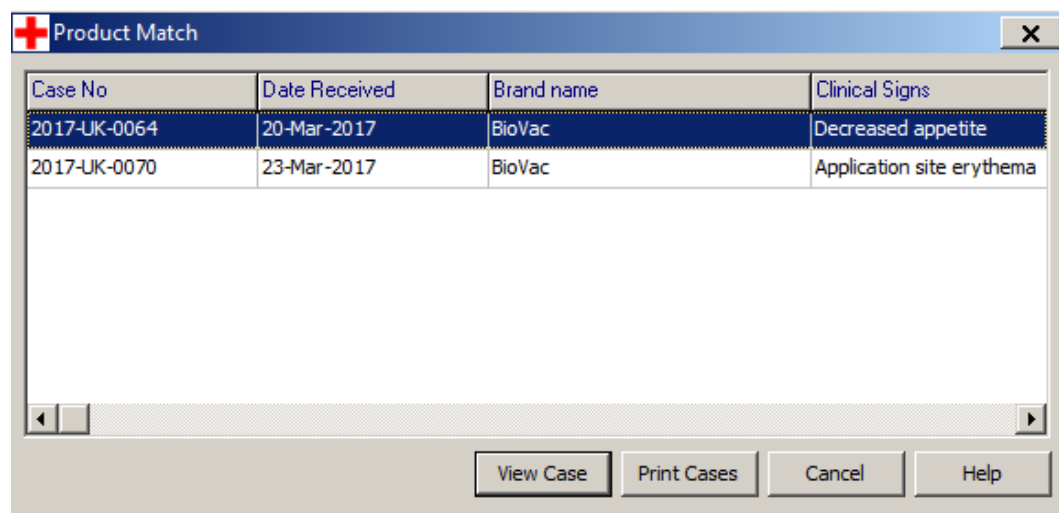
The 'reason for use' field may be entered from a list of pre-set reasons or by free-text entry. The reasons in the drop down list are a combination of reasons defined for all products and reasons specific to the selected product.

Further Product Details

By clicking the button 'Further Product Details' additional information may be specified about the product as shown in Figure 6.7.6:

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Figure 6.7.6: Further Product Details

The ingredients list cannot be edited directly from this screen. Its definition is taken from the Company Product Dictionary which can be amended by the System Administrator using the PV-Admin program.

Dose Details

By clicking the button 'Dose Details' information may be entered for one or more dosing episodes for the product. The screen shown in Figure 6.7.7 is displayed:

Figure 6.7.7: Dose Details

Dose information may be entered in a structured format in line with ICH E2B or as free text. Where free text is specified, this will be used in preference to the structured information on all reports.

The Dosing information entered is used to build a description of the dose from data items such as amount, units of dose and frequency and to calculate the cumulative dose.

If the start date / end date / duration fields become inconsistent due to data edits, the system will warn that this has occurred and will offer to correct the duration field. The 'date patient last dosed' field will be greyed out if the "Ongoing" value is set to any value except "Yes".

Indications

By clicking the button 'Indications' the reasons why the product was taken may be entered. The screen shown in Figure 6.7.8 is displayed:

Figure 6.7.8: Product Indications

A product may have up to 999 indications. Each indication may be entered as free-text or may be selected from a list of common indications created by the System Administrator. This list is displayed by clicking the 'Common Indications' button as shown in Figure 6.7.9

Figure 6.7.9: Common product indications

Indications may be coded either during data entry or as a separate step in the pharmacovigilance process. Coding indications during data entry will display the same screens and functions as described in section 8.

5.8 Medical Devices

In many ways devices share similar characteristics with drug products in that all company devices are defined in the Company Product Dictionary and the device can be either suspect or concomitant. For simplicity and to reflect the different data fields that are captured, medical device product data is entered on a separate screen to drug products.

The 'Medical Devices' screen will comprise four record cards:

- Medical Device details
- Device Event / evaluation
- Device Event coding
- Addresses

It is possible to enter the details of multiple medical devices if necessary.

Figure 6.8.1: Medical Device Details

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All devices are company products and will be selected from the product dictionary. The first device to be entered will be considered primary. The dictionary will provide the following fields:

- Device type
- Device class
- Model no.
- Catalog no.

If these fields are not provided by the dictionary the user should be able to edit them, otherwise they will be read-only.

All dates are historical except for expiry date. All dates may be approximate and partial.
/Either implant or explant check box may be checked, but not both.

Device Event / Evaluation Screen

While details of the event itself will continue to be entered on the adverse event screen (section 6.5), this screen will contain details of any evaluation that took place on the device itself.

Figure 6.8.2: Medical Device Event / Evaluation

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For each device there will be one event/evaluation. The narrative types will contain the following values:

Additional narrative
Corrected data
Initial investigation
Further investigation
Corrective action
Projected timing
Similar incident reports

The user may add a new narrative to the device record by selecting its name in the drop down list and entering text in the memo window. The navigation bars will change the current narrative to the next one in the database – presentation order is 'alphabetical order of code'). Alternatively, the user may select a narrative directly via the drop down list.

It is not possible to add more than one narrative of the same type.

Device Event Coding Screen

Medical Device incidents are coded according to a three tier coding system required by FDA. The three levels are:

Method
Results
Conclusions

Conclusion codes must be entered even if the device was not evaluated.

Figure 6.8.3: Medical Device Event Coding Screen

Addresses Screen

The 'Addresses' tab (Figure 6.8.4) will allow the user to enter three names and addresses:

- the manufacturer of the device
- the distributor of the medical device
- the reprocessor of the medical device (used where a device is refurbished and re-used).

While the screen design will be based upon the 'Contacts' screen, the storage of data will differ. Since the user will be the manufacturer of the medical device, manufacturer names and addresses will be taken from the Contact Dictionary. Details will be copied to the case.

Figure 6.8.4: Medical Device Addresses

5.9 Narratives

Narratives are free-text data fields that may hold up to 200,000 characters of data. The system will support any number of narratives. Narratives differ from 'notes on data fields' in that they are used in reports. Each narrative has two key properties:

1. Type
2. Language

The 'type' of a narrative indicates its contents and purpose. Many types are fixed by PV-Works as they are required for regulatory reports, eg case narrative, PSUR comment. However, additionally the Systems Administrator can define any company-specific narratives that are required to support local processes, eg internal company assessment.

Each narrative may be entered in any language. The same narrative type may also be entered in different languages. For example, a case reported in France will require its narrative in French. This is likely to be translated to English for international reporting.

Any number of narratives may be entered for a case and each may be recorded in multiple languages. In practice it is likely that most narratives will be in English. A summary grid shows the narrative / language combinations that already exist.

It is possible to display the text of a narrative in 'read-only' format at the same time as another narrative is being entered or edited. This function is useful when:

- narratives are being translated from one language to another.
- when a new narrative is derived from another, e.g. a PSUR comment might be a précis of the case narrative.

Narrative text may be auto-generated by merging user-defined templates with case data. (see section 13.3) for further details.

Figure 6.9.1: Narrative Screen

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5.10   Literature

Literature reference may be recorded for cases originating from published sources. In the Literature screen shown in Figure 6.10.1 p to 999 literature references may be entered for each case.

Figure 6.10.1: Literature Screen

A warning is given if the user tries to add a literature reference without either an author or a title.

5.11   Clinical Trial

Study data is entered using two screens:

1. General clinical trial data
2. Treatment unblinding information

The reason for separating these is to allow different access rules to apply to the more sensitive unblinding data. For example, a user may be able to view and edit the trial description data but is not permitted to see the unblinding data.

This section describes the basic entry of study data and the unblinding of a single case. Other Clinical Trial data entry functions such as the Clinical Trial dictionary and unblinding all cases in a study are described in section 9.

Figure 6.11.1: Clinical Trial Screen

The data that describes the clinical trial in which the patient is participating may be entered as free text. However, it is recommended that, wherever possible, the user should set up an entry in the PV-Works Clinical Trial Dictionary to define fixed reference data. This data will be used to provide a hierarchical data entry system, ensuring accurate data and minimised data entry effort. This approach is described in section 9..

If the selected study is amended on this screen and the data is available in the Clinical Trial Dictionary, the user may be prompted if the name of the principal investigator is changed. The consequence of this prompt is that the new investigator details can replace the current data in the Contacts Screen (Figure 6.2.1).

When the case is a clinical trial or post-marketing study, the study identifier will be displayed in the update container header. If the patient number is entered this will be appended to the study identifier in parentheses.

Patient check

The 'Patient Check' button will perform a duplicate check for the patient and will find all cases reported previously for this patient (identified by patient number) in the same clinical trial.

The user must enter both the study and patient number fields, otherwise the 'Patient Check' button is disabled. PV-Works will search the database for previous cases with these details. If no matches are found, the system will inform the user with a simple message:

Figure 6.11.2: No matching patients found
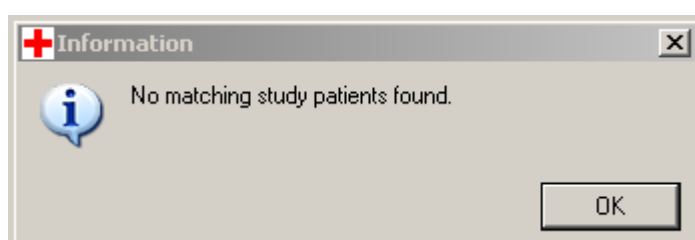
If matches are found, PV-Works will display a simple grid of matching cases at the foot of the clinical trial screen:

Figure 6.11.3: Clinical trial matching patients
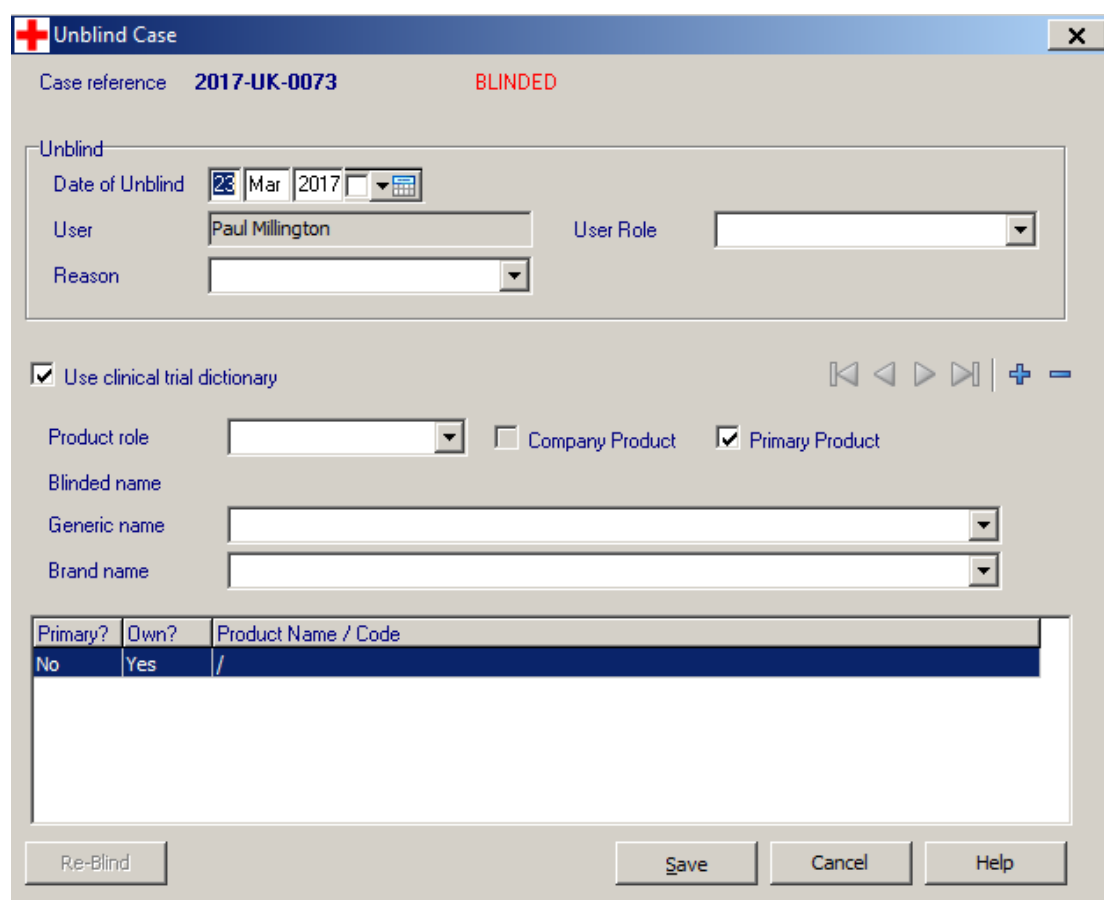
The user can select one of the matches (by default the first will be selected) and, provided there is no patient data already entered into the current case, can copy the patient information from the previous case into the current case.

If patient data is copied, PV-Works will add an explicit link between the two cases with a link reason of 'same patient'.

Study unblinding – Single case

To unblind a single case click [Unblind] on the 'Clinical Trial' screen. Popup 6.11.4 will be displayed.

Figure 6.11.4: Single case unblinding screen

This screen will only be displayed if:

- the case is a clinical trial or PMS type;
- the study is defined as 'blinded'; and
- the user has security permission to access the screen

One blinded product can lead to multiple 'unblinded' products; in other words, the pseudo product name 'Blinded Test Product' is masking the fact that more than one product was dosed. The plus (+) button allows the user to enter multiple products.

When the case is unblinded, the unblinded product definition(s) are copied to the product screen. If there is a one:many relationship between blinded product and unblinded products, this PV-Works will create multiple product records.

The delete button (-) will only be available before the initial save of the unblinding information. Once the case has been unblinded, individual unblind rules cannot be edited due to the complexity of the onward processing (see below). However, the user can 're-blind' the case and revert the product definition to its original blinded state. Thus if the unblinded product definitions need to be edited, the user should 'Re-blind' the case and then 'Unblind' it again.

Only one 'blinded product' record may exist in a case. While it will usually be the primary suspect product, this rule is not enforced.

The process of unblinding and re-blinding is as follows:

Process	Actions
To unblind a single product:	a) User selects the correct generic and brand name either from the Clinical Trial Dictionary (if study is defined) or from the Company Product Dictionary b) PV-Works will save this unblind product rule as part of the study data c) Replace the 'Blinded Test Product' record on the product screen with the unblinded product d) A link is made between the study unblind product rule and the records that it has generated on the product screen
To unblind a patient's treatment to reveal more than one product	a) Select correct generic and brand name as above for the first product. b) PV-Works will save this unblind product rule as part of the study data c) Click '+' button. A new record is displayed. Details for second and subsequent products may be added and are stored as before. d) Replace the 'Blinded Test Product' record on the product screen creating multiple product records one per unblinded product. Initially any dosing information entered for the unblinded product will be copied to each new product record e) A link is made between the study unblind product rule and the records that it has generated on the product screen

To re-blind a case	a) Click the 're-blind' button on the Unblinding screen
	b) User will confirm that the case should be reblinded
	c) The primary Product record will be re-labelled as 'Blinded Test Product'
	d) If there were other product records generated as a result of the unblinding, these will be deleted
	e) Unblind details stored on the Clinical Trial screen will be reset

5.12 Parental Data

Data may be added to a case to describe the reaction of a parent to the same drug. This data also includes the parent's medical history, personal details and products taken. Parental data is implemented as a plug-in screen titled 'Parental data' that consists of two record cards:

- Parental data / Medical History (Figure 6.12.1).
- Parental Drug History (Figure 6.12.2).

Figure 6.12.1: Parental Data / Medical History Screen

The parental data / medical history screen bear a strong resemblance to the Patient screen (Figure 6.3.1) with the following processing rules:

- Height and Weight values will be translated into imperial / metric units (as per patient screen)

- Body mass index will be calculated (as per patient screen)

- Only 'Female' patients may be pregnant (as per patient screen)

- Last period date will only be enabled if the patient 'is pregnant' (as per patient screen)

- Multiple medical history verbatims may be entered (as per medical history screen)

A narrative will be added for Medical History comments. There will be one such comment per case – not per verbatim. This narrative has a maximum size of 10,000 characters. In order to facilitate easier entry, the narrative will also be available on the Narratives screen (current functionality).

Figure 6.12.2: Parental Drug History Screen

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The Parental Drug History screen follows the same principles as the product screen:

- The 'company product' check box controls whether the product may be selected from the drop down list of company products or entered as free text.

- One reason for use may be entered and this may be coded using MedDRA

- The duration for dosing is calculated from a completed start and end date

- A new area 'reaction to drug' allows the entry of a single reaction to the drug. This may be coded.

- Products from other countries and inactive products can be selected via the "Find" button.

5.13 Medical Factors

Medical Factors are pre-defined lists of items that could be considered to influence the case. These are separated into two groups:

Primary factors; these are the more commonly assessed set of factors and which may be required for regulatory reports. This list is fixed by PV-Works

Additional factors; these may be defined by the Systems Administrator to handle local requirements not met by the primary factors.

The user may move between each set of factors by clicking the record card name shown in Figure 6.13.1.

PV-Works will allow a maximum of over 1.5 million factors to be stored for each case. If there are more factors defined than can be displayed on one screen, the display can be scrolled vertically.

The data collected for each factor is the same regardless of whether it is primary or additional:

- A check box indicating whether the factor influences the case, does not influence the case or whether this relationship is unknown.

- If 'unknown' is selected this may be further qualified using a codelist defined by the System Administrator.

- If a positive relationship is noted, the user may add a free-text comment of up to 40 characters in length.

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Figure 6.13.1 : Data Entry : Medical Factors

5.14 Regulatory Reports

The regulatory reports screen (Figure 6.14.1) records each time that a regulatory report is sent to any authority. Both the list of regulatory authorities and the list of report types are defined as codelists by the Systems Administrator.

There is no limit to the number of records that may be made. For example, a particular report can be sent to one authority many times over and each submission recorded.

Figure 6.14.1: Regulatory Reports Screen

Before an entry is saved in this screen, the user is prompted to confirm that it has actually been sent to the authority.

The report type displayed as the current entry may be printed directly using the print button added to the navigation buttons using the latest case data. Note that this button takes the user directly to the report options screen for the selected report. It is possible, therefore, to set the options differently to those used for the actual submission and thus generate a different report.

The list of report submissions is displayed in the 'Reports submitted' grid that allows the user to sort, filter and group records such that it is easy to find particular submissions regardless of the number made.

The screen also shows any PSUR reports in which the case has been included. Data in this panel is entered automatically by the PSUR generation function. (See section 11.9).

'Skeleton' records are added into this screen when an 'official' single case report is printed. This reduces the task of the user to one of confirming that the report has indeed been submitted.

If the report type is "XML" and so indicated an electronic submission, it is possible to view the XML file that contained this report by clicking the `View XML` button. This displays a screen such as the one in Figure 6.14.2

Figure 6.14.2: XML file viewer
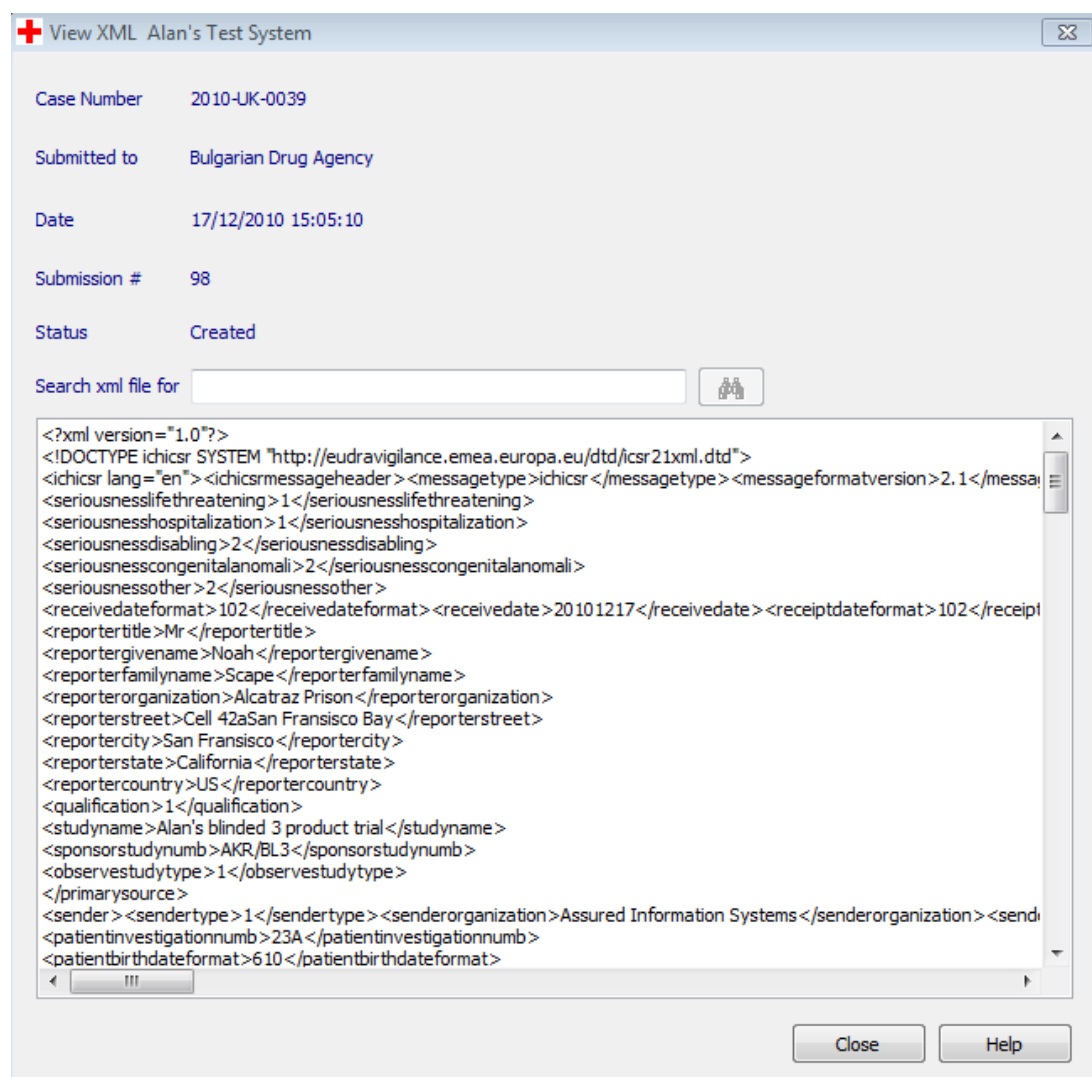
There is a useful search box that will look through the file to find particular strings. Be aware that it is possible that this case was submitted in a batch report. The XML viewer shows the submitted file as a whole i.e. for all cases in the batch not just the XML for the current case.

It is possible to view errors in transmission via the "Review Comments" button. See section 12.8 for more details.

5.15 Call History

The Call History screen can be used to record internal notes about a case.

In principle the Call History page is a multi-purpose note function that can record:

- Further 'conversations' with the caller or other company personnel
- Notes on issues, internal queries, etc.
- Actions taken e.g. fax documents
- Interim conclusions

The Call History screen has been integrated with Action Board Tasks such that these tasks are always recorded on this screen and the assigned user may respond to them from this screen.

Figure 6.15.1: Call History Screen

Each entry is maintained as a separate record with a free-format narrative block to record the notes. Each entry will permit a note of 2000 characters. Each case may have an unlimited number of call history notes attached to it.

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The call history items are presented in a standard PV-Works multi-record format in descending order of action date.

The list of possible actions will be controlled by a codelist.

The Case Contact name may be selected from a drop down list containing the names of all external personnel involved in the case (as recorded on the Contacts screen Figure). The user will be able to select one of these names or type in a different name.

Where Company staff are involved in the action, e.g. receiving a phone call, sending a fax, their name may be selected from a drop down list (as the 'Created by' field). This will be taken from a staff list maintained in the PV-Works contact dictionary.

Certain PV-Works functions will automatically add records to this screen, e.g. noting that an official regulatory report was generated. These notes may not be edited or deleted even by the user responsible for their creation. This ensures that a complete record of case actions is maintained.

If a user has access to a case, then they have access to all notes for reading. The user may create new comments, but may only edit or delete a comment if they are the author of it.

The Call History screen uses a grid which provides functionality to sort, group and filter call history records.

Action Board integration:

Action Board tasks are ad-hoc workflow steps that can be assigned to a user. These can support the tasks of a primary workflow process or can be used as a substitute where customers do not use the PV-Works workflow functions.

For Action Board tasks only, three are a number of additional fields and buttons such as the 'Action Board task activity' which is the title of the task category, e.g. 'Follow up question', 'Review case'. The 'description' field contains the task definition, i.e. what the user is being asked to do. The 'start date' and 'due date' fields show the target times set for the task by the requester.

These fields are intelligently greyed out depending upon the nature of the Call History record being displayed (i.e. action board task or standard note) and the user involved (note author or not).

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When the user executes an Action Board task (e.g. by double-clicking the 'Todo list'), PV-Works will load the correct case data for update and will display the Call History screen with the relevant task showing.

If the user viewing the Call History screen is the recipient of the task, they will be able to:

- record the completion of the task – by entering a completion note, the date of completion and clicking 'Complete'

- reply to the requestor – by entering a reply note and clicking 'reply'. (Note that a reply will leave the original question 'open' and will create a new Action Board task).

Note that the Call History screen is only used to respond to existing Action Board tasks. To create a new Action Board task either the Actions button on the Main Menu screen or the Action Board icon on the update container should be used.

Call History Report:

A 'Print report' button will allow the user to create a simple report of all (or selected) entries. The user will be able to select entries based upon any or all of the following:

- Type of action
- Date range (of Action)
- Caller / Recipient
- Company staff member involved (or all)

The report sort order will default to descending date, but may be altered to

- Ascending date
- Type of action and within action, descending date.

Figure 6.15.2: Call History Log Report

5.16 Surveys

The PV-Works Survey function is a user-defined screen that is displayed if the product with a survey configured against it is added to a case. Initially it was designed to support for Customer Surveys where an additional list of product-specific questions are posed to customers calling a Customer HelpDesk. However, its applicability is potentially wider.

Responses to survey screens are held in the PV-Works database and may be used in queries and ad-hoc reports. However, this data will not be included in any regulatory report.

Creation and editing of survey definitions is a function of the System Administrator using a separate function in the PV-Admin program.

- A survey will have the following attributes:
- A name (must be unique)
- A product family, product name (generic), or trade name to which it belongs
- One or more questions, containing the question string, plus a response
- A 'guidance' note – intended to give the MCC user guidance over whether to complete the survey for this case, and if so, how to do it.

The response may be one of the following types of data:
- Yes/No/Don't Know/No response
- A text string either as free text or selected from a drop down list
- A number
- A date

PV-Works will 'trigger' a survey if the user adds a product that is linked to a survey to a case.

The user will be informed that a survey is available either on entry to the Data Update screens or after the manual entry of a product in the Products screen (i.e. on exit from the Product screen).

The user will be shown the 'guidance' note (which could offer advice on the applicability of the survey to the current case or completion instructions), and given the option to 'Accept' or 'Decline' the survey. This screen is shown in Figure 6.16.1

Figure 6.16.1: Invoking a survey
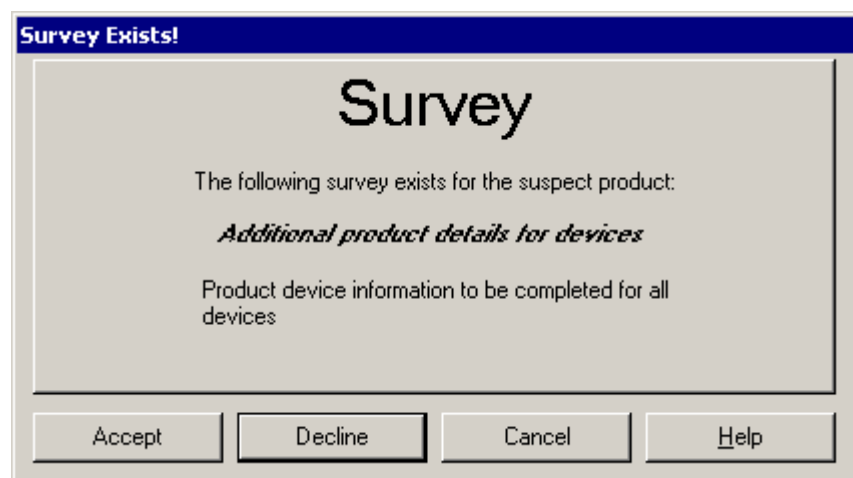
If the user declines the survey the pop-up will disappear, and the user will not be prompted about this survey again. This does not preclude the user from manually completing the survey unprompted at a later date.

If the user accepts the survey then the survey tab will be shown, containing the questions to be answered (see an example in Figure 6.16.2).

Figure 6.16.2: Survey completion screen
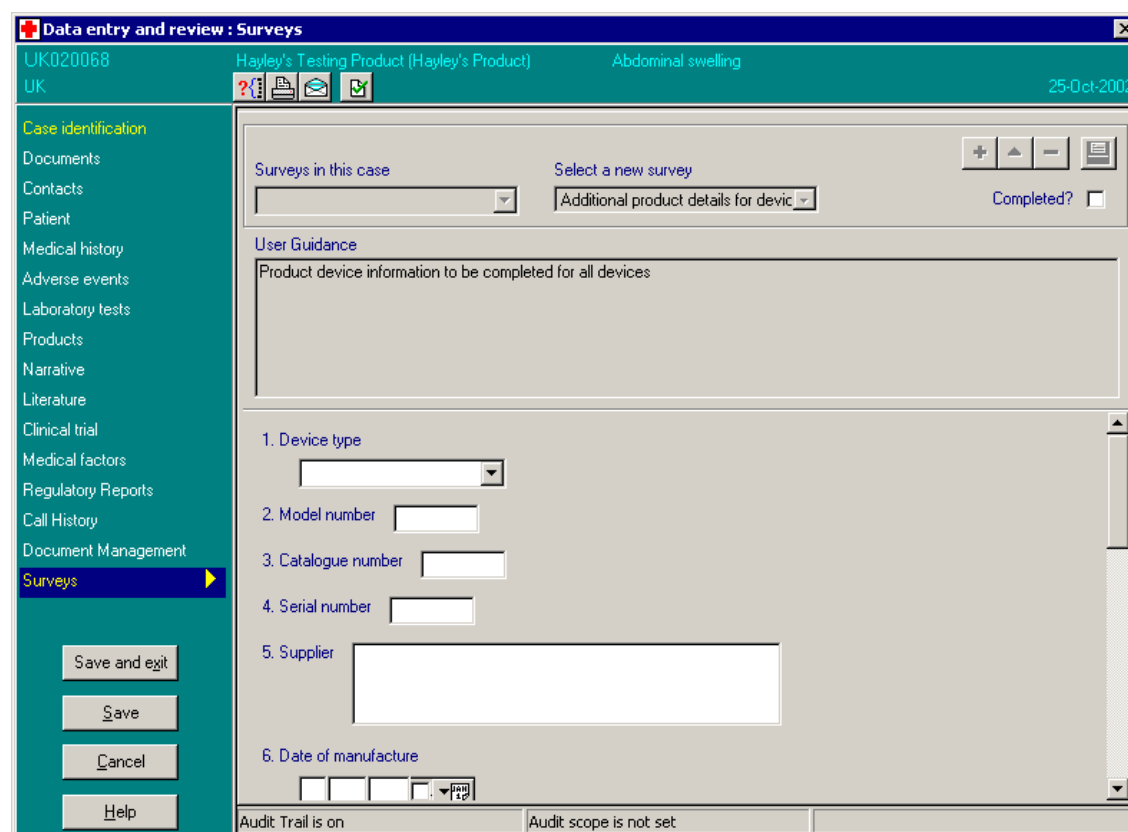
5.16.1 Completing a survey

The aim of this screen is to allow the user to perform the following operations:

- Select a new survey for the current case, and complete it
- Select a survey that has already been completed (may be partially?) and update it
- Delete a survey related to a case
- Mark a survey as complete or incomplete

The screen will allow the user to scroll through the surveys that have been completed or partially completed for the current case to review the results.

5.16.2 Selecting a survey

This pull-down list allows the user to select a survey for completion for the current case. The list contains all of the surveys that have been defined within the system for any of the products involved in the case– irrespective of the product to which they are attached.

The user may only define each survey once per case.

The questions are listed in 'Question/Answer' pairs – running from 1 to the number of questions defined for the survey. The question portions appear on the screen as text labels.

A 'Survey notes' field is always appended at the end of the questions and will hold any miscellaneous notes that could not be captured elsewhere in the survey.

The survey may be marked as 'Complete' or 'Incomplete'.

5.17 User defined data entry screens

Customers may create their own screens that can capture additional case data where specific fields are not present in the database. These fields can be included in main screen grid query results and crystal reports. They will not be used for any regulatory report as PV-Works is unaware of their nature.

The System Administrator is referred to the separate PV-Admin Functional Specification for a description of the design and set up process.

