Assured Information Systems

PV WORKS
PHARMACOVIGILANCE
WORKFLOW MANAGER

PV247 Configuration Guide

Completed Date 25 Feb 2014

Acknowledgement of Trade Marks

PV-Works® is a registered trademark of Assured Information Systems Ltd.

Assured Information Systems Ltd acknowledges the trademarks of the companies and products referenced in this document.

CONTENTS

LIST OF FIGURES

1 Document Information

1.1 Software Release

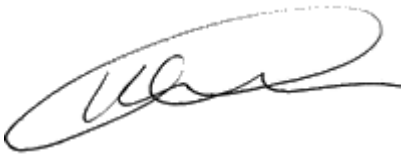
This document relates to PV-Works versions Human 3.7 and Vet 4.1

1.2 Authorisation

The PV247 Configuration Guide for PV-Works versions Human 3.7 and Vet 4.1, dated 25 Feb 2014, is authorised for release to customers.

Author

M R Walker



Mark Walker
03/03/2014 12:36:17 GDT
Author

QA Director

K W Edmonds

Keith Edmonds
Monday, 03 March 2014 15:35:06
Document Review

1.3 Document History

Product Version	Completed Date	Author	Revision Details
Hum 3.7 & Vet 4.1	25 Feb 2014	M R Walker	• Initial Release

2 Overview

2.1 Scope of this Document

This Configuration Guide describes the additional functionality provided to allow PV247 administrators to configure specific aspects PV-Works.

This document describes the functionality of PV-Works Configuration screens including its interfaces and dependencies upon third-party software. It does not specify the functionality of any third-party software.

2.2 PV-Works : General Description

PV-Works combines a commercial workflow product with flexible product safety functionality to produce an integrated application that meets both business and regulatory needs. 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 same system is suitable for pharmaceutical companies, generic manufacturers, CROs, medical device manufacturers and, in fact, any company that needs to comply with the requirements of drug safety.

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 gathered, managers are able to measure actual performance against targets, allowing the identification of bottlenecks, over-allocated staff, under-tasked staff and training needs.

The process management function is optional. Whether or not it is implemented is a local customer decision. Even without this function, PV-Works still offers process control functions with individual task assignments and a regulatory clock.

The design of the pharmacovigilance modules supports:

- international reporting requirements for single case reports and line listings from the key regulatory authorities world-wide
- generation of electronic reports in format for transmission to regulatory authorities and licensed partners. Cases can also be imported into PV-Works in the same format.
- easy to use, intuitive data entry and review screens that may be tailored to meet local business requirements
- assessment of case seriousness, expectedness and causality
- automated expediting of cases to subsidiary offices and partners
- full compliance with authority guidelines, including electronic reporting
- fully integrated proactive workflow
- several coding dictionaries with emphasis on MedDRA and VeDDRA

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. This includes defining specific codelist 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.

2.3 Background to the Pharmacovigilance Process

All companies that test, manufacture and market medicinal products are responsible for collecting and disseminating product safety information. This responsibility covers prescription and 'over the counter' medications including biologics and medical devices. Safety data is processed in line with global regulatory requirements both at an individual case level and cumulatively to provide product safety profiles.

Despite continuing efforts towards a standard, harmonised international procedure, formats and time-lines for reporting safety data still vary from country to country.

The initial report of an adverse event to one of their products may be received by the manufacturer or their agent from one of many different sources. For marketed products the consumer, a health care professional, a regulatory authority or published literature are the most common. Data quality and completeness varies widely according to data source. The manufacturer is able to exert most control over data quality with information arising from clinical trials that it has sponsored. Follow-up requests for further information are commonly required in order to make a reasoned assessment of a case.

Generally the manufacturer's approach is to establish a separate 'Product Safety' or 'Pharmacovigilance' function responsible for the collection, analysis and reporting of safety data. This function may be centrally located with all information funnelled to one point via fax or e-mail for consolidation, assessment and world-wide reporting. Alternatively, larger companies may establish a corporate safety group together with local safety offices in major geographical markets. In this decentralised model, the local offices are empowered with local or regional responsibility for pharmacovigilance, while the corporate group oversees the products' global safety profile.

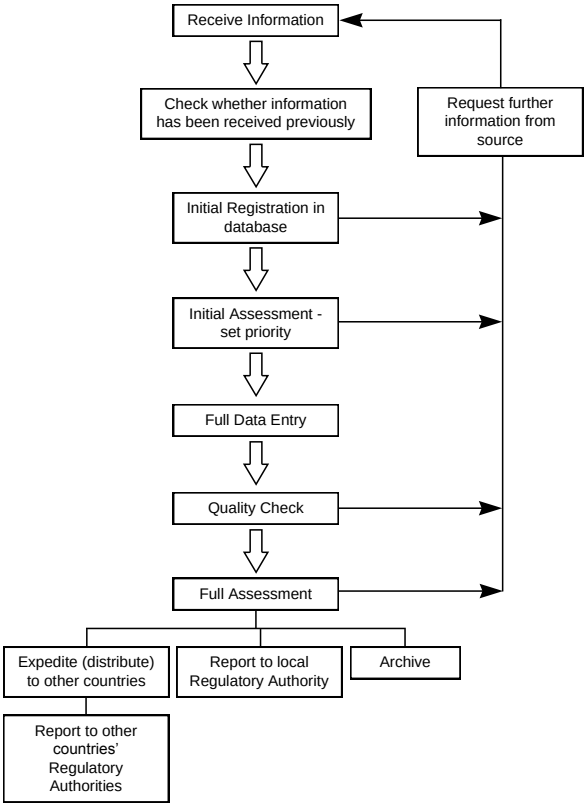
Whatever the corporate structure of pharmacovigilance and the geographic spread of its operation, a computer system to support the above needs must:

- support the pharmacovigilance business process
- be flexible to adapt to individual company organisation structures and procedures
- provide ready compliance with international and national regulatory requirements
- operate in an international setting
- ensure data security and integrity with comprehensive access controls
- promote compliance with quality objectives and target reporting times

Fundamentally, pharmacovigilance is a business process. The process is complicated by the variety and quantity of cases handled, the need to meet deadlines derived from both business and regulatory sources and the number of 'hands' through which a case passes from receipt to closure. Figure 1shows the steps of a simplified process for adverse event reporting.

It is immediately recognised that the process must be controlled if temporal and quality goals are to be met. But this process is no more complicated than others found in manufacturing, banking and other business sectors where software already supports workflow management.

Figure 1 : Sample Pharmacovigilance Workflow Process



Process or workflow management is an integral part of a product safety system and one that must be incorporated from the outset.

Focusing on the business processes of pharmacovigilance is not to deny the importance of the underlying database and its need to be comprehensive and adaptable to changing business and regulatory requirements. However, the database is a tool that supports the business, it can not drive the process.

2.4 Introduction to Pharmacovigilance Functionality

PV-Works allows users to enter, update, query and report adverse event data. Reporting includes regulatory and internal report formats for individual cases as well as multi-case reports.

The data entry functions provide a flexible environment that can be configured to mirror the actual input forms as closely as possible whilst retaining key functionality such as data validation, audit trail and data notes.

The PV-Works database is designed to ensure compliance with the ICH (International Committee on Harmonisation) E2B Guideline that requires companies to submit electronic copies of case data to regulatory authorities. Each data field required by ICH E2B has a clearly defined and documented entry in the PV-Works database.

There are several PV-Works pharmacovigilance functions that may be configured by the user in order to tailor the product to the user's business requirements and processes. These include:

- Selectable screen layouts and order (not available in PV247)
- Customisable report options (not available in PV247)

- Letter templates (not available in PV247)
- System options and defaults
- Codelists of acceptable entries for a field
- Pre-defined queries (not available in PV247)

These functions are the responsibility of the Systems Administrator and are discussed further in the separate Systems Administrator Functional Specification document.

All data changes may be recorded in an audit trail. The audit trail complies with regulatory requirements for recording data changes and may be switched on, case by case, at a specified point in the process, eg after first data entry and quality check.

Internal, working notes may be attached to any field in any data entry screen.

2.5 Introduction to Workflow Management Functionality

PV-Works incorporates an internal workflow engine that controls the processing of each case and gathers performance data about each task. This module is called Pipeline.

The heart of PV-Works's workflow management function is a process template. Each company may define several process templates using a graphical tool to represent the different ways in which cases are handled. The process template may include the business rules that determine whether a particular step is required or omitted.

When a new case is created, one particular template will be assigned to a case. Thus different types of case can follow different processes. For each task within a process template the user may define several factors such as its expected duration and the role or name of the person who should normally perform it.

By reviewing all active processes, PV-Works promotes timely completion of all tasks by presenting a 'to do' list for each user at log-on. Outstanding tasks are colour coded to highlight those that are overdue.

The 'to do' list is fully integrated with the safety functions of the system. A user may click on any task in the list and will be taken to the appropriate part of the system with the relevant data loaded so that the task may be carried out.

Upon completion of an individual task the target dates for all remaining steps are re-calculated. Milestone dates may be defined for each case. These are tasks that must occur by a certain date, for example a 15 day report to the regulatory authority. In calculating new target dates for remaining steps in the process, the system will try to ensure that these key dates are met.

For a workload supervisor or manager additional functions are provided to monitor the current (and future or past) workload of a team or individual. The supervisor may re-assign tasks to other staff to overcome bottlenecks or to handle absences (eg holiday, sickness).

PV-Works collects and stores detailed data describing how each case actually progressed and how each task was performed. There are a number of standard reports and graphs that provide performance measurement and process health checks, such as:

- case volume versus time versus case type
- achieved performance versus predicted / standard times for individual action steps,

workgroups or individuals

The workflow function of PV-Works can also be used to manage processes that are not related to individual cases. For example the preparation and submission of a Periodic Safety Update Report (PSUR) could be defined as a process and its tasks would appear in the PV-Works ‘to do’ list at the appropriate time for each product.

3 Configuration within PV-Works

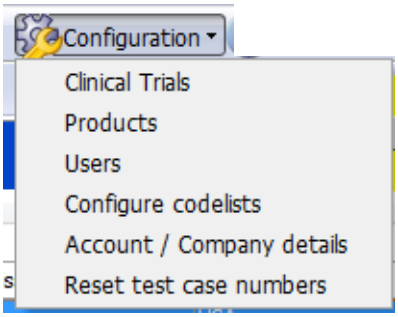
3.1 Introduction

The ability to configure certain key reference data types without the use of a separate Admin application has been introduced for Assured's PV247 solution. Access to the configuration module is controlled by the use of a specific role which must be allocated to a user by an Administrator. Some of the modules described below are only appropriate to Premium PV247 systems and these are clearly indicated in the text.