The additional fields are presented in a separate screen that has four sections:

- Case data – where data applies to the case as a whole, e.g. to the patient, to the study or to the collection and receipt process. See Figure 6.17.1

- Events – this is found under the "Multi-case data" tab and allows additional data items to be entered for each event. See Figure 6.17.2

- Products – this is found under the 'Multi-case data' tab and allows additional data irems to be entered for each product. See Figure 6.17.3.

- Reporters – this is found under the 'Multi-case data' tab and allows additional data items to be entered for each reporter. See figure 6.17.4.

Figure 6.17.1: User Case Data - case level

Figure 6.17.2: User Case Data – events

Figure 6.17.3: User Case Data - products

Figure 6.17.4: User Case Data - reporters

Each screen may be designed with a combination of the following field types

Field type	Description
Text	A single edit box taking the width of the screen. Maximum length 200 characters
Code	A dropdown edit box controlled with a PV-Works codelist
Date	A standard Oracle date with approximate flag and precision
Number	A numeric field. The user can control the precision of the value as an integer or a real number with 1, 2 or 3 decimal places
Memo	A memo box with maximum length of 2,000 characters. The user may define the number of lines to be displayed on the screen. A vertical scroll bar should be available. (note that if the user requires a larger memo they can use the current Narrative screen!)

While the order of presentation of these fields may be controlled, the layout is simple – one field per line.

On the multi-data screens the user may select the particular product, event or reporter to which the data applies. To do this either use the navigation buttons or click on the index record at the foot of the screen.
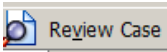
For multi-case data this additional data is applied to an existing product / event / reporter. It follows that the user must enter the basic product details before entering data into these additional fields.

By the same token when a base product / event / reporter record is deleted then its associated additional data is also deleted.

All additions, amendments and deletions of user case data are audited in the same manner as all other case data.

5.18 Data Review

The Data Review function allows a user to review the case information but they are not able to make any changes to it. All data is displayed in dark grey text to indicate clearly that it is in a read-only state. The order of the screens displayed in a Data Review function can be controlled by the Systems Administrator and may differ from those available in Data Entry if required.

Reviewing a case can be performed using the menu option 'Data' -> 'Review Case' or by using the toolbar icon . Only the 'Cancel' (named 'Close') and the 'Help' buttons are available to the user.

6 Assessment

6.1 Introduction

The assessment option is invoked either from the Data menu on the Main Menu screen or via the Assess button on the Main Menu.

The name of the assessor and the date of the assessment are recorded for each assessment. The name defaults to that of the logged on user, i.e. PV-Works assumes that an on-line assessment occurs. The date of assessment defaults to the current date.

The assessment screen is shown in Figure7.2. The screen comprises record tabs:

- Company assessment — Records the assessment of the case made by the company, ie the reporting safety group. It is this assessment that is used for reporting to regulatory authorities

- Imputability — A screen to calculate and record an assessment of the case based upon the French Imputability Algorithm.

- Reporter assessment — Records similar assessment data to that of the company assessment, but as the opinion of the person who reported the information to the reporting safety group / company

- Summary — Is a 'read-only' screen that compares the assessment made by the Company and the Reporter and highlights differences

The presence of the Imputability assessment record tab is controlled by a system option such that it is possible to suppress its display.

The presence of the Reporter assessment and summary record tabs is also controlled by a system option such that it is possible to display both company and reporter tabs or just the company assessment record tab. If the Reporter tab is displayed, the summary tab is automatically displayed.

A system option controls whether the list of products displayed is restricted to suspect products owned by the user's company or whether all suspect products, including third-party products, should be displayed.

The Company assessment and Reporter assessment screen each comprise three panels or areas:

- Case Assessment   To record case level assessment(s)

- Seriousness Assessment   To assess the seriousness of each adverse event (and to justify this with reasons)

- Expected and Causality Assessment   To determine whether each event is expected with the user of each suspect product and to assess its causal relationship

When the screen is first displayed for a case and no previous assessment has occurred, the user will be asked if they wish to populate the assessment screen with data from the adverse event screen (Figure 6.5.1). If the user agrees, then reasons for seriousness will be copied from the adverse event screen and seriousness will be set both at an event and case level

6.2 Company Case Assessment panel

This panel allows the user to specify the following assessments:

- Case level assessment of seriousness (with reasons if 'serious')

- Case level assessment of expectedness (set automatically by PV-Works based upon the expectedness of each product / event combination).

- Reportability – i.e. how the case should be reported, e.g. 15-day, periodic, not reportable. This will be checked by PV-Works against the case serious and case expected values for compatibility. However, at all times the user is in control of this setting and may override the suggestion of the system.

- Case level assessment of causality

- Entry of a validity check for Events, Products, Reporters and Patient (set automatically by PV-Works based upon case data entered).

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Figure 7.2: Company Assessment Screen

6.3 Company Serious Assessment panel

The seriousness assessment panel is a grid based upon the adverse events that have been entered for the case. If any ICH serious outcome has been assigned to the case, this is imported into the assessment screen and will cause the seriousness of the event to be set to 'Yes'. If any event is determined as 'Yes', then the case seriousness is also set to 'Yes'. The automated import of data from the adverse event screen will not set the serious value to 'No' under any circumstances.

The user may select an event by clicking any part of the row in which it is displayed. The list of events is scrollable vertically and is presented in sequence number order. It is not possible to add, delete or amend the text of an event verbatim in this screen. One event may be marked as 'most important'. If no event is marked as 'most important', the system provides a warning message on exit.

The 'Reasons' button displays the 'Reason for Seriousness' pop -up window so that the reason why the selected event is serious may be defined. See section7.5. This button is only enabled if the case is defined as serious at case level.

If the user edits the seriousness of an individual event, then a warning is fired on exit from the assessment screen that prompts the user to review the adverse event screen for internal consistency.

6.4 Expectedness and Causality panel

Assessment of expectedness of an event and its possible causality is made on a 'per suspect product' basis. Each suspect product will be displayed as a 'tabbed record card', with the primary suspect product first.
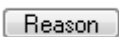
- On each tabbed record there are a number of data entry areas:
- Expectedness
- Causality
- Dechallenge / Rechallenge result
- Action taken with the drug post-reaction
- Time to onset.

The user will be able to move from event to event either by using next/previous buttons or by selecting a different event in the 'serious assessment' grid.
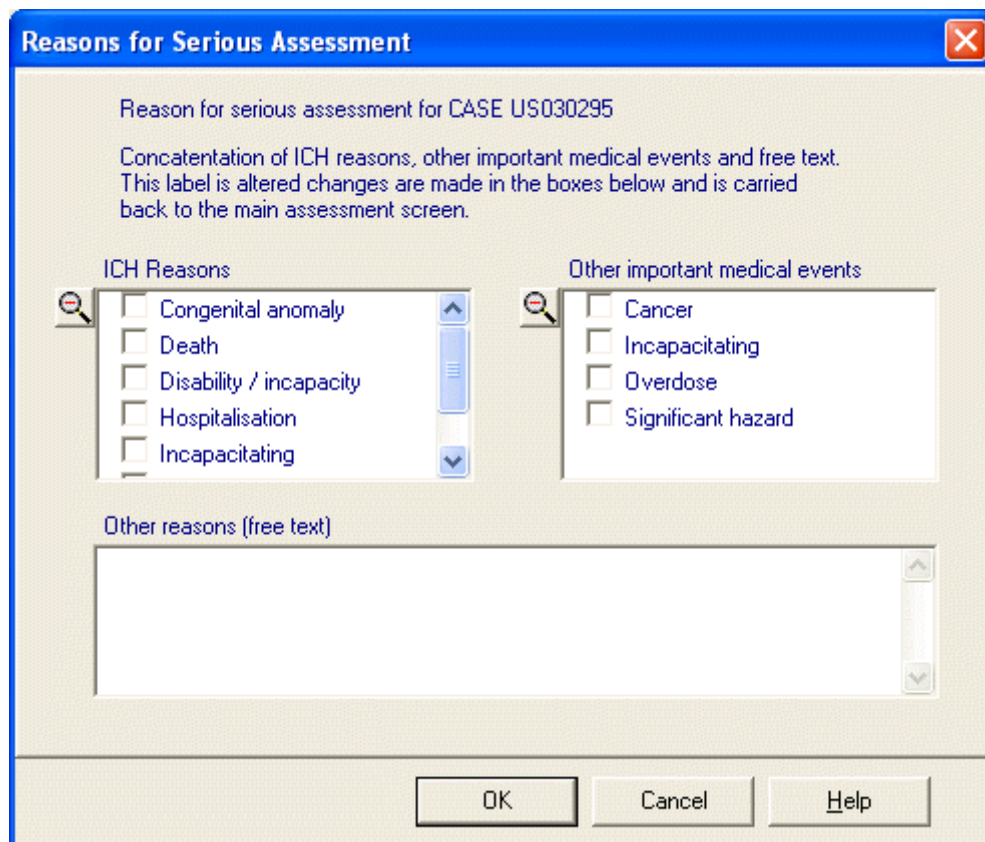
The System Administrator will set a 'default label list' for each user. This could vary from user location to location and will be used as the 'label against which expectedness is assessed' on this screen. Where other labels are assessed in parallel see section 7.6.

Potentially a customer may need to assess expectedness against several labels, e.g. core list, local country labels, investigator's brochure etc. One list, the default list, will be displayed directly on the screen. The others will be available via a pop-up window. The user may further qualify the causality assessment with a comment.

6.5 Reason for Seriousness popup screen

When a case or event is assessed as 'serious', the Reason for Seriousness pop-up screen will be available

via the button [Reason] . This screen is shown in Figure 7.5

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Figure 7.5: Reason for Seriousness Pop-up

Using the selected codelist value(s) and the optional free text, the reason for seriousness will be displayed on the main screen (Figure 7.2) as the user changes the selection/text. It will be created by concatenating the ICH reasons (decoded descriptions) followed by the other important medical events (decoded descriptions) followed by the free text.

When the user presses save, this text is copied to the main assessment screen and saved in the appropriate tables.

6.6 Expected Assessment for Other Data Sheets

The main assessmennt screen in Figure 7.2 will only permit assemment of expectedness against one data sheet – the users 'default' data sheet. To assess the event against other data sheets the pop up screen shown in Figure 7.6 may be displayed by clicking the button.

The use of a pop-up screen for this information is designed to make the presentation of data on the main screen simpler.

Figure 7.6: Expectedness Assessment for Other Data Sheets

When this pop up window is first displayed, the selected event will be the currently selected event on the Main Assessment screen. Users may select any event and any or all of the defined data sheets / labels.

6.7 Local Causality Assessment

This screen is a pop-up window that is accessed from the 'local causality button' on the main assessment screen [image] . It provides the user with the option to specify a causality grading assessment for each event/product for each defined regulatory authority. The Local Causality Assessment screen is shown in Figure 7.7

If a local assessment exists for a regulatory authority to whom an XML e-report will be sent, the local causality assessment will be used in preference to any other assessment.

Figure 7.7: Local Causality Assessment screen

6.8 Company Causality Assessment Summary Table

This screen is a pop-up window that is accessed from the 'table button' on the main assessment screen

. It provides the user with a visualisation of all causality assessments displayed in a grid of events versus suspect products. All data items are read-only. The Causality Assessment Summary table is shown in Figure 7.11

6.9 Imputability Assessment panel

This panel similar to the 'Expected and causality assessment' panel of the Company Assessment screen in Figure 7.11, i.e. there will be one record per company suspect product.

Figure 7.9: Imputability Assessment Screen

For each event / product combination the user may enter either the 'intrinsic' or 'extrinsic' imputability assessment or both. When an event is selected in either panel, the same event should also be selected in the other panel. Once the 'chronological criteria' and the 'semiological criteria' of the 'intrinsic imputability' panel are entered, the 'intrinsic imputability' itself may be calculated as follows:

Intrinsic Imputability Algorithm Rules table

	Sémiologie		
Chronologie	S1	S2	S3
C0	I0	I0	I0
C1	I1	I1	I2
C2	I1	I2	I3
C3	I3	I3	I4

6.10 Reporter Assessment screen

The reporter assessment panel is very similar to that for the company assessment and is displayed in Figure 7.10.

Figure 7.10: Reporter Assessment Screen

The differences between the company assessment record tab and the reporter assessment screen are:

- Case assessment : no field is available for the reporter's assessment of reportability
- Case assessment : the assessor details and validity check data has not been replicated from the company record tab
- Expected & Causality assessment: the pop up functions 'look up label', 'show expectedness' and 'causality summary' are not available/

When the Reporter Assessment tab of the Assessment screen is displayed the system pulls the seriousness and reasons for seriousness and causality from the Reporter's Assessment on the Event screen. Note that the value on the Event screen is assessed at an event level while the assessment screen

uses an event / product matrix. Therefore the causality from the event screen will be the default value for all products. The defaulting process will only occur if there is no value in the Assessment tab's field; i.e. once the user has saved assessment data from the above screen then this will not be overwritten.

6.11 Summary screen

The Summary record tab offers a read only view of all assessment data – Company and Reporter – and offers an easy to see comparison of the two assessments. The screen is shown in figure 7.11. The user may select a different data sheet from a drop down list which causes the lower panel data to be re-displayed. When the data sheet is amended it is only the 'expected' column that will be changed – the other columns apply commonly to all data sheets.

Figure 7.11: Assessment Summary Screen

The screen will highlight any differences between the assessment made by the company and that of the reporter by displaying this data in red text or with the phrase 'different'. In figure 7.11 all the causality assessments differ as do the assessments of the rash.

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6.12 EU Clinical Trials and Causality

From the EU guideline on reporting adverse events from clinical trials, the company assessment of causality should not be lower than that of the reporter. This restriction / concept does not apply to spontaneous cases.

To implement this a warning is given on exit from the assessment screen and when the user changes the product tab in the 'Expected and Causality Assessment' panel of the assessment screen. If the system detects that the company causality assessment, which is the one that is used in regulatory reports, is lower than that of the reporter, a warning message is displayed. It is the user's decision whether to change the assessments and no attempt is made to force this as PV-Works cannot determine which assessment is correct and which invalid.

7 Code with MedDRA

7.1 Introduction

Within PV-Works it is possible to code adverse event terms, medical history terms, laboratory tests, causes of death, products and product indications against their relevant dictionaries. For most of these elements MedDRA is the dictionary of choice. Potentially, each term or product in a case may be coded against any number of dictionaries. These could be different dictionary types or different versions of the same dictionary.

In practice MedDRA has become the only dictionary required for pharmacovigilance reporting and so all comments about other dictionaries in this specification can be ignored by most readers.

For example in addition to MedDRA coding, an adverse event could be coded:

- against both Costart and WHO-ART

- against standard Costart and against a local 'company extended' version of Costart

- against different versions of WHO-ART

PV-Works supports MedDRA coding using the latest production version of the dictionary but also supports earlier versions where customers have not upgraded to the most recent issue. Assured will endeavour to make each release of the MedDRA dictionary available to customers within one month of its release, subject to no changes to the underlying data structure.

- The coding functions of PV-Works may be accessed in the following ways:

- from the Data drop down menu of the Main Menu Screen

- from a 'Code' button on the Main Menu screen

- from an icon at the top of the Data Entry functions (MedDRA only)

- from within the Data Entry function, e.g. adverse events may be coded from the screen where event data is entered or edited.

The following commercial dictionaries are supported in the current version of PV-Works:

Cause of death	MedDRA
Events	MedDRA Costart WHO-ART HARTS
Indications	ICD-9 MedDRA
Laboratory Tests	MedDRA
Parental data	MedDRA
Products	WHODRUG

Given the migration to MedDRA as the single coding dictionary, a delivered PV-Works system is now set so that MedDRA is the only available dictionary. The flexibility of PV-Works to code with different dictionaries still exists but is hidden.

7.2 MedDRA Coding

The latest production version of MedDRA is included in PV-Works. Individual customers will be responsible for obtaining a subscription licence for MedDRA.

PV-Works keeps its coding results in a separate table in the database to avoid confusion or misuse with results derived from other dictionaries. Such separation is important so that users can distinguish between codes for legacy dictionaries such as Costart and WHO-ART that were determined manually versus those inferred by MedDRA.

In addition to the selected preferred term, this table records the full MedDRA hierarchy for the selected code to assist ad hoc querying.

The data recorded against each code for a case includes the version number of the MedDRA dictionary used to derive the code. This item assists customers in the management of codes across different versions of the MedDRA dictionary.

Searching the MedDRA dictionary may be initiated either:

- at the Low Level Term (LLT) or Preferred Term (PT) level (see section 8..2.1)
- across all levels of the dictionary (see section 8.2.2)

Coding against MedDRA follows the same basic principles as coding against any other dictionary. The search text is matched against the dictionary, alternatives are displayed and the search text itself may be amended for improved searching.

However, the searching functionality with the MedDRA dictionary offers two further features:

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- the ability to use two search terms e.g. 'head' and 'pain' – and to make the conjunction of these an 'AND' or an 'OR', i.e. 'head' and 'pain' versus 'head' or 'pain'.

- the ability to maintain multiple versions of the MedDRA dictionary in a single database and to select the one that will be searched.

Before the actual searching takes place, the user is shown the summary screen in Figure 20.

Figure 17 : MedDRA Coding : Codes for selected verbatim term(s)

When MedDRA coding is initiated from a particular data entry screen, the screen above will only show the single item to be coded. The user may choose the method of searching – i.e. LLT, PT or all levels. This may be set as a default by the System Administrator.

7.2.1 Search for Low-Level or Preferred Terms

Searches may be initiated at either the Lowest-Level-Term (LLT) or Preferred Term (PT) levels. From the preferred term it is possible to select a LLT term.

The search text may consist of one or two strings – these do not need to be whole words but equally each can be multiple words. Using the AND / OR radio group it is possible to define how the two search strings will be used.

Valid search terms include:

'Headache'
'Head' and 'ache'
'Head' or 'ache'
'hypera'
'hypera' and 'low'
'ism' or 'itis'

A search may be defined as:

- 'Best Fit' – if the search text matches a coded term precisely; this will be returned with no further choices. If not, the search term is matched from the start of the coded dictionary terms. Finally, the system returns coded terms that 'sound like' the search text (be warned that this final option often produces some bizarre ideas of what constitutes a match).

- 'Exhaustive' – this is a similar search except that the search text may appear anywhere in the coded terms. This is the default option.

Note that the MedDRA searching algorithm is text sensitive and has no medical intelligence.

An additional user selection may be required depending upon the data returned from the MedDRA dictionary. For example, the screen below shows alternative codings for the search text 'Hypertension'. The user has selected 'Hypertension renal'. In the MedDRA hierarchy this term belongs to two different High Level Terms (Renal failure and complications, Increased Blood Pressure). In turn these lead to two different High Level Group Terms and two System Organ classes.

Where a search result returns more than one MedDRA entry, PV-Works will display the alternatives and the user must select the most appropriate one.

Users may code the following against MedDRA:

- Adverse Event verbatim
- Medical History
- Cause of Death
- Indication for use

- Laboratory Tests*
- Parental data

note that Laboratory tests are normally coded outside of PV-Works and held in a dictionary. See PV-Admin Functional Specification.

MedDRA coding : Result of Dictionary Search

The MedDRA coding function in PV-Works returns all MedDRA database entries for both the MedDRA Preferred Term and the MedDRA synonym. The code values held in the MedDRA database can include:

- WHO-ART event code
- HARTS event code
- Costart coded indicator
- J-ART event code
- ICD-9 indication code
- ICD-9CM indication code
- ICD10 indication code

7.2.2 Search All Levels of the MedDRA Dictionary

A third method of searching the MedDRA dictionary is termed 'all levels'. In this the search text is tested against each of the five levels of the MedDRA dictionary in a single pass (i.e. against System Organ Class, High Level Group Term, High Level Term, Preferred Term and Low Level Term). The result of this search style is the display of all five levels of the hierarchy with results shown in five columns. It would be possible to drill down from these levels on the screen to find the best match by double-clicking the + sign in the grid.

This is an ideal option if the user is keen to review potential codings around the search term or is less familiar with the MedDRA dictionary.

The ability to use one or two search terms is identical to the functionality of a search based on LLT or PT. The screen for the display of search results is shown below.

MedDRA Matching Terms for All Level Search

A search term could be found in any or all of the five levels. Many terms will be found in both the Low Level (LLT) and Preferred Term (PT) Levels e.g. Aggression, Anxiety. In fact 'Anxiety' is found at four levels – not in the System Organ Class.

Of course if the user searches for a common string of characters e.g. 'en', then it is bound to be found in all levels – not that this search is very helpful to coding but it demonstrates that the proposed implementation needs to be ultimately flexible.

It is proposed that any term that matches will be displayed, regardless whether this results in a duplicate row. Thus if the user searches for 'Anaemia', then there will be 4,332 rows returned (with MedDRA version 12.0) as follows

1 for HLGT
8 for HLT
25 for PT
4,003 for LLT.

This allows the user to start drilling down at the level most appropriate to their needs.

Where matches occur in the System Organ Class (SOC), HLGT, HLT and PT levels, these will be presented in an explorer style with (+) buttons to allow the user to expand and contract the hierarchy.

The user may only select a code for inclusion in the case from a row in which a full hierarchy (SOC, HLGT, HLT, PT, LLT) is shown. Note that the whole hierarchy is shown in the coloured list above the results grid.

Unless the user has selected a row that is defined at all levels, the 'Save' button is disabled, making it impossible to select an incomplete row.

For example:

Suppose that the user searches for the term 'Anaemia'. This term is found in four levels of the dictionary as described above and will be presented as shown below (which represents a fraction of the total search results).

Presentation of MedDRA Search Results

In the first row the displayed match occurs as the Low Level Term ('Anaemia prophylaxis'). All five levels are displayed as a simple data line. The user may select this line and copy these codes into the case.

In the fourth row the displayed match occurs as the Preferred Term level ('Anaemia of pregnancy'). The SOC, HLGT and HLT are displayed as fixed data items, the LLT is not displayed and the PT shows an explorer-style expansion symbol (+). The user cannot select this row to copy codes into the case, but first must expand the display (by clicking the + symbol) to show the related Low Level Terms. This will result in a display similar to

Presentation of MedDRA Search Results - expanded

The user may now select one of the Low Level Terms and copy these codes into the case. Alternatively, the user may close the expanded view and drill down in other areas of the hierarchy.

The same principles apply to matches found at the higher levels.

7.2.3 Using multiple MedDRA versions

The System Administrator can install more than one version of MedDRA. This function may be useful when it is determined that a particular clinical trial should be coded to a particular MedDRA version to ensure internal consistency. This function has less value for cases from marketed products.

When a clinical trial is defined by the System Administrator it is possible to 'force' a particular MedDRA version and apply this version to all cases for the selected study. If this definition is made, then the user is forced to use the selected version of MedDRA.

As new versions of MedDRA are issued, Assured will release a revised dictionary to its customers. Normally, this update will be applied to replace the current version such that only one MedDRA version is active.

However, it is possible to apply the new MedDRA dictionary as an additional version to the version or versions that already exist. Note that a function in the administration program allows the System Administrator to delete versions of MedDRA as required.

If one version of MedDRA is installed (or the case is from a clinical trial with a pre-defined MedDRA version) then the user is forced to use this version when coding.

If more than one version of the MedDRA dictionary is loaded then by default PV-Works will select the version that is defined by the System Administrator as the default; typically this will be the latest version. However, each of the search screens displays a drop down list of available MedDRA versions and the user may select a different one for the case / clinical sign in question.

Note that a verbatim term can only be coded once; it is not possible to code it against an older version of MedDRA and the current version simultaneously.

The version of MedDRA that is used for coding is recorded against each coded term stored in the database.
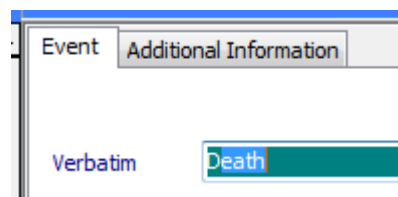
7.3 Auto-Coding to MedDRA

The MedDRA auto-coding function is intended to reduce the amount of effort required by the user in entering the MedDRA coding for common verbatim terms.

As the user begins to type in the Verbatim field of the Adverse Event screen, the system will list common verbatim terms whose name begins with the same letters that the user types. For example, when the user starts typing 'RA' into the verbatim field, the system will automatically pop up the suggestion 'RASH'. If the suggestion is accepted, then the full verbatim term is entered together with its associated MedDRA coding.

An accompanying administrative function is available in PV-Admin that allows customers to define their own list of common verbatim terms and their mapping. This list may need to be reviewed as new versions of MedDRA are introduced.
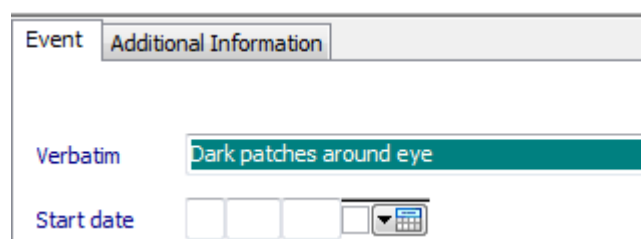
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Automated MedDRA Coding
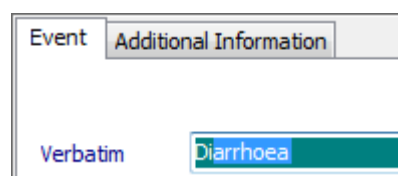
Given that a list of common verbatim terms exists and the user types the letter "D" then the drop down list, similar to the 'Automated MedDRA Coding' screen shown above, would be displayed. Since there are items in the common verbatim list beginning with 'D' the first one is selected. (For reference the common list in this sample configuration is Death, Diarrhoea and Dizziness).

If none of these suggestions is appropriate the user should continue typing the required verbatim term and this will replace any auto-suggestion e.g.
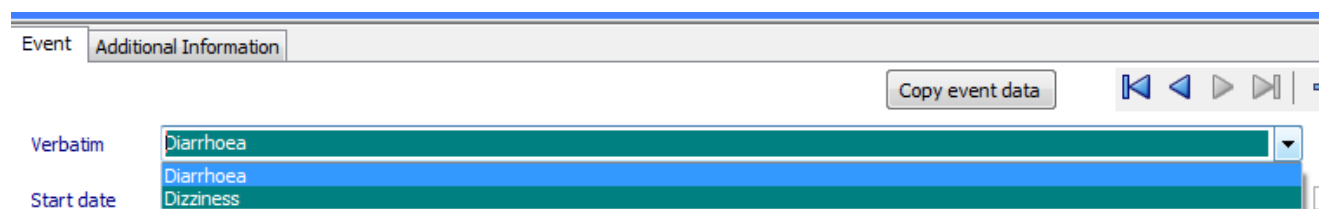
Alternatively, if the user types the letter 'I' or 'i' after the 'D', the auto-suggestion moves to the first term that begins with 'Di', namely Diarrhoea.

The user can continue typing until the required term is found or may open the drop down list and select from the filtered list that is offered:

If the user selects a term from the pre-defined list of suggestions then the MedDRA coding will be added as soon as cursor is moved out of the verbatim field.
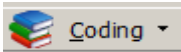
The backspace key will delete the user's typing so that entry can be re-started.

7.4 Upgrading MedDRA

The MedDRA dictionary is refreshed twice per year (currently March and September) and the new version should be implemented two months later. Assured provides scripts to update the dictionary in a timely manner. While this process is outside of the scope of this specification users should be aware that the upgrade process will determine any codes that have become obsolete or have been changed in the latest MedDRA release.

7.5 MedDRA Browser

A MedDRA browser option allows a user to browse the MedDRA dictionary without making any changes to a case. This function is based upon the 'all levels' search screen described in section 8.2.2. It is invoked by clicking and then selecting 'MedDRA Browser' and will display the following screen:

MedDRA browser screen

Note that the MedDRA browser also supports two search strings.

The MedDRA browser will also allow the user to select any of the installed versions of MedDRA for browsing purposes. (see section 8.2.3 for details on the ability to store multiple versions of the MedDRA dictionary simultaneously).

The MedDRA browser can be run from:
- the Coding button on the Main Screen
- the Data menu of the Main Screen

The search level drop down will be populated with the following values:
- System organ class (SOC)
- High level group term (HLGT)
- High level term (HLT)
- Preferred term (PT)
- Low level term (LLT)
- All levels – the default value

The text entered into the search text will be tested against the MedDRA dictionary at the specified level and all matches will be displayed. It is possible to drill down from the level displayed on the screen to expand the results by double-clicking the '+' sign in the grid.

7.6 Principles of coding in PV-Works with other dictionaries

Coding of reported terms against dictionaries is an 'assisted' task in PV-Works rather than one that is fully automated. When a coding task is started, PV-Works will search for all dictionary entries that either match the reported term or product name perfectly or that contain it. If more than one entry is found the user is presented with a list of alternatives from which to select. (see Figure 8.6).

Users may widen the search to include dictionary entries that are spelt like the search term. Alternatively, the user may alter the search term and re-search. Amending the search term does not alter the data stored in the PV-Works database. PV-Works is not case sensitive and will convert all search text to upper case before searching. This conversion does not affect the data stored in the database.

Figure 8.6: Coding Case Data : Results of Dictionary Search

7.7 Company Product Dictionary

The Company Product dictionary describes the products owned by the customer, including the generic and brand names, marketing authorisation holder and international birth date. The data in this dictionary is maintained by the Systems Administrator.

The dictionary is used wherever data about the company's product is entered, e.g. Initialise Case, Data Entry / Update, and generates a company-specific look up list on the product screen. By default this drop down list shows active products only and is also restricted to products that are marketed in the country where the adverse event occurred.

On the product screen the user may amend the list to show all products regardless of market country. This may be necessary for 'cross-border' cases. However, this list may be extremely long. As an alternative the user may click the 'Find' button and search for a product. This is the only method of selecting an inactive product.

7.8 Expected Adverse Events

The Expected Adverse Events dictionary is created and updated by the user to record the events that define the product label. Different sets of events may be defined for different labels. This information can be used in the Assessment screens to automate the assessment of labelledness. The use of this dictionary is as a guide to the user; the user may overwrite the answer retreived from this list.

Figure 8.8: Coding Adverse Events against Expected Events List

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7.9 Common Indications

The Common Indications dictionary is created and updated by the user to record the indications that each company product may be used for. This information can be used in the Data Entry / Update screens to reduce the need to type long indication names for products.

Figure 8.9: Coding using Common Indications Dictionary
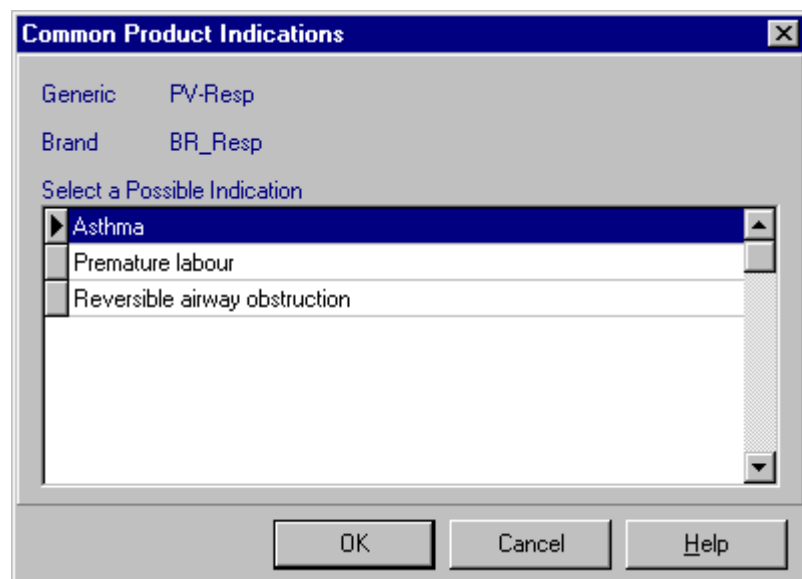
7.10 Equivalent Products

Where product brand names vary from country to country, these may be defined as part of the case data. When a single case report such as FDA 3500 or CIOMS-1 is printed, PV-Works can use these alternative brand names to print the name used in the country to which the report will be submitted.

Note that PV-Works includes a system option set by the System Administrator to determine whether reports should include local brand names for the country of report submission or whether the name in the country of case occurrence should always be used. For example, all FDA 3500 reports submitted to the FDA could show US brand names if these are known.

If the local brand name is not known, the report will show the brand name from the country where the case occurred. This approach is considered preferable to one where the user is required to select the correct brand name at the point when a report is generated. By making these alternate brand names part of the case record, each report can be re-printed consistently and the assessment of product equivalence can be performed by the person with the most appropriate knowledge (who may not be the person printing the report).

For each product in the case, PV-Works will record an alternate brand name for any country using the screen shown below

International Equivalent Products

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8 Clinical Trial Case Data

8.1 Clinical Trial Selection

On the Case Identification screen the user is prompted to select a study from the clinical trial dictionary as soon as the case type of 'Clinical Trial' is set. The pop up screen in question (Figure 9.1) allows the user to select the Trial Centre from which the case originated.