If any of the PV-Works configuration modules are available to the user, then a "Configuration" button is added to the ribbon bar on the Main screen:

The menu under this button shows the available functions:

Figure 2 : PV-Works Configuration Modules



The available modules are:

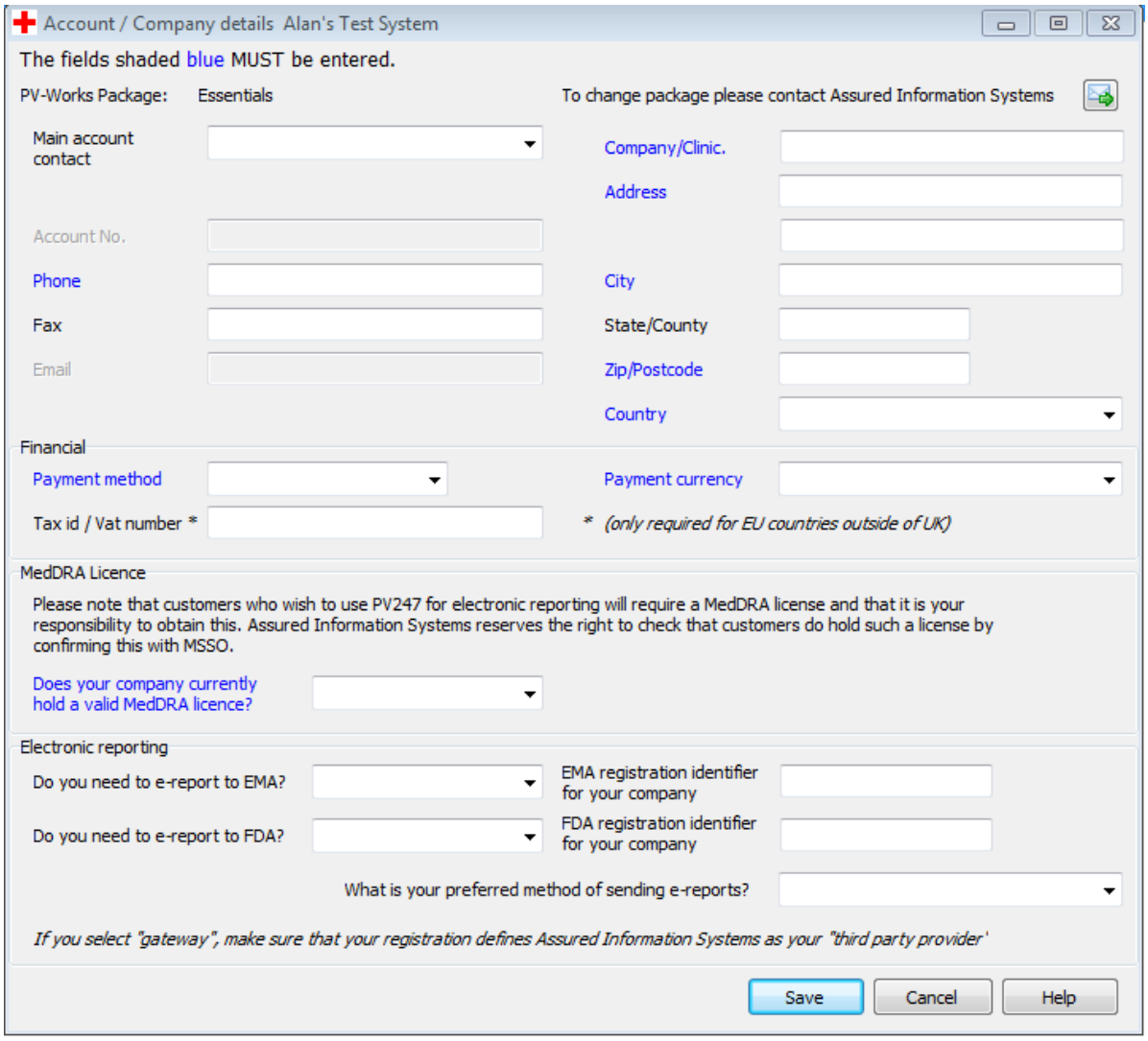
Clinical trials (Human only)	Define clinical trials, their centres and products administered	See section 3.5
Products	Define company products	See section 3.4
Users	Add users to the system	See section 3.3
Configure codelists	Amend vocabulary lists used in dropdown boxes and /or amend the mapping of these items to ICH XML files for e-reporting	See section 3.6
Account / Company details	Update details of the company owning the PV247 system eg names, primary account holder etc	See section 3.2
Reset test case numbers	Soft-delete all cases entered while testing the application and reset case seeds so that the first production case is number 1	See section 3.7
Names and Addresses	Add and edit names and addresses of key contacts such as regulatory authorities, clinical trial centres and local offices	See section 3.8
System options	Amend the values of system	See section 3.9

	options to meet local requirements	
Case Subsetting (Human Only)	Define case subsets	See section 3.10
Re-activate Cases	Unlock locked cases	See section 3.11

3.2 Account / Company details

On clicking the Configuration | Account / Company details option, the following pop-up screen will be displayed:

Figure 3 : Account / Company Details screen



The company details are stored when an account is first created. This screen will allow a user to amend them and is a replica of the web page used when the PV247 account was first created.

Fields whose labels are shown in **blue text** must be completed otherwise the record can not be saved.

Notes:

a) You can change the payment frequency from monthly to yearly (or vice versa) using the payment method.

b) Companies outside of EU and outside of UK can ignore the question on Tax id / VAT number. Companies based in EU should add their VAT number to this screen, otherwise VAT will be added to their invoices.

c) Due it its mandatory nature Assured requires that you maintain a current subscription for the MedDRA dictionary. This is one of the terms and conditions of system use that is included in the legal agreement. (Not applicable to PV247 Vet systems)

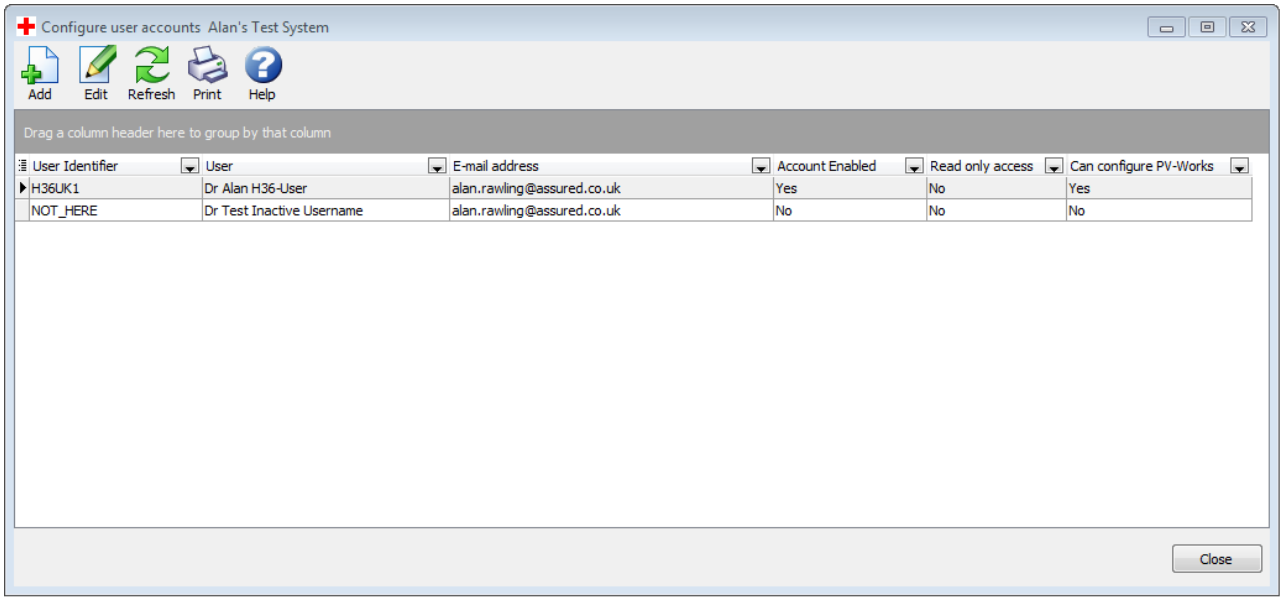
d) The EMA registration number is the sender identifier to be used in XML e-reporting files sent to EMA

e) The FDA registration number is the sender identifier to be used in XML e-reporting files sent to FDA

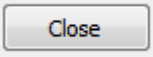
3.3 Users

On clicking the Configuration | Users option, the following pop-up screen will be displayed:

Figure 4 : User Configuration screen



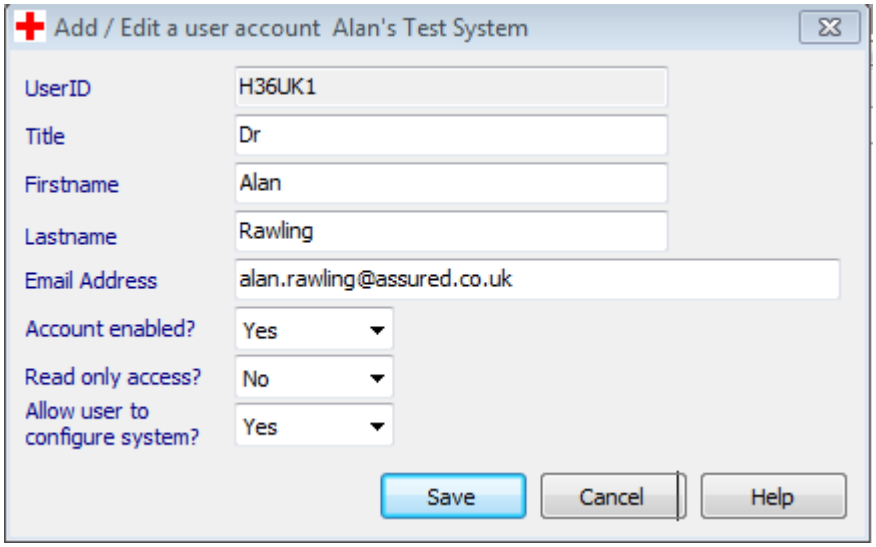
Buttons

Button Function	Function
	Add a new user
	Edit the details of a current user
	Refresh grid results – standard grid behaviour
	Print grid results – standard grid behaviour
	Close the screen

Add / Edit a new user

The screen shown in Figure 5 will be displayed.

Figure 5 : Add / Edit a User



For a new user the UserID is assigned by the system. This is the user's PV-Works "username".

There are three options that can be set on this screen:

a) Account enabled

This Yes/No field controls whether the user is active or not. When a user leaves the company their details remain in the system for regulatory purposes, eg attributing their full name to data entry records. They should be marked as "inactive" (account enabled = No) so that their PV-Works licence may be re-assigned.

b) Read only access?

A user may be granted read access to all cases such that they can not amend case data by setting this field to "Yes".

c) Allow user to configure system

A user may be allowed to configure the system (ie use the functions described in this document) or may be denied this privilege using this option. If granted, then they have access to all of the configuration functions.

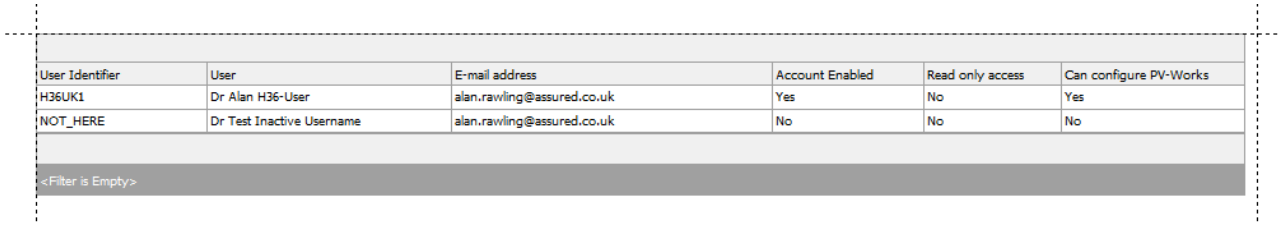
Note it is not possible to set every user to "can not configure". There must be one member of the team who has this right.

When a new account has been created by the system, the new user will be sent an email to confirm its creation. This includes log-in instructions. A copy of this email is also sent to the user who created the new account.

Print:

This function creates a simple listing of the defined users as shown below:

Figure 6 : User list print out



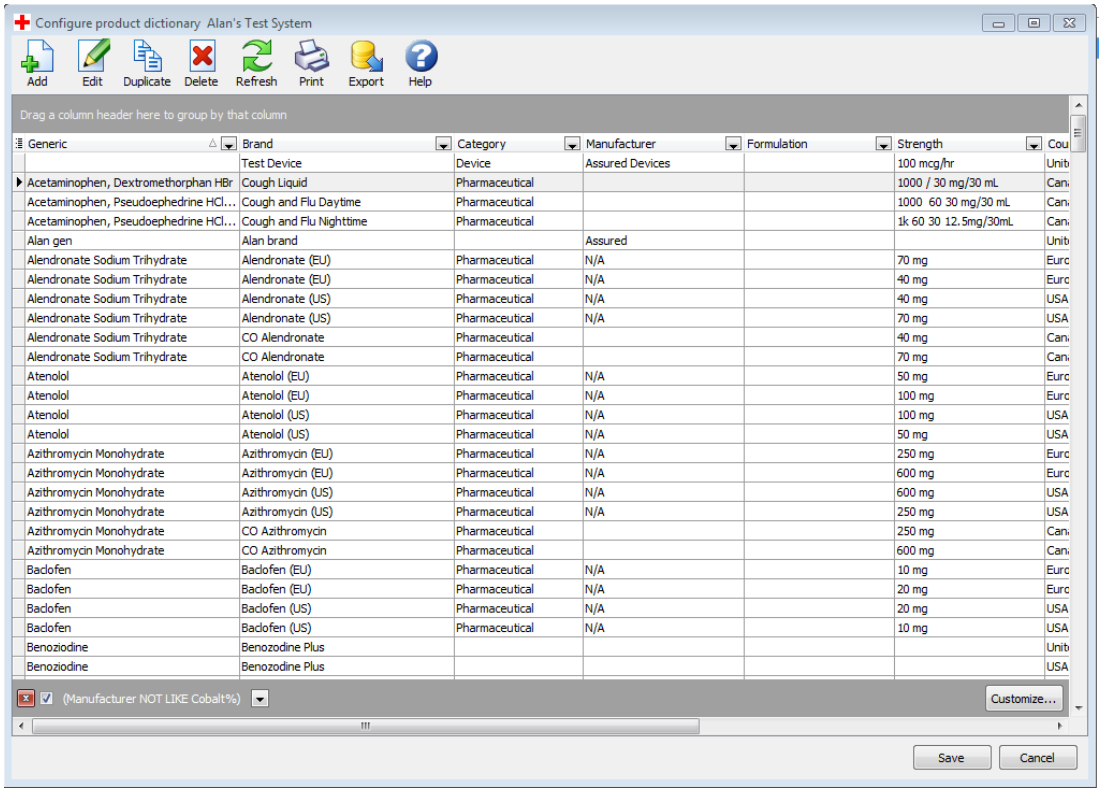
User Identifier	User	E-mail address	Account Enabled	Read only access	Can configure PV-Works
H36UK1	Dr Alan H36-User	alan.rawling@assured.co.uk	Yes	No	Yes
NOT_HERE	Dr Test Inactive Username	alan.rawling@assured.co.uk	No	No	No