Figure 9.1: Select a study
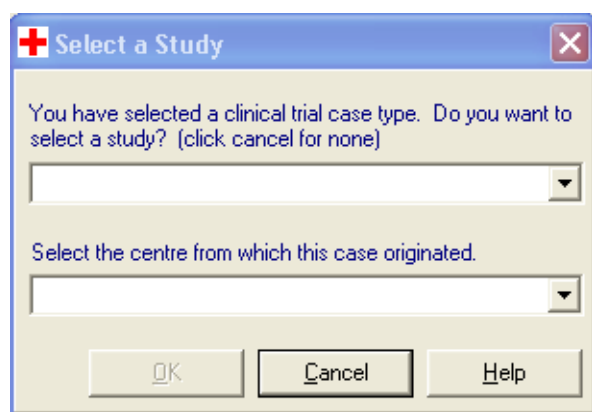
The user may also select these data items on the Study Screen.

Regardless of which screen is used to define the study and centre then once a study centre has been selected and, assuming that there are no existing contacts in the case, the primary reporter set for the selected study will be copied to the Contacts screen. Note it will be possible to define the investigator centre (i.e. location) without entering the name of the investigator.

If the selected trial is defined as 'blinded' then a record is added to the product screen with the product name is set to 'Blinded Test Product'. This infers that one or more actual products have been taken, but the precise treatment is not available.

8.2 Unblinding a complete Clinical Trial

In section 6.11 a function was described that allows a case to be unblinded, e.g. for regulatory need. There is a complementary function that allows a user to unblind all the cases of a single clinical trial in a single operation. This is accessed from the Data Menu as 'Unblind Clinical Trial'.

The following screen is displayed:

Clinical Trial Unblinding Screen (End of study)

The user will select the sponsor and clinical trial to be unblinded. The user will confirm this request and the following screen will be displayed:

Clinical Trial Unblinding at end of study

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All cases from this study will be displayed – regardless of whether they have been individually unblinded or not. The results may be sorted. The user will mark all cases (i.e. patients) who received the same treatment. A case with status of 'Unblinded' cannot be marked. Until one or more cases are marked, the 'Define Product' button is greyed out.

The user will click the 'Define Product' button to define the product (or products) that were actually dosed. This follows the same principles as were outlined in section 6.11 and this data is entered using the following screen:

Figure 18 : Clinical Trial Unblinding : Define Products

The button 'unblind' is greyed out until the user has selected the product(s) that a patient took. This process requires the user to unblind the trial in a series of blocks of cases. A running count of the number of cases, the number unblinded and the number remaining will be displayed on the screen.

The user is warned if they attempt to cancel the function before all cases have been unblinded but is permitted to exit this function with the trial partially unblinded.

Where more than one case exists for the same patient (identified by patient number), it is not possible to select different unblinded product names for each case, ie a patient always takes one set of products. An error message is given if this situation is detected.

When the UNBLIND button is clicked each case in the selected block is unblinded.
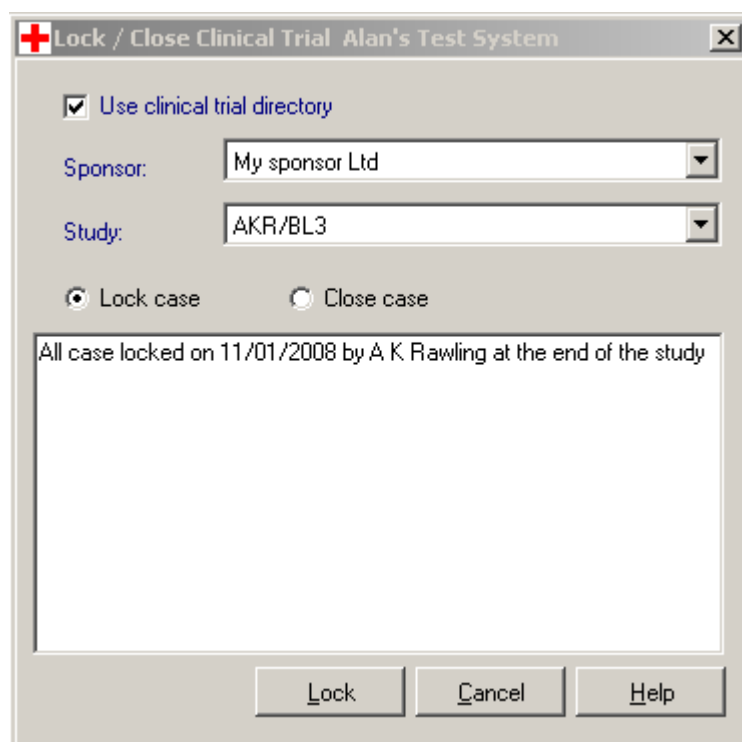
It is also possible to lock all cases of the trial that have been unblinded by clicking the 'Lock cases after unblinding' button. This will lock all cases that have been unblinded (and are not already locked) and will add a reason for locking as "Locked during trial unblind. Trial was unblinded due to <user reason>.".

8.3 End of Trial Lock Function

In section 9.22 unblinded cases can be locked in a single step. However, this function is not available for 'open' studies. A function can be accessed from the File Menu ('Lock/Close a Clinical Trial') that will allow the user to lock all cases from a single clinical trial regardless of whether it is blinded or open.

The following screen is displayed:

Clinical Trial Locking Screen (End of study)

In addition to the standard security access rights, this function may be further protected with an electronic signature (section 21). The user may 'lock' or 'close' the cases of the trial as defined by the radio group. The default option will be 'lock case'.

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9 Reporting: Single Case Reports

9.1 Introduction

An essential part of a pharmacovigilance system is the generation of specific reports that are submitted to regulatory authorities. PV-Works collects and reports data to meet all common international regulations including CIOMS, FDA, EMEA, MHRA and PSUR. In addition to these external requirements PV-Works includes reports for use within a company. These include a case report and an audit trail report.

Whether the report is required internally or is sent externally, and regardless of whether the report takes its data from one case or several, the general principles of operation outlined in section 10.2 apply to all reports. All reports can be printed either on A4 (11.69 x 8.26 ins, 297 x 210 mm) paper or Letter paper (11 x 8.5 ins).

This section describes how single case reports are generated. 'Single case reports' are those reports that display case data from one case only.

Section 11 provides details of the generation of multiple case reports such as PSURs as well as functions that will generate multiple 'single case reports' in one step. However, the reader is advised that the principles in this section need to be understood before the approach taken with multiple-case reports is reviewed.

Section 12 provides details of the generation of XML files with the intention of electronic submission to regulatory authorities.

9.2 General Principles of Operation

The report style to be generated is selected from a sub-menu which is displayed from

- the Report menu of the Main Menu

- by clicking the 'Report' button on the Main Menu

- by clicking the 'Report' button on the Data Entry / Update screen.

Internal reports generated by the customer may be 'published' to PV-Works and accessed from PV-Works via the screen in Figure 10.2. Internal reports may be assigned to any number of categories and are displayed in a 'windows explorer' style with + and – expansion / contraction symbols.

The reports shown on the 'Select Reports' screen are restricted to those reports that the user is able to run, i.e. has been given security access for the currently selected case. All other report names are invisible rather than 'greyed out' and so the actual screen shown to the user is likely to have less options that the one in Figure 10.2.

Figure 10.2: Report Selection sub-menu
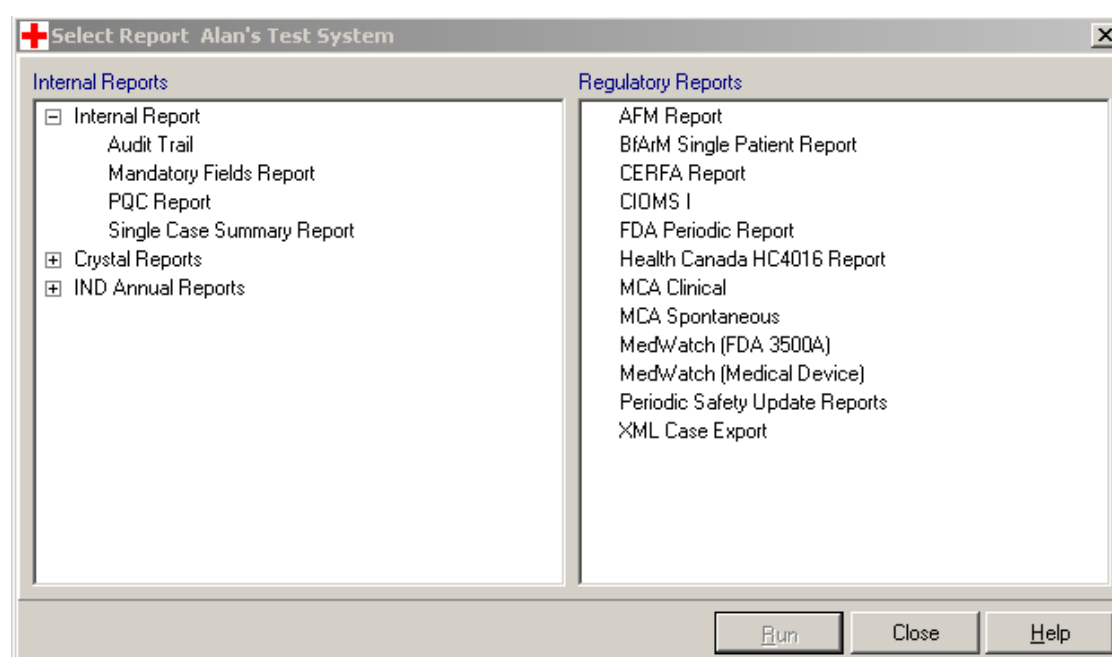
If the report style is for a single case the user will need to select the appropriate case on the Main Menu before invoking the Reports option. Where the report style is for multiple cases, the actual case currently selected and displayed on the Main Menu is irrelevant.

Most reports allow the user to tailor the report by specifying options such as:

- Draft or Official format

A 'draft' report is an internal working copy of a regulatory report. It is stamped with the word 'DRAFT'. An 'official' report is one that is intended for submission.

- case identification format

- default text where data is missing

The actual options available vary from report style to report style and are discussed further in the sections below.

When an official report is created, an image may be saved automatically in the PV-Works document repository when the report is printed. The purpose of this is to create an electronic library of all reports that have been sent to a regulatory authority. This function will be controlled by a system option which will be given a value of either:

NONE   - implying that no copy should be created

<<folder>>   - the name of the document folder in which the copy should be saved.

The document will be assigned the name '<<report type>> official report copy', e.g. 'FDA3500 official report copy'.

This option will apply to every report type for single cases. All official reports created by a user will be stored in the same document folder. However, it will be possible for different users to save these images in different folders, e.g. a USA user stores reports in a different folder to a German user.

The Systems Administrator can determine default settings for each option and may also determine security rights such that only certain users may amend these defaults at run-time. Reports may be printed directly to the currently selected Windows printer or may be displayed on screen as a Print Preview. The actual printer used may also be changed to any printer connected to the user's Windows system.

From the Print Preview screen the user can navigate the report from page to page, zooming in and out as necessary. The Print Preview screen includes options that allow the user to:

- print the report
- close the report without printing
- save the report to a PC file
- export the report to an Adobe PDF file
- export the report to Microsoft Word
- export the report to an E-mail system
- export the report to the PV-Works document repository

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If a case needs to report more information than will fit into the available space on a single sheet, then a continuation page is used. This situation is common with the regulatory reports where there is no control over the format required. Any of the following conditions is likely to cause the case to require a continuation sheet:

- several adverse events
- long narrative text
- several laboratory test results
- several suspect products
- several concomitant drugs
- several concomitant diseases

It is also possible to send a single case report to a licensed partner. Available licensed partners may be defined by the Systems Administrator. These reports may also be stored electronically in the PV-Works document repository upon printing and a record of their 'transmission' to the partner made in the same manner as regulatory authorities.

9.3 Regulatory Reporting Approval

The report approval function is a user-customisable option that builds upon the Mandatory Data check described in this guide and provides a mechanism by which cases must be approved formally before official regulatory reports may be generated. Prior to this approval, data from a case may be presented in draft regulatory reports and may be included in any internal report that is generated.

Once a case has been approved for reporting, an official report may be generated in the format of any of the PV-Works regulatory reports. In other words, the approval of reportability is global.

A series of options are proposed and customers may decide to implement all or some of these. System options will be created for:

1. The report approval function as a whole (the "report approval" option)
2. The creation of a version of a case when the report is approved
3. The restriction to generate official regulatory reports only from approved case versions, i.e. never from the master case.

version of PV-Works implements the report approval elements for single cases only.

The 'report approval' function will be found as an item of the Reports menu on the Main Menu screen. It can be run at any time as a method of checking the completeness of a case for reporting.

Alternatively, the option may be run from within the Update screen via an icon button in the Update screen toolbar, as shown in Figure10.3:

Figure 10.3: Report approval Button
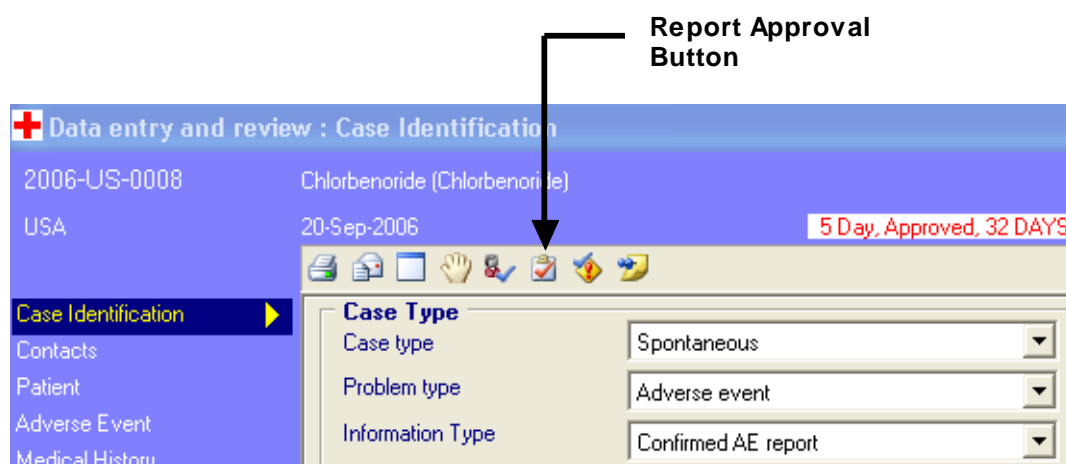
9.3.1 Simple Report control

If the regulatory approval function option is set to 'false', then the remainder of section10.3, does not apply to the customer's implementation of PV-Works.

Assuming that report control is implemented, then the mandatory data check screen will be extended as shown in Figure10.3.1. Standard security/access rules will be applied to this screen so that the users able to approve cases for reporting is restricted.

This screen will operate in the same way as that described for Mandatory Data items, i.e. the user will be able to branch to the screen where the missing data needs to be input. (Note that it may be necessary to start an update session for the user if they wish to amend data. The standard user security / access rules will apply to this.)

Figure 10.3.1: Report approval screen

The fields marked as 'error' are those set by the user as 'mandatory for reporting', while those marked as a 'warning' are set as 'warning for report'.

The 'approve regulatory report' button will only be enabled when there are no data fields marked as 'error' and a reason/timing selection has been made. When this button is clicked an electronic signature challenge will be made upon the user to approve the case for official regulatory reporting. If the user successfully passes the electronic signature challenge then the case status will be changed from 'open' to 'reportable'.

If the reportability system option is invoked, then any attempt to create an 'official' regulatory report from a case whose status is not set to 'reportable' will be denied – the print and preview buttons on the set up screens will be disabled.

If the user runs the 'report approval' function for a case that already has a status of 'reportable', it is possible to remove the reporting approval by clicking the 'revoke' button. Removing approval will also require an electronic signature approval.

This represents the simplest level of control:

- Cases must be approved for generation of official reports
- Approval requires an electronic signature which is recorded

9.3.2 Automated versions and version control

In principle (and without further controls beyond those described above), the official report can be created from the master copy of the case or any 'versions' taken during its processing. The next stage in the control of reporting is to automate the creation of a version of a case at the point of approval and then restrict reporting such that the master version (i.e. the one that can be edited), may not be used for official reports.

("Versions" are read-only copies of a case's data frozen at a certain data point. See 'Case Versioning' for details of the versioning process).

The advantages of this are:

- All regulatory submissions are taken from the same version of the case, leading to global consistency.

- Any questions from the authority can be directed to the data at the time of approval.

- Any follow up information arriving after the case has been given approval status but before submission to the authority, may be entered into the master version of the case without impacting the original submission

To implement this level of control, the system option 'creation of version when approval is given' will be set to 'true'. If this is the setting, then the approval for reporting will lead to the following changes:

- User will add a reason for the approval related to the processing of the case, e.g. initial report, follow up. (This is entered via a drop down list next to the 'approve report' button.

- Creation of a case version (i.e. a read-only snapshot of the data)

- The version control data will note that the version is available for reports

- The reason for the creation of a case version will be set automatically.

Any attempt to create an 'official' regulatory report from a version whose status is not set to 'reportable' will result in an error message and the report request will be rejected. With the above rules implemented, this means that the case/version selected must be a version that was created at the point of report approval.

The 'report set up screens' will be amended to show whether 'official reports' may be generated for the current case and for which version(s). This is shown in

Figure10.3.2.

Figure10.3.2: Report Set Up Screen – with report approval shown

When a regulatory report set up screen is displayed the 'report print status' is set to 'DRAFT'. This is intended to be an internal, working copy of the report. A draft report may be generated at any time and is not subject to report approval. The 'preview' and 'print' buttons are greyed out and thus inaccessible.

If the user changes the 'report print status' to 'official' to generate the copy for submission and version control is invoked, all approved versions will be displayed, in descending order of approval date. If version control is not invoked an official report may be generated provided the case has been approved.

The user may select any version for the official report. This offers an improved level of control:

- Cases must be approved for generation of official reports
- Approval requires an electronic signature which is recorded
- Official reports can only be generated from safe copies of the case data ('versions') created when approval is given

Note that only cases that have been "report approved" may be generated as "official" reports. When the user selects "official" a check is made of the report approval status. If the case is "approved" then the user may continue the process.

If the case is "unapproved" then the following message is displayed:
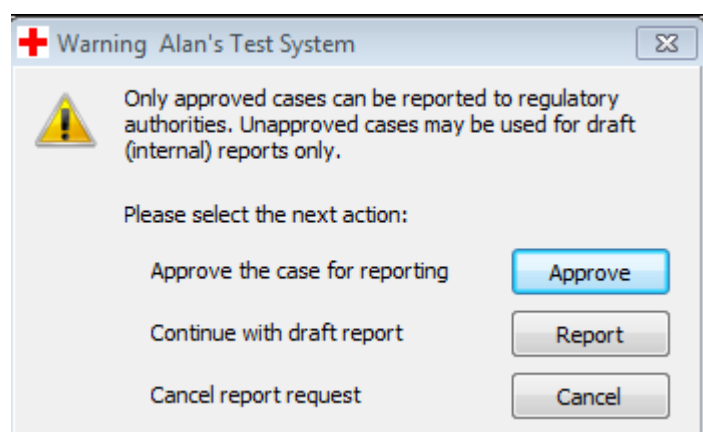
If the user has security access to the Report Approval function, they will be able to branch to this screen in order to approve the case before reporting it. The user may continue to generate a draft report using the unapproved case.

9.3.3 Regulatory Reports Screen

The regulatory reports screen allows the user to record dates of submission of a report to an authority. This is a manual process. Generation of 'official' reports is assumed to lead to submission to an authority. As such the program will record this action as follows:

- Whenever an official report is generated, a record will be added to the regulatory reports screen with a status of 'generated, but not submitted'. The system will note which version of the case was used to generate the report.

- Users may delete the 'generated' record, if the report was never submitted

- Users may confirm submission and provide a submission date

- A simple report could be created of reports 'generated' but not 'submitted'

To achieve this, the regulatory reports screen is shown in Figure 10.3.3. The submitted reports are shown in the grid. The status of the submission is also shown.

Figure 10.3.3: Regulatory Reports screen

9.4 Version dates on regulatory reports

If the customer has configured PV-Works such that cases are approved before official regulatory reports are generated (see section10.3.1), then each official report will carry the date and time of approval. This is added as a footer of each page of the regulatory report. outside of the 'frame' of data defined by the regulatory authority.

The following reports will be amended:

- FDA3500 / MedWatch
- CIOMS-I
- Any regulatory report for a single case developed in the future

Note that this requirement does not apply to PSURs.

The following table shows the message text that will be printed based upon the 'Report Approval' configuration options invoked in section10.3. In addition to the option settings, a draft report may be created from a case prior to approval or from a case version created for a reason other than reporting. These situations are also covered by the table:

Figure 19 : Version Messages on Regulatory Reports

Report type	Case / version approved for reporting	Report Approval option set OFF	Report Approval option set ON Version reporting option set OFF	Report Approval option set ON Version reporting option set ON
DRAFT	Unapproved	None	Unapproved	Unapproved
	Approved	None	Date / time of approval	Date / time for version approval
OFFICIAL	Unapproved	None	Not possible	Not possible
	Approved	None	Date / time of approval	Date / time for version approval

Key to message formats in the above table:

- None   no message text printed
- Unapproved   "Version: unapproved"
- Date / time of approval   "Version: 24 Jan 2002 at 13:11" ...from latest approval
- Date / time for version approval   as date/time but values taken from case version that is used for printing

9.5 Regulatory Reports for single cases

9.5.1 CIOMS I

The CIOMS-I report summarises single case data in a format defined by the document 'International Reporting of Adverse Drug Reactions; Final Report of CIOMS Working Group; CIOMS, Geneva'.

CIOMS-I report options include:

- define default text for empty fields
- define the event description field e.g. verbatim versus coded
- define the Case Identification field, e.g. case number, case number with local reference number
- source of Name and Address to be used as Manufacturer
- language that report is to use for case narrative
- suppression of all personal case data, i.e. reporter's name and address details

Figure 10.5.1: CIOMS Report Options screen

9.5.2 MCA Clinical

The MCA Clinical report summarises single case data for submission to the MCA (Medicines Control Agency – now MHRA). It is used for expedited reporting of serious unexpected Adverse Events which occur during a clinical trial. The report is also known as the EMEA Clinical report.

MCA Clinical report options include:

- define default text for empty fields
- define the event description field e.g. verbatim versus coded
- define the Case Identification field, e.g. case number, case number with local reference number
- source of Name and Address to be used as Manufacturer

9.5.3 MCA Spontaneous

The MCA Spontaneous report summarises single case data for submission to the MCA (Medicines Control Agency – now MHRA). It is used for expedited reporting of serious unexpected Adverse Events which occur post-authorisation. The report is also known as the EMEA Spontaneous report.

MCA Spontaneous report options include:

- define default text for empty fields
- define the event description field e.g. verbatim versus coded
- define the Case Identification field, e.g. case number, case number with local reference number
- source of Name and Address to be used as Manufacturer

9.5.4 FDA 3500A MedWatch

The FDA 3500A or MedWatch report summarises single case data for submission to the FDA (Food and Drug Administration). It is used for both expedited and periodic reporting of Adverse Events. This specification follows the guidelines set out in the MedWatch document 'Instructions for Completing FDA Form 3500A'.

MedWatch report options include:

- report type: 5-day, 10-day, 15-day
- define default text for empty fields
- define the event description field e.g. verbatim versus coded
- define the Case Identification field, e.g. case number, case number with local reference number
- source of Name and Address to be used as Manufacturer
- suppression of all personal case data, i.e. reporter's name and address details

9.5.5 3500A MedWatch for Medical Devices

The FDA 3500A or MedWatch report for Medical Devices summarises single case data for submission to the FDA (Food and Drug Administration) and is used where the product involved in the case is a device. The layout is very similar to that of the 3500A for drugs but with additional sections. Most of the principles of reporting and available options are identical.

The MedWatch Medical Devices form is implemented as a separate report type within PV-Works to allow different security / access settings to be defined.

A further eMDR electronic report has been implemented in PV-Works – see chapter 12 for further information.

9.5.6 HC 4016 Report

The HC 4016 report summarises single case data for submission to the Canadian regulatory authority. (Health Canada).

HC 4016 report options include:

- define default text for empty fields
- define the event description field e.g. verbatim versus coded
- define the Case Identification field, e.g. case number, case number with local reference number
- source of Name and Address to be used as Manufacturer

9.6 Internal Reports: Case Report

'Internal' reports are those produced for medical review, data check or any other 'non-regulatory' requirement during the processing of a case. These reports are in the form of safety data summaries, listings or frequency of occurrence tables.

The PV-Works philosophy is that users need to be able to define their own reports wherever possible. Every company has its own set of 'standard' reports which share many common features from company to company. However, it is also true that these 'standard' reports vary widely from company to company and that any generic set offered by PV-Works is unlikely to satisfy the company's requirement without amendment. Such customisation can be part of an agreed PV-Works implementation programme.

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PV-Works provides various options to support the internal report requirements:

- Case Summary Report (see 10.6.1)
- Product Quality Complaint Report (see 10.6.1, 10.6.2)
- An integrated interface to Crystal Reports (see section 18.4)
- An interface to other third party report writing software (see section 18.4)
- An Audit Report.
- An option to export data to a comma-separated values file (.csv) or to print data from the main screen grid (see 17.5,17.6)
- The option to export data from the 'Find Case' function to a comma-separated values file (.csv) which can be processed by third party software including Microsoft Excel and SAS.

Note that the use of any third-party query or reporting software that is compatible with Oracle is a further option for the generation of Internal Reports. These products include Crystal Reports, Brio Query, Impromptu and Business Objects.

9.6.1 Case Summary Report

PV-Works generates a basic case report that displays all case data and administrative data such as details of case submission to regulatory authorities. This should prove acceptable to most companies without further customisation.

The report has a simple format grouping all similar data together into a section e.g. product and dose information, patient data. All data in a section is printed as a block and each section of the report expands to the required size according to the data to be printed.

9.6.2 Product Quality Complaint (PQC) Report

PV-Works generates a report that displays all key product complaint data for product defects recorded in a case. See section 15 (and 15.3 in particular) for further details.

9.7 Interfacing reports with Microsoft Office and other software

As described in section 10.2 PV-Works can export a report to Microsoft Word, Adobe Acrobat (pdf file), the user's email software or to a PC file. In each case the report is exported as an image that cannot be edited. However, the receiving software may process this report image as appropriate, e.g. integrate the image with text, re-size the image, print the image.

Examples of the uses of this feature might include:

- addition of case reports to management reports or medical assessments in Word
- addition of reports to PowerPoint presentations

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- storage of case reports sent to a regulatory authority in a document / image repository

To export a report the user previews it using the report preview option. All preview screens display the toolbar shown:

Print Preview Screen Toolbar
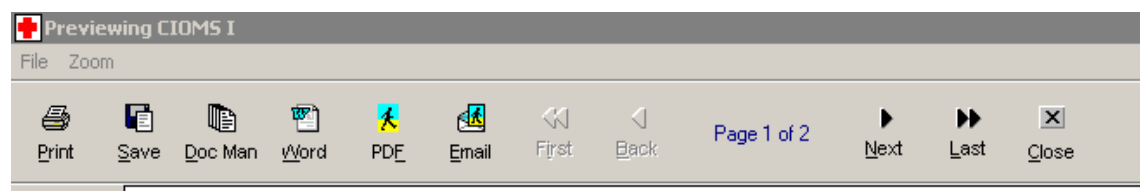
In addition to a 'Print' button to print the report on paper, this toolbar has five export options:

1. Save - Save the report to a PC file in a Windows Metafile (.wmf) format. This format is compatible with most graphics and image software. Once this button is clicked the user is able to name the output file and define its storage folder using standard Windows dialogue boxes. The save report dialogue box is shown below.
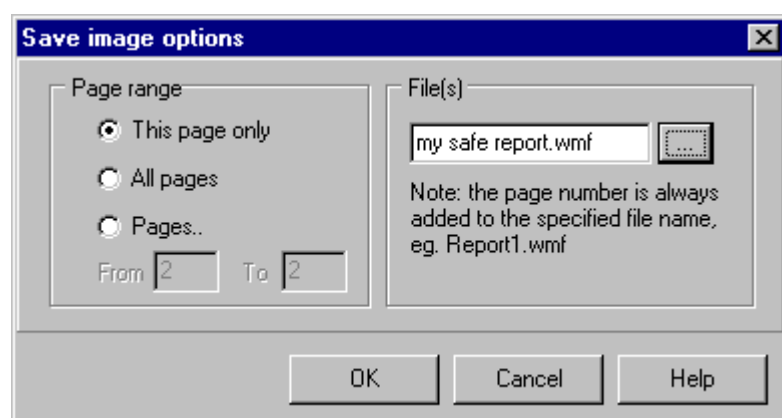
The user may also specify whether the whole report, the current page or a range of pages should be saved. The option to save a range of pages will be particularly useful for multi-page reports such as PSURs and the audit trail.

2. Doc Man - Export the whole report to the PV-Works document repository (i.e. the 'Document Management' screen). This is an image library held in the PV-Works database. Images may be retrieved from the repository, viewed and printed but may not be changed.

3. Word - Export the whole report to Microsoft Word. If Word is not running at
             The time that this button is clicked, PV-Works will load it. The report
             Is inserted into a new Word document with each page in a separate
             Image. Images may be copied to other Word documents (e.g. insert
             into a management report) via the clipboard.

4. PDF - Export the whole report to Adobe PDF format (Portable Document
            Format). Once this button is clicked the user is able to name the
            output file and define its storage folder using standard Windows
            dialogue boxes.

5. Email - Export the whole report to the user's email software as an attachment
              to a new message. The user's default email system is activated so that
              the user may insert the address of the recipient, add a message and
              send the email. This feature operates with any MAPI-compliant email
              software. This includes most of the commonly used applications
              including MS Mail, MS Outlook and Lotus Notes.

9.8 Sending and Recording Single Cases sent to Licensed Partners

Section 10.3.3 describes how submissions of single case reports to regulatory authorities may be recorded. In a similar manner it is also possible to record "submissions" of single case reports to licensed partners.

Note that although the term 'licensed partners' is used throughout this function, the names of these partners is set by the System Administrator. As such this list could include sponsors, ethics committees, CROs or any other person / group.

While these two functions are broadly similar there are a number of minor differences in the approach to reports for licensed partners:

a) for regulatory authorities only 'official' reports generated post-report approval may be submitted. With licensed partners it is possible to send either a 'draft' report or an 'official' report.

b) While 'official' reports to regulatory authorities are saved automatically to the document repository and the regulatory reports screen, this same functionality only occurs for licensed

partner reports if the user requests it.

Each single case report set up screen has two additional fields on the 'set-up' tab. These are:

- A check box that confirms that the user intends to send the report to the sponsor / partner
- A drop down box to define the partner

Figure 10.8.1: CIOMS Set Up Screen

The partner dropdown list will be greyed out until the 'store/send' check box has been checked. It will re-grey out if this check box is unchecked. This dropdown is optional.

When the user clicks Preview or Print and 'store/send official report' is clicked and the report being generated is 'official', a warning should be given. ('Please confirm that an official report should be stored / sent to a licensed partner'). This is not required for a draft report.

As with reports to regulatory authorities, when the user prints a report where the 'store / send draft report' check box is marked, then:

- a copy of the report is stored in the appropriate folder

- a skeleton report record is created in the "licensed partner" screen (Figure10.8.2)

Note that it is necessary to print the report even if the intent is to send it to the licensed partner as a pdf file via email as it is the print operation that triggers the saving mechanism. Tip: If a printout is not required, then 'print' the report to a non-existent printer; this has the effect of triggering the save function without generating a print-out.

The regulatory reports screen has two tabbed record cards – one for regulatory reports and one for partner reports. The licensed partner tab is similar to that for regulatory authority reports with some label changes and the deletion of the 'cases included in periodic report' grid:

Figure 10.8.2: Regulatory Reports Screen - licensed partners tab

10 Reporting: Line Listings

10.1 Printing Reports for Groups of cases

In handling adverse event cases on a regular basis, there are occasions when the user wishes to print the same single case report for a group of cases.

NOTE: Whereas the 'Batch Printing' function described in this section will generate reports for a set of cases, the reader should also review the Expedited Report Submission function described in section 11.2. 'Batch Printing' is a function linked to a Find Case search and may print any report type, e.g. a regulatory report or an internal report such as an audit trail report. On the other hand, 'Expedited Report Submission' is a function designed to manage the submission of official regulatory reports. Both functions have a role to play in a pharmacovigilance process.

'Batch Printing' of reports is a two stage process:
- Select the cases to be reported
- Select the report type and print it for the selected cases.

This screen will allow the user to select a group of cases which are displayed as shown in Figure 11.1.

By default, none of the cases are marked for printing. The user may alter the cases chosen for printing using the 'unmark/mark' and 'unmark/mark all' buttons. Since the user has fine control over exactly which cases are to be printed, it is not critical that the search criteria entered in the Find Case screen define the precise reporting set.