<Filter is Empty>

3.4 Products

On clicking the Configuration | Products option, the following pop-up screen will be displayed listing all of the products currently defined:

Figure 7 : Product Configuration Screen



Buttons

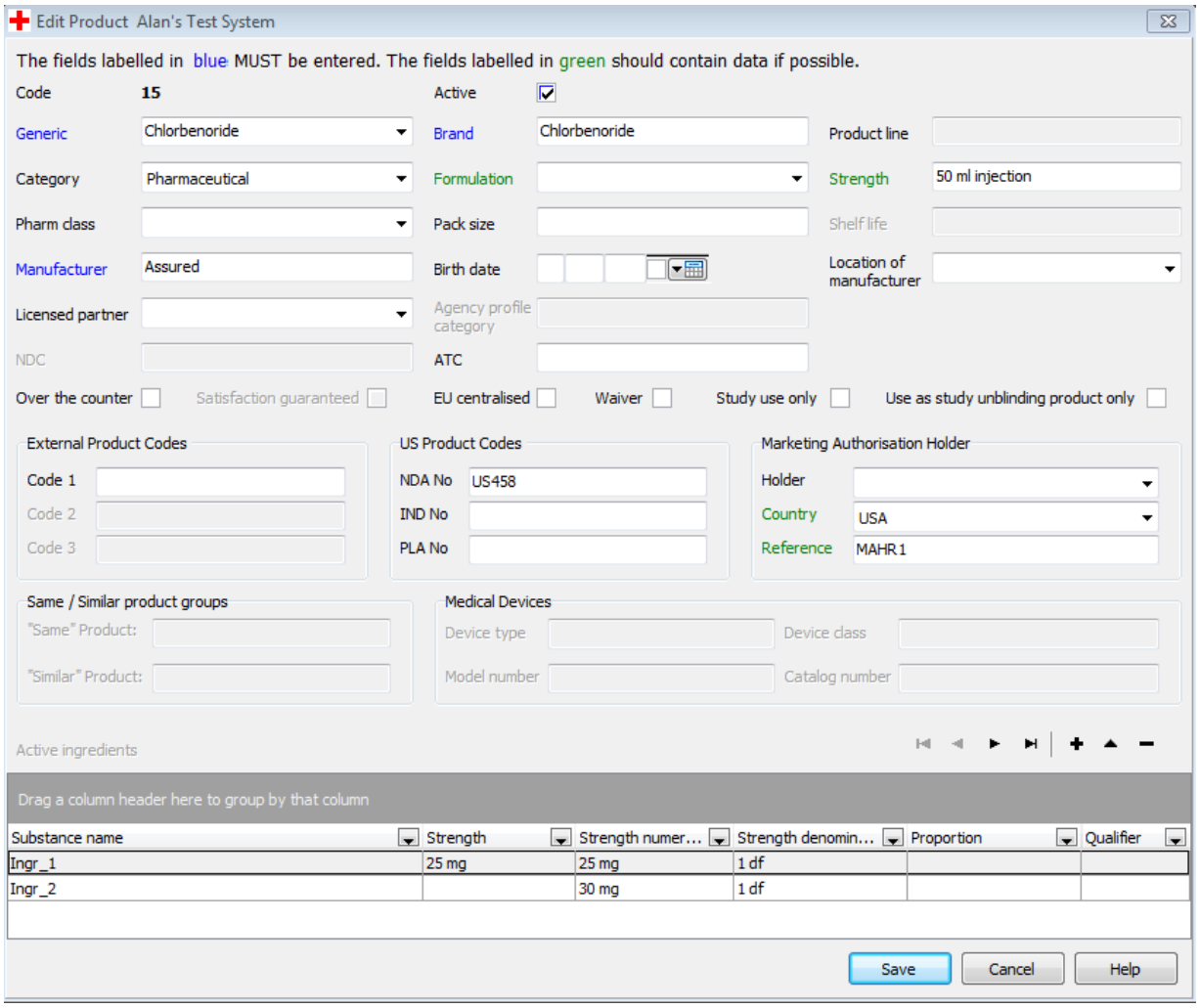
Button Function	Function
	Add a new product
	Edit the details of a current product
	Duplicate a current product
	Delete a current product
	Refresh grid results – standard grid behaviour
	Print grid results – standard grid behaviour

Export	Export grid results – standard grid behaviour
Save	Save all data to the database
Cancel	Return to main screen without changing data

Add or Edit a product

When the Add or Edit icon is clicked, the screen shown in Figure 8 will be displayed. For the edit option this will contain the data of the currently highlighted row.

Figure 8 : Add / edit a product definition



Fields whose labels are shown in **blue text** must be completed otherwise the product can not be saved. Fields whose labels are shown in **green text** should be completed if possible.

Note that the Marketing Authorisation Reference number is green rather than blue in order to support clinical trial cases. However, for marketed products it should be entered.

The generic name may be selected from the current product dictionary generic names or may be entered manually.

The field "code" is an internal product code number generated by and used by PV-Works. It is never reported. Gaps in this numbering sequence can occur and are permitted.

On save, the changes made will be rolled through all existing cases

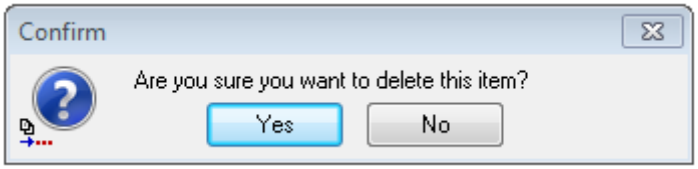
Duplicate:

This function allows the user to take the details of an existing product and use them to create a new one. The screen shown in Figure 8 will be displayed and will contain the data of the currently highlighted row.

On saving the system should confirm that the record has been changed. If any of the blue or green fields have NOT changed, then a warning to this effect is given.

Delete:

This function allows the user to delete the details of an existing product. Follow the current principles from PV-Admin and ask the user to confirm this:



If the product code has been used in a case then it can not be deleted – this is also current functionality in PV-Admin.

Print:

This function creates a simple listing of the defined products as shown below:

Figure 9 : Product list print out

Generic	Brand	Category	Manufacturer	Formulation	Strength	Country	MAH refere…	External produ…	PV-Works c…	Active
	Test Device	Device	Assured Devices		100 mcg/hr	United Ki…			12	Y
Acetaminophen, Dextr…	Cough Liquid	Pharmaceutical			1000 / 30 mg/3…	Canada	DIN 02289…		COB0115	Y
Acetaminophen, Pseud…	Cough and Flu Daytime	Pharmaceutical			1000 60 30 mg…	Canada	DIN 02289…		COB0116	Y
Acetaminophen, Pseud…	Cough and Flu Nighttime	Pharmaceutical			1k 60 30 12.5m…	Canada	DIN 02289…		COB0117	Y
Alan gen	Alan brand		Assured			United Ki…	12346		14	Y
Alendronate Sodium Tri…	Alendronate (EU)	Pharmaceutical	N/A		70 mg	European…	N/A		COB0217	Y
Alendronate Sodium Tri…	Alendronate (EU)	Pharmaceutical	N/A		40 mg	European…	N/A		COB0216	Y
Alendronate Sodium Tri…	Alendronate (US)	Pharmaceutical	N/A		40 mg	USA	N/A		COB0326	Y
Alendronate Sodium Tri…	Alendronate (US)	Pharmaceutical	N/A		70 mg	USA	N/A		COB0327	Y
Alendronate Sodium Tri…	CO Alendronate	Pharmaceutical			40 mg	Canada	DIN 02258…		COB0066	Y

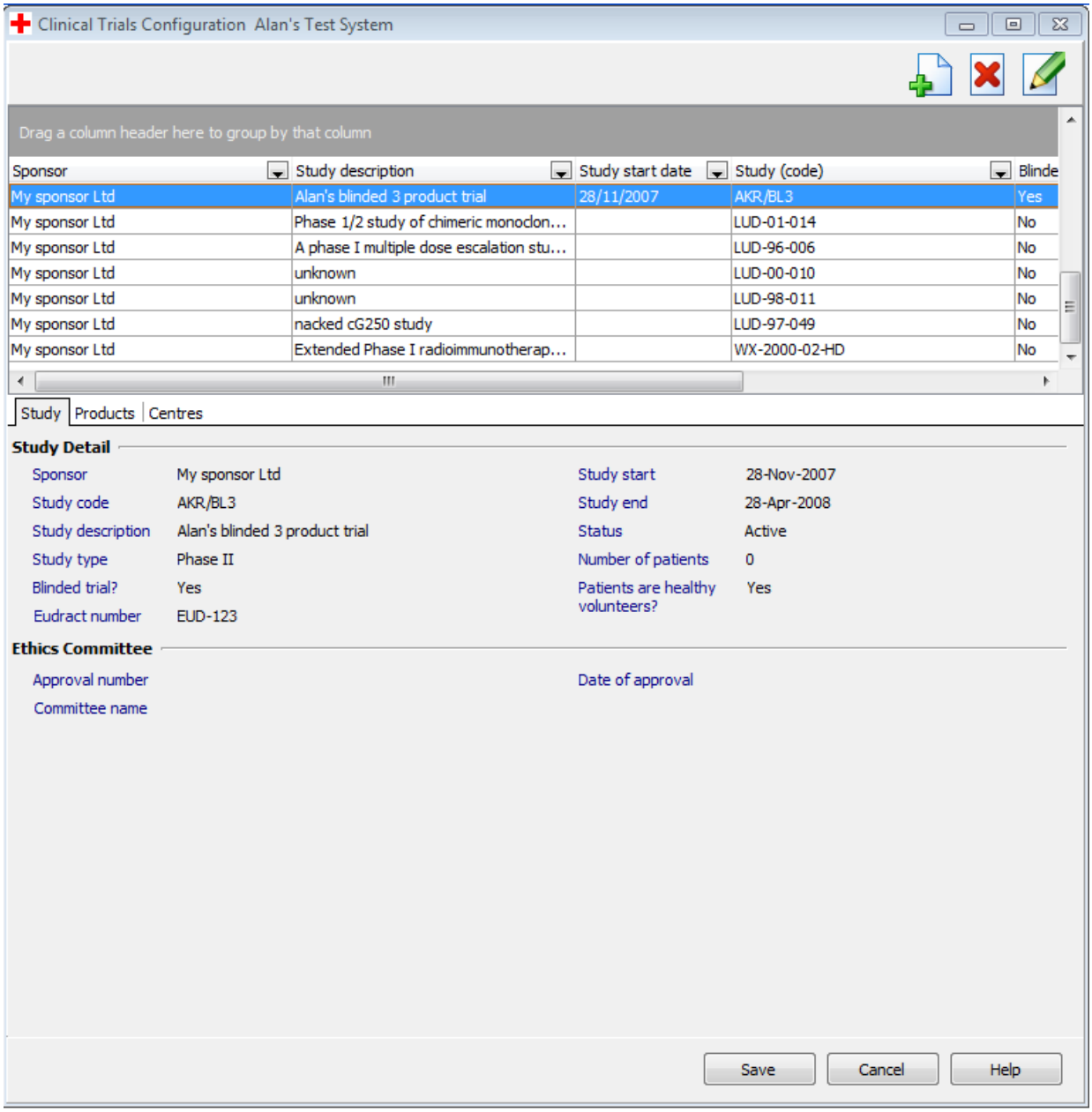
Export:

This function will export the product list to Excel.