Figure 11.1: Matching cases for batch printing

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When the desired set of cases is marked, the 'report' button will follow the same route as that taken when a single case is displayed, i.e.

- display the list of available reports.
- display the appropriate option screen for the selected report

The options selected for the report will be applied to every case in the set.

With the batch printing option, it is not possible to preview the reports, only print them. Printing occurs as a foreground task and the user is not able to continue work until the last report has been generated. While print generation occurs a progress bar will show which case is being printed. An example is shown below:

Batch Printing Progress Bar
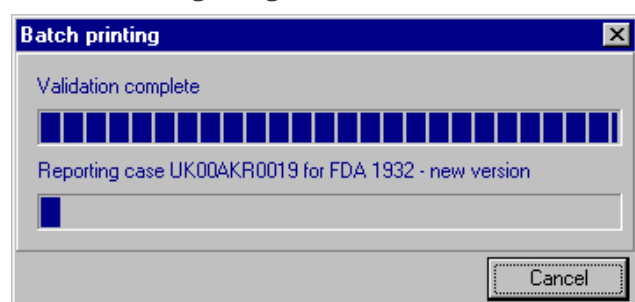
After the last report has been printed, PV-Works will generate a list of all cases reported. If another user is making changes to a case at the time of reporting, this may invalidate the accuracy of the report. Where a case is being updated by another user at the same time as it is being reported, the report will usually be printed successfully. However, the list will show which cases were being updated and by whom.

10.2 Introduction - Expedited Report Submission and PSUR Generation

For many companies the volume of cases handled and the number of expedited cases is relatively low. On the other hand the largest customers of the PV-Works product family process many tens of thousands of cases in a year. For the majority of users in the lower volume category, the workflow module is ideal as a method of tracking the progress of each case and ensuring its 15-day report is submitted on time. (See section 16 for more details).

For a few customers such an approach would be inefficient. The 'Expedited Report submission' function resolves this by finding cases that are due to be reported and generates reports in batch as a single block. The fundamental requirement is to find a set of cases that need to be reviewed and/or need to be reported.

However, many customers will need to use this function as its principles are also a useful approach to reporting 'all cases that are due to be reported and are now ready to report'. The basic design of this function is:

There are two methods of operation of this function:

- Expedited Report Submission – a standard pre-defined query that finds cases that are ready to be submitted
- Advanced Report Submission – allows the user the option to define the query that will find the target cases. User-defined queries may be saved and re-played.

The function can generate two categories of report:

- Single Case Reports – as defined in section 10.5 with one copy per case. All reports are of the same type in a single run, e.g. all are FDA 3500s or all are CIOMSs.
- XML e-report files

Reports may be created as "official" reports for submission or "draft" reports.

The System Administrator may define any number of pre-defined queries for the most common search requirements. These may be parameterised, e.g. the user may be asked to select the product name so that the same query can be restricted to a particular product. Examples might be:

"find all approved cases for brand X to be reported as 15-day report"

"find all Canadian reports for periodic reporting"

"find all foreign cases to be reported"

The system will also support the concept of a sampling review by the report submitter. As a result of the review a case may be placed 'on hold' so that it cannot be reported until some discrepancy or concern with the data is resolved.

Customers should ensure that Validation of PV-Works confirms that multi-case reporting functions return the correct data and, in particular, that the customer's business processes will ensure case data is entered that will lead to a correct report.

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10.3 Expedited Report Submission – basic method

Expedited Report Submission in its simpler form is based upon standard, pre-defined queries. While these may take parameter data to filter the database, the query itself may not be amended by the user. The customer may define any number of these queries and users may execute them by clicking the 'pre-defined queries' radio button and selecting one from a drop down list as shown in Figure 11.3.

(Note the use of the 'my queries' option is discussed elsewhere in this guide).

Figure 11.3: Expedited Report Submission: Query Selection

If a predefined query is selected, all other fields on the form will be disabled. Also, all filter value entry fields will be cleared - Qualifier fields cannot be cleared and will be disabled only. The Query Description field will be read and will display the description of the selected query. If the 'Query Name' field is subsequently cleared, all fields will become enabled again. In essence the user is able to select a predefined query, or specify a manual filter, but not both at the same time.

After selecting the query, it may be run. No other parameters are specified on the screen. Any parameter values required by the pre-defined query are prompted when the 'Show Matches' button is pressed. (Note that this last point is true even if the pre-defined query requires a filter criteria value that is present on this screen).

10.3.1   Expedited Submission – Matching Cases

When the query has been run the results are shown in the 'Show matches' screen.

Figure 11.3.1: Expedited Submission - matching cases

At the top of the screen the user should specify the recipient of the reports. This can either be a regulatory authority or a partner company. The drop down list will change its contents according to the radio group selection.

The user should also select the report type to be generated from the "Output" list. Note that the contents of this varies depending upon the selected recipient and the list may be controlled by the System Administrator.

No reports may be generated unless both of these fields are specified.

This screen consists of two tabbed records:
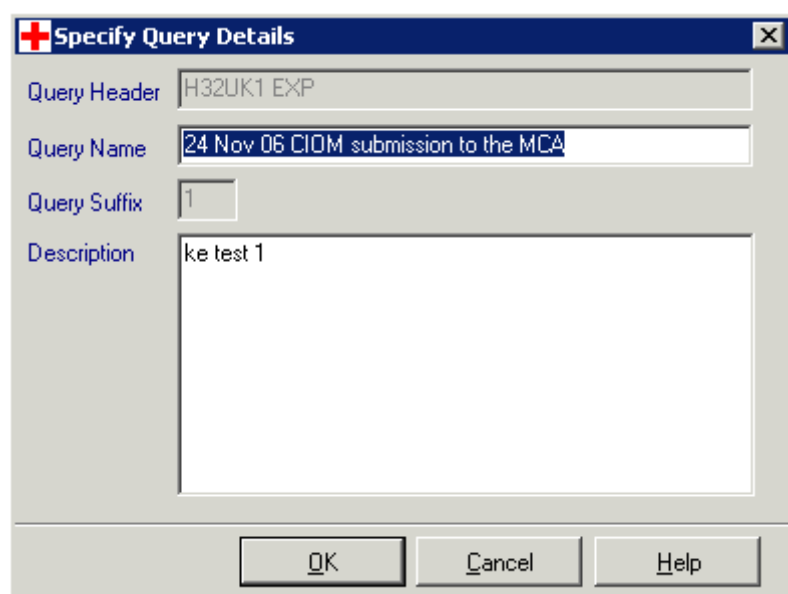
a) Case Selection – allows the user to review and refine the list of cases filtered from the database. This screen is always displayed first.

b) Display – allows the user to define the output formats required. This screen is described in section 11.4

The user may review any case that has been selected by the query. After such a review, the user may set the case status to 'on hold' such that the case is not reported event though it fits all other reporting criteria. When a case is held, the user takes responsibility for managing its further processing, e.g. discussing the case with the case owner. Alternatively, a case can be placed 'on hold' without a review of its data. The user may also clear the 'on hold' status of a case, thus releasing it for submission.

Whenever a query is run, PV-Works will find all cases that satisfy the query criteria including those that are currently 'on hold'. These will be displayed in the results window so that they cannot be 'forgotten' and will be highlighted in red text.

By default, all cases 'on hold' will not be marked for reporting. The user may save the query definition for later use / re-use. A popup window (**Figure**11.3.2) will appear and the user will be prompted to enter a name and a full description for the query.

Figure 11.3.2: Save Query Definition for Regulatory Submission

Since a customer may build up a large library of queries over time, it is possible to place an age limit on each query. While all queries will continue to be retained in the database, the list displayed for selection for future runs will only display the names of queries that are less than 'x' days old. This value is controlled by the System Administrator.

The use of the creation date rather than the submission date as the basis for determining the age of a query means that any submission run that is created but never submitted will also disappear from the list after 'x' days. Saved queries will be visible in the Predefined Query section on the Regulatory Submission screen.

When saving the query, the currently selected Agency, Report, Cover Letter, PDF Path and Printer field values will be saved along with the query filters. When the saved query is subsequently selected, the values of the abovementioned fields will be restored to their saved values.

Queries saved by users will save the actual filter field values. When subsequently 'replayed', the filter values will be restored and the user will have the ability to modify the filter values. Note that users can only see queries saved by users in the same location.

Also note that queries cannot be modified and overwritten. Predefined query maintenance is an administration function.

Via buttons on this screen, the user may:

- mark all cases for printing without review by clicking the 'Mark all' button. Note that this excludes those cases that are being held.

  By default the user may not select cases that are "unapproved" (see section10.3). However, it is possible to include unapproved reports for draft runs only, by checking the

   box. Note that this forces the run to a "draft" - see section 11.4.

- Unmark cases that are already marked for inclusion

- Review cases individually by clicking the 'Browse' button. This will lead to the standard update screens.

- Update cases individually by clicking the 'Update' button. This will lead to the standard update screens.

- Save the user query that generated the matching cases. The query is saved as a 'personal query' for this user only and may be replayed (and edited) only by its author. (To make the query available to all users it should be converted to a pre-defined query by the System Administrator).

- Print the reports requested in Figure 11.3.1.

10.4 Single Case Display Options and Outputs

The second tab on the Matching Cases screen (Figure11.4) is labelled 'Display'. The defaulted values of the Display screen may be specified via system options and for many runs will be acceptable to the user.

Figure 11.4: Matching Cases - Display Options
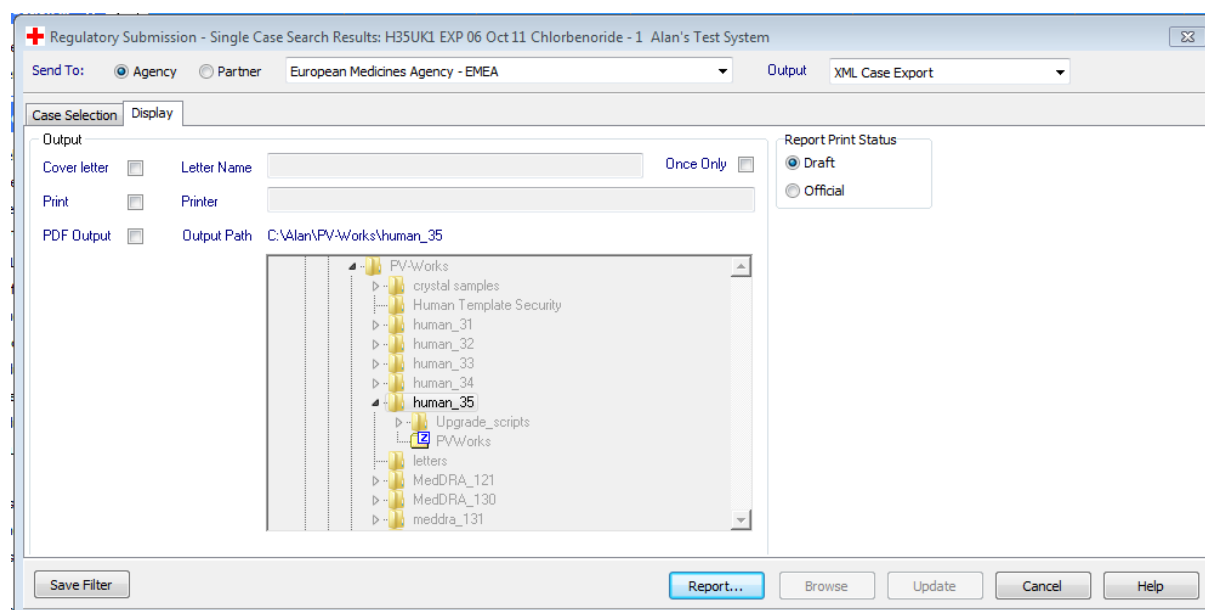
The user may define the report as an "official" or "draft" by checking the status radio group. The differences between these are:

Official report	Draft report
Only reports approved cases	Can include unapproved cases
	Includes the text "DRAFT" in the query identifier
	The pop up screen in Figuredoes not display for a draft report
When the run executes a record is made in the database of the run parameters and the cases included to permit a re-run.	No record of the cases is made in the database of the draft run

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The user may specify the type of output required and may include:

- A Cover letter using a pre-defined letter template (see section 13 for a description of letter writing). If 'once only' is checked, the letter is generated once for the run. Otherwise (and by default) a separate letter is generated for each NDA/MA number in the run.

- Report generation directly to the printer. The user may select the printer.

- Report generation to a pdf file. The user may specify the output directory which must be one to which the user has been granted write access and file create permissions. The file will be named by PV-Works (vet) as:

   User name

   'EXP'

   Date of run as dd mmm yy

   Report type e.g. XML, CIOMS

   Submission to <recipient>

   Run number – to make each run in a day unique

E.g. V40_US1 EXP 27 Jul 04 Submission to EMEA - 1.pdf.

Page alignment of the PDF file will be corrected with the addition of blank pages to allow duplex printing of the file such that each case starts on a 'front page'.

If an error is encountered during a report run, the PDF will not be generated, but the Internal Summary Sheet will be printed and will show the nature of the error encountered.

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In a single run it is not possible to print to both printer and pdf file.

The output comprises:

1. A letter (optional)

2. A list/index of all cases suitable for sending to the agency.

3. All cases with the same market authorisation or NDA number. These are printed in the following sort order:

    - Causality ABO as a single group

    - Causality N (or blank)

    Within these two causality blocks, cases are presented in ascending case number order.

4. A list/index of all cases. This is always printed to the default printer if the pdf file is generated as well as being included in the pdf file as a precaution against print failure.

Before the output may be generated, the appropriate single case report setup form for the selected report will be shown at the start of the reporting sequence. The values from the setup form will be reused for each report in the run.

For purposes of report generation:

- Each report's Send Status will be set to the appropriate value of Initial / Follow-up for each case. The 'Status' section of the report setup form will therefore be disabled and no status needs to be selected.

- Print Status will be disabled and defaulted to 'Official'.

- Receiving Authority will be the authority selected on the Results form, and will be read-only.

- The 'Send Report to Authority On' field will, if it exists on the setup form, be enabled or disabled according to the existing functionality.

- Report Type will be determined from the value set on the assessment screen for each case/authority. A case without this information would have failed the validation check and caused

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the run to terminate.

- Follow-up date will be set as is appropriate for each case. The 'Follow-Up Date' section of the report setup form will therefore be disabled and no date will be shown.

- The signature selection box will become enabled and will be defaulted to Report Approver.

- The display tab will be available and Event Descriptions will display in the default manner.

- The 'Preview' button will not be enabled.

If the user clicks on 'Cancel', the entire report sequence will terminate. If the user clicks on 'Print', the first report run will start.

Validation

Report-specific validation will be applied against all cases to be included in the report run. All cases that fail the validation will be noted in the internal summary sheet. If any case fails the validation process, no PDF will be generated and the report run will terminate with only the internal summary sheet being printed.

The user will be given visual feedback on the progress of the validation process. If all cases pass the validation process, the next step will be initiated.

As the selected output is generated a progress bar indicates completion.

Expedited Submission Progress Bar
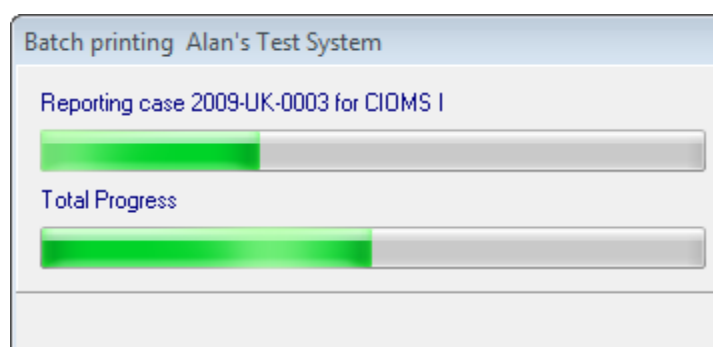
The system will progress through a series of steps:

- Validating case data
- Reporting case
- Creating pdf file (assuming option selected)
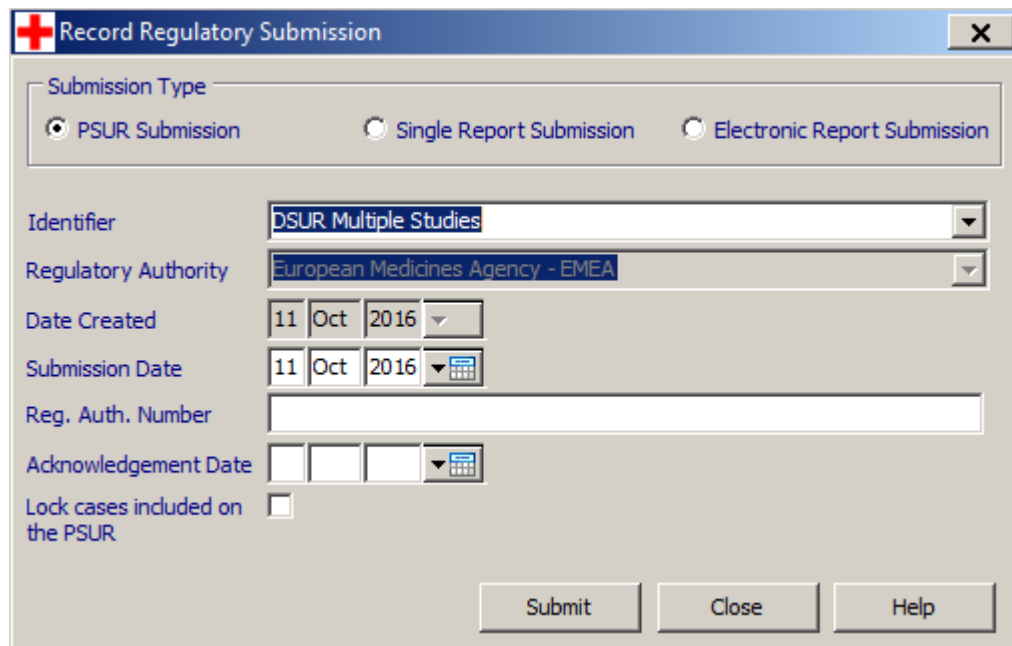
This will be repeated for each MA/NDA number.

10.5 Recording the submission of reports

The Record Regulatory Submission screen allows the user to record the submission of cases generated via this function to a regulatory authority (whether paper-based or electronic). This applies equally to single case reports and to PSURs. As a result, this fact of submission is recorded in the record of the data of each included case. It also, optionally, allows the user to lock all of the cases included in the PSUR.

Note also that the function also allows users to record the submission of electronic reports (see section 12). The screen also allows the user to record the submission of a PSUR. This marks the PSUR definition as "submitted" such that this fact becomes visible on the Regulatory Reports screen of the included cases. The Record Regulatory submission screen is shown below.

Record Regulatory Submission Screen.

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Depending upon the selection made in the radio group, PV-Works will retrieve a list of PSURs or single case runs generated as 'official' versions. The user will enter the date of submission for the reports and this will be applied to all of the cases contained therein.

Lock all cases included on the PSUR:

- This check box allows the user to specify whether all cases included within the PSUR should be automatically locked by PV-Works when recording the submission date.

10.6 Advanced Report Submission

The 'standard' Expedited Report Submission function is based upon pre-defined queries. Where the user requires further flexibility, they may build a query by specifying certain criteria (Figure 11.6) is displayed.

Note that by separating the advanced function from the standard function it is possible for the System Administrator to determine which user may run it. This could be a subset of the users who have access to the standard function described above.

Figure 11.6: Regulatory Reports screen for user query definition

There will be a number of filter criteria that can be applied to the case. These include:

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- Problem type – e.g. to find all lack of efficacy cases to review.

- Date range – type of date and range. Date type will be 'last time mandatory field changed', 'last audit change', 'received date', 'follow up received date', 'report approval'

- Product definition – Multiple products may be selected either by generic, brand, product family or market authorisation reference number (NADA in USA). The product selected may be further restricted by formulation.

- Report approval – i.e. has the case been approved or not. The user may select whether the approval has occurred since the last submission as a method of detecting follow up reports. Options are:

    Never approved

    Has been approved

    Approved since last submission

    Not approved since last submission

    Not approved since mandatory field change

    Approved, but never submitted

- Submitted – ie has the case been submitted to the target regulatory authority or not. This option may be used separately from Report Approval or in conjunction with it. Both combinations are valid depending whether the user is trying to find cases to report or looking for cases that should be reported and may be stalled in the business process. Options are:

    Never submitted

    Not submitted since follow up info received

    Not submitted since approval

- Receiving Authority – The regulatory authority that receives the cases must be defined. Apart from allowing PV-Works to print the correct address, this is essential for the searches related to submission.

- Seriousness

- Country of occurrence – to select local or foreign cases, e.g. 'from USA', 'not from USA' based upon where the adverse experience occurred

- Market country – to select local or foreign cases, e.g. 'from USA', 'not from USA' based upon the country where the product is registered.

As a rule of thumb, any field or field-set that is blank, means that the field is not part of the filter. For example, if no products are selected, it means that products are not to be part of the filter query and so ALL products will be selected. It does not mean that only cases with no products are to be selected.

For fields where qualifiers are associated, such as 'Include / Exclude', actual field values must be entered for qualifiers to be included in the query. E.g. It makes no sense to 'Exclude' certain case types when no case type has been selected. In this instance, Case Type will not be a filter criterion for the selection query.

Submission-related criteria will be interpreted in the context of the agency selected, and the product selected, if reports to the selected agency are made on a per-product basis.

As described in section 11.3 the user will define the type of report required – single case versus PSUR – and will display a set of matching cases as shown in 11.3.1. Processing of cases into reports follows the same steps as those described in section 11.4.

Users may save query definitions entered in this manner using the 'save filter' button on **Figure**. User-defined queries are private and may only be re-played by the user who created them. To select a personal query click the 'my queries' radio button and select it from the drop down list. Note that when a personal query is re-displayed all of the filter criteria are available on this screen such that the query may be amended.

The expected outcome of an expedited reporting run depends upon:

a) the target products for the run, i.e. the products defined on the selection screen
b) the report type for the receiving agency, i.e. 'by product' or 'by case'.

Assuming that a run expects output for more than one mah number, then the expected output is:

a) for a 'by product' agency*, one file / printed block per mah number containing every case that includes the target mah number of the block. As a result a single case can be included in more than one block. Note that a case involving two similar products with the same mah number (e.g. different strengths of the same product will only be included once).

b) for a 'by case' agency, one file / printed block per run containing a single example of every case to be reported.

* Note that the current policy of all regulatory authorities is 'by case', ie a case is reported once to the agency as a report for all product licences that are involved in the case. This functionality is required in veterinary pharmacovigilance and is left in this version of PV-Works for potential needs.

For example a run based on the MAH numbers 123 and 124 for the following cases:

Case #	Product 1 MAH #	Product 2 MAH #	Product 3 MAH #	Product 4 MAH #
1	123	-	-	-
2	124	-	-	-
3	456	789	345	-
4	456	123	155	765
5	456	123	124	322
6	124	123	-	-
7	222	124	121	123

Will generate the following report blocks:

a) by product reporting:

    Block 1:   MAH 123:   Cases: 1,4,5,6,7
    Block 2:   MAH 124:   Cases: 2,5,6,7

b) by case reporting:

    Block 1:   Cases: 1,2,4,5,6,7
    These cases will be sorted into MAH number order, i.e. 1,4,5,6,7,2

10.7 Regulatory Report Submission: Undo a Submission

If a user has marked a 'package' of cases as 'submitted', then it may occasionally be necessary to 'undo' a set of reports so marked. This is available from the Main Menu | Reports menu and will display the screen in Figure 11.7.

Note that if an individual (paper) report is 'pulled' from a submission, its record of submission should be deleted individually from the Regulatory Reports screen shown in **Figure**. However, the record itself remains on this screen in an "unsubmitted" state.

Note also that the function also allows users to "undo" the submission of electronic reports (see section12). This marks the case as unsubmitted in the Regulatory Reports screen shown in **Figure**

The screen also allows the user to undo a PSUR submission where this has been marked in error as "submitted" using the function described in section 11.5. This effectively resets the status of the PSUR itself and the individual cases it contains.

Figure 11.7: Undo a regulatory submission

The user will define the Regulatory Authority to whom the submission was made and the date of submission or creation. This date can be defined as a range. The system will display the matching submissions in the grid. After selecting the correct identifier, the user may click 'Undo' to undo the submission record. Before processing the user is asked to confirm this step.

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10.8 Regulatory Report Submission: Delete a Submission

Occasionally a user may create an official PSUR or expedited report run in error and wishes to delete it from the various display screens and drop down lists described in this chapter.

If the run's definition has not been used for a submitted report the user is referred to the function described in section 11.10. If the run's definition has been submitted then individual identifier / recipient records may be deleted if necessary.

To do this run the "Delete Regulatory Submission" option from the Main Menu | Reports menu. This will display the screen shown below.

Delete a regulatory submission

A "submission" does not need to be marked as "submitted" before it is deleted. Therefore it is possible to use this function to delete draft or test runs from these functions. After selecting the correct identifier, the user may click 'Delete' to delete the definition of this PSUR / expedited report run and any associated submission records. Before processing the user is asked to confirm this step.

10.9 Periodic Safety Update Report (PSUR) / Development Safety Update Report (DSUR)

The Periodic Safety Update Report (PSUR) provides a common format for the submission of periodic reports to multiple regulatory authorities. The report follows the definition laid out in the ICH E2C and Volume 9a documents.

The DSUR report (Development Safety Update Report) is intended as an annual / periodic reports concerning drugs under development, i.e. in clinical trials. In many regards it is similar to the PSUR as its name suggests. The DSUR can be used instead of the US IND reports and the EU annual safety report. The report follows the definition laid out in the ICH E2F document.

PV-Works PSUR functionality will produce Section 6 of the report, 'Presentation of individual case histories'. This is made up of a line listing of individual cases.

There are three PSUR formats available for selection:

    a) Standard ICH E2C / Volume 9a format
    b) EU Clinical Trial format
    c) Alternative ICH E2C format with improved display of narrative comments

There is a single DSUR format.

A record is made in each case when it has been submitted to an agency as part of a PSUR / DSUR.

Cases are included in the PSUR for 'similar' products (as defined below) and
- received by the company within the defined date range
- Or those where follow-up has been received within the defined date range

Cases selected due to follow up are NOT automatically marked for inclusion in the report. These cases need to be considered and marked for inclusion manually.

Cases for DSUR reports will typically be selected by study name or generic for a given time period. Cases to be included can be blinded and these should not be unblinded for the purpose of their inclusion in this report.

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10.9.1   Defining a PSUR / DSUR Report

When the PSUR / DSUR report is selected from the 'Select Reports' screen, the following screen will be displayed:

PSUR / DSUR Definition: Case Selection

While there are many options that can be used to filter cases in the database for the PSUR, only a few are required:
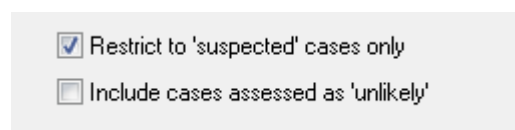
- A unique identifier (given name) for the PSUR / DSUR so that it can be recognised in the future (e.g. to re-run, to generate further reports).

  Note that in time identifiers will be created that are no longer required. These may be deleted – see section 11.10.

- The regulatory authority to whom the PSUR / DSUR will be sent
- A label list (used to assess expectedness, i.e. the label that is appropriate to the selected regulatory authority)
- A product or products that must be included in the selected cases … or the study from which cases should be selected
- A date range for the date the case was received
- The criteria (or some of them) to indicate the case source, seriousness and expectedness that will be included
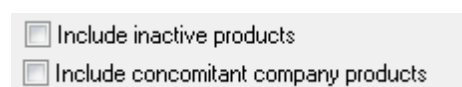
If the user selects a study then the product selection fields are greyed out and the product definition is taken from the Clinical Trial Dictionary. If the study involves more than one product, the user may further filter the cases returned by removing any of the defined study products, e.g. placebo.

It is also possible to restrict clinical cases to "suspected" reactions (ie causality = 'probable' or 'possible') and "suspected plus unlikely" reactions by checking the following boxes:

It is also possible to control product selection to determine whether inactive products should be included – by default these are excluded. Similarly it is possible to determine whether or not to include cases involving the target product but where its role is marked as "concomitant" – by default these are excluded. These two options are controlled via check boxes in the "Select Products" panel:

10.9.2   Same and Similar Products

The method used by PV-Works to select 'similar' products from other countries ideally relies upon a fully populated product dictionary so that matches based upon generic name, formulation and strength can be performed on a global basis. Where the dictionary is deficient inappropriate products may be selected. In addition, local variations on individual customer sites make it inevitable that a single algorithm for determining same / similar products will always be fallible in certain circumstances. PV-

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Works overcomes these problems with a 'selected product review' screen that allows the user to fine-tune the product list.

The selection of global products depends upon the method by which the product was defined in the 'Selected products' box (see below).

- Selection via one or more product families – Returns the products defined in the product family only
- Selection via generic name, brand name or MAH number – Returns equivalent products globally, based upon the following algorithm:

Firstly, all products deemed to have the same licence number (MAH reference number) and same country of market as those chosen for inclusion in the report are considered to be 'the same'.

Note, when matching products, records which contain a null data value (i.e. missing MAH #) are not returned. This helps to avoid problems with incomplete dictionaries.

Subsequently, for each product in the license number set above, an attempt is made to find other equivalent products. PV-Works queries the dictionary to identify all products that have the same generic, formulation and strength.

Note, when matching on generic name, product records which contain a null data value should not be returned. Null values in the FORMULN and STR_TEXT fields will be honoured, such that a record with a blank formulation (or strength) will match to other products with a blank formulation – providing of course that the generic and strength data also match.

The user may review selected products before PV-Works searches the database for matching cases (a check box on the create PSUR / DSUR submission screen controls whether this product review screen is displayed).

☐ Review selected products before processing

The PSUR / DSUR product match screen (see Figure 11.9.2) offers two grids:

- The upper grid shows all products selected according to the PSUR same / similar products algorithm
- The lower grid contains all other products in the company product dictionary.

There are two editing options available:

- Delete a product record from the PSUR / DSUR definition. This is achieved by highlighting a product in the upper 'selected products' section and clicking the 'Remove Product' button

- Add a product record. This is achieved by highlighting a product in the lower 'unselected products' section and clicking the 'Add a product' button.

Note that the grid supports the standard shift-click and ctrl-click Windows functions to allow multiple product selection.

Figure 11.9.2 : PSUR / DSUR Matching Products Screen

Both grids support comprehensive grouping and sorting functionality that allow the user to re-sequence the information displayed and in this regard the two grids act independently. This includes:

- Sorting on any column by clicking on the column header label – sorts can be ascending or descending

- Grouping data by dragging the column header label into the navy blue area. Multiple header labels can be dragged into this area to create a multi-level hierarchy. The hierarchy can be expanded and collapsed so that products of interest are found quickly

- Filtering the presented contents by clicking on the drop down symbol on each column header – note that this is similar behaviour to Microsoft Excel's data filter.

Using these techniques in combination allows a user to review and find products with ease.

The 'Save Family' button allows the user to save the set of selected products in the upper grid to create a new product family. This family can be used for subsequent PSUR / DSUR runs or for any other reporting purpose. During definition of the PSUR / DSUR, a user has access to all product families regardless of who created them.

Users may delete or overwrite product family definitions made in this manner. Warning – a user can delete a product family created by a different user (but only after a suitable warning message is given). Product families created by the System Administrator cannot be deleted via this screen.

10.9.3   PSUR and DSUR reports – Matching cases

When the query is run the results are shown in the 'Show matches' screen shown below

Report Submission - matching cases : PSUR / DSUR

The purpose of this screen is to allow the user to review and refine the list of cases filtered from the database by removing some of them from the included list. The user may review any case that has been selected by the query by clicking the 'Browse' button. The cases in the grid are displayed in various colours that indicate their status in the selection:

Colour / shading	Status
Bold black text	Approved cases.
Black text	Unapproved cases, ie cases that will be included in the PSUR but as in a quality process ought to be in an approved state.
Shaded grey	Cases that have not been assessed

Via buttons on this screen, the user may:

- mark all cases for printing without review by clicking the 'Mark all' button. Note that this excludes those cases that are being held.

- Unmark cases that are already marked for inclusion

- Review cases individually by clicking the 'Browse' button. This will lead to the standard update screens.

10.9.4   Display Options and Outputs

The PSUR / DSUR Display screen below is displayed when the user clicks 'OK' on the Matching Cases screen and allows the user to specify the Sort order for the PSUR / DSUR and to set other print layout criteria.

PSUR / DSUR Display Screen

Display Options tab: Sort Criteria

This panel allows the user to specify up to five levels of sort order on the PSUR / DSUR.

On entry to the screen, the left hand text box will contain the candidate sorting criteria, and the right hand box the selected sorting criteria. The sorting criteria will be applied in descending order based on the order of the items displayed in the right hand box. The user can transfer the values between boxes using the two buttons between the boxes, and can re-order the values in the right hand box using the buttons on the right hand side.