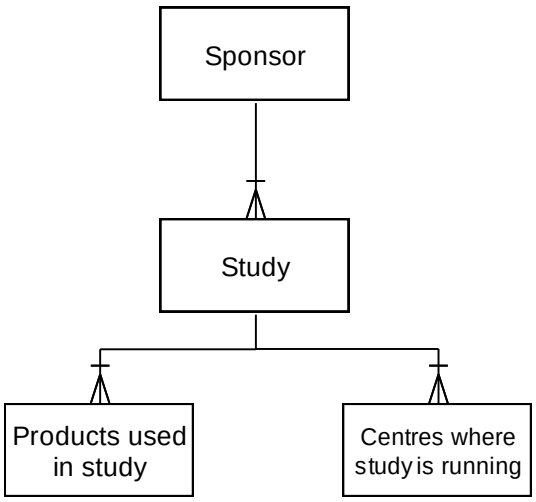
3.5 Clinical trials (Not applicable to PV247 vet systems)

On clicking the Configuration | Clinical Trials option, the following pop-up screen will be displayed listing all of the clinical trials currently defined:

Figure 10 : Clinical Trial Definition



The clinical trials dictionary is a reference list of all studies run by the company and it has the following structure:



The concept of a 'Sponsor' is intended for use by CROs. For pharmaceutical companies this will commonly be set to a standard value, eg 'My Pharma Co'.

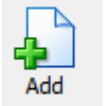
Since the list of studies is displayed in a standard grid, the normal sorting, filtering and grouping functions are applicable.

On first display the pop up screen will show the currently defined studies sorted by Sponsor. Under the grid the screen shows details for the selected clinical trial in three tabs:

a) Trial definition
b) Product – defines product(s) administered in the trial
c) Centres – defines trial centres

Of these, entry of information on the Trial definition tab is mandatory, the product tab is optional but recommended and the centres tab is optional but will improve data entry efficiency.

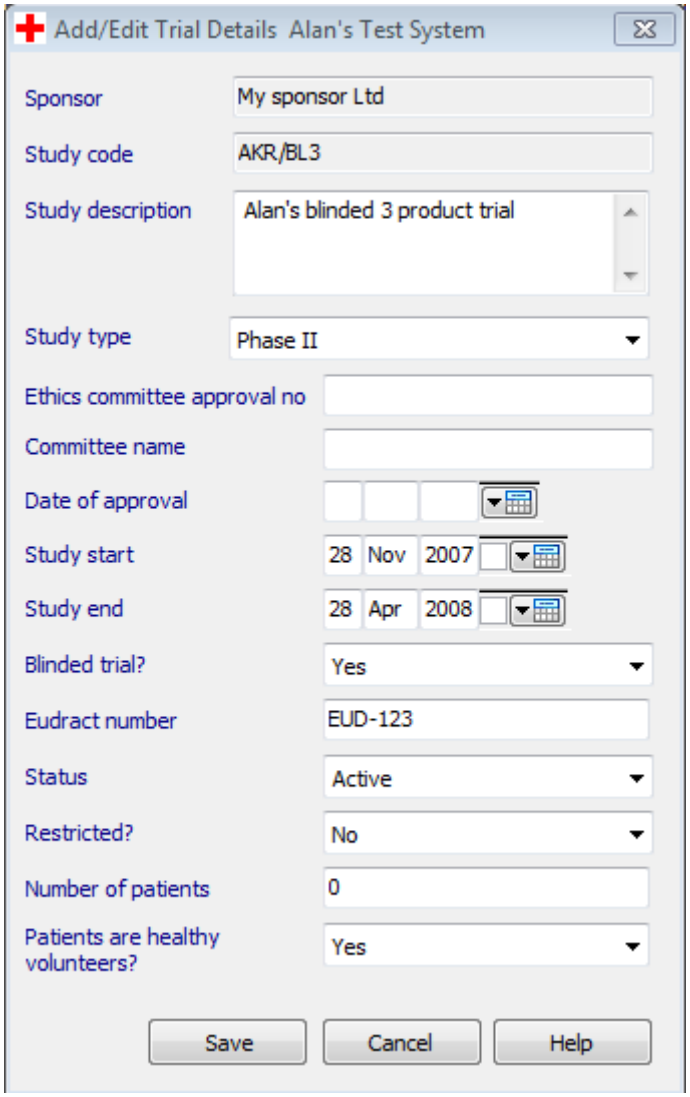
Buttons:

Button Function	Function
	Add a new clinical trial definition
	Delete the details of a clinical trial and its product and centre definitions
	Edit the details of a clinical trial

Study tab

When the Add or Edit icon is clicked, the screen shown in Figure 8 will be displayed. For the edit option this will contain the data of the currently highlighted row.

Figure 11 : Add / edit a clinical trial definition

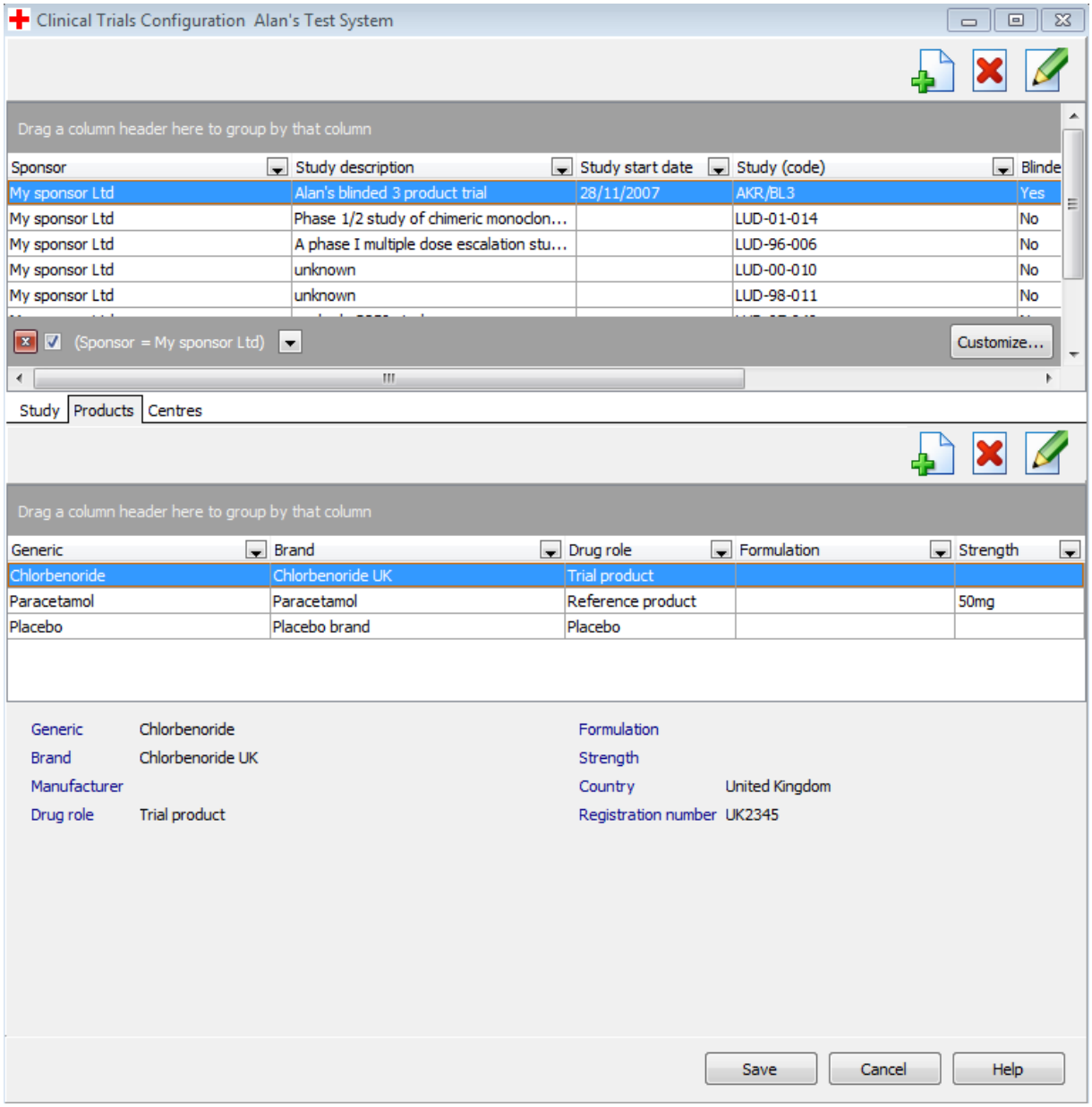


When a clinical trial is added the user will be able to enter the Sponsor and Study code. The Sponsor may be selected from the dropdown list or can be typed.

Product tab

The product tab will display the products associated with the trial selected on the Study screen. The following screen will be displayed:

Figure 12 : Clinical Trial Products Definition

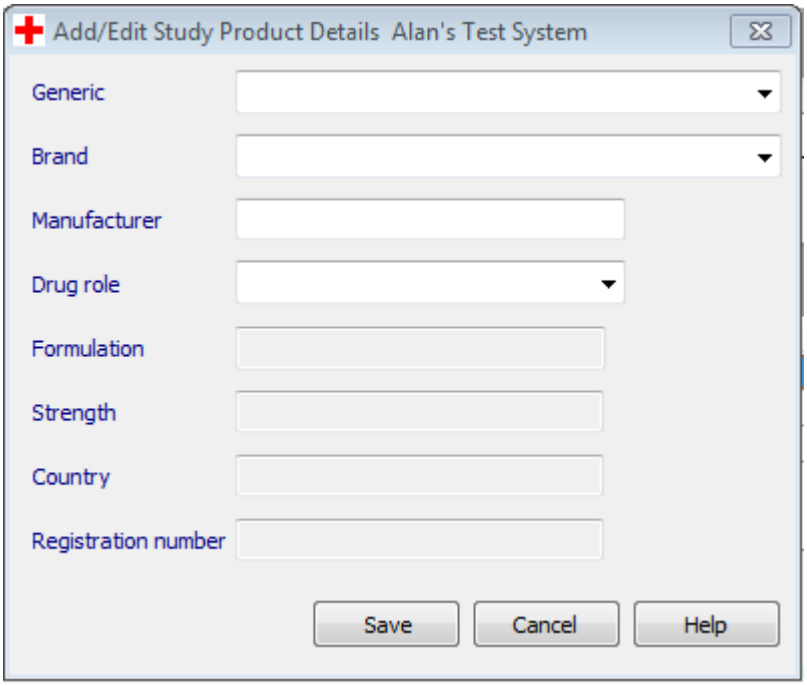


Buttons

Button Function	Function
 Add	Add a new product to the current study / clinical trial
	Delete a product from the current study / clinical trial
	Edit the details of a product

Add / Edit a Product

Figure 13 : Add / edit a product in a clinical trial



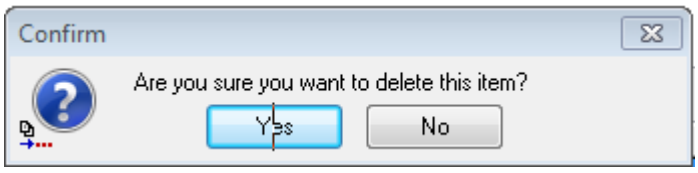
When a product is assigned to a trial it must be selected from the dropdown lists. It can not be entered as free text. This means that all products need to be entered in the product dictionary (see section 3.4).

For clinical trials this may mean entering third party comparator products or "pseudo-products" such as "placebo" even though these are not truly "company" products.

The user should select the generic name first in order to filter the brand list to associated brands. The fields formulation, strength, country and registration number will be filled from the product definition entered in section 3.4.