The list of sorting criteria, which will be configurable in the Administrator's module, will contain the following values as standard:

The following list of sorting criteria is available:

- Brand name   Product brand name

- Case type   User defined case type

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- Causality   Case causality

- Clinical trial   Cases will be grouped by study identifier

- Country   Country of occurrence of the case. Sorted by ascending country as defined by its ISO code, eg Germany (DE) will appear before France (FR)

- Domestic versus Foreign cases   local cases will be reported first. All foreign cases will be reported as a single block, ie not further sorted by country.

- Expectedness   Case expected / labelled.

  This is determined from a hierarchy:

    - Use the assessment given for the country to which the PSUR is being submitted;
    - Else if not found and country to which the PSUR is being submitted is in the EU, use the EU assessment
    - Else if not found and spontaneous use CORE
    - Else if not found and clinical trial use INV
    - Else set to 'unassessed'

- MedDRA preferred term

- MedDRA system organ class

- Problem type   Cases will be grouped according to the problem type.

- Seriousness   Case serious

- Source category

Will group case source into four or five groups: – medically substantiated spontaneous (vet), non-medically substantiated spontaneous (owner, farmer), market support programs (ie solicited), studies and regulatory authorities.

The default sort order is defined by five system options:

PSUR_SORT1 … PSUR_SORT5.

These options hold the value of the sort option from the codelist PSURSORT. For example to sort cases by seriousness and within seriousness by country, set:

PSUR_SORT1 = 'SERIOUS'

PSUR_SORT2 = 'COUNTRY'

PSUR_SORT3 = null

PSUR_SORT4 = null

PSUR_SORT5 = null

At each break point in the sort sequence a new page will be started and a complete heading will be inserted describing the selected sort/break levels:

Sort option	Heading text
Brand	"<<Brand>>"
Case type	<<codelist description>>, e.g. 'Human reactions'
Causality	"Causality assessment <<causality – decoded>>"
Clinical Trial	'Study: XXXX'
Country	"Cases occurring in <<country description>>", e.g. "Cases occurring in France"
Domestic / foreign	Local: 'Cases occurring in XXXX' Foreign: 'Cases occurring in the rest of the world'
Expectedness	Expected cases Unexpected cases

MedDRA preferred term	"decoded preferred term" name
MedDRA System Organ Class	"decoded system organ class name"
Problem type	"<<Problem type – decoded>>"
Serious / Non-serious	Serious cases Non-serious cases Note that if both seriousness and expectedness are used as sort criteria, then the heading should be combined, eg 'Serious, unexpected cases'
Source category	Medically substantiated cases Non-medically substantiated cases

Display Options tab : Output

The user will select:

- The PSUR / DSUR required e.g. ICH E2C or EU Clinical Trial format or DSUR
- Whether the listing is a draft or official report
- Whether the PSUR / DSUR data should be exported to a comma-separated value file and the location and name of this file.
- Additional reports that should be generated, e.g. CIOMS or 3500.

Display Options tab : Appearance of 'previously acknowledged' cases

For each of the case 'types' (considered individually below) the user can specify the appearance of relevant cases within the line-listing. If the user wishes to include cases of a particular type an optional indicator can be selected from a user-defined codelist of key characters – the chosen indicator will be represented on the line-listing, next to the case number, to identify the particular cases. Alternatively the case may appear unmarked in the line-listing and no attempt will be made to distinguish it from other cases. Finally the user can elect to exclude all cases of a certain type altogether.

As with other options on the Display sub-screen the default values for these selection boxes can be configured via the Admin program. An existing system option (PSUR_FIXED) can be used to 'lock' these default options to prevent users producing reports that may contradict with company reporting policy.

The number of cases to be omitted from the line-listing report by selecting the 'exclude' option is demonstrated on the selection tab of the PSUR setup screen. The number to be excluded will be indicated alongside the 'Matches Found'. In addition, the relevant cases that will be omitted are greyed out (text displayed in light grey) in the grid listing.

There are four 'PSUR / DSUR Case Sets' that can be used as filters for inclusion or can be indicated with a symbol in the line listing. These are:

- Cases included on previous summary report (for defined product)
- Cases included on previous summary report (for other product)
- Cases reported individually to this authority
- Cases previously sent to Regulatory Authority by reporter

PSUR / DSUR Case 'Set':

Cases included on previous summary report (for defined product)

A case may have been included on a previous PSU line-listing report produced for the same product to the regulatory authority in question. This may occur if a second PSUR / DSUR is required with an overlapping time period.

As an example, a 6 month line-listing report is produced for ProductA and a particular case is included. Some time later a 5 year renewal PSUR may be produced for ProductA. Since these time periods overlap the case in question will once again be included in the report.

In the example given above, it seems logical to include the case in the subsequent renewal line-listing, but it may be reasonable to use a suitable indicator so that attention can be drawn to the fact the receiving authority has previously been notified of this case. No attempt is currently made to identify the previous line-listing in which the case was included.

Cases included on previous summary report (for other product)

A case may have been included on a previous PSU line-listing report submitted to the Regulatory Authority in question, for an additional product associated with the case. This may occur when considering cases that involve multiple products.

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As an example, a certain case may involve two suspect company products, ProductA and ProductB. The case will be included in a line-listing report prepared for ProductA. Some time later it may be necessary to produce a line-listing for a ProductB renewal.

In the example above, company policy may be to include the case in one or both of the line-listing reports. If cases are to be included in subsequent reports it may be appropriate to identify those cases that have already been notified to the regulatory authority in question within previous line-listings for other relevant products.

Cases reported individually to this authority

A case may have been previously expedited to the regulatory authority in question (for example, in order to comply with regulations associated with the reporting of serious cases).

It is likely that a line-listing report would also include cases that have been previously submitted to the regulatory authority. However, it may be desirable to mark these cases accordingly in order to draw attention to the fact that case has been submitted previously, albeit as an individual report.

Cases previously sent to Regulatory Authority by reporter

Some cases are notified directly to the Regulatory Authority by the case reporter. It is common practice for the Authority to then forward details of such a case to the Marketing Authorisation Holder. These cases are identified in PV-Works by setting the source of the report as the Regulatory Authority.

Also, on occasion, a case reporter will send case notification to both the Marketing Authorisation Holder and directly to the Regulatory Authority. A field on the Case ID screen is used to identify that the reporter has also submitted the report to the domestic health authority.

In either of the above situations the Regulatory Authority is already 'aware' of the case before the submission of the case within an appropriate line-listing. Therefore, it may be appropriate to exclude cases where the source of the case is the Regulatory Authority. Alternatively, and as with other case sets, the cases might be included and marked with a suitable indicator as required.

(The specific Regulatory Authority is not recorded in association with the source data. The assumption will be made that if the Regulatory Authority to which the line-listing is to be

submitted is in the same country as the country of occurrence defined in the case, then this will be the same agency defined as the source of the case).

With respect to the other case sets discussed previously, the Marketing Authority Holder has previously notified the Regulatory Authority of the case in question and has consequently made the agency aware of the company case reference number. In contrast, where the case has been received via the Regulatory Authority (or indeed the agency has been made aware of the case by the reporter directly) the agency may not have a company reference number by which they can identify the case when it is subsequently included on a line-listing report. To counter this situation, in the event that a user chooses to mark cases that have been received via the authority, the intention is to append the Regulatory Authority reference number (where available), quoted by the agency (usually in their correspondence to the Marketing Authorisation Holder regarding the case report), in brackets after the case number. This additional reference may be entered on the Case ID screen as an external reference – a fixed codelist element will be reserved for this type of reference.

Appearance of Indicators on Report:

Where a case had been notified to the Regulatory Authority on a number of previous occasions (for example, as an individual serious case report and in a previous PSU line-listing produced for an earlier overlapping time period) each of the relevant indicators would be placed next to the case number on the report shown below

PSU line-listing report

Non-serious cases

2006-U S-0065	U S A	--U N KN OW N--
2006-U S-0123	U S A	43 (F)

Serious cases

2006-U S-0008 / @	U S A	6 (F)
		d
2006-U S-0031	U S A	31 (M)
		t
2006-U S-0039	U S A	49 (M)
2006-U S-0079 / @	U S A	25 (M)

Please note that it will be possible for a single indicator to be used for multiples of the case types above. Consequently, a broader approach may be to assign a particular indicator to identify all those cases of which the Regulatory Authority in question has been previously made away, irrespective of the means in which they were notified. In this situation each unique indicator will only be represented once on the line-listing report even if the case 'qualifies' on multiple counts.

PSUR Line Listing Alternative Format

An alternative format PSUR will be introduced in an attempt to obtain a more 'output friendly' variation of the report defined in the regulations. The new version of the PSUR will move the 'Comments' field so it is printed beneath the item data items for each case rather than at the right hand side of the 'line'. The Comments field can then be printed in an area of greater width to increase its readability. The new version of the PSUR will be available from the PSUR type drop down list on this PSUR display screen.

Print Options tab : Other print options

The user may define:

- Format of the 'unknown' text string to be used for missing data
- Page numbers for the report
- The format of the case identifier number. Up to three case numbers may be printed:
    The PV-Works case number – mandatory

    One of the additional 'external' case numbers

    An agency reference numbers

- The format of the event / clinical signs column. If specified, the level of the MedDRA term to be printed may also be specified.
- Whether the list of products displayed in the report header should be a global list or just those marketed in the country of the regulatory authority to whom the report will be sent.

Display Symbols

As determined by the functional specification, 3 options are given for the display of the above case types.

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'Exclude'

With this option selected the cases meeting the criteria will be omitted from the line-listing report. The number of cases to be omitted should be made clear on the PSUR / DSUR setup screen, next to the 'Count' the number of excluded cases to be shown in brackets. In addition the specific cases should be greyed out in the grid (text displayed in light grey).

'Unmarked'

Cases are to be included in the line-listing as normal, with no additional detail shown on the selection tab of the PSUR setup screen.

'Marked with'

Where this option is selected, cases meeting the required criteria are indicated on the line-listing report with the appropriate symbol. A symbol is assigned to each case type from the codelist PSUR_SYM. It may be appropriate to fix the elements of this new codelist depending on the implications of printing different symbols – 6 suitable options should be sufficient? Care needs to be taken with the selection of symbols and their support with different fonts and different printers.

The symbol should be printed on the line-listing report as a superscript immediately after the case number as currently shown. (Please note that where the user has chosen to also display a cross-reference number any applicable symbols will appear before these data).

With regard to the option to mark '*Cases received via the Regulatory Authority (in the country of this agency)*' the Regulatory Authority reference is to be appended, in brackets, to the case references already displayed.

Population of the Product List in the PSUR / DSUR Header:

When the PSUR / DSUR line listing is generated the header block lists the products to which the report relates. A radio button on the PSUR / DSUR display tab allows the user to control the display of product names in the report header field labelled as 'Products displayed.'

With the radio button set to 'All' the header will display the name and marketing authorisation reference of all products selected for the report regardless of the country in which they are licensed. If the 'Local to agency' option is selected the report header will display only products marketed in the country of the agency to which the report will be sent.

The default value of the radio button is controlled by a system option.

Please note that in both situations the report header will show a product record even if no cases have been returned on account of that specific product.

Processing rules:

1. Processing of Follow-up Cases with Initial Receipt Date outside the defined period

   Cases with an Initial Receipt Date outside of the defined date range will be included in the list of cases presented in this screen if Follow-up is received within that date range, or if the case has not been submitted in a previous PSUR. However, these 'outlying' cases will NOT automatically be marked for inclusion in the report (i.e. the Mark field will be blank) and the case information will be displayed in a prominent colour (i.e. red). These cases need to be reviewed by the user and marked for inclusion manually.

   All other cases (i.e. those with an initial receipt date within the defined date range) will be marked for inclusion automatically.

   A case will only be added once to a PSUR report, i.e. if the case was received as an initial report in the selected time window and follow-up reports were also received in the same time window, then only one instance of the case will occur in the report. Since the case was received as an initial report in the selected time window (as well as follow up), then it will be marked for inclusion by default.

2. Processing of PSURs Only Previously Executed in Draft Mode

   If the PSUR / DSUR has not yet been executed, or has previously only been executed in draft mode the cases listed on this screen are retrieved by searching the database using the criteria defined. Also, in these situations the user may change the set of cases to be included in the report – using the 'Add Cases' and 'Unmark' functions. This may result in a different set of cases to be reported.

If the PSUR / DSUR being executed currently is official, and a draft version exists, then an appropriate warning message will be displayed if the set of cases has changed since the draft report was executed.

If the PSUR / DSUR being executed currently is official, and no draft version exists then it may be executed using exactly the set of cases derived by the search criteria specified. Alternatively that set of cases may be changed: cases may be removed from or added to the list by the user.

3. Processing of PSURs / DSURs Previously Executed in Official mode
If the PSUR / DSUR has previously been executed in official mode then the cases linked to that official report will be loaded into this screen without the need to re-search the database using the criteria defined. In this case, the set of cases may not be amended, so that the previous set is re-played in its original form.

The Mark field will be checked but greyed out for cases belonging to a previously executed official report. If a previous set of cases is re-used and a target case has been deleted since the original run (an unlikely occurrence), then the system will give the user a warning but will be able to continue with the process.

10.9.5 Managing the submission of a PSUR & DSUR

There are three functions to manage the PSUR / DSUR once it has been generated. These are

a) Mark the PSUR / DSUR as "submitted" to its intended recipient. See section 11.5 for further details.

b) Undo the "submitted" status of a PSUR / DSUR so that it does not indicate that it was submitted. See section 11.7 for further details.

c) Delete the definition (and submission status) of a PSUR/ DSUR that is no longer required. Typically this will be used for draft or test runs. See section 11.8 for further details.

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10.9.6   Data Update Container: Case regulatory reports screen

For completeness, the regulatory reports screen will have a scrolling read only block showing the PSURs / DSURs in which the case has been included. This can be displayed in the empty bottom right section of the screen. The grid will show the PSUR / DSUR identification, date submitted to authority, submitted to. This means that the same PSUR / DSUR may appear multiple times if it has been submitted to multiple authorities. If the case is included in a PSUR / DSUR that has not yet been submitted, only the PSUR / DSUR identification will be displayed.

Regulatory Reports Screen showing PSUR / DSUR Submission

10.9.7 PSUR & DSUR Crystal Reports

Several Crystal Reports are provided with PV-Works that tabulate counts derived from the cases within a particular PSUR / DSUR. It follows that these may only be run once the PSUR / DSUR line listing has been created as described above.

These reports are

a) PSUR Crystal Summary Tabulation by EU
b) PSUR Crystal Summary Tabulation by Problem type
c) PSUR Crystal Summary Tabulation by clinical sign
d) PSUR Case Counts by Country and ABON
e) PSUR Case Counts by Country
f) PSUR Summary – counts AEs and patients/cases, displaying counts by SOC/lower level and by case type
g) ICH Periodic Benefit Risk Evaluation Report (E2C R2): Table 6 Cumulative Tabulations of Serious AE from Clinical Trials
h) ICH Periodic Benefit Risk Evaluation Report (E2C R2): Table 7 Numbers of Adverse Drug Reactions by Term from Post-Marketing Sources

In addition the DSUR line listing may generate a report of "Cumulative Summary Tabulation of Serious Adverse Events (SAEs) as described in ICH E2F.

10.9.8 PSUR & DSUR Reports from the main grid

It is possible to select cases on the results grid and present them as a PSUR / DSUR line listing.

The user should select the cases to be included using the standard windows shift-click and ctrl-click operators to refine the selection. With a selection made, right-click the mouse on the grid and select "Run PSUR with these cases".

Main Grid Results : PSUR / DSUR Interface

Note: The user is totally responsible for the selection of cases to be included in the PSUR. Only those cases selected will be included. A PSUR set up screen will be displayed as shown below.

PSUR / DSUR Set up Screen from Main Grid

While many of these fields are similar to the search screen described in section 11.9,1, the fundamental difference is that the fields here are used for naming the filter criteria or display on the line listing and not for selection of cases.

However, it is important that the products that are selected on this screen cover the products administered in the selected cases. In other words there is no cases where one of the suspect products is not listed on this screen. Failure to list all of the products will lead to a case being omitted from the final listing.

On clicking "Run", the next screen shown is the "Matching Cases" screen and the process follows the same steps as described in section 11.9.3 and subsequent sections.

10.10 Deleting unwanted PSUR and Expedited Report Identifiers

Where identifiers for PSURs and Expedited Reports are no longer required, these may be deleted. Performing this housekeeping task from time to time will reduce the size of the list presented to the user for "previous runs" and should make this list easier to handle. In order to do this run the function "Delete PSUR / Expedite Report IDs" from the Reports menu of the Main Screen. The pop up screen in Figure 11.10 is shown:

Figure 11.10: Delete PSUR / Expedited Report IDs

Using the radio button at the top of the screen the user may switch between a list of PSUR identifiers and Expedited Report Identifiers. Since the List is presented as a grid it is possible to sort and filter the list to help find particular items.

To delete an identifier the user should select its title (click on the row) and click the "Delete" button.

This is a very powerful function that will delete the definition of the identifier selected but will not delete records of its submission. The user is asked to confirm the deletion process before it is executed:

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10.11 FDA Periodic Report

The FDA (NDA) Periodic Report is a US-specific line listing that is a predecessor of the PSUR. Although the PSUR report is accepted by FDA as its replacement, some customers prefer to submit the FDA Periodic Report until the PSUR is mandated.

The method by which this report is defined and executed is similar to the PSUR – with the user selecting product, date range etc. Therefore it is proposed that similar screens are created to allow the creation, execution, and recording of submission of the FDA Periodic Report to that which exists for PSURs as described in section 11.9. The FDA Periodic Report is simply a report selection from the PSUR set up screen. The format of the FDA Periodic Report line listing will comply with the old FDA regulations regarding periodic reporting of US-licensed drugs (21 CFR 314.80).

10.11.1   Defining a FDA Periodic report

When the FDA Periodic report is selected from the 'Select Reports' screen, the following screen will be displayed:

FDA Periodic Definition: Case Selection

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The Case Selection tab will enable the user to define the selection criteria for cases in a FDA Periodic, and to assign a unique label to that FDA Periodic.

Most importantly, the user is able to define a 'FDA Periodic identifier'. This is a user-assigned name given to a FDA Periodic selection criteria set. Alternatively, from the drop down list the user may select a previously defined FDA Periodic definition for replay or may enter a new name.

Apart from re-generating a FDA Periodic, the name can also be used as a starting point for an ad hoc analysis using a query tool such as the integrated query program or any third party query software.

If the user selects a previously executed FDA Periodic that was executed in 'Official' mode from this pull-down list (or types a previously executed FDA Periodic name into the field), then all of the fields on this tab will display the previous criteria and will be disabled except for:

- Regulatory Authority
- FDA Periodic Status (Draft or Official)

This will allow previously executed FDA Periodics to be re-played for additional authorities; in official mode; or with a different set of incidence tables.

Products may be selected by NDA number or by product family.

The FDA Periodic report will share functionality with the Periodic Safety Update report (PSUR). Some options are inappropriate to a FDA Periodic Report and consequently will be greyed out at all times.

The user may optionally select only the cases that have been formally approved.

10.11.2   Exceptions Report

The exceptions report is a simple list of cases that would be included in the selected FDA Periodic report except that one inclusion parameter is missing or incorrect. These are cases that the user may choose to review before proceeding with the actual periodic report as the presence of a case in this list may indicate that the case has been incompletely or incorrectly processed.

Each case is listed in numerical order in one or more sections. The tests performed and hence the categories listed are:

- Cases not approved

Case has not been approved formally using the PV-Works report approval process. In itself this may not be a condition for exclusion but it may indicate that processing is incomplete

- Cases not assessed

Case has not been assessed. Reportability assessment is the critical assessment for the FDA Periodic report.

- Outliers

Cases that were received in an earlier period and should have been submitted in a previous periodic report. A system option will determine whether these cases will be included in the current periodic report or will be handled separately by the customer.

- Cases not valid for the report

Case meets all other criteria but is not valid due to reportability / country / waiver.

Cases are reported in three sub-sections:

- reportability e.g. 3 day
- country i.e. not USA
- waiver i.e. is a waiver product

10.11.3   Running a FDA Periodic

The 'Run FDA Periodic' button on the case selection screen, takes the user to the selected cases screen. This screen is shown below:

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This screen will be a pop-up window, automatically populated on invocation with case data for the specified FDA Periodic.

Unlike the PSUR report the user will not be able to drop (Unmark) individual cases from the selected set. However, they will be able to browse the data of a case for review.

It will also allow the user to preview and to print the report, and all attached MedWatch outputs.

Case will be highlighted:

- Bold text – if the case has been approved using the standard Report Approval function

- Red text – if the case was received before the start of the target period and is included as it has never been sent to the agency in a previous report.

10.11.4   Recording the submission of a FDA Periodic

The PSUR submission screen allows the user to record the submission of a FDA Periodic to a regulatory authority. As a result, this fact is recorded in the record of the data of each included case. It also, optionally, allows the user to lock all of the cases included in the FDA Periodic.

The screen also allows the user to reject a FDA Periodic. This effectively deletes the FDA Periodic from the system, i.e. deletes its definition and its list of included cases. This function is necessary for situations where an 'official' FDA Periodic is generated but never submitted.

The FDA Periodic submission screen is shown below

PV-Works will retrieve a list of periodic reports generated as 'official' versions.

The user will enter the date of submission for the FDA Periodic and all of the cases contained therein. The date of submission will also apply to each of the FDA 3500 reports associated with it.

Lock all cases included on the FDA Periodic:

- This check box allows the user to specify whether all cases included within the FDA Periodic should be automatically locked by PV-Works when recording the submission date.

10.11.5   The FDA Periodic Line Listing Format

The FDA Periodic Report consists of seven separate listings, thus:

1	Summary of criteria used to generate the report. Note that this page is for internal use only.
2	FDA3500 forms submitted during the specified period as15 day alerts, either as initial reports or follow-up reports

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3	Tabulation by Body System of all clinical signs for all cases submitted as 15 day alerts
4	Index of 3500 reports submitted as part of this periodic report
5	Tabulation by Body System of all clinical signs for all cases submitted as 3500 reports in this periodic report
6	NDA Line Listing of 15-day reports submitted during the specified period
7	History of actions taken since the last report (heading page only)

10.12 IND Annual Report

Four Crystal Reports are available that provide the summary listings required as part of the IND Annual Report as defined in 21 CFR 312.33. These are:

1. Tabular summary of all adverse events by body system:

2. Summary of all IND Safety reports submitted during the year

3. A list of subjects who died with cause of death

4. A list of subjects who dropped out due to an adverse experience

10.13 Printing Grids of Data

PV-Works displays data in a grid format in many parts of the application, e.g. Query results These grids allow the user to sort, filter and group data. Some of them include a print function – easily identified by the presence of a 'Print' button.

Note that the 'print grid' function is supplied via a third-party software component used to deliver the grid functionality itself. As such Assured has little or no control over the formatting capabilities that are offered.

The Print function allows the user to create a simple report of the grid data and offers some basic layout controls:

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a) from the File | Design menu option (or cog icon), the user may amend several aspects of the report layout but the only one seen to be of value is to change the report title (also available from Format | Title).

b) from the File | Page Setup menu option the user has access to a standard set of Windows print functions e.g. set paper size, margin and header / footer contents.

Figure 11.13.1: Sample Grid Print

If the user has grouped records in the grid, this grouping is honoured in the print image. This can be useful if it is only one group that needs to be printed, but as Figure 11.13.2 shows, it is also possible to print a completely collapsed grid.

Figure 11.13.2: Sample Grid Print compressed

11 Adverse Event Reporting –Electronic reporting

11.1 Introduction

The International Committee on Harmonisation (ICH) has been tasked with defining standards for the electronic submission of data to regulatory authorities. As well as defining the technical standards of transmission, it has been charged with defining data standards for safety data as the first data type for submission.

Two ICH Guidelines are applicable:

- ICH M2 Electronic Transmission of Individual Case Safety Reports ('ICSR') Message Specification; Final Version; February 2001 and subsequent revisions

- ICH E2B: Data Elements for the Transmission of Individual Case Safety Reports; July 1997 and subsequent revisions

M2 defines the format and transport mechanism, while E2B defines the contents of the message.

M2 allows transmission of the exported XML files either by CD-ROM or via an Internet gateway using secure EDI. This gateway will be bi-directional and will be capable of receiving many different types of message including documents and images, as well as safety data and other scientific information.

In addition, PV-Works has been extended to support the submission of cases related to medical device products in the eMDR format.

Furthermore, guidance documents have been issued from time to time by various agencies. As a general principle PV-Works will adhere to these in addition to the basic guidelines.

Figure 12.1: Sample E2B Export File
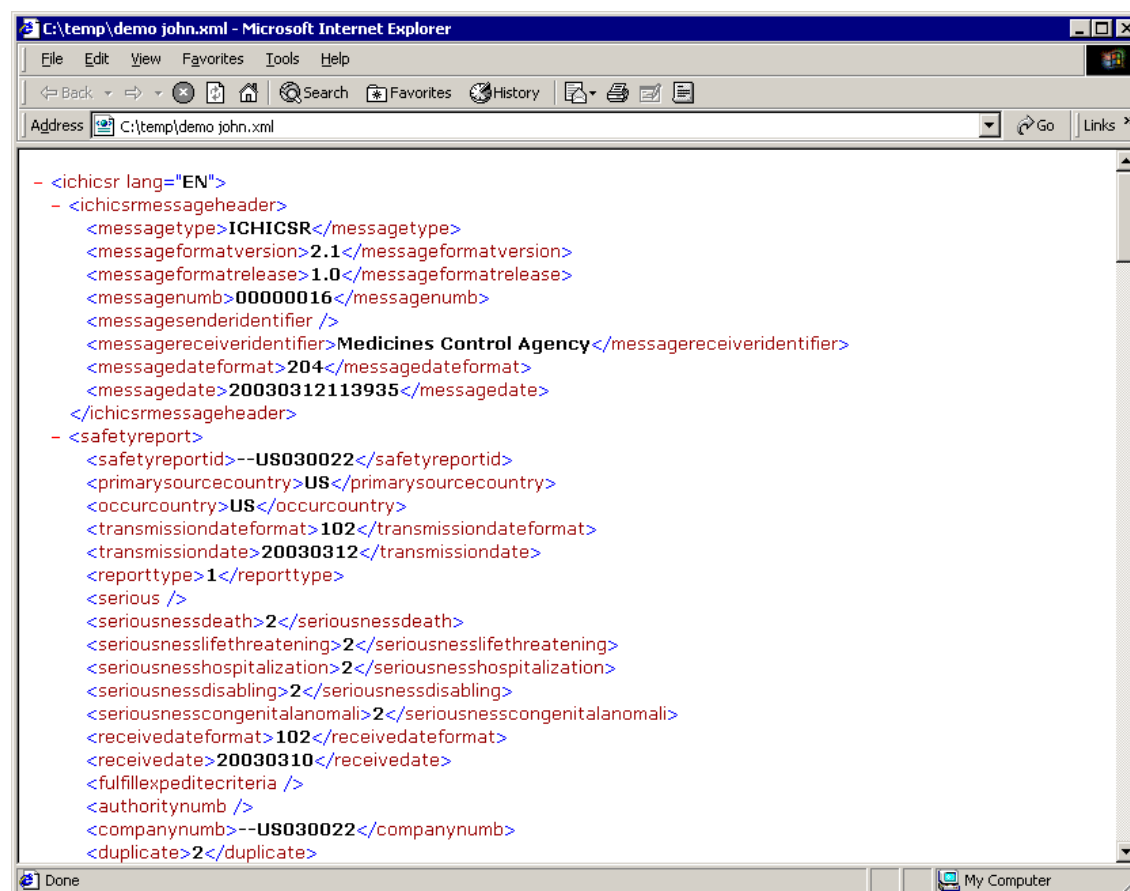
This section defines the method by which a PV-Works customer will export cases to the required XML format. While the primary goal of this function is to describe electronic reporting to a regulatory authority (e.g. EMEA and FDA), it is recognised that a case import/export function will also support exchange of case data between two PV-Works customers – e.g. licensee and licensor.

While these formats are similar to one another with XML as a common thread, they vary in detail. For the user, their usage is common.

The basic premise is that an XML file is basically a report albeit presented as a computer file rather than a paper output.

One of the principles of electronic reporting is that all cases are uniquely identifiable globally by their worldwide case number. The worldwide number is defined by the country where the case occurred, an organisation identifier and a local reference. Typically the worldwide case number is established by the organisation that first reports the case to another organisation, as a result PV-Works will construct and

save the worldwide case reference number at the time of generating the first report. If a case is imported into PV-Works the worldwide number will be loaded at the time of import.

The electronic reporting function creates an XML file containing one or more cases. The XML file is submitted to the regulatory authority or licensed partner; thus an XML file is also termed a 'submission' in PV-Works.

The basic steps of generation are:

- A single case could be exported directly from the Main Screen or from within an update or review session.

- Multiple cases will be selected using existing case filtering functions, e.g. Find Case. Multiple cases may also be identified for export via the 'Create Regulatory Submission' function (see section 11.3) This later method is recommended for customers with larger case volumes.

- A new pseudo-report called 'XML Case Export' will be offered as a menu option. Current security measures will determine which users are able to run it – i.e. are able to export cases.

- As with all reports, a set-up screen will be shown in which the user may define the nature of the XML export required. This screen will allow the user to select the output format – ICH or PV-Works. The destination folder of the XML file will be defined. Other options and selections may be necessary e.g. the name of the responsible contact.

- The XML file will be created.

- PV-Works is not responsible for automated transmission of the exported file. However, the XML file will be stored in a designated folder on the server and this can be polled by a commercial gateway software product and transmitted immediately.

In 2011 global harmonisation of electronic reporting is showing some signs of fragmentation. Two examples of this have been implemented in PV-Works:

a) Adoption of a different character set (ISO 8859-1) for transmission to FDA compared with all other agencies

b) Special rules covering the presentation of reporter address data for submission to the Spanish authority where the reporter resides in Spain

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11.2   Validation of Cases for Export

A case has to meet a certain standard to be considered to be "valid" for electronic reporting. This infers that it must contain an identifiable patient, product, event and reporter. PV-Works has addressed this check at the "report approval" stage of the data entry, assessment and reporting process. (See section 10.3 for a discussion of report approval).

Issued with PV-Works are a number of scripts that will define mandatory field checks to be applied during report approval. Failure to pass all of these tests during report approval will mean that the case cannot be approved.

Since PV-Works will not generate an electronic report for unapproved cases and only valid cases will pass these checks, it follows that invalid cases cannot be submitted electronically.

There is one exception to this rule. It is possible to send XML files to either a regulatory authority or to a licensed partner company. PV-Works allows unapproved cases to be sent to a licensed partner as this may be necessary depending on the business relationship established between the two companies.

However, it is always true to say that unapproved cases can NOT be sent to a regulatory authority.

11.3   Selecting Cases for Export

There are three functions that may filter the database to retrieve a case or set of cases that need to be reported:

- 'Create regulatory submission' (see section 12.3.3)
- 'Find Case' (see section 12.3.2)
- 'Single case export' (see section 12.3.1)
-

Each of these will be starting points to create an XML export file containing single or multiple cases.

In addition it is possible to create an XML file to report data relating to a single case, this functionality is driven from the single case reporting function used to generate other regulatory and internal report outputs.

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11.3.1 Single Case Export

If the user wishes to export a single case then the case should be selected on the Main Menu screen. The user will click the 'reports' button and will see the 'Select report type' screen shown below.

Only approved cases can be submitted electronically. The latest approved version of a case is used automatically and no facility is provided to allow a user to select a previous version. If an attempt is made to produce an individual case report for an unapproved case, an error message is generated from the select report screen.

Select report type screen
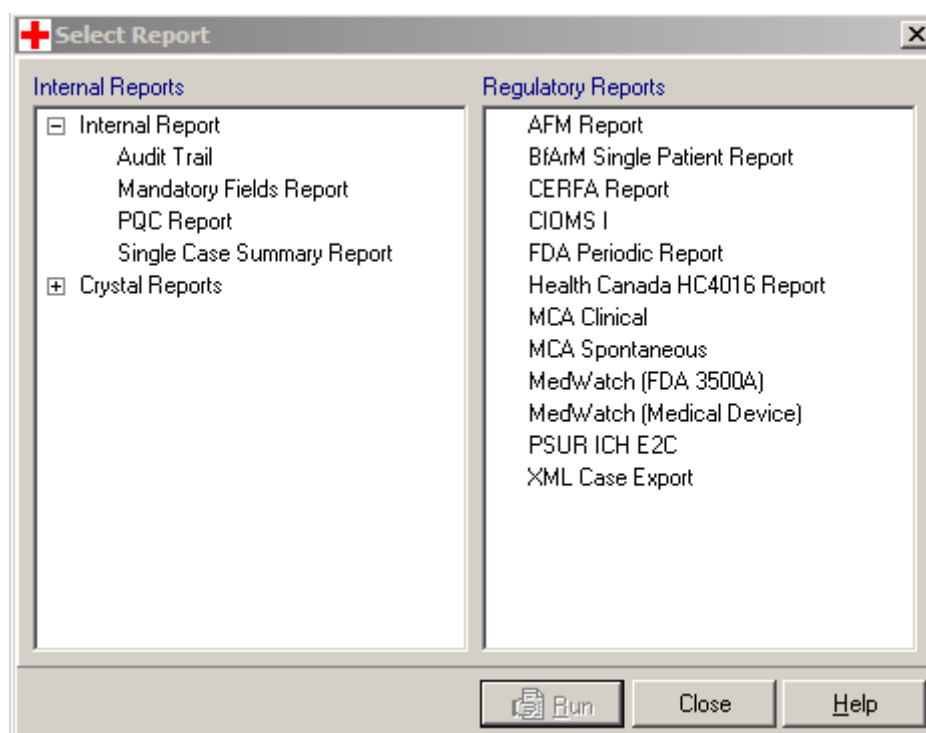
Only cases that have been "report approved" (see section 10.3) may be exported to regulatory authorities. However, it is possible to export unapproved cases to a partner company. After 'XML Case Export' is selected a check is made of the report approval status.