Delete a Product

If the user clicks the 'Delete' button, prompt them to confirm that the highlighted product should be deleted:

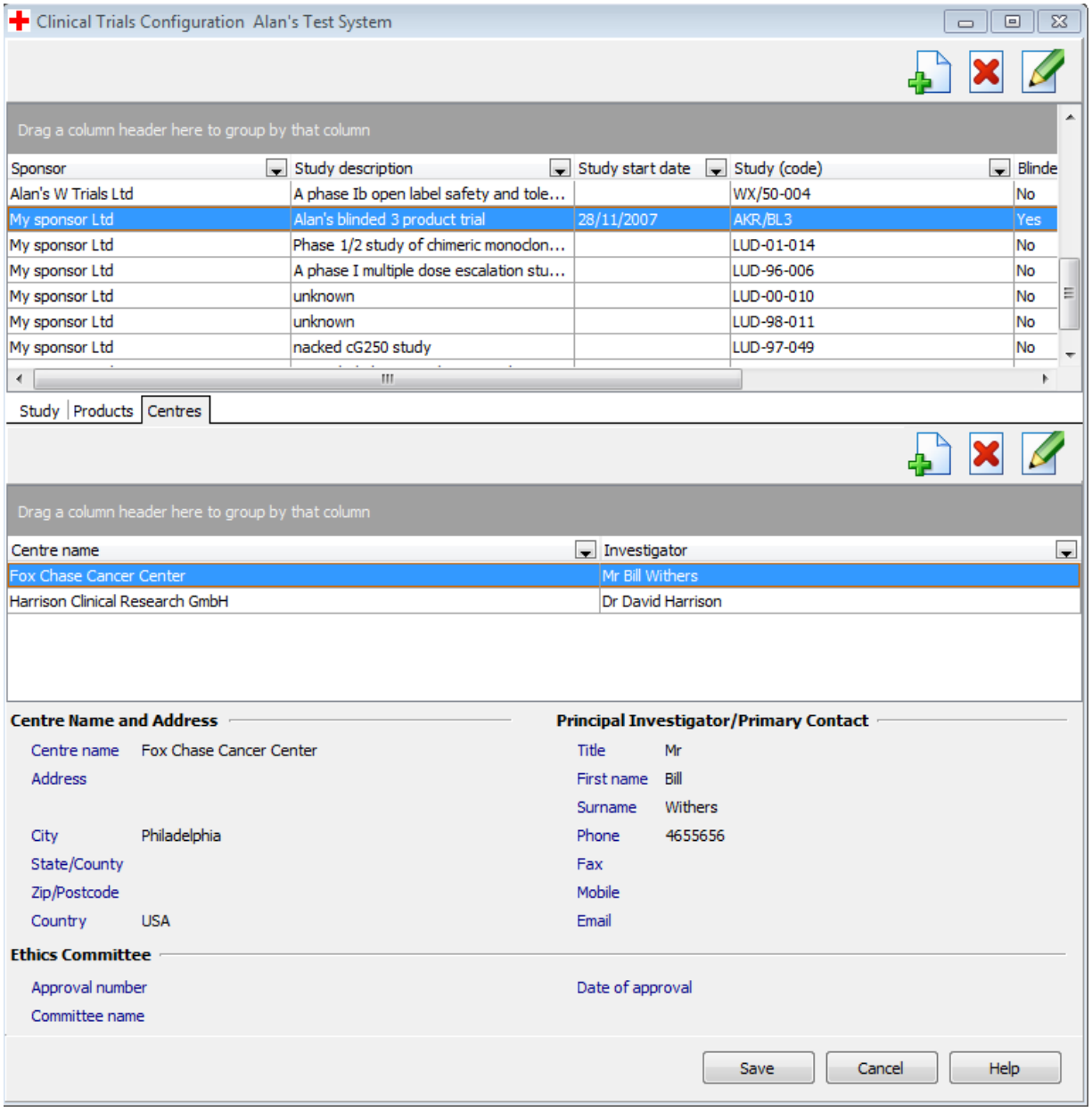


If the user confirms the deletion then the product is no longer associated with the selected trial. Its definition in the company product list (section 22.4) is NOT deleted.

Centres tab

The Centres tab will display name and address details of the hospitals / centres where the clinical trial is being executed. The following screen will be displayed:

Figure 14 : Clinical Trial Centre Definition



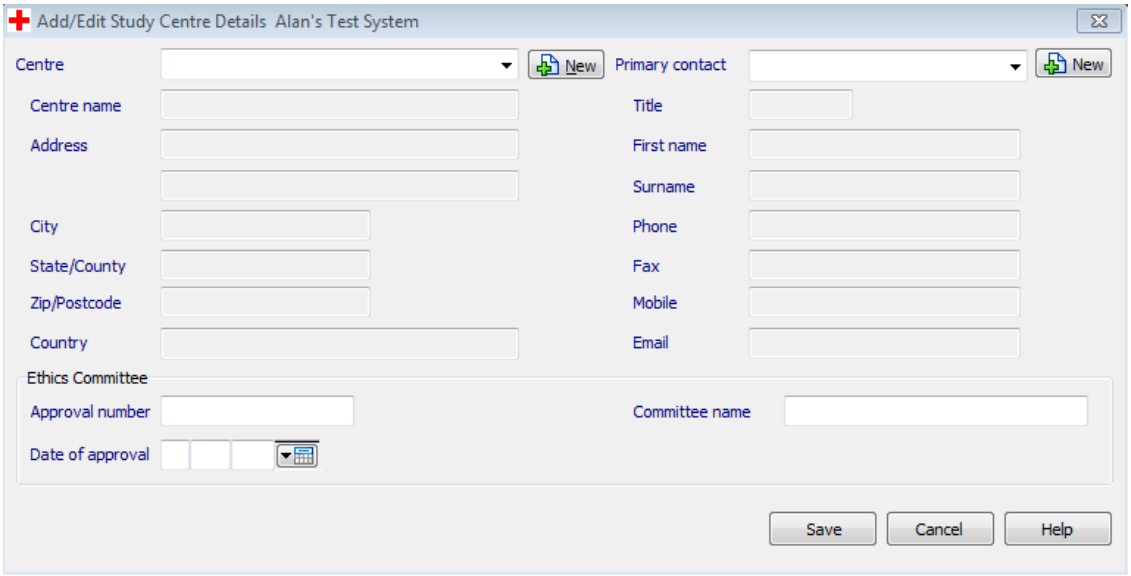
Buttons

Button Function	Function
	Add a new Centre to the current study / clinical trial
	Delete a Centre from the current study / clinical trial

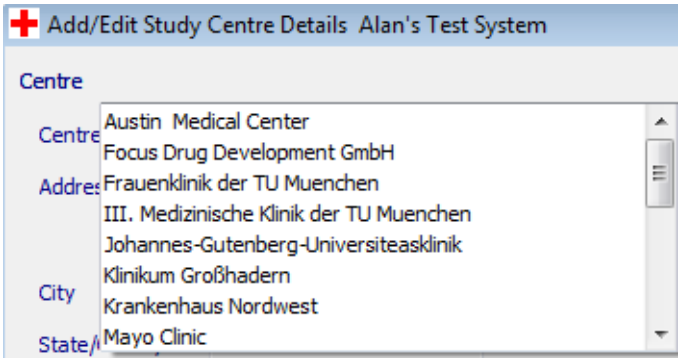
	Edit the details of a Centre

Add a Centre

Figure 15 : Add a Centre to a Clinical Trial definition



The screen on which Centres are added is shown in Figure 15. By default the user is encouraged to re-use the name of a Centre that already exists by selecting from the Centre dropdown box:



If the Centre has not been used before, click 

and enter its details manually.

The same principles apply to the primary contact.

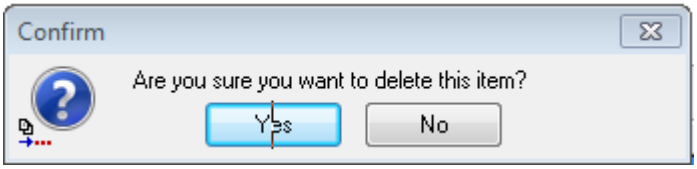
When a new case is created and a clinical trial selected, the user will be able to select the Centre from which the case was received. As a consequence PV-Works will add the Centre and the primary contact from this screen as a reporter / contact.

Edit a Centre

This function will allow the user to correct spellings, phone numbers, add missing data etc. In other words "edit" the existing records but not change the basic 'trial / centre / investigator' relationship. The same screen as shown in Figure 15 is used for this.

Delete a Centre

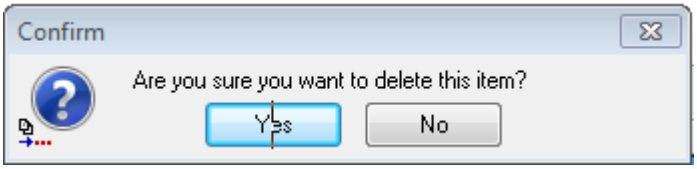
If the user clicks the 'Delete' button, prompt them to confirm that the highlighted Centre should be deleted:



If the user confirms the deletion then the Centre is no longer associated with the selected trial. Its definition in the list of potential centres is NOT deleted.

Delete a Trial

If the user clicks the 'Delete' button to delete a clinical trial, they will be prompted to confirm that the highlighted study should be deleted:



If the user confirms the deletion then the clinical trial definition is deleted. This operation has no effect on case data or the product dictionary.

3.6 Configure codelists

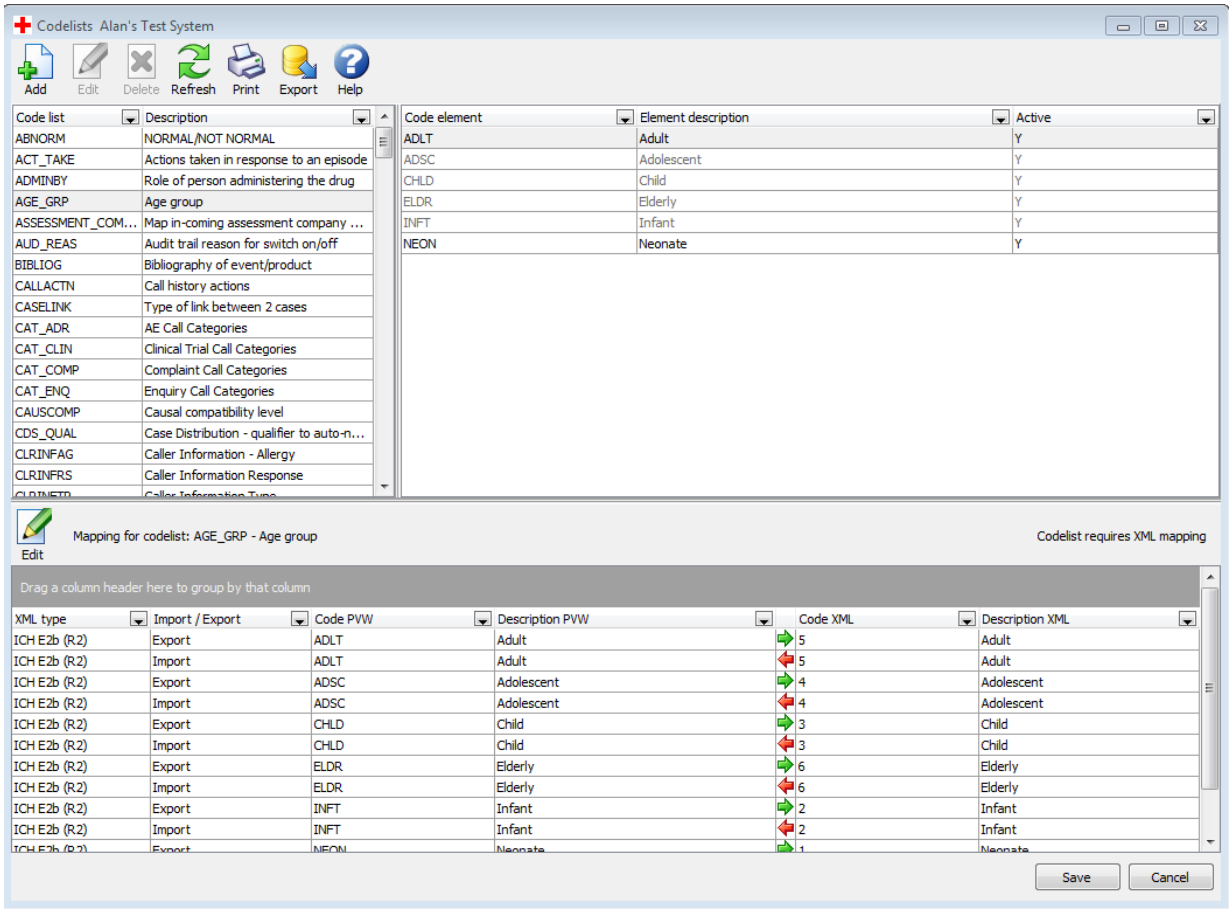
This function allows the user to add or edit codelist entries and at the same time amend their mapping to XML files.

> *This function is only available to Premium package customers*

On clicking the Configuration | Configure codelists option, the following pop-up screen will be displayed listing all of the codelists currently defined that are not set as "fixed":

("fixed" codelists are ones whose contents are set by Assured and can not be edited by customers).

Figure 16 : Codelist Editing screen



The screen shows a list of the available codelists in the top left hand panel with the contents of the selected codelist displayed in the top right hand panel. The lower panel shows a list of mapping rules between the code and term used in PV-Works and the vocabulary defined for e-reporting in ICH.

Note that only a subset of codelists require mapping for e-reporting. Where a codelist is only used in PV-Works and is not required to create the XML e-report file, the user will not be able to create a mapping for it.

The example above shows the AGE_GRP codelist containing the age groups such as adult, child. In PV-Works these have been assigned alphabetic codes eg ADLT, CHLD whereas a

numeric value in the range of 1 to 5 is required for XML e-reporting. While this example shows a simple map it is often necessary to map more than one PV-Works term to a single XML term.

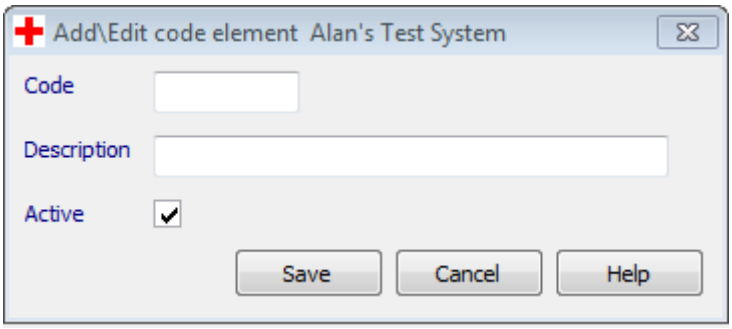
Buttons

Button Function	Function
	Add a new element (ie term) to the selected codelist
	Edit the current description of a code element
	Delete a Centre from the current study / clinical trial
	Print grid results – standard grid behaviour
	Export grid results – standard grid behaviour

Add a code element

To add a new element, click the "add" button to display the following screen:

Figure 17 : Add code element pop up screen

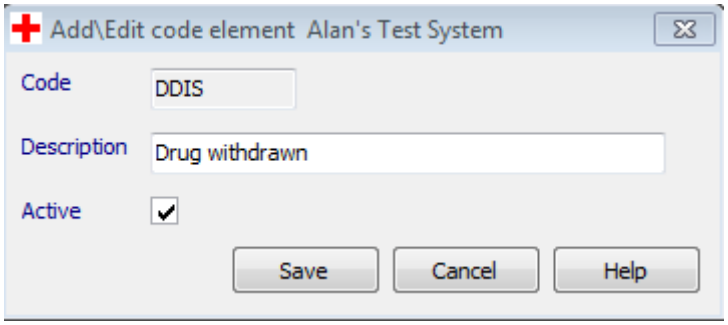


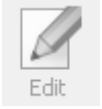
Create a unique code – the code must only be unique within the codelist as it is possible to use the same code in different codelists. The description is the text seen in PV-Works.

Edit the code element description

To edit the description of an existing element, click the "edit" button to display the following screen:

Figure 18 : Edit code element description pop up screen

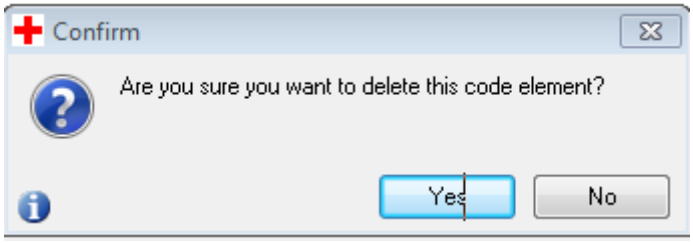


Note that some code elements are fixed and so can not be edited. If this is the case then the edit button will be greyed out: 

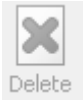
Delete a code element

To delete an existing element, highlight the code to be deleted and click the "delete" button.

The user will be prompted to confirm that the highlighted code should be deleted:



If the user confirms the deletion then the code element is deleted. Note this operation may affect the case data if the code has been used. While the code will remain in the case record, it can no longer be translated on screen, giving the impression that the case data has been deleted.

Note that some code elements are fixed and so can not be deleted. If this is the case then the delete button will be greyed out 

.

Print:

This function creates a simple listing of the selected codelist as shown below:

Figure 19: Print out of a codelist

Code List Report Language English Date 14/06/2012

Name NORMAL/NOT NORMAL

Code ABNORM Max. Length 4 Type Variable

Element Description	Element Code	Element Type	
Abnormal	ABNM	Fixed	Y
Normal	NORM	Fixed	Y
Result abnormally high	HIGH	Fixed	Y
Result abnormally low	LOW	Fixed	Y
Unknown	UNKN	Fixed	Y

End of Report

Export:

This function will create an XML mapping file based on the mapping rules defined in this screen.

3.6.1 Introduction to Mapping PV-Works codelists to XML

In the E2B definition of the XML file, several items need to be coded using vocabulary lists and associated codes defined in the ICH guidelines. These E-reporting lists rarely line up perfectly with a pharmacovigilance system designed for a wider remit than reporting and so a mapping function in PV-Works allows users to map the codelists used in their implementation of PV-Works to the required output format.

While PV247 systems are set up to reflect the official ICH codelists as closely as possible, PV-Works typically uses different codes internally tending to favour alphabetic mnemonics rather than meaningless number systems.

For PV247 systems with a "Premium package" and all other PV-Works implementations, the codelists are configurable and where configuration occurs to meet local business need there is an implied need to ensure that the XML mapping requirement is met.

For example, the required output values for Patient Gender are defined by ICH as:

Sex: 1=male, 2=female

However, a standard codelist (SEX) in PV-Works might be:

Sex: M=male, F=female, U=unknown

When an ICH E2b file is created, it is necessary to map each term used by PV-Works to the correct code required by E2b, ie "M" to "1" and "F" to "2". Since ICH has no concept of "unknown", cases with this value will ignore the gender field and report it as a blank.

The following reference lists are required by E2B:

E2B TYPE	MAPS TO PV-WORKS CODELIST
Action taken with drug	ACT_TAKE

E2B TYPE	MAPS TO PV-WORKS CODELIST
Age group list	AGE_GRP
Case type	CASETYPE
Country code	CTRY
Dose duration	TIMEUNIT
Dose interval	DOSETIME
Dosage unit	DOSEUNIT
Event duration	TIMEUNIT
Gestation period	TIMEUNIT
Outcome of event	OUTCOME
Product type	PRODTYPE
Reporter role / qualification	REP_PAT
Reportability	RPT_WHEN
Route of administration (patient and parent)	ROUTE
Serious and seriousness criteria	YESNO
Sex (of patient and parent)	SEX
Study type	SDY_TYPE
Time unit (age)	AGE_UNIT
Time unit (others)	TIMEUNIT

The following PV-Works codelists also need to be present in the PVW to E2b mapping. These codelists are used for lookup on the source side only and therefore do not need to be mapped to an E2b vocabulary.

CODELISTS USED FOR E2B EXPORT	PURPOSE
ASS_METH	To find human (non-automated) assessments (GLBI)
EXPORT_MEDDRA	Used to determine the MedDRA level to be exported for particular regulatory authorities
EVNTTYPE	To find Medical History (PREV, ALGY) To find reactions (ADR)
FORM	Description of formulation
LABUNIT	Laboratory test unit
LINKTYPE	Type of case link
MAH_HOLD	Description of licence holder
MED_FACT	Description of medical factors
NARRTYPE	To find Case narrative (NARR), Company diagnosis (CDIA), Literature narratives (LITR), laboratory test narratives (LABT), Parental narrative (PNAR), Reporter's comments (RCMT)
REL_ASS	Description of causality
TESTUNIT	

In practice, codelist mapping needs to be replicated - Once for export and once for import. These maps will be different.

While this sounds a daunting prospect, any implementation of PV-Works is accompanied with a standard set of codelist vocabulary lists and their appropriate mapping both for export and import of ICSRs. So most customers will only find themselves making the occasional change to this metadata.

3.6.2 Mapping PV-Works codelists to XML and XML vocabularies to PV-Works

Mapping rules are stored in an XML transformation file called

CODELISTDATA.XML

This is a simple XML file with its own schema definition (codelistdata.xsd). The file is saved in the appropriate transform folder with the PV-Works software.

The configuration tool makes it easy to manage these files using the simple process:

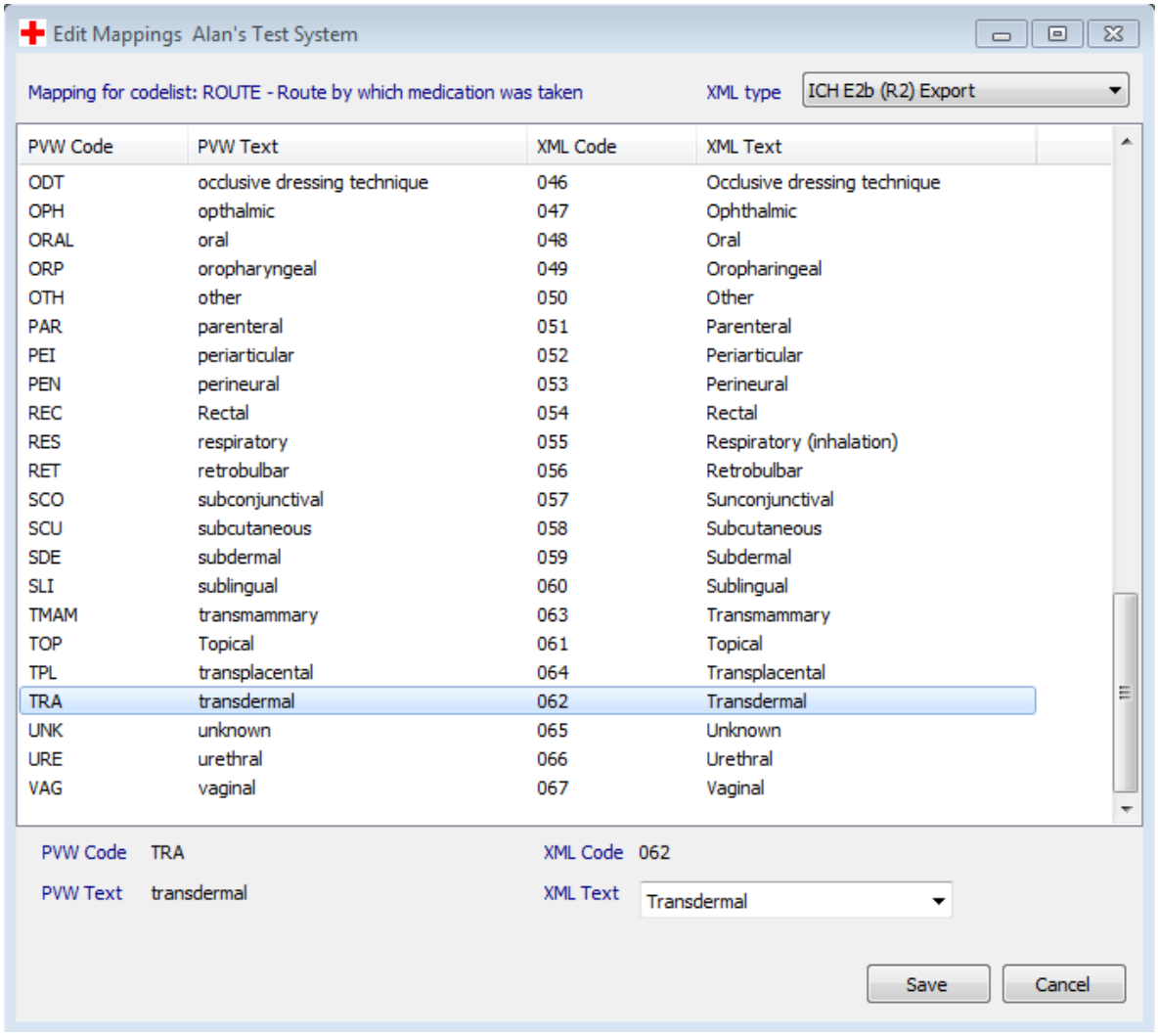
1. Amend the codelist mapping using the function described below
2. Export the revised mapping to recreate the CODELISTDATA.XML file.

The current mapping is shown in the panel at the foot of the screen in Figure 16

The code mapping can be edited codelist by codelist. If the user clicks on the 

button above the mapping grid, the following screen is displayed:

Figure 20: Editing XML mapping screen

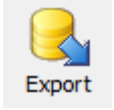


The user may select either the Import or the Export mapping definition for the selected codelist using the dropdown box in the top right hand corner of the screen.