If the case is "unapproved" then the following screen will be displayed:
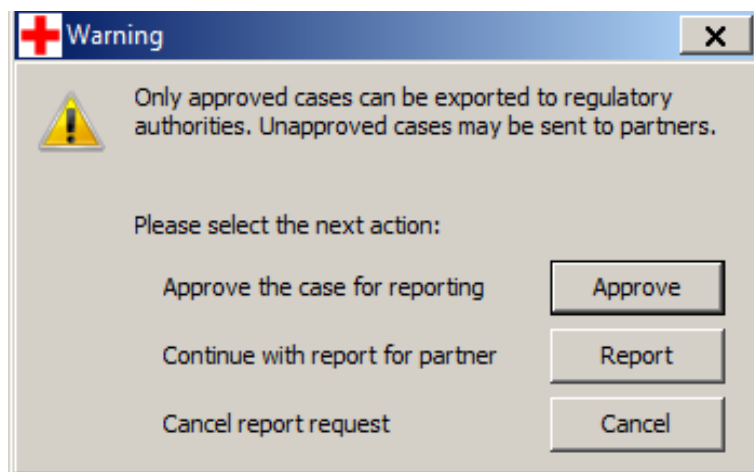
If the user has security access to the Report Approval function (see section10.3), they will be able to branch to this screen in order to approve the case before reporting it.

The user may continue to generate an XML file for a partner company using the unapproved case. If this option is taken the set up screen shown below is displayed.

If the case is "approved" then the set up screen below is shown.
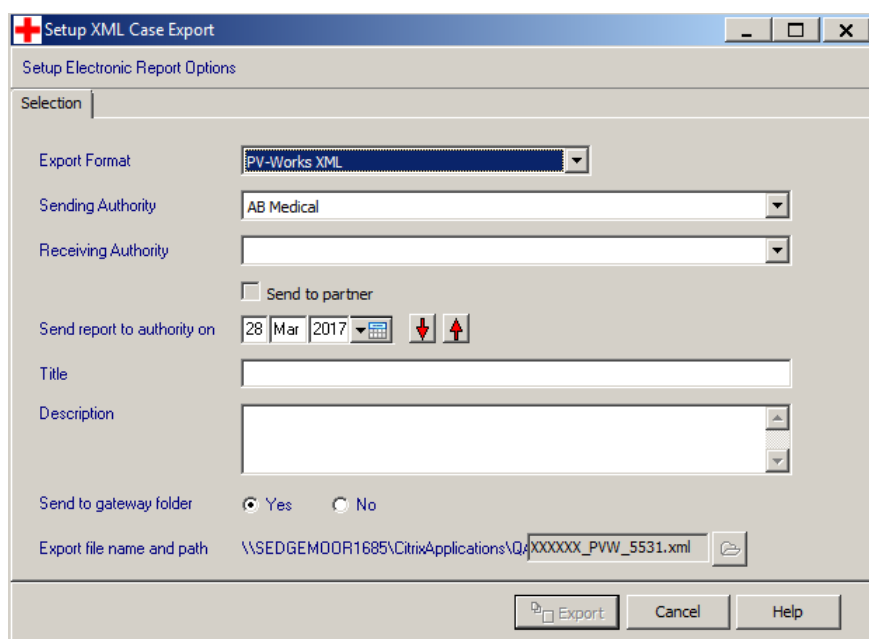
The available export formats are:

- ICH / Eudravigilance XML EMA
- ICH / Eudravigilance XML FDA (with different character set)
- eMDR report (for medical device reports)
- PV-Works XML (for "customer to customer" data exchange).

It is possible to define multiple "Sending authorities" in the contact dictionary to handle situations where one customer needs to create XML files with different sender identifiers. An obvious use of this feature will be by CROs.

Electronic reports may be sent to licensed partners as well as to regulatory authorities. To send to a partner, click the check box 'send to partner'. This will change the contents of the "Receiving Authority" dropdown box such that it contains a list of partner companies.

The name to be given to the export file will be defined by the program – its format is

<<company name>> <<format>> <<unique number>>.XML.

The path (folder) in which it will be stored will usually be defined via a system option so that the use does not need to define this. However, it will be possible for a user to set this entry. The user may also enter a title and description, which are saved to the electronic report log (and are for internal identification purposes only).

When the user clicks on the 'Export' button, the selected cases are exported initially to the proprietary PV-Works XML schema. For a ICH formatted report, the data are then transformed to fit the appropriate XML schema.

Once an XML file has been created successfully the selected cases will be exported in the required format and stored in the named file. The identifier (defined above) will be allocated when the report is generated. A message is generated upon successfully creation to notify the user of the allotted number.

An option exists that allows the customer to mark all cases exported to the XML file as 'submitted to their intended recipient' immediately upon creation.

11.3.2 Find Case

The 'Find Case' function can be used to return matching cases that can then be marked for export and the 'Reports' button will be clicked. The user must select the 'report type' and the process continues along the same lines as for a single case. A single output XML file will be generated that contains all of the selected cases.

Note that XML Case Export will not be available from the reduced Find Case function available on the Main Menu screen.

11.3.3 Create Expedited Submission

The Create Expedited Submission function requires no alteration in order to support electronic reporting. The filter criteria will be applied and the results are displayed on the 'Matching Cases' screen in Figure.

An output type of XML Case Export is available and, as is current practice, the cases to be reported / exported are marked with a red cross. When the 'report' button is clicked the 'XML Case Export' set up screen is displayed.

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11.4 Submission status of an electronic report

It is important that PV-Works is able to track the sending, receipt and processing of the file. In order to achieve this aim a log of XML files is maintained in the database. The log will record the lifecycle of an XML file according to the pattern outlined below:

- At the point of generating an XML file, the log function will record each output produced and the agency to which it will be submitted. The log also records a list of all of the cases exported including their intended destination.

- Initially the status of the XML file and each case report within the file is set to 'Created'.

- The user will mark that the XML file has been submitted and the status of the file and each case record will change to 'Submitted'

- At some point after submission the recipient (agency or company) will first perform an integrity check on the XML file. If the file meets the expected format an acknowledgement will be returned and the status in the electronic reporting log will change to 'Received'. The 'Received' status will be inferred to all cases contained with the electronic report. If the XML fails this integrity check the XML package will not be accepted. An acknowledgement message will be returned to the sender, and the status of the file in the log (and the cases contained within the report) will be set to 'Failed on receipt'.

- After receipt the recipient will commence a review process of the individual cases contained within the report. Acknowledgement messages will now be received by the Marketing Authorisation Holder for each case in turn. The status of each case described in the log will change according to the type of acknowledgement received – the case report status will be set to 'Accepted' if the case is accepted, 'Rejected' if the case is rejected, and 'Accepted with questions' if the case is accepted but has questions from the regulatory authority outstanding.

  (Note that ICH does not currently include an outcome of 'accept with questions' and so this response will only apply to company-to-company transfers.)

- A further case level status change will be seen for cases that have been rejected or accepted with questions, as appropriate responses are made. However this functionality is described in section12.8.

- The overall status of the XML log will also change to reflect the review of the individual cases by the regulatory authority. Potentially, once the first case review acknowledgement has been received the status of the complete file will change to 'In review'. (Note this does not seem to be current EMEA practice and all cases are acknowledged together). Finally once a message has been received for all cases in the file, the status will change to 'Processed'.

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Please note that there is no concept of a draft or official status in the electronic reporting module.
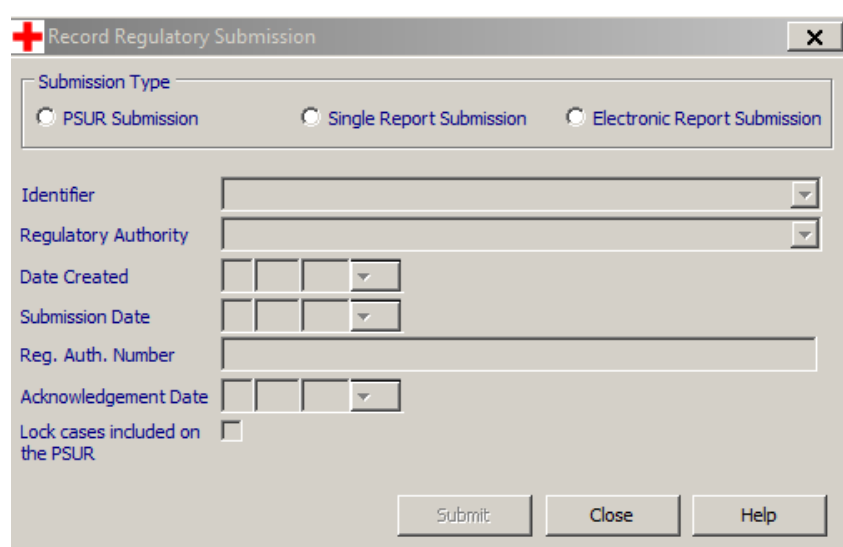
In order that the submission status is updated automatically, the user must import acknowledgement messages using the PV-Importer program supplied by Assured with PV-Works. This program can be set to poll the inbox generated by a gateway.

11.5 Recording the submission of an XML file

If a PV-Works user is submitting XML files directly and automatically via a gateway, then its cases could be assumed to be submitted as soon as it is saved in the output folder. However, if cases are submitted manually, e.g. via the EMEA's EVWeb tool, then this is not valid. The system allows either approach to be adopted with control exercised via a system option.

When an XML file is created a record is added to every case in the file that shows that an XML export was created for submission. This is visible on the regulatory reports screen. Each report is assigned a status of 'generated, not submitted'. If the system option for automated submission is set on, then the status is marked as 'submitted' and the date of submission will be taken from the value entered in the 'Send report to authority on' field on the XML report setup screen.

An additional main menu option has been established to allow the user to record that the XML has been sent to the intended destination. The screen is shown below

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When the radio button 'Electronic Report Submission' is checked the fields for 'Reg. Auth. Number', 'Acknowledgement Date' and 'Lock cases included on the PSUR' are greyed out as they have no relevance for a submission of this type.

The radio button 'operation' controls the display of the 'Submit' and 'Reject' buttons and is consequently the contents of the 'Identifier' drop down list. For example, this prevents the user from rejecting submissions that have been submitted.

The 'Identifier' drop down displays the names of all created XML files which have not yet been submitted (i.e. where the status in the XML report log is set to 'Created'). When a file is selected, the regulatory agency to which the file was generated, and the date created is displayed in read-only format – this information is taken from the log record for the specified XML file. The user can specify the 'Submission Date' for the electronic report, future dates will be allowed. The submit button will remain greyed out until an identifier and submission date have been entered.

When the 'Submit' button is clicked a confirmation message will be displayed. Once this submission has been confirmed the status of the XML file in the log will be changed to 'Submitted', and the date of submission will be recorded. The status of each cases included in the XML file will also be updated to 'Submitted' and the submission date is recorded.

The 'Reject' button will allow the user to clear an unwanted XML file from the drop down. A confirmation message will again be displayed when this button is clicked. Once confirmed, the status of the XML file, and the status of each associated case record, will be set to 'Deleted'.

A system option (XML_AUTO_SUBMIT) has been added which when set to 'Y' will cause any XML file generated to be automatically marked as submitted. The date of submission will be taken from the value entered in the 'Send report to authority on' field on the XML report setup screen. In reality it is likely that this option will only be used when sending electronic reports via an automated secure gateway established with a regulatory authority or for company to company case transfer.

11.6 Tracking the status of submitted Electronic Reports

It is important that the user can review the status of previously submitted XML files.

A mechanism for reviewing the status of submissions is provided by the main screen grid – a number of specific queries are available to show reports submitted and submissions requiring further attention. Additional queries can be developed as necessary.

Main screen grid tracking of XML submissions

There is a small query function within the E-reporting block of the Main Screen grid. Click the query name "E-report New" to display the following screen:

This provides a simple query tool with fixed fields / parameters that allows the user to filter all reports submitted electronically to display a sub-set in the grid. Any number of the parameter fields may be selected in combination, remembering that each one is combined with an AND operator, i.e. each parameter further restricts the submissions received.

An additional facility to review submissions is provided via the main screen, using the electronic reporting interface via the 'Files sent' screen (see below). To access this run the menu Reports | E-report status.

(Note that this is complementary to the regulatory report screen of the case in question and operates at a "submission level").

Files sent screen

The user must first specify whether they are interested in seeing previously submitted regulatory or licensed partner XML files. A radio button allows the user to specify the type of submission. By default the regulatory XML radio button is checked.

Note the "pseudo- authority / partner" of <ALL> which allows the user to select all regulatory authorities / licensed partners within a defined date range.

The top half of the screen area is used to filter the XML files that are displayed in the grid below.

The user must first specify whether they are interested in seeing previously submitted regulatory or licensed partner XML files. A radio button allows the user to specify the type of submission. When a regulatory submission is selected the 'Licensed partner' drop down field is greyed out, likewise when a licensed partner submission is selected the 'Agency' field is greyed. By default the regulatory XML radio button is checked.

The user may specify a combination of criteria including the agency / licensed partner to which the report was submitted, the date of submission, or a specific submission identifier. The 'Submission title' field will support wild card searches using the asterisk to indicate a number of unspecified characters.

By default no values are selected in the filter fields and no submissions are show in the grid. The 'Find' button is used to execute the query according to the defined query, whilst the 'Clear' button will reset the filter criteria and results to default values. The grid will display information taken from the XML electronic report log. The list of XML files displayed will be limited to exclude all files with a status of 'Created' or 'Deleted'. Valid status values are:

Status	Meaning
Submitted	The XML file has been placed in the 'outbox' ready to go to its intended recipient. In other words the file is outside of PV-Works's control. It is expected that a gateway would transmit this file immediately, but equally this is the next potential point of failure in the chain.
Received	The XML file has been received and the file is accepted as having the correct structure. However, none of the cases has been reviewed.
Failed on receipt	The XML file has been received and the file is rejected due to its incorrect structure.
In review	The first case has been reviewed – and accepted or rejected – but there remain cases in the submission that have not been reviewed. (Note that this is determined by receipt of case level acknowledgement messages, not an insight into the recipient's system!)

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Processed	All cases in the submission have been reviewed and either accepted or rejected.

The user can also elect to exclude all 'Processed' XML files in the filter section. XML files with a status of 'Failed' are displayed and the status is shown in red text. The number of cases associated with the electronic report is displayed along with the current status of the report. An option has been provided to allow the user to review the XML file in its native format. With a row in the grid highlighted the 'View XML' button will access the XML file in the following screen:

XML viewer screen

A search box is provided to help find particular data items. Bearing in mind that the submission may contain multiple cases, this is a useful feature.

The user may explore the submission status data presented and filter it in order to focus on a particular submission or status. There are three basic options to explore the data displayed (and these may be used in combination):

- Expand the report by clicking on the plus (+) button to display details of each case in the submission

Files sent screen with one submission expanded

- Sort the data by clicking on the column header, e.g. "status"

- Group the data by dragging one or more column headers into the grey box

Figure 20 : Files sent with status "grouped"

With a case selected, the user may review any error or warning message issued by the recipient (see section 12.8).

With an individual case selected, the user may

- Review any error or warning message issued by the recipient at a case level (see section 12.8).
- view the XML data for the case
- Update the case – e.g. to respond to an error or warning message
- Browse the case

11.7 Tracking rejection or questions on submitted Electronic Reports

Cases which have been accepted require no additional activity. While the 'Files sent' screen can be used to examine all previous submissions including ones that were accepted without any further action, the 'Response required' tab only shows cases where a response is required. As this is considered more important, it is the default data display for this function (see below).

The label text on the 'Response required' button is designed to change to red if any of the case counts for the selected agency have a positive value, otherwise it will remain black.

'Response required' screen

The top half of the screen area is used to filter the XML files and their cases that are displayed in the grid below. The user may specify a combination of filter criteria including the agency / licensed partner to which the report was submitted. By default the regulatory XML radio button is checked. The grid will display information taken from the XML electronic report log with one case per line as a default.

The list will be limited to exclude all submissions with a status of 'Created' or 'Deleted'. The user can also elect to exclude all 'Processed' XML files in the filter section. Each value in the grid represents the number of cases in the category – divided into the reportability under which the case was submitted.

There is a colour coding system used to display the data:

- GREEN   Case submitted but not acknowledged

      Cases in this group have been submitted but the recipient has not acknowledged the receipt of the submission. Clearly if the submission occurred in the last few minutes, this is to be expected. A delayed acknowledgement may give cause for concern.

- RED   Case failed

      Failure means that the XML file is incorrectly formatted and that all cases in the submission will be rejected by the recipient. The failure is accompanied by a reason. Note that PV-Works (vet) will check the format upon generation, making this category unlikely unless there has been a corruption in transfer.

- PURPLE   Case rejected

      A rejection can occur at a case level if the recipient's reviewer takes exception to the data within the case. The rejection is accompanied by a reason.

- BLUE   Case accepted with questions

      The recipient's reviewer may accept the data in the case but wish to ask a supplementary question or comment on the data, its presentation or format. The acceptance is accompanied by a question or comment.

      NOTE that this category cannot occur with ICH. At present this state will only occur with submissions to licensed partners.

With a submission selected, the user may review any error or warning message issued by the recipient (see section 12.8).

With an individual case selected, the user may

- review any error or warning message issued by the recipient at a case level (see section 12.8).

- view the XML data for the case.

In addition, the 'Refresh' button is used to update data displayed in the grid, without requiring the user to exit and reopen the case listing.

Please note that as responses for rejection messages and questions are confirmed the case submission status is updated. Such case submissions are no longer considered as rejected or accepted with questions and consequently the refresh function will cause these case submissions to disappear from the list of cases requiring response. In this way the 'Response Required Review' popup screen can be used as a working list of cases that require response.

11.8   Responding to rejection or questions on submitted Electronic Reports

A company will be required to answer questions or rejection messages raised in response to an electronic report submission. The electronic reporting interface allows the user to respond to any outstanding rejection messages or questions associated with all cases.

Note : Questions cannot be raised by EMA or FDA in their current design.

11.8.1   Responding to rejection comments and questions via the electronic reporting interface

In practice it is likely that a user will periodically review the list of cases with outstanding rejections or questions. In the first instance the user will wish to read the comment returned in the acknowledgement message from the regulatory authority or licensed partner.

By highlighting a case in the Response Required Review screen grid and clicking the 'Review Comment' button a popup screen will open. The 'Review Comment' screen (see below) is displayed containing comment messages associated with this case submission – the data displayed is saved in the electronic report log when the acknowledgement message is processed.

Review Comment popup screen

The left hand side of the header block details information relating to the case submission, as recorded in the electronic reporting log. The right hand side of the header block, shows some basic case information.

A read only block in the centre of the screen, identifies the comment text as returned in the acknowledgement message and shows the original data that caused the comment. The screen has been

designed to accommodate multiple comments per acknowledgement. A grid displays a summary of the individual questions, and the user can select each record separately. Video navigation buttons are also provided for this purpose.

In order to complete the response to a rejection or question, a company comment must be entered for each message. The 'Response by', 'Response on', and 'Comment' fields relate to the specific message selected in the grid above, such that values can be set for each message in turn.

The 'Response by' field will default initially to the current user when the message is first reviewed, but other free text can be manually entered.

The 'Response on' date field will remain greyed out until text has been entered into the comment box and the 'Response by' field. Once the date has been entered the 'Confirmed' column in the message grid will show the confirmed on date – this allows the user to see which messages still require a response.

The 'Confirm Response' button will remain greyed out until a response and date has been entered for each comment. This button is then clicked to close the response, and in doing so the status of the case submission in the reporting log will be updated. When a response is confirmed for a case submission with a status of 'Rejected' the status is now set to 'Rejection closed'. Clicking the 'Confirm Response' button also saves all of the company comments to the electronic report log for the current case submission.

The 'Export' button is used to copy information contained on the 'Review Comment' screen to the clipboard, such that it can be pasted into a Word document or an email message.

The 'Print' button will send the same text block that is exported to the user's default printer for offline review.

In many cases it may not be possible to respond to the comment without reviewing the case. The 'Cancel' button will close the 'Review Comment' popup without saving any data and return the user to the 'Response Required Review' screen

A further button 'Save' will save the data entered in the comment field to the electronic report log for the current case submission, but will not cause the case status to be updated.

11.8.2　　Re-approving rejected cases or cases with questions outstanding

Cases that have been approved (since a previous submission to a given agency) are considered available for submission via the electronic reporting interface. It may not be appropriate re-approve a case with outstanding rejection comments or questions, as this might mean that the case is re-submitted before these issues have been fully addressed.

In an attempt to avoid this situation a check has been added to the report approval process. The following confirmation message (see below) will fire if any case submissions with the status 'Rejected' or 'Accepted with questions' are found in the electronic reporting log for the current case. No further attempt is made to automatically control the potential re-submission of a case with outstanding electronic submission comments.

Re-approval confirmation message
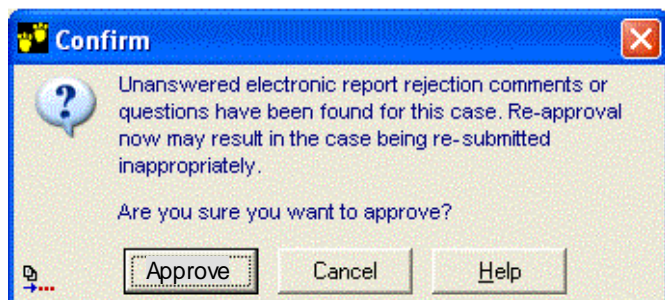
11.9 Nullify Previously Submitted XML Report

If a case has been sent to a recipient in E2B format and that case needs to be withdrawn, a 'nullification' message must be sent. This is a complete case of data with the 'Report nullification' flag set to 'yes' and a reason given. From the 'Reports' menu of the Main screen the sub-menu item 'Nullify e-report' will display the following screen:

E-report nullification screen

In order to illuminate the 'OK' button a 'reason for nullification' must be given. This is the text that will be submitted to the e-report recipient. After confirmation of the nullification request, the export tables will be updated to record the nullification within the PV-Works database and an XML file of the correct format will be generated and sent to the recipient(s). The nullification information will also be visible on the Regulatory Reports screen.

11.10 Importing XML Data into PV-Works

As well as sending cases electronically, it is possible for PV-Works users to receive cases in the same format or an agreed format. These may be sent by a regulatory authority or a licensed partner.

The XML file containing the new cases is saved to a local disc and is then read and processed from this location automatically. (This is achieved by a separate program, the "XML importer" written by Assured. See the separate document, "PV-Works XML Importer Functional Specification"). This is normally the responsibility of the Systems Administrator.

Cases derived from received XML files will

- Be imported into the database and assigned a new case number. The sender's case number will be retained as an 'external case reference number'.

- An Action Board task can be initiated for each case imported.

A report of cases imported will be created at the end of the import process. This will describe the message and will list all cases imported, giving their case number as defined in the import file and their PV-Works case number. This is essentially a print-out of the above tables.

11.11 Follow-up Management

PV-Works includes a function to manage follow up reports that are imported from files received electronically with further information to a case that was imported previously. Follow-up reports are identified where the worldwide case number already exists in the receiving database. New follow-up data will be imported into a quarantine area within PV-Works such that it is not automatically available for use.

The follow-up management review is a comparison of the current data to the new data – where the user will be presented with a list of fields that are different. The list displayed to the user can be configured as required.

Follow-up management screen

The user can see changes in three categories, each broken down by functional area:

- Records removed
- Records modified
- Records added

A grid at the bottom of the screen allows the user to see the details of the records in the selected category. In addition, the user is presented with the both the old and new case narrative (if different). The user can then decide to append the new narrative to the old, or replace the old with the new. For reasons of space this is shown on a pop-up window which is displayed by clicking the button "Review narrative".

Follow-up management, review narrative screen

The user then has the opportunity to merge the new information with the old case data with each change being audited. After review the follow-up report will be attached to its original case as a 'version'

so that it can be viewed in its entirety. A version of the case record prior to the merging of the new follow-up information will also be retained.

12 Letter Writing

At many points in the processing of a case it is necessary to generate letters based upon the data of the case. These include:

- requests for further information (follow-up)
- reminders for follow up information not received
- regulatory submission cover letter
- fax header sheets

Most of these are standardised by individual companies and a template library will already exist in the Word Processing system for manual preparation. PV-Works allows the System Administrator to create an 'intelligent template' that can be used to merge case data with fixed text automatically.

In versions prior to version 3.2, the letter writing function of PV-Works operates with Microsoft Word (any version). From version 3.2, the word processing function is delivered by an internal engine for reasons of performance and robustness.

The System Administrator has total control over the template and can create any document style using a set of word processing functions that are remarkably similar to the common functions of Microsoft Word. These might include letters, faxes, memos, tables etc. The general user may only print letters from the PV-Works application.

12.1 Creation of letters

By clicking the 'Letter writing' button on the Main Menu screen or by selecting 'Letter writing' from the External menu of the Main Menu screen, the screen below is displayed.

Letter Writing Template Selection screen
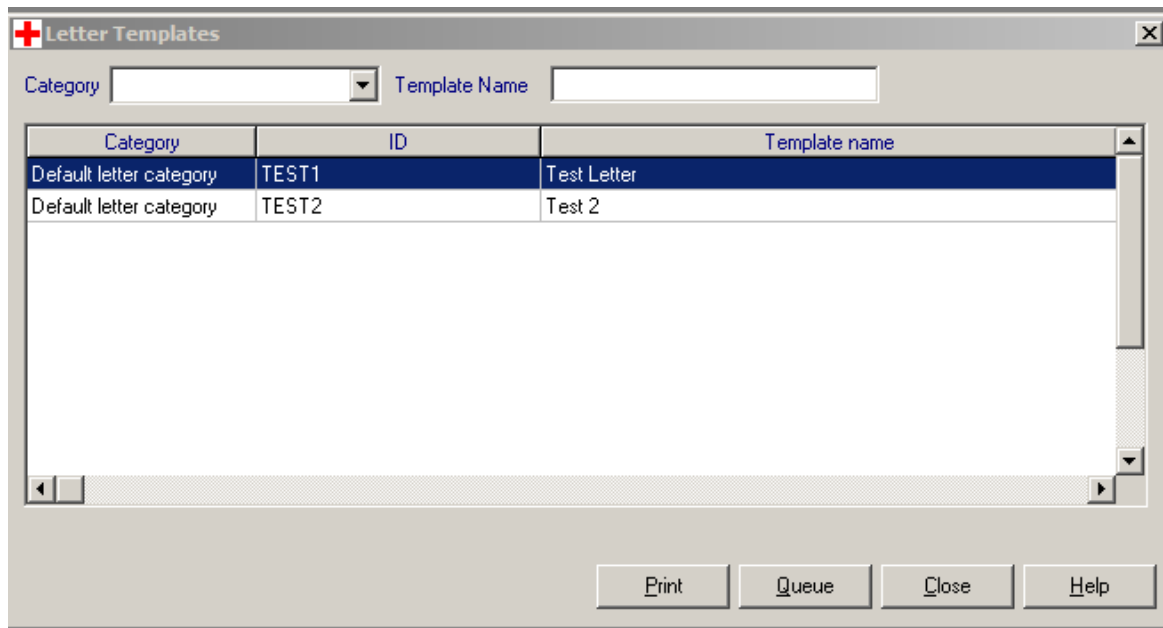
The letters displayed are secured at a pool level. This means that the System Administrator may control which letter templates are available to which users. The user may generate the letter immediately or may defer printing to a batch operation by queuing a request for the letter. See section 13.2.1 for details of the function to print queued letters.
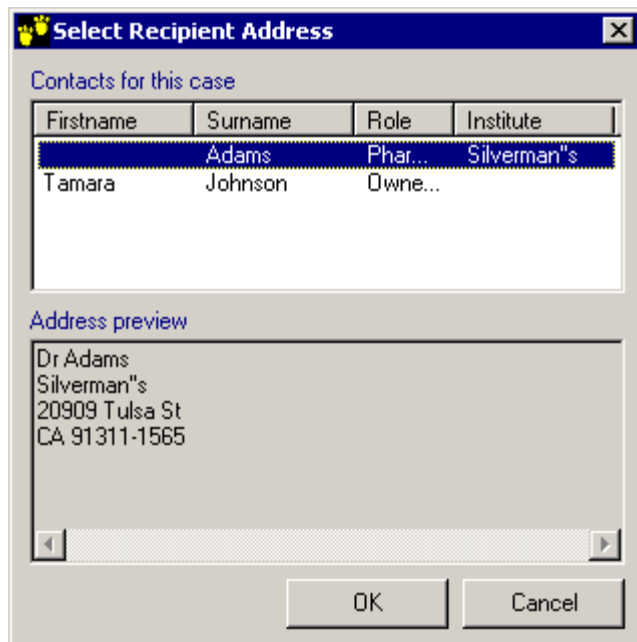
12.1.1   Immediate Generation

To generate the letter immediately, the user should pick the required letter and click 'Print' to generate the letter. The selected template will be merged with data from the current case to generate a new text document.

If the letter template includes a contact name and address block, the user will be able to select any of the contacts entered into the case (i.e. via **Figure**) to be the letter recipient. The screen shown below allows the user to make this choice and shows a preview of the address label. Selection is made by clicking on the appropriate row of the grid and clicking 'OK'.

Letter : Select Recipient
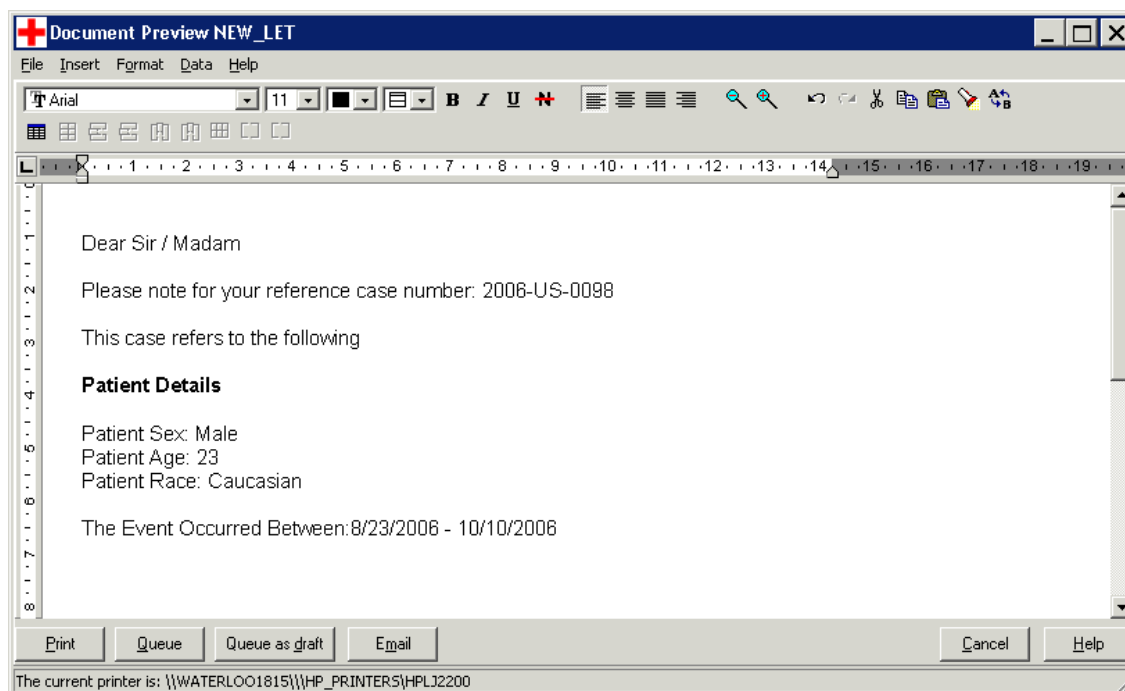
The user has two further options:

     a) Print the letter immediately (on the default Windows printer)
     b) Preview the letter before printing. The letter Preview screen below is displayed.

Letter Preview Screen

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The user can edit the resulting letter before printing, e.g. to personalise it or to add non-standard text. Note that it is possible to alter the data that has been derived from the database although this has no effect on the database itself. The decision to leave the generated letter 'open' to further amendment has been taken to provide greatest flexibility. Letters may be saved automatically in the Document Repository upon printing.

Case letters may often take considerable effort to compose, even when written from standard letter templates. It is often necessary to consider the content over a period of time or with the input of colleagues. The button labelled 'Queue as draft' allows a user to save a letter in draft format. When the 'Queue as draft' button is clicked the letter is saved to the letter queue but will be marked as a draft.

Apart from editing the letter, the user may:

- Select a printer for the output
- Print the letter
- Send the amended letter to the letter queue for subsequent printing and / or editing
- Send the letter as an email – using the user's email system
- Close the preview without printing

12.1.2   Deferred Generation

To print the letter at a later point, the user should select the required letter and then click 'Queue'.

1. All letters that are added to the queue will be generated at the time that the 'queue letter' request is made.

2. The format of the letter in the queue will be a rtf file.

3. When a letter is generated (and provided that the letter template has been suitably defined), PV-Works can generate the name and address (or company name and address) of the recipient in a label format. This will permit printing and re-printing of address labels.

With regard to printing the name and address of the recipient on a label:

Two pre-defined letter fields will be made available – one for an individual's name and address and one for a company name and address. These must be added to the letter template for this function to operate correctly. Labels will be printed on a dedicated letter printer which will be identified to PV-Works (vet) via an existing system option (LABELPRINTERNAME). The label printer will need to

be a dedicated label printer holding address labels that are on a roll, one label across the 'page'. A typical label printer is the Dymo LabelWriter range.

12.2 Automated storage of letters

Customers can configure PV-Works so that an electronic copy of the letter will be saved automatically in the document repository upon printing. This function will be controlled by a system option that will be given a value of either:

NONE - implying that no copy should be taken automatically

<<folder>>   - a copy will be made automatically when the letter is printed and will

be stored in the document folder named <<folder>>

ASK   - the user will be asked if they wish to store the letter and where using 'Document folder selection' screen shown below)

Document folder selection
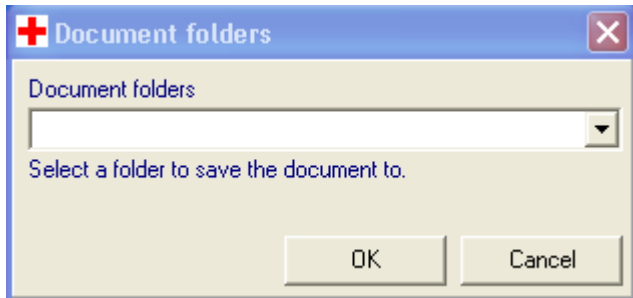
Regardless of the setting of the above option, whenever a letter is printed a record will be added to the 'sent letters log'. This will occur if the letter is printed from the letter queue or is printed immediately upon generation. Whenever a letter is printed an entry will be added to the Call History log in the form:

"Letter printed: <category> <letter type> queued on <date> by <user>. Printed on <date> by <user>"

If the letter was printed directly, i.e. without queuing the text "queued on <date> by <user>" will be deleted from this entry. If the letter that has been printed contains a pre-defined name and address block, this will be printed to a dedicated label printer at the same time as the letter itself is printed.

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12.2.1 Batch printing of letters

PV-Works will allow the user to 'schedule' the generation of a letter for a case as a background activity, i.e. to queue a request: either by menu option or by a button on the toolbar and then print them as a block at a later time. Letters may be printed by their author from the queue or by a designated user.

PV-Works will maintain a list of scheduled letters for all cases.

The scheduled letters screen provides the following functionality:

- Enable the user to view cases with pending letters
- Enable the user to select multiple letters, and to print then in a batch (in Draft or Final mode)
- Enable the user to de-schedule a letter for a case, if it is no longer required
- Filter the letters in the queue by category, originator or case number
- Browse an archive of previously printed letters for re-printing
- Send an 'action board' task to a user relating to a letter in the case
- Return to the case from which the letter was generated

Batch printing letters

Batch Letters — Letters Awaiting Printing

	Category	Letter	Case	Queued On
☐	Default letter category	Test Results	UK020075	04/11/2002 12:21:13
☐	Default letter category	Fiona's copied template	UK020054	06/11/2002 13:14:56
☐	Default letter category	Fiona testing	US020021	15/11/2002 16:13:33
☐	Default letter category	Follow up Letter	US020017	06/11/2002 19:54:43
☐	Default letter category	Appointment Reminder	US020008	29/11/2002 10:13:07
☐	Default letter category	Follow up Letter	US020064	09/12/2002 10:23:58
☐	Default letter category	Test Results	US020002	10/03/2003 09:46:30

Draft ⦿   Official ◯

[Mark] [Mark All] [Print] [Delete] [Cancel] [Help]

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If the user prints a letter, then that letter is removed from the 'scheduled' list.

Delete button:

> The delete button will remove the letter from the queue. A warning will be given before the deletion occurs, e.g. 'Are you sure you wish to delete this letter?'

> The warning will be more strongly worded if the user tries to delete a letter queued by another user. E.g. 'This letter was created by <<user>> and not by you. Are you sure you want to delete it'? However, the user will be able to delete the letter after this warning.

> Note that the user can only see letters created by co-workers in the same location and cannot view, print or delete letters created by a user in a different location.

> Once deleted, there is no record of the letter in PV-Works. If deleted in error, the letter must be re-generated.

Print button:

> In addition to the letter, the 'print' button will print an address label if one was specified in the template that added the letter to the queue. [Note the only time that an address label would not be present would be for letters that are internal forms or were not designed to include a label or if the user did not have a label printer]. Draft letters cannot be printed.

12.2.2 Separate Printers for different letterheads

PV-Works will support the automated selection of an appropriate printer for a case. For example, if a follow-up letter is required for a 'Product XYZ' case, then the letter will be printed on a printer that contains the appropriate pre-printed stationery for Product XYZ.

The definition of special stationery is defined in the Company Product Dictionary on a 'per product' basis by the Systems Administrator.

12.3 Auto-Narrative Generation

PV-Works will support the generation of 'Auto-Narratives' – i.e. narratives that are generated automatically based on a predefined template made up of a set of 'conditional' paragraphs. In effect this is very similar to the creation and processing of a letter template, except that the resulting text is copied to a data field of PV-Works.

The function is very flexible. For instance:
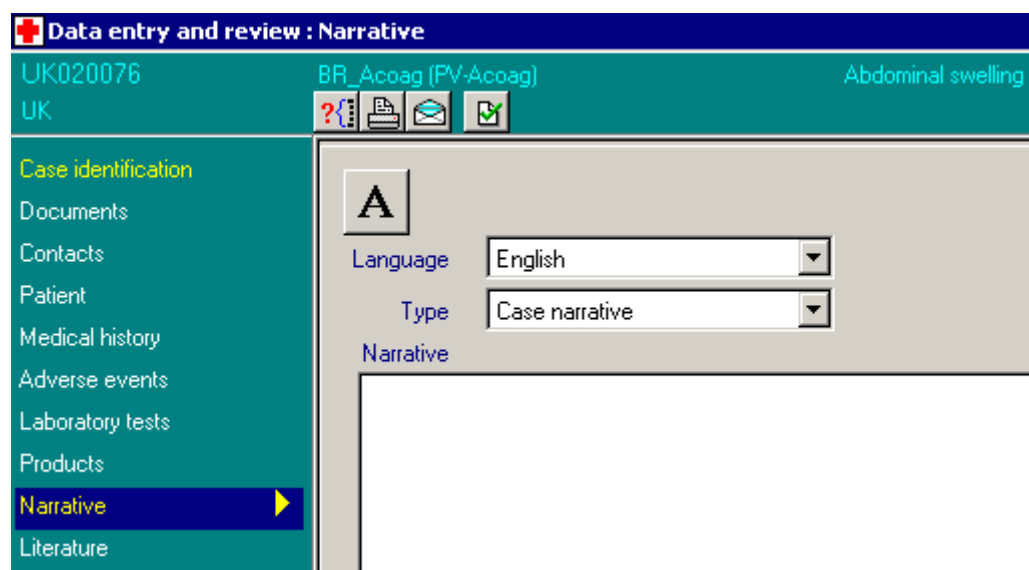
- A paragraph may have a condition attached to it. If PV-Works evaluates the condition to be True then the paragraph is included. If False, then the paragraph is not included. For example, a paragraph may be conditional upon a particular case type, the source of the case, the product taken etc.

- A paragraph will contain a mixture of plain text and 'placeholder' fields (i.e. markers for values of case data, such as the suspect product name, that will be populated when the narrative is generated)

During data entry a user may elect to generate an auto narrative for any of the 'narrative' type fields.

Template management is included in the Administrator module (PV-Admin).

The auto narrative feature will be available from the Narrative Data Entry screen shown below

Narrative screen with auto narrative button

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The Auto narrative button will only be available when the user selects one of the available narrative types e.g. Case narrative; PSUR comment.

On pressing the button PV-Works will perform the following processing:

- If no narrative template is defined display an appropriate warning message.

- If a narrative template is defined generate the auto narrative, and place it in the selected Narrative field with a narrative type of 'Case Narrative'

Note that if the narrative field already contains a value, then a warning will be given. At this point the user will be give the options to 'replace', 'append' or 'cancel' the auto narrative generation using the screen below

Confirm auto narrative dialog
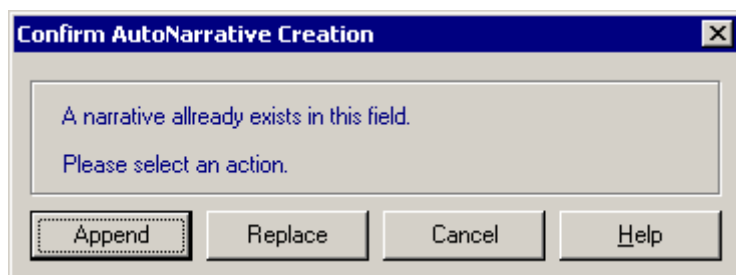
If an auto narrative is generated then it is NOT saved to the database automatically: the user must do this manually as with all other data using the 'save' or 'save and exit' button.

13 Complaint Management Functions

13.1 Introduction

PV-Works includes a complaint management module that allows customers to record details of any call (or correspondence) with customers. In addition to adverse events, this includes complaints and technical enquiries. Each call is stored in the standard PV-Works database and is assigned a 'case' number. Transfer of calls between categories, e.g. upgrading or downgrading a complaint to/from an adverse event is, therefore, very simple. The Complaint Manager also records the conclusion made by the company.

Calls entered via the Complaint Manager take advantage of the standard PV-Works infrastructure and utility functionality, including:

- Audit trail
- 21 CFR Part 11 compliance
- Security
- Find call / querying
- Case versioning
- Workflow process integration

13.2 Complaint / Enquiry Data Entry

Figure 14.2: Complaint / Enquiry Data Entry Screen

The 'Complaints Screen' allows a user to record the key information about the call either during a telephone conversation or after initial receipt. Certain data fields are duplicated on this screen and other

data entry screens. Any data entered or edited in either presentation of these fields is automatically reflected in the other. The intention of this duplication is to avoid the need to change screens during the entry of the basic call data.

PV-Works will retrieve any previous calls from the same caller. The program will display all calls received in the previous 12 months. These will be summarized at the foot of the Complaint page as shown in Figure 14.2 Apart from providing background information on the caller, it is possible that the caller is following up on a previous call or the user wishes to review an earlier call for relevance to the new call. Thus the user may:

1. Browse a previous call to review the data without the ability to change it. This will be achieved by highlighting the row containing the call of interest and clicking the 'browse' button.

2. Update a previous call. This option will abandon entry of a new call and move directly to edit/update of the previous call. This will be achieved either by highlighting the row containing the call of interest and clicking the 'select' button or by double-clicking the row describing the call.

A number of special situations may occur during the entry of a new call:

13.2.1   Update Existing Call Details

At any point in the entry of a new case the user may recognize that the caller is following up a previous call. It is expected that this will be identified early in the call conversation.

At the foot of the Complaints page the user will see the previous calls from the current caller in the last 12 months. To select a call for addition of follow up information, the user may double-click the row containing the previous call to abandon entry of a new call and move directly to edit/update of the previous call. If any text has been entered into the Description field of the new call this will be copied to the clipboard automatically and will be available for addition into the previous call record at the user's discretion using the paste command (or 'ctrl-v').

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13.2.2   Two complaints in one call

A caller may report more than one 'incident' in one call, resulting in more than one call record ('case' in standard PV-Works terminology). To facilitate this the toolbar at the top of the page may display a 'New' button.

The New button will have the following function:

- Save the current call (assigning a call number if necessary)

- Open a new call for entry of the next incident being reported

Note that making the 'new' button available during data update allows a caller to provide follow up information for a previous call and report a new incident in the same conversation.

13.2.3   Call Notes Side Panel

Call notes may be captured on the Call History screen. In addition, a separate call notes display side panel may also be used to view / edit call notes. This is made available via a toolbar icon toggle function and can be viewed from any data screen. A fresh call note field will be made available for every case editing session and scroll buttons allow the user to review previous entries. The side panel areas may be re-sized and the system will remember the user's previous settings.

14 Product Quality Complaints (PQC)

14.1 Introduction

The Adverse Event Management functions can record details of Product Defects. Frequently the products associated with these cases and with other complaints are investigated to determine the cause of the problem and to recommend corrective action.

The Product Quality Complaints ('PQC') module extends PV-Works to allow quality assurance groups to record details of such investigations and to track progress. Key features of this module are:

1. Any responsible QA group (or approved designee) with access to PV-Works may enter the complaint directly

2. A complaint may be assigned to an investigation team

3. The results of the investigation are recorded and the case closed

4. The workflow functionality of PV-Works is used to ensure that all personnel are notified of cases / tasks assigned to them in a timely manner and in compliance with the business process

5. Responsible PQC managers are able to track the progress of individual cases

14.2 PQC Data Entry

Product Quality Complaint Data Entry follows the same principles and screen design as the current PV-Works program for adverse events. This includes:

1. A 'New case' option to enter a new complaint

2. An 'Update case' option to amend data previously entered

3. A 'Review case' option to examine case data in a 'read-only' format without recourse to amendment.

4. An integrated audit trail.

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Data entry of PQC data can occur with a separate set of data entry screens (i.e. dedicated to QA personnel) or as an extension of the adverse event screens. Security rights will control the presentation of the appropriate screens.

14.2.1 Case Identification

Figure 15.2.1: Product Quality Case Identification Screen

The Case Identification screen is very similar to the Case Identification screen for adverse events (see **Figure**). It will show other external case numbers for cross reference. Case links may be established with other cases that are directly related to this case. Note that there will be no requirement to link cases that are:

a) the adverse event data / complaint data of the same case. These are automatically linked in the 'References' block
b) for the same manufacturer, product, lot number. These are linked dynamically by data.

Where a single call leads to multiple investigations these may be recorded as a single PQC case and each investigation documented and monitored separately within the case.

14.2.2 Product / Narrative

Figure 15.2.2 : Product Narrative Screen

Products will be selected from the Company Product Dictionary shared with the Pharmacovigilance users via the Brand name. The Generic name will be populated automatically as it is in the PV Product screen.

The Internal Product Code will be populated from the Company Product Dictionary when a brand is selected, but may be edited by the user.

While it would be possible to derive the manufacturer name from the Company Product Dictionary, it has been agreed that this source of information is not always maintained accurately. As a result a new 'manufacturer's dictionary' will be developed and the actual manufacturer will be selected manually.

When a manufacturer of 'Other' or a third party 'Toller' is selected, the 'manufacturer other' box is available for entry of the actual manufacturer name. Otherwise it is not available.

A new dictionary will be created to record the relationship between a particular manufacturer and a QA investigation. This dictionary will be created and maintained by the System Administrator and will include:

- Manufacturer name
- Manufacturer type (Company, Toller, Other)
- Name of default QA responsible person at manufacture site
- Location of QA at investigation site (or responsible for the site)
- Name of default QA responsible person at/for investigation site
- Country of manufacture
- Workflow role of investigator

When a manufacturer is selected, the system will assign the investigation task in the workflow process to the role defined in the above dictionary.

Batch number checks on other cases from the same batch will be performed in exactly the same way as the adverse event product screen.

If no PQC narrative has been entered and the case exists as a 'complaint' or as an 'adverse event', the previously entered narrative text will be copied into the PQC narrative field. Changes made to the PQC narrative text derived from this source will be saved as part of the PQC record but will not affect the original.

When the PQC Product / Narrative table is displayed and the 'Customer relations' box options 'product replaced' or 'reimbursement' are not set, then the system will look to the complaint data to determine which actions have occurred.

The following actions will be set automatically according to the following business rules:

Customer Action	Rule
Product replaced	If a request has been made for product issue
Reimbursement	If a request has been made for a payment / credit to the customer

The remaining 'customer actions' cannot be detected.

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14.2.3 Investigation Summary
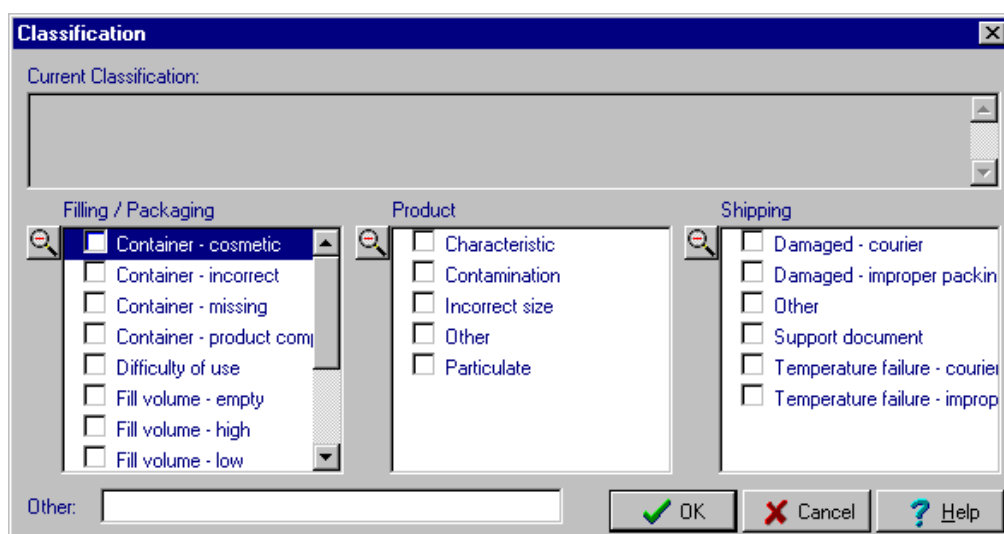
Investigation Summary Screen

The Investigation Summary screen records the Verification of the case by QA and the QA response to the investigation. Finally QA may 'close' the call. There will be one 'QA response' per investigation that is initiated as a result of the call (or for each 'follow up cycle'). As such this screen will behave as a standard PV-Works 'multi-record' screen (i.e. as Contacts, Products), but with one exception. It is not possible to add or delete an investigation record on this screen, only navigate between them. (n.b. To add or delete investigation records see section15.2.4).

There are four buttons on this screen which offer the following functions:

1. Batch Check - The 'Batch Check' button will perform the same batch check routine that is automatically invoked when a batch/lot number is entered on the product screen. This allows the QA user to review these cases after data entry.

2. Classify - The 'Classify' button displays a pop-up window in which the user may classify the call. The following screen will be displayed.

Classification Pop-up window

The classification terms will be controlled by the System Administrator via codelists. (Note that the sample classification items in the above figure are erroneous). If the user selects 'other', they may enter the classification manually.

The selected classification(s) will be displayed on the main Investigation Summary screen in read-only form. The use of a pop-up screen is necessary due to space constraints on the Investigation Summary screen, but this approach will allow additional security to be applied to the classification process.

3. Verification Complete
   When QA has completed verification of the case and wishes to instigate the investigation, the 'Verification Complete' button will be clicked. Access will only be granted to this function if the user correctly enters their electronic signature password. This challenge will follow the implementation of electronic signatures already available in PV-Works, including the recording of the authorisation. After confirmation that this task is truly complete, PV-Works will automatically complete the 'verify' workflow task (if applicable), thus setting the investigation in hand.

4. Close Case
   When QA is satisfied that the investigation(s) is complete and that all information has been received and evaluated, the case may be closed. The 'Close Case' button will be clicked. Access will only be granted to this function if the user correctly enters their electronic signature password. This challenge will follow the implementation of electronic signatures already available in PV-Works, including the recording of the authorisation. After confirmation that this case should be closed, PV-Works will automatically complete the 'close case' workflow task (if applicable) and will change the status of the case to 'closed'.

14.2.4   Investigation Response Detail

Investigation Response Detail Screen

The Investigation Response Detail screen records the investigation request made by QA at the originating site and the QA investigation response at the investigation site. Finally the investigating QA group may return the call to the originating QA group for review and closure. Of course, the originating and investigating QA groups could be the same person.

The three main data fields, 'request investigation', 'investigation summary' and 'corrective action summary' may be repeated as many times as necessary for a single case. This allows for:

- Multiple investigations from a single Product Quality Complaint, e.g. a contamination investigation occurring alongside a courier shipping damage investigation.

- Rejection of the investigation by the originating QA group with a request for follow up investigations.

Each iteration of the investigation cycle will be separately recorded and will be controlled by a separate workflow process. With the exception of the initial investigation, the addition of a subsequent investigation will lead to the creation of an ad-hoc workflow process to control it.

There is one button on this screen with the following function:

1. Response Complete
   When QA has completed the investigation response for the case and wishes to return the case to the originating QA group for review, the 'Response Complete' button will be clicked. Access will only be granted to this function if the user correctly enters their electronic signature password. This challenge will follow the implementation of electronic signatures already available in PV-Works, including the recording of the authorisation.

   After confirmation that this task is truly complete, PV-Works will automatically complete the 'Investigation Response' workflow task (if applicable), thus setting the investigation review in hand.

14.3 Product Quality Complaint Report

The Product Quality Complaint Report is available as a standard PV-Works report from the 'Select Report' option (see section 10.2). The report is a print out of the product quality complaint and its investigation.

It will only be used if the case has a PQC case number, i.e. it cannot be used to print cases in the database that are adverse events but are not associated with product quality investigations.

Note that certain boxes (particularly narratives) have the potential to contain more data than may be printed in the allocated space. When this occurs the program will print data until the box is filled and the remaining text will be printed on a continuation page. This approach allows the appearance of the report to remain standard. All continuation text blocks will have an appropriate heading. The format of the report is defined in a separate Report Specification document (Internal use only).

Product Quality Complaint Reports can be marked as "draft" or "official".

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15 Function Keys

You can navigate around PV-Works using keyboard functions. The tables below explain the keys functions available

15.1 Menu Options

To	Press
File Menu	ALT + F
Duplicate search	ALT + D
Reports Menu	ALT + R
Tasks Menu	ALT + T
External Menu	ALT + E
Help Menu	ALT + H

15.2 Moving between data entry screens and multiple records

To	Press
Next data entry screen	PAGE DOWN
Next record card (right)	RIGHT ARROW
Previous data entry screen	PAGE UP
Previous record card (left)	LEFT ARROW
Last record	CTRL + DOWN ARROW
First Record	CTRL + UP ARROW
Next Record	CTRL + LEFT ARROW
Previous Record	CTRL + RIGHT ARROW

15.3 Moving between fields and around the screen

To	Press
Backwards between fields	SHIFT + TAB
Display a drop down list	F4
Down a drop down list	DOWN ARROW
Down a scroll box	DOWN ARROW
Down radio buttons	DOWN ARROW

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Forwards between fields	TAB
Up a drop down list	UP ARROW
Up a scroll box	UP ARROW
Up radio buttons	UP ARROW

15.4 Updating records

To	Press
Add a new record	CTRL + ' +'
Cancel changes	ALT + C
Clear a check box	SPACE BAR
Delete a record	CTRL + -
Save a record	ALT + S
Save and Exit	ALT + X
Select a check box	SPACE BAR
Undo typing in a text field	Shift F10

15.5 Editing text

To	Press
Copy text	Highlight text and CTRL and C
Cut text	Highlight text and CTRL and X
Highlight Text one word at a time	CTRL and SHIFT and ARROW KEY
Highlight Text one word at a time	SHIFT + ARROW KEY
Select all text	CTRL + A
Paste Text	CTRL + V
Undo Typing or last action	CTRL + Z

15.6 Help keys & Exit

Help	F1
Exit from current window	ALT + F4
Exit from PV-Works	ALT + F4

16 Querying Case Data

16.1 Grid Introductions

The query tool in PV-Works is both powerful and flexible. Based on a mixture of pre-defined queries that accept parameters to make their application generic and a function that allows a user to build their own query, the potential exists to answer any question. The standard library of queries provides a sample set that answer process question such as "which cases need coding?" as well as safety questions such as "do we have any cases where product X was administered and clinical sign Y occurred?"

The results are returned to an Excel-like grid that allows the user to sort, filter and group data to find any subset. The user may also alter the display layout by adding, removing and re-ordering columns. Finally, the results may be output – printed or exported to Excel.

In the PV247 system the available query list is determined by Assured. In a hosted PV-Works environment or a local installation, the customer's system administrator may add further queries using the PV-Admin tool.

In order to control the overall performance of PV-Works and prevent a single user 'taking over' the database, two checks have been added:

a) a warning that more than 'x' cases have been found as a result of the query. After acknowledging the warning, the user may continue with the query, but is now aware that the display of results will not be instantaneous

b) an 'error' that states that more than 'y' cases have been found as a result of the query and that this is too many to process. This prevents a user running a query that consumes too many resources.

16.2 Query Selection Panel

The left hand side of the main screen holds a list of queries separated into Query Blocks – the currently selected query will be highlighted accordingly. The following sample blocks may appear:

- Workflow / action board
- Pre-defined queries.
- My queries.
- E-reporting.
- My favourites.

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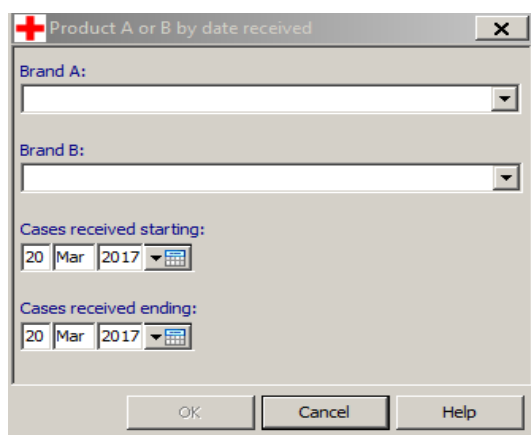Query selection functionality:

- Collapse or expand the whole list of queries using the buttons shown below.
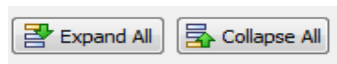
- Expand a single query block by clicking on .

- Close a single query block by clicking on .

- Run a query by clicking on it.

The execution of a predefined query will be performed when the query is selected from the main screen list. Any parameters associated with the query will be presented to the user in the standard popup box, before the results are presented in the main results grid.

Figure 46: Sample Parameter screen

Figure 47: Query Results

16.3 Case Display Grid – Results Population

The purpose of the main screen case grid is to display the results of the selected pre-defined or a user-defined query.

Once the query has executed each individual case may be opened for edit by double-clicking any part of its row in the grid. Alternatively, a different function may be executed by selecting the case (click once on its row) and then select the appropriate function (e.g. coding, assess, report etc.). The results set can also be manipulated within the grid using the standard grid functionality, namely:

16.3.1 Sorting Results

Sort each column (ascending or descending) by clicking the column header. Click the column once and its data are sorted in ascending sequence. Click it again and the sort becomes descending…. And then ascending and then descending.

16.3.2 Filter Results

Filter the display based upon the contents of each column using the dropdown list

This displays a list of values that are present in the column. Click on one item to filter the results grid to show only records for that value.

When a column has been filtered, its 'black arrow' changes colour to blue to indicate this fact:

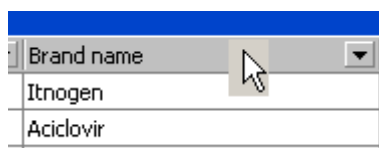Remember the filter of '(All)' to return the display to all records for that column.

16.3.3   Grouping Results

The area above the Column Headings is the 'grouping bar' (see below) and is used to group the grid records into user-defined sets.
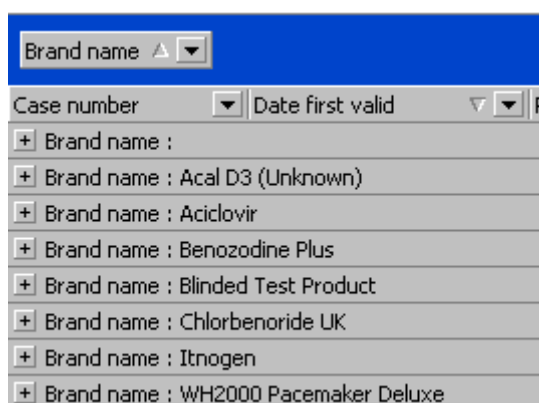
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Place the mouse over the column heading e.g. 'Brand name'

Hold the left mouse button down and drag the column title up into this 'grouping bar' and release the mouse button. (You can drop this title anywhere).

You can open and close a group of records using the '+' and '–' button to the left of the group title.

You can perform the following operations on the cases within a group:

- Update, report, code a case
- Apply a filter to a group
- Apply a sort to a group

Note it is possible to group more than one item e.g. brand within country of occurrence (or vice versa).

16.3.4 Changing the columns in the results grid

Re-order the columns by dragging the column header to its new grid position.

To remove a column from the results grid:

- Click on the column heading and drag the column heading to an area outside of the grid. Release the Mouse button. The precise location of this "drop" point is not critical but it must be outside of the grid. You can tell that the location is suitable as the mouse pointer changes shape to:
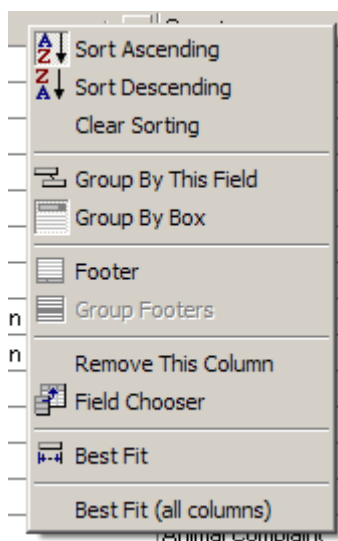

- Alternatively, right click on the column to be removed from the grid and select the 'Remove This Column' option.
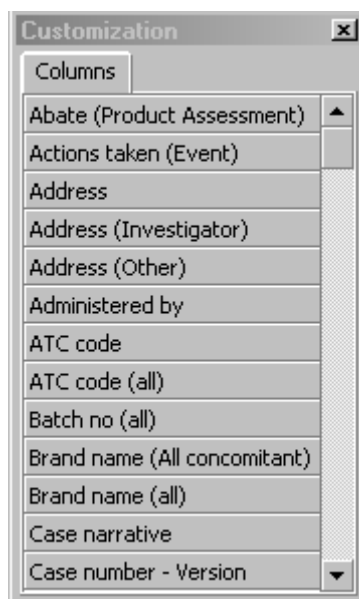
Note that "deleting" a column is only removing it from the results grid, not from the database.

To add a column to the results grid:

- RIGHT click on any column heading to display the following sub-menu:

- Click on 'Field Chooser' and a menu of available fields will be displayed similar to:

- Find the field you wish to add from the list.

- Click on the column name and drag the column name to the vertical line that separates the two columns in the grid column titles where you wish to add the new column. Note the green arrows indicating where the column will be placed. (This is similar to re-organising existing columns in Exercise 4).

- Release the Mouse button

Note that the data of the new column is not always displayed immediately. If it isn't, click the `Refresh` button. As a general principle the more columns you display the worse the performance and the less usable the grid becomes. Just because you can display 100 columns in the grid (and you can) doesn't mean you should!

16.4 Counting Results

It is possible to count records in a grid by adding a "count" function.

To add a grid count, add a footer bar to hold the result:

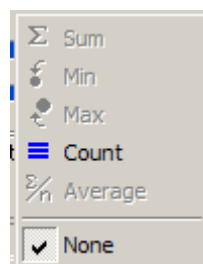- RIGHT click on any column heading to display the following sub-menu:

- Click 'Footer'.

- A grey row appears at the foot of the grid:

This is the grid footer.

- Now define its contents by RIGHT clicking the grid footer to display a choice of two 'None' or 'Count'.

- Select 'Count' and the footer row will display the number of records in the grid, i.e. the number of results.

16.5 Printing the results grid

It is possible that a user may want to produce a simple print out of all or part of the results grid. To achieve this, it is possible to print the grid using the print button .

Note that only the defined data columns in the current display configuration will be printed, and collapsed groupings will not be expanded.

16.6 Exporting grid results

The data presented in the grid may be exported to one of the following formats:

- Text file.
- HTML file.
- Excel file.
- Clipboard copy.

To export the results grid, click the 'Export' button and select the required format from the list.

Figure 48: Export format selection

With the exception of the 'Clipboard' option, the user will be presented with a dialogue box to select the folder in which the exported file will be stored and the name of the file.

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Figure 49: Export 'Save as' dialogue screen

A sample of exported grid data in html format is given in Figure 50.

Note that if the grid has been grouped prior to export then the grouping is reflected in the resulting export file. However, each 'group of data' is presented in its expanded form (i.e. not with the group collapsed and hiding data as is possible ion the screen).
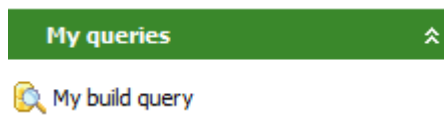
Figure 50: Sample Exported grid data

Case number - Version	Case number	Internal case number	Date first valid	Reported name (primary product)	Case owner	Reported name (all products)	Case type
2017-UK-0060	2017-UK-0060	00000003716	10-Feb-2017		Paul Millington		Spontaneous
2017-UK-0063	2017-UK-0063	00000003722	6-Mar-2017		Paul Millington		Spontaneous
2017-US-0011	2017-US-0011	00000003724	3-Jan-2017		Paul Millington		Spontaneous
2017-US-0001	2017-US-0001	00000003647	3-Jan-2017		Chaitanya Adudodla		Spontaneous
2017-US-0010	2017-US-0010	00000003723	3-Jan-2017		Paul Millington		Spontaneous

16.7   Build a Query

The build-a-query function allows the user to define the search criteria from a pre-defined list of data fields in order to answer questions not addressed by the pre-defined queries. For performance reasons a user is advised to run a pre-defined query in preference to building their own query.

Build-A-Query may be accessed from two points:

- the find case binoculars icon from the Standard Main Screen

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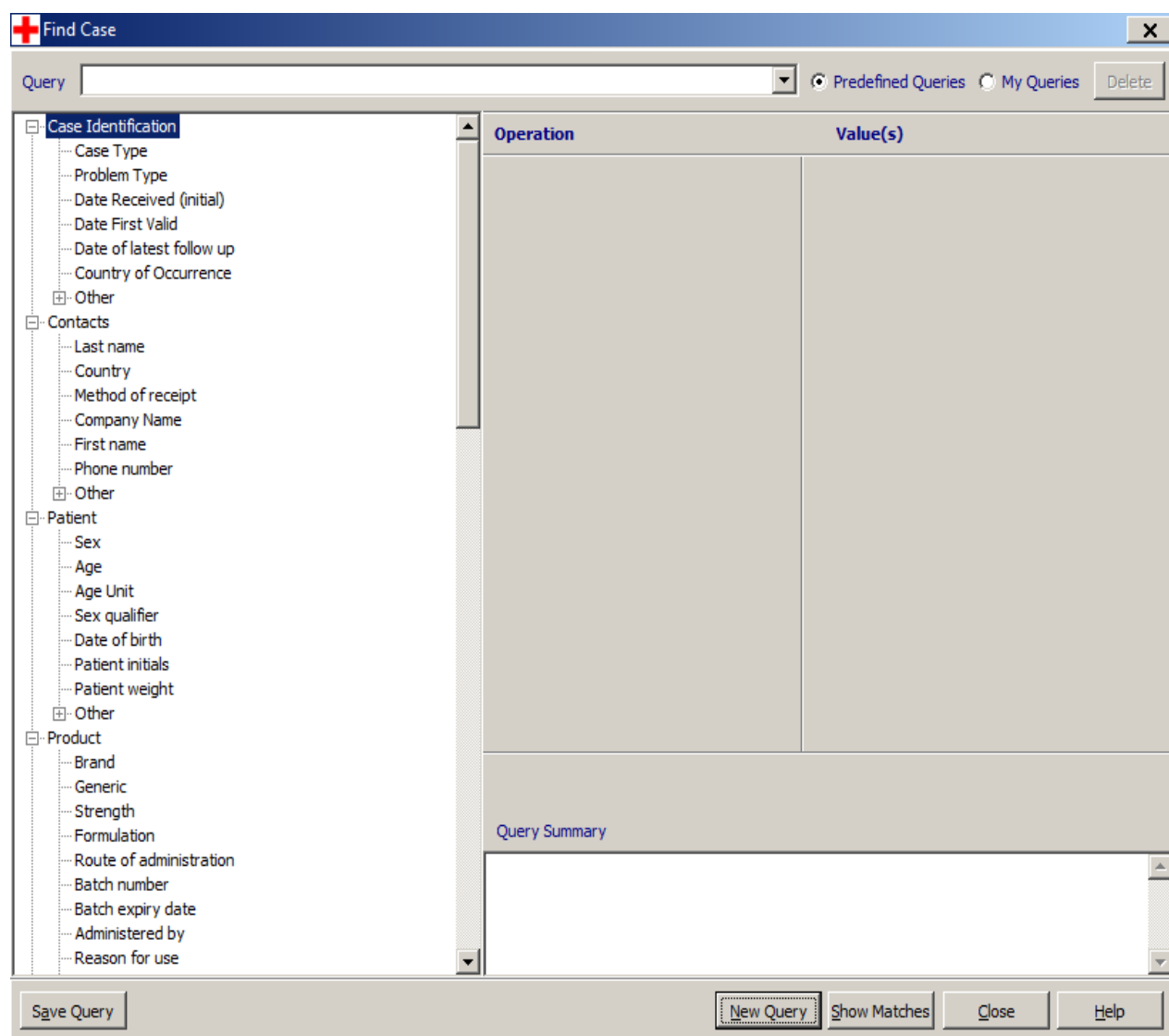
- as a query from the 'my queries' list

The "Find" button method is discouraged because the "query" method provides the user with an opportunity to modify (and re-save if necessary) the definition as well as manipulating the results.

The Build A Query screen (Figure 51) shows a list of fields that can be chosen as filter criteria. These are presented in sections that reflect their location in the case update / edit screen.

Figure 51: Build a Query screen

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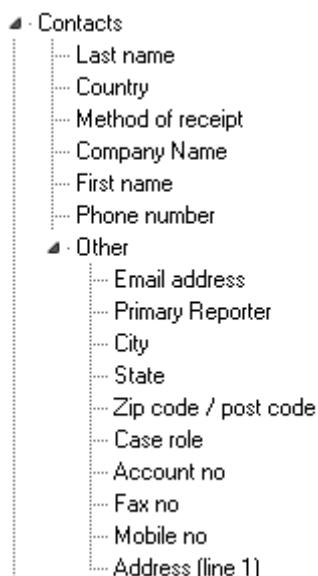
Within each section the fields are divided into two groups:

- Fields that are always visible – as these are thought to be the more important or commonly used filters
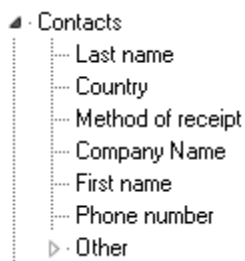
- Fields that can only be displayed by opening the 'other' list.

Once a filter field is selected, the user must choose an appropriate operation to apply to it (e.g. 'equals', 'is not', etc.) and also a data value for the comparison.

The operators that are available will depend on the type of field selected:

Field type	Operators	Note

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String / text - data field controlled by vocabulary list (i.e. a dropdown list)	<> = is ANY OF is EMPTY is NOT is NOT EMPTY	<> means "not equal to" "is ANY OF" is used with fields controlled by vocabulary lists so that the user can select more than one item (e.g. route = oral or rectal).
String / text - free text entry	<> = CONTAINS is EMPTY is NOT EMPTY STARTS WITH	<> means "not equal to"
Number	< <= <> = > >= is BETWEEN is NOT BETWEEN	
Date	< <= <> = > >= is BETWEEN is NOT BETWEEN	
Record exists	DOES NOT EXIST EXISTS	This is a special field type to test whether a record is present or not. For example it can be used to find cases where no assessment has been made

The search criteria can be extended with as many data fields as necessary. All search items are joined together with 'AND' logic.

The cases that meet the conditions specified by the filter are displayed in the main screen grid (see Figure 47).

17 Case Lock

PV-Works provides the ability to lock a case in order to prevent it being accessed. It is also possible to unlock a locked case.

How to lock a case

1. From the main screen select menu option 'File' -> 'Lock Case'.
2. The user must enter their 'Electronic Signature Authorisation' when prompted.
3. The 'Lock case' screen is displayed as shown in Figure 48.

Figure 52: Lock / Unlock Case screen

4. Select a 'Reason for Change'.
5. Selecting **OK** takes you back to the main screen which will display a "case status" value of "locked" to show that the case is locked. See Figure 53.

Figure 53: Case Lock – locked case

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How to unlock a case

1. Highlight the locked case in the main grid.
2. Select menu option 'File' -> 'Unlock Case'.
3. Enter an 'Electronic Signature Authorisation' when prompted.
4. Select the 'Reason for change'.
5. Selecting **OK** takes you back to the main screen and the lock has been removed. The case 'Status' is shown as 'open'.

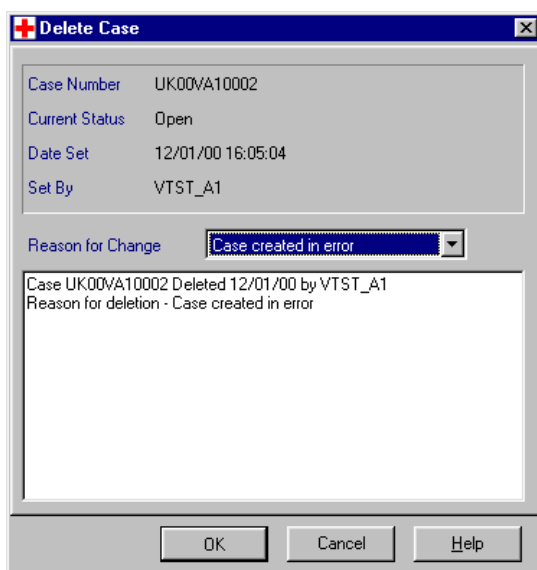Ennov property. Reproduction or disclosure strictly forbidden without prior written consent.

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18 Delete Case

PV-Works provides the ability to delete cases from the system. This option does not actually delete the case from the database but changes the 'deleted' flag for the case to **Yes** (the default is No). This case is then unavailable for queries, data entry and reporting activities.

If a case is deleted in error there is a Case Undelete option available to Systems Administrators only, this will restore the case to the database.

How to delete a case:

1. Highlight the case to be deleted in the main grid.
2. Seelct menu option '**File**' and then '**Delete Case**'. The 'Delete Case' screen will be displayed (see figure 54).
3. The screen displays the current case number and case status information.
4. Select a 'Reason for Change' from the drop down list.
5. Click **OK** to delete the case.
6. The system will return to the main screen, but the deleted case will no longer be displayed.

Figure 54: Delete Case screen

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19 Copy Case

On occasions users may wish to generate two cases from a single call. To reduce the data entry necessary for this, it is possible to copy the data of one case as a starting point for a new case.
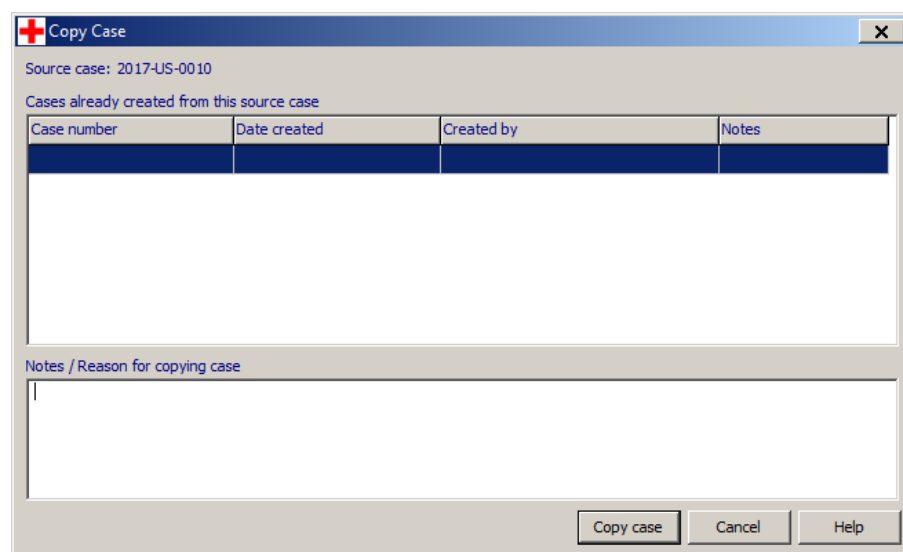
Thus the user will enter all data for the first case and will then copy it to create a second case in which certain data will need to be changed to make the case unique. The copied case will be assigned a new case number and will show the number of the source case as a 'linked case'. The source case will also record the numbers of all cases generated from it as 'linked cases'.

Once the second case is created, data amendments to the original case are NOT replicated into the copy (or vice versa). Similarly coding and assessment data are not copied into the copied case; this ensures that these are performed individually for each case.

It is possible to copy a case as many times as necessary to create 'n' copies. Repeating the steps described below generates each copy. It is also possible to create a new case by copying a case that was previously a copy of another case!

To copy a case, the user will select the original case on the Main Menu and will then choose the option 'Copy Case' from the File drop down menu. A screen similar to Figure below will be displayed:

Figure 55: Copy Case screen

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The system will display the numbers of any other cases copied from this source case. Before clicking the 'copy case' button, the user must specify a reason for creating the copy in the 'notes/reason' window.

PV-Works will create a new case that contains all data from the source case. A progress bar similar to Figure 52 will indicate progress should the copying process take a substantial amount of time:

Figure 56: Copy Case progress bar
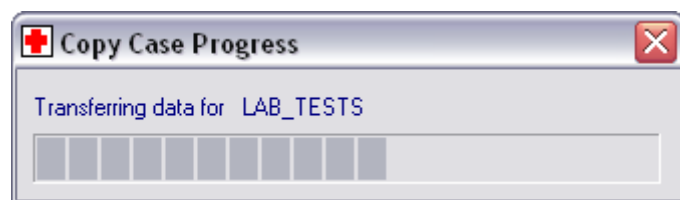
When all source data is copied, PV-Works will display the 'new case' in the standard Data Entry screens. At this point, the new case has not been saved to the database and the user is able to cancel the creation of the copied case and leave the database unaltered.

The user should amend the copied case to distinguish it from its source. When the user saves the case using the 'Save and Exit' button, an additional warning is given as shown below.

Figure 57: Warning message when saving copied case
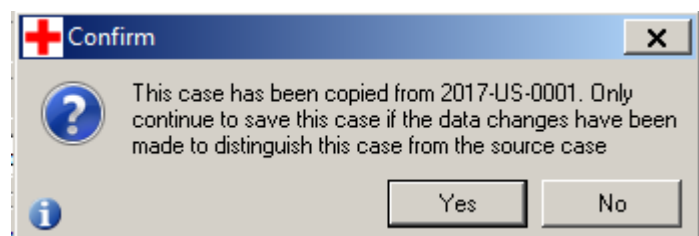
Once created in this manner, the new case behaves as an individual and separate case with no reference to its source case other than a note of its origin.

The 'Case Identification' screen of the Data Entry / Update function will indicate that the case was originally copied from another. A case link entry will be given and the source case number will be displayed as part of the 'case' block (see Figure 58). The user is able to update, browse the source case using the buttons shown.

Figure 58: Case Identification screen showing case copy information

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20 Electronic Signature Authorisation

The comprehensive PV-Works security module ensures that only authorised users have access to particular system functions. The electronic signatures function takes this a stage further by ensuring that the user invoking a key function is truly the logged-on user and by recording their authorisation to carry out the function.

The PV-Works functions to which electronic signatures may be applied are:

- Generating a FDA 3500 report
- Generating a CIOMS-1 report
- Creating a version of a case
- Locking a case

Each of these is controlled by a separate system option so that Customers may decide which function(s) require electronic signature.

Figure 59: Electronic Signature Authorisation Question
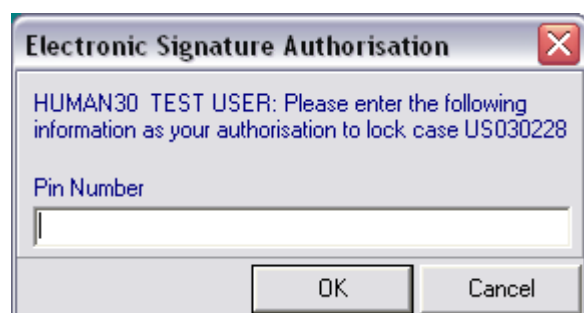
These report functions can be controlled more tightly so that the electronic signature check only applies to the generation of 'official' reports, i.e. those without the 'draft' heading and in a format that can be submitted to a Regulatory Authority.

The password check follows the same principles as that defined for logging in, using any of the second-level password tests defined by the System Administrator. It is also possible to define the user account password used for log-in as a password test and for this to be the only test type, thus enforcing re-entry of the main user password.

Access to a function that is protected with an electronic signature will only be granted if both of the following are met:

a)   The user has been granted the necessary security rights.

b)   The user responds correctly to the electronic signatures password check.

A record of the case number, password test, date and time and PV-Works function that was authorised is recorded in the database.

To prevent a colleague misusing the rights of a user who leaves a screen unattended, the PV-Works session will be locked out after a time period set by the System Administrator (see figure 60). The session may be re-started without loss of data by re-entry of the user's password. However, the session may also be cancelled (with loss of any unsaved data changes) to overcome situations where a user has left the office and the PC needs to be switched off.

Figure 60: Electronic Signature Lock out
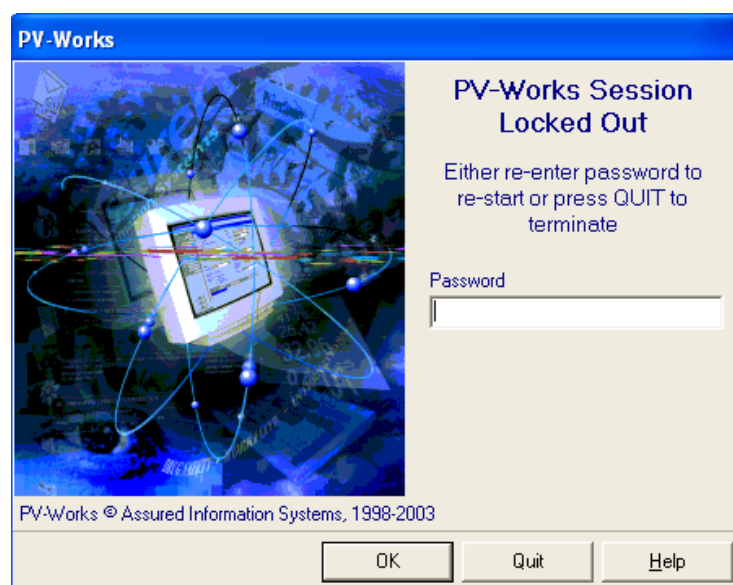
21 Case Linking

PV-Works provides the ability to link cases together for such reasons as 'Same patient', 'Duplicate', 'Parent-child report'.

How to link a case:
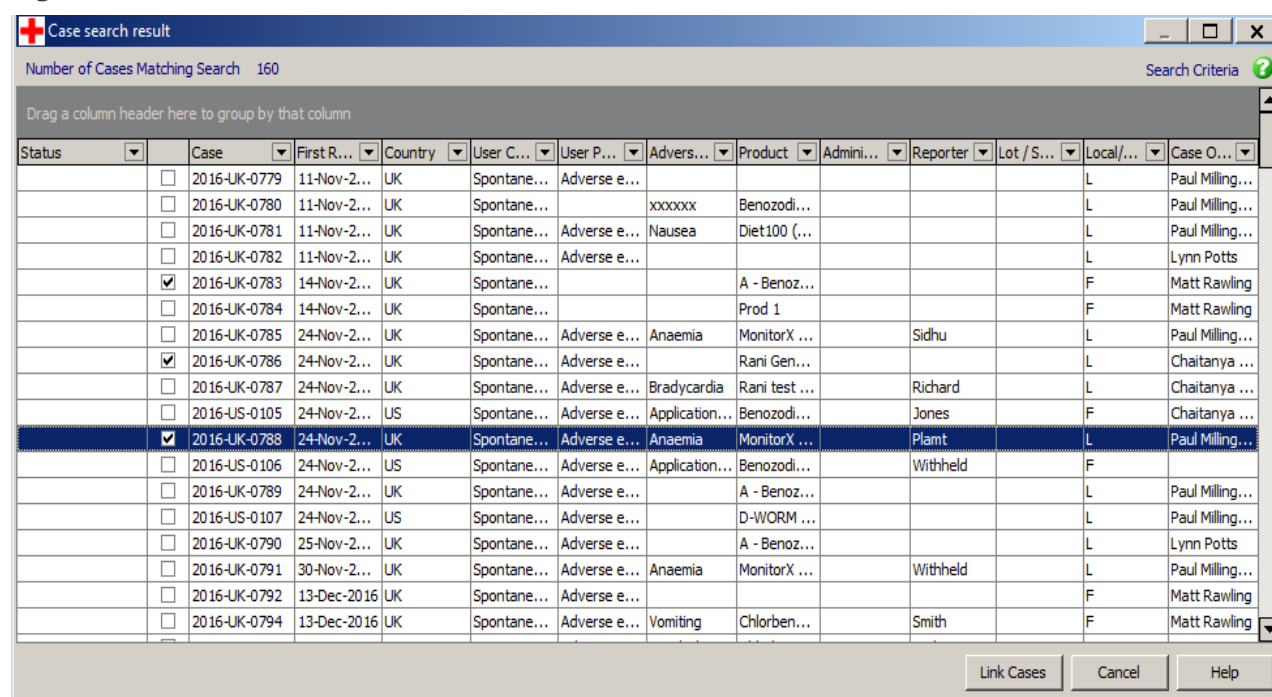
1. You can access the Link Cases option from either of these 2 ways:

    ❑   The Data Entry/Update screen 'Case identification' using the Link button

    ❑   From the menu options '**Data**' -> '**Link Case'.**

2. The system displays the Find Case - Linking records search screen. This screen has the same functionality as the Find Cases search screen. For further information see section 17.7.

3. Once you have completed the search screen the system displays any matching cases on the Link Marked Cases screen.

Figure 61 - Linked Marked Cases

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4. Select a case you wish to by ticking its checkbox i.e. ☑ 2016-UK-0713

5. Continue to selecting the cases to link in the same way.

6. If you need to de-select a case then simply click on its checkbox to untick it.

7. Once you have selected all of the cases to be linked then click '**Link Cases'** and the 'Reason and Type of Case Link' screen will appear (Figure 62).
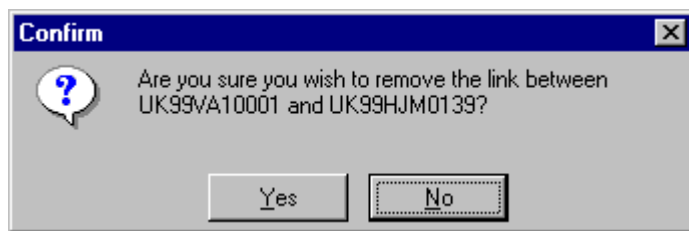
Figure 62: Reason and Type of Case Link

8. This screen needs to be completed for each case being linked. Clicking '**OK'** moves the system onto the next record to be linked. Both of the fields required are Mandatory.

- Type   The type of case linking (e.g. Duplicate, Same patient).
- Reason   The reason why they are being linked.

9. Once you have completed all of the links the system returns to the previous screen.

How to remove a linked case

1. You can remove linked cases from the 'Case identification' screen.

2. Highlight the case you wish to remove and click Remove link .

3. The system will ask you to confirm removing the link between the two cases. Selecting 'Yes' removes the details from the screen and you can then repeat the process for further linked cases.

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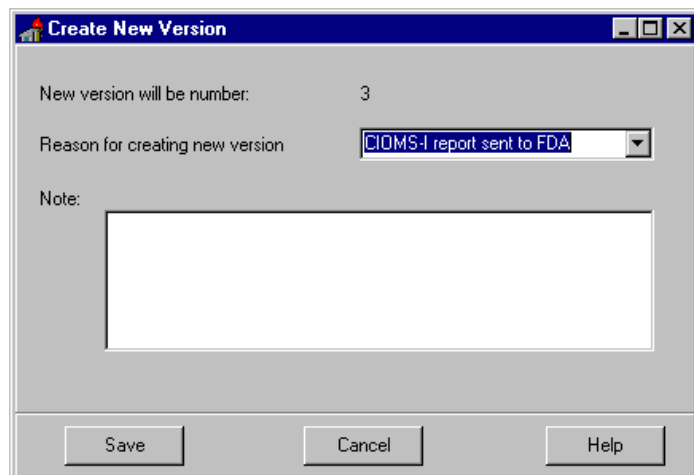**Figure 63: Remove link confirmation message**

22 Case versioning

Users may wish to take 'snapshots' of the data in a case at a particular time so that subsequent reference may be made to the data at a critical point in the process. A typical example of this is the moment when a regulatory report is sent to an authority, thus allowing the company to answer any queries on this case based on the information known at the time of the report as well as on the latest data.

Changes to the case are made to the master version of the case and are not replicated in any of the 'snapshots'.

Case versioning provides a further method of tracing data changes to a case.

A case version is created from the File menu of the Main Menu screen. Before a version is created the user must give a reason for taking the snapshot. The version number is assigned automatically.

Create new case version screen

Access to a specific version of a case is controlled via the Main Menu. When a case number is set and verified on this screen, the version being accessed is the master version (zero).

From the File | Select Version the user can display a screen of all versions and select one to view and/or report.

Select version of case
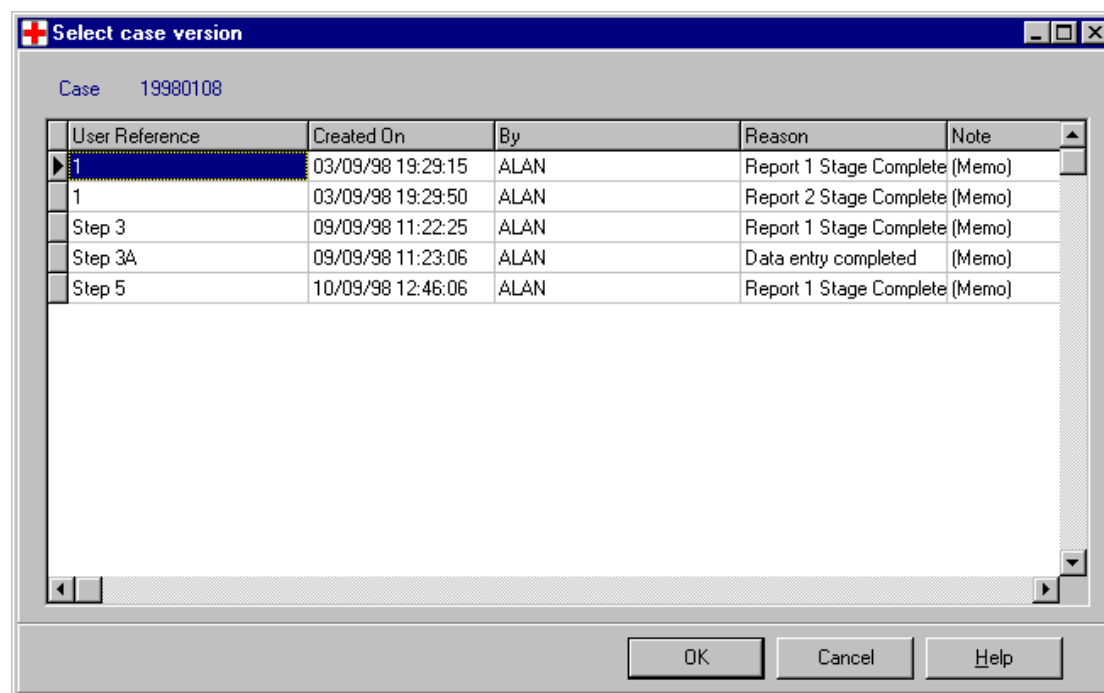
Once a particular version is selected:

- the version number will be displayed on the Main Menu

- the version number will be displayed on all subsequent screens (typically in the top panel next to the case number)

- access to all functions of PV-Works will be granted in read-only mode (for non-master versions)

If the Main Menu displays a case version that is not the master version, the user can re-select the master version by choosing the 'Select Version' option from the File menu. An additional button appears on the screen above 'Select Master Version'.

23 Case Comparison

The Case Comparison utility can compare two cases or two versions of the same case and report differences. Its use includes:

- Comparison of two cases suspected to be duplicates of one another

- Comparison of two versions of the same case to determine the changes made to the case between two time points

There are three methods of invoking a case comparison:

- From the File Menu

    From the 'File' menu of the Main Menu screen, the user will select the 'Case Comparison' function

- From the results on the Main Screen Grid (see figure 4.2.2)

    The user can select one (or two) cases by clicking the results row. Use ctrl-click to select two rows. With the row selected, right click the mouse to select the option "Compare Cases". The advantage of this method is that it will pre-populate (see.below).

    Note that if more than two cases are selected then the option "Compare Cases" is greyed out as it is only possible to compare two cases at a time.

Selection of Case Comparison via the main grid

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- From the 'Duplicate Check Results' screen (see section 5.2.4)

    This screen follows the same approach as the main screen grid in that the user may select one (or two) cases by clicking the results row and then selecting the option "Compare Cases" from the right-mouse click menu.

Each of these starting points will display the following pop up screen from which the cases are selected for comparison and results shown. The File Menu approach will not show any case numbers, while the other two methods will show one or two case numbers.

Select cases for comparison

Case comparison results

The user can see differences in three categories, each broken down by functional area:
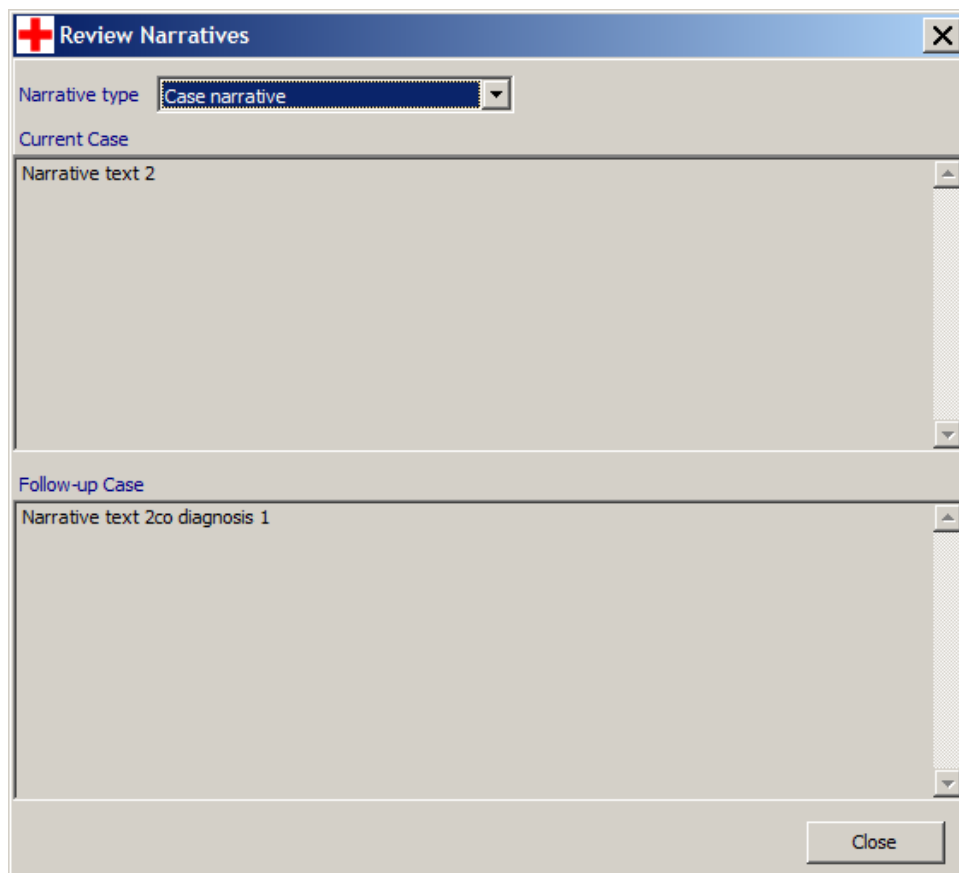
- Records removed
- Records modified
- Records added

In defining removed / modified added "case 1" is considered to be the base and "case 2" its comparator.

A grid at the bottom of the screen allows the user to see the details of the records in the selected category. That is by clicking on the label "Patients", the user will only see differences related to Patient data. In this manner the user can review differences "section by section". At the same time the user has full grid manipulation functions such as sort, group and filter that can be applied to the results.

In addition the user is presented with the both the old and new case narrative via the "Review Narrative" button.

Case Comparison – review narrative screen