This screen shows all elements of the selected codelist so that multiple mapping changed may be made in one step.

With a particular mapping rule highlighted, its mapping rule may be visible at the foot of the screen where a revised mapping selection may be made. The choice of destination mapping terms are those defined in the ICH guideline.

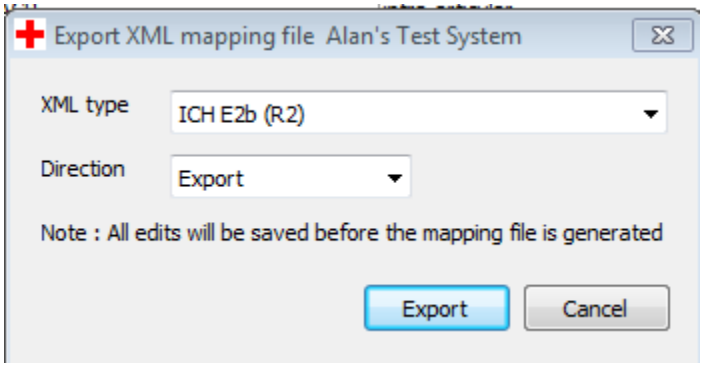
Once the mapping terms have been updated they should be saved using the “Save” button.

When all changes have been made, the revised mapping rules need to be exported to an XML file. This function is essential as the XML file creation process is unable to read the PV-Works database and must be able to find the mapping rules in a simple XML file. To create this file, click the 

button.

This will display the following screen:

Figure 21 : Export XML codelist mappings



which allows the user to select the type of XML file (ICH E2b is currently the only option) and the direction of the mapping – import or export.

When the user clicks "Export", the file of mapping rules is created in the correct format in the correct folder.

The format of the XML mapping file is shown below:

Figure 22: Sample XML Mapping File

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- 1.17 FDA Codelist for transform file to IMPORT cases From FDA to PVWorks Aug 2009-->
<LOOKUP_TABLE xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
xsi:noNamespaceSchemaLocation="C:/XML/Schemas/codelistdata.xsd">
    <LOOKUP_ITEMS Codelist="AGE_UNIT">
        <ITEM SourceCode="d" SourceText="Day(s)" DestCode="D" DestText="Day(s)"/>
        <ITEM SourceCode="h" SourceText="Hour(s)" DestCode="H" DestText="Hour(s)"/>
        <ITEM SourceCode="min" SourceText="Minute(s)" DestCode="MIN" DestText="Minutes"/>
        <ITEM SourceCode="mo" SourceText="Month(s)" DestCode="M" DestText="Month(s)"/>
        <ITEM SourceCode="s" SourceText="Second(s)" DestCode="SEC" DestText="Seconds"/>
        <ITEM SourceCode="wk" SourceText="Week(s)" DestCode="W" DestText="Week(s)"/>
        <ITEM SourceCode="a" SourceText="Year(s)" DestCode="Y" DestText="Year(s)"/>
        <ITEM SourceCode="UNK" SourceText="Unknown" DestCode="UNK" DestText="Unknown"/>
    </LOOKUP_ITEMS>
    <LOOKUP_ITEMS Codelist="TIMEUNIT">
        <ITEM SourceCode="d" SourceText="Day(s)" DestCode="DAY" DestText="Day(s)"/>
        <ITEM SourceCode="h" SourceText="Hour(s)" DestCode="HR" DestText="Hour(s)"/>
        <ITEM SourceCode="min" SourceText="Minute(s)" DestCode="MIN" DestText="Minute(s)"/>
        <ITEM SourceCode="mo" SourceText="Months" DestCode="MON" DestText="Month(s)"/>
        <ITEM SourceCode="m" SourceText="Month(s)" DestCode="MON" DestText="Month(s)"/>
        <ITEM SourceCode="s" SourceText="Second(s)" DestCode="SEC" DestText="Second(s)"/>
        <ITEM SourceCode="wk" SourceText="Week(s)" DestCode="WK" DestText="Week(s)"/>
        <ITEM SourceCode="a" SourceText="Year(s)" DestCode="YR" DestText="Year(s)"/>
    </LOOKUP_ITEMS>
</LOOKUP_TABLE>
```

3.7 Reset test case numbers

> *This function is only appropriate for PV247 customers using the "Essentials package"*

This function allows a customer to reset their initial test system such that test cases are hidden and case numbers used in testing can be re-assigned for production cases (ie re-used).

It is recognised that some customers are likely to enter a production case during their testing as a parallel test and may wish to retain this data whilst discarding others. Therefore PV-Works will not guess which cases should be discarded but will rely on explicit instruction from the user.

The process will be:

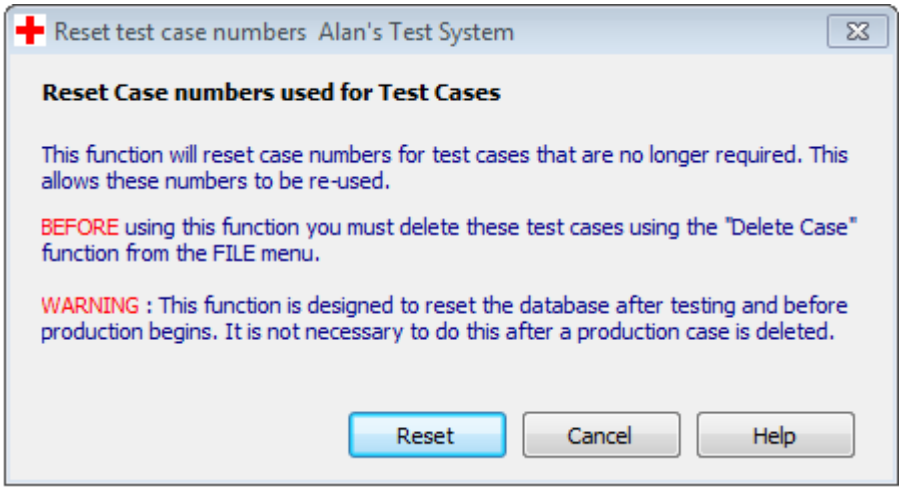
1. User will soft-delete every test case that is not required

2. User will run the "reset test case numbers" function to re-use case numbers

Cases are "soft-deleted" using the File | Delete function from the main screen. This is a "soft" delete because the case data is not actually deleted from the database but is marked as "deleted" and then ignored by PV-Works. As such a "soft delete" is reversible if the wrong case is so marked.

Once all of the test cases have been "soft-deleted" the user should click the Configuration | Reset test case numbers option. The following pop-up screen will be displayed:

Figure 23 : Reset Test Case Numbers screen



After noting the instructions and warning, the user should click "Reset" to reset case numbers.

The test cases that are marked as "deleted" are renumbered with the word "DELETED" and a unique number as a suffix to the existing case number. This allows these case numbers to be re-used with production cases and avoids confusion between the test case data and the production data that has overwritten it.

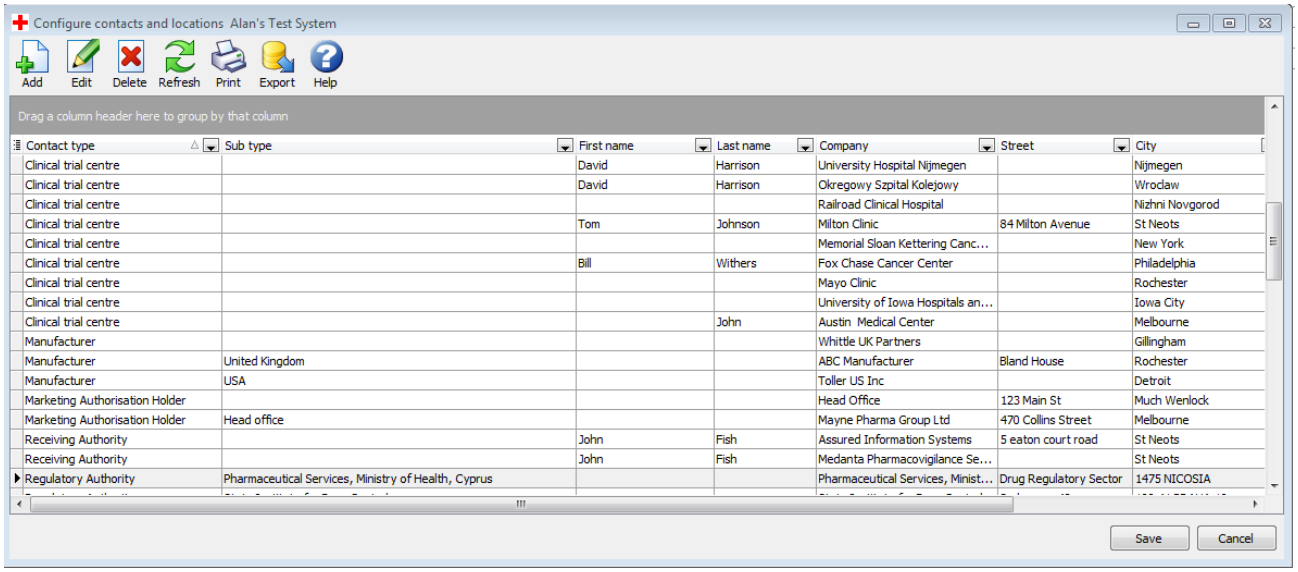
PV-Works will assign the lowest possible case number to the next case entered but will avoid any case number that already exists. In other words it will fill in any gaps left where only some of the test cases were deleted.

3.8 Configure Names and Addresses

PV-Works uses several pre-defined names and addresses. Typically these are used on reports and so include regulatory authorities, customer addresses, clinical trial centres etc. This function allows an administrator to add and edit these addresses.

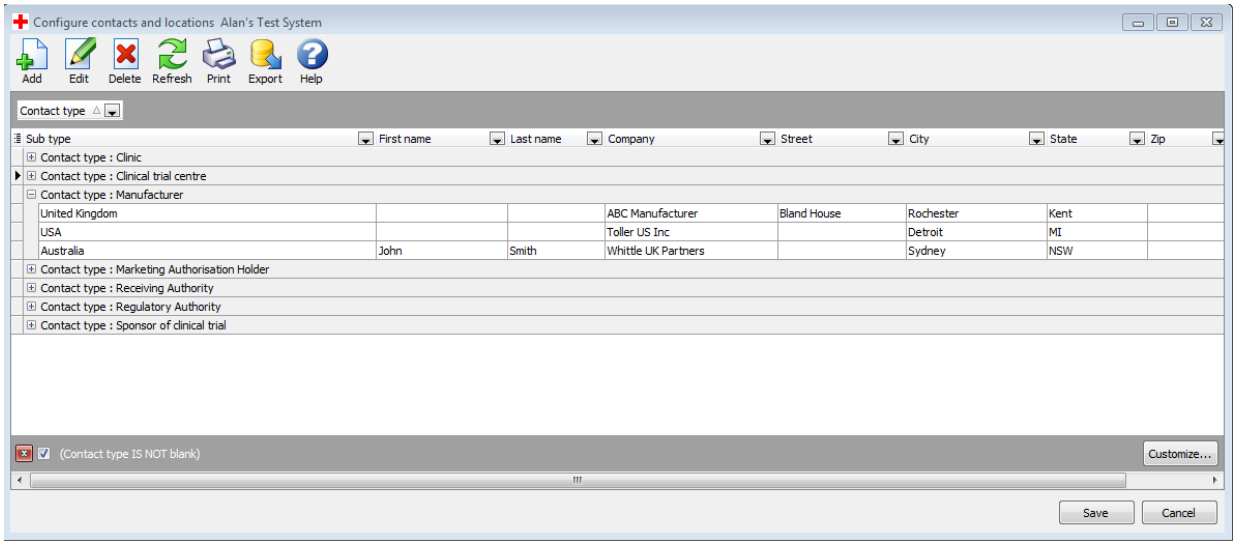
On clicking the Configuration | Contacts and Locations option, the following pop-up screen will be displayed listing all of the contacts currently defined:

Figure 24 : Contact Name and Address Configuration



Note that the format of presentation of this data is a grid of the type used in the PV-Works main grid. Given that there are likely to be many entries in this grid using the filtering, sorting and grouping functions is advised. For example grouping by “Contact type” will simplify the display as shown below:

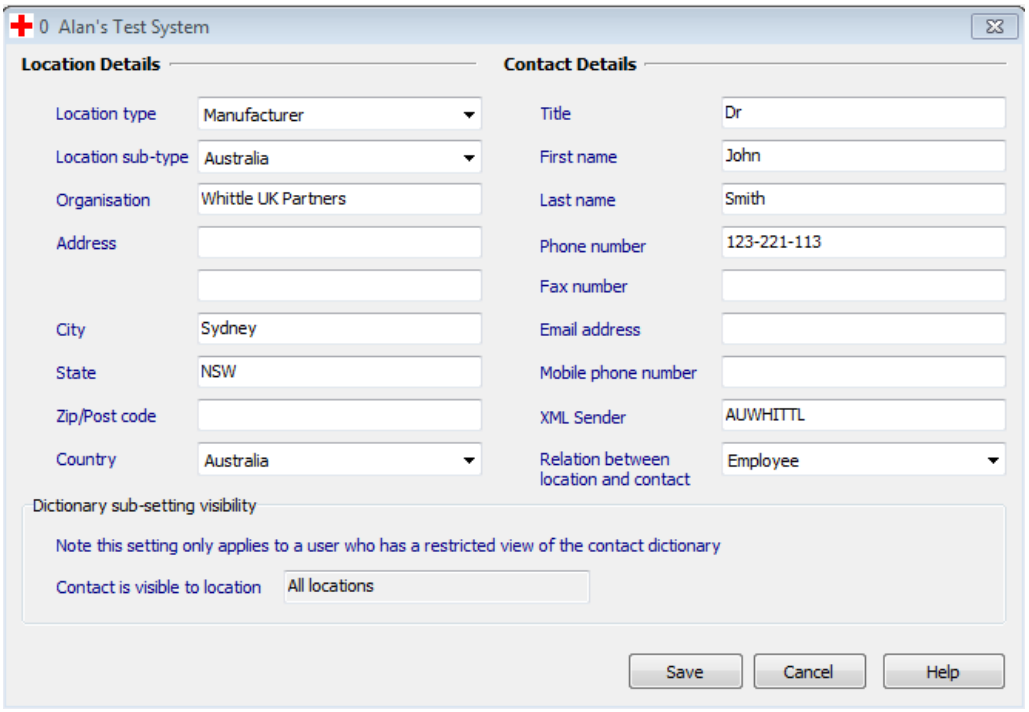
Figure 25 : Contact Name and Address Configuration - grouped



To amend the dictionary of names and addresses use the Add, Edit or Delete functions at the top of the screen:

The add and edit buttons will display a pop up screen (Figure 26) where the company name and address may be added / edited. In addition the primary contact person for the company may be identified if required.

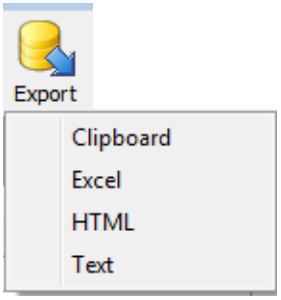
Figure 26 : Contact Name and Address edit screen



Changes should be "Save"d back to the grid. After all edits have been applied they must be saved to the database using the SAVE button underneath the grid.

If an external list of all contacts is required, it is possible to create a print out or export the whole list to four different formats.

Figure 27 : Contact Name and Address export options



Of these Assured recommends Excel as the preferred option.

3.9 Configure System Options

> *This function is only available to Premium package customers*

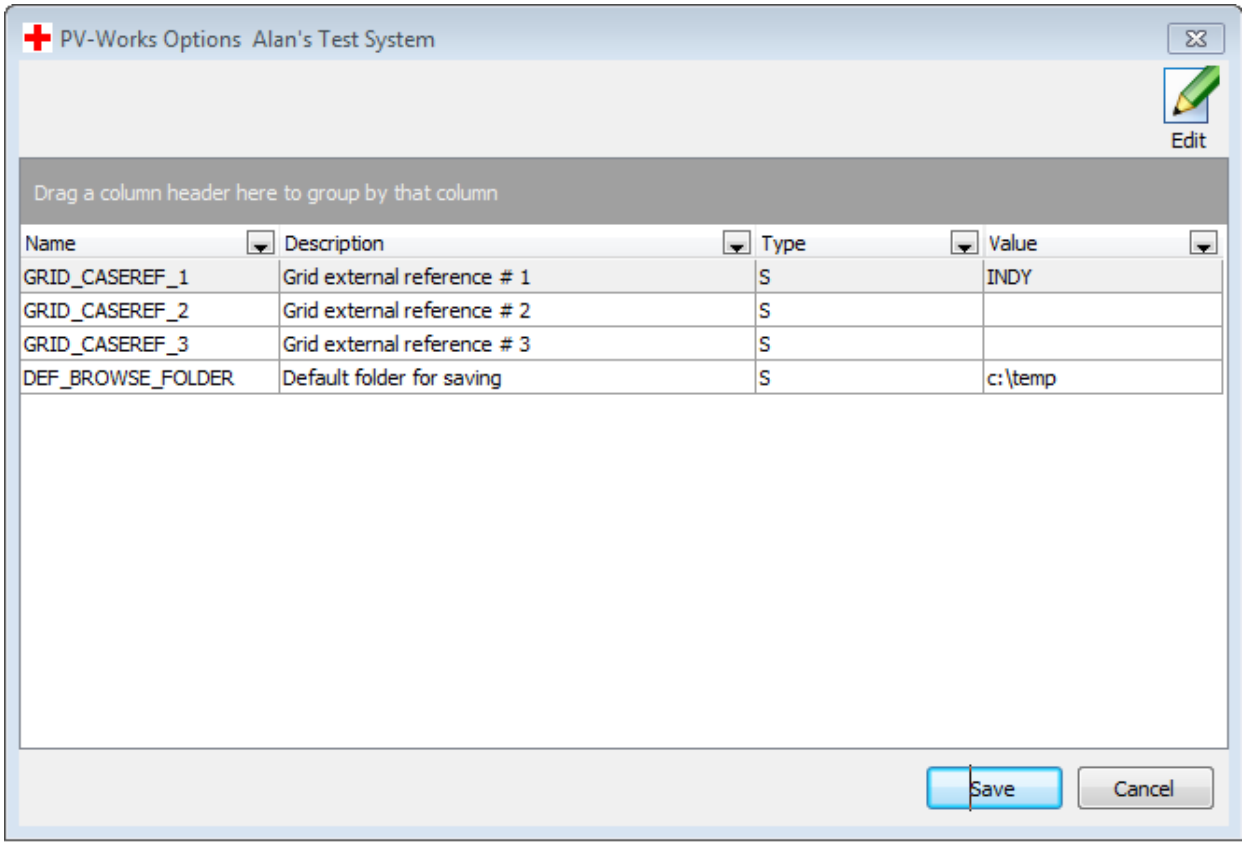
PV-Works is a very configurable system part of which is managed by over 300 system options. Fortunately for customers these are set to sensible values in a standard installation and for PV247 systems are pre-set. However, there are a few options that even a pre-defined PV247 user may wish to change. Typically these refer to local environment variables.

By default all system options are defined such that they can not be amended in this function. For a PV-Works implementation the System Administrator needs to determine which option(s) may be amended. This is achieved via the PV-Admin program. For PV247 implementations this list is managed by Assured.

Note that option values may only be changed at a system level (this concept only applies to PV-Works implementations).

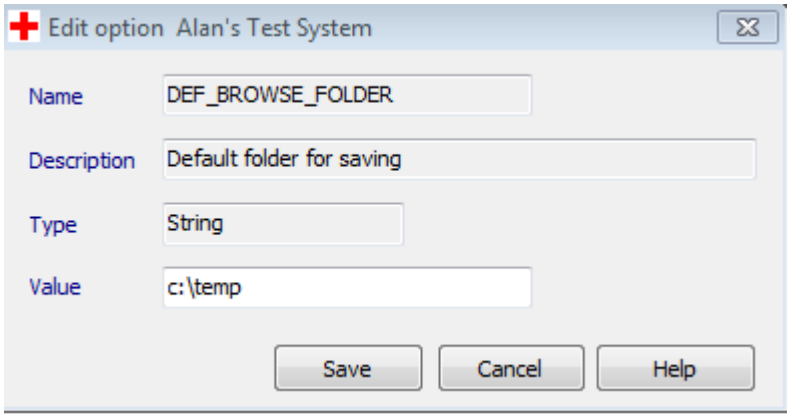
To amend a system option value click on the Configuration | System Options option, the following pop-up screen will be displayed listing all of the system options that may be amended, together with their current values:

Figure 28 : Configuration of System Options



To amend the value of a system option, highlight its row and click on the EDIT button to display a pop up screen:

Figure 29 : Edit a system option value



The new value is entered in the "Value" field" and "Save"d back to the list of all options. The administrator must ensure that the value entered conforms to the format expected for the option being edited. No validation is performed.

To commit these changes the administrator must click the "Save" button on the screen in Figure 28.

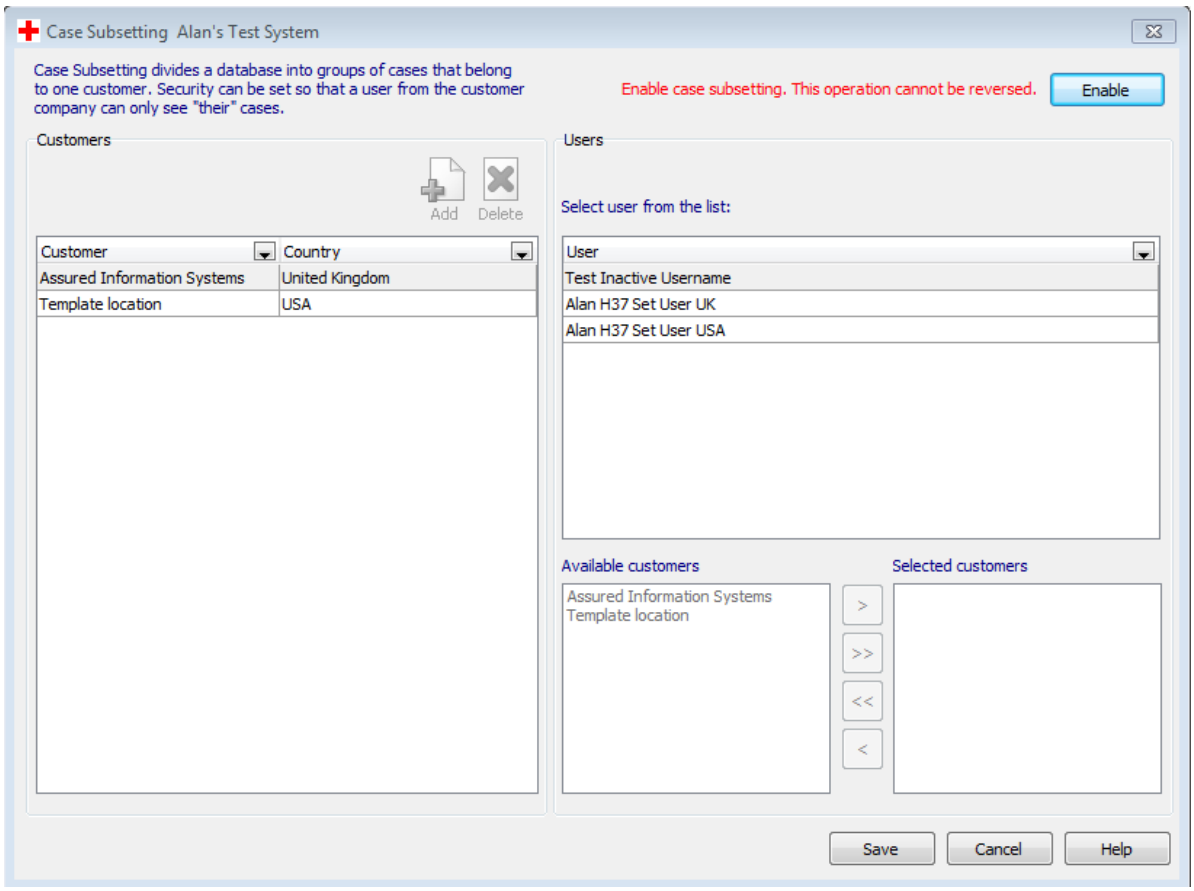
Note that all users, including the administrator, will only use the new value for amended system options after they re-start the PV-Works application.

3.10 Database Sub-setting (Not applicable to PV247 vet systems)

A database may be divided into logical partition called "sub-sets". In a PV247 implementation this is restricted to a partition based on a "customer" and so is primarily intended for use by PV247 companies who are CROs. Further details of the principles of sub-sets is given in section 4.4.

On clicking the Configuration | Case Subsetting option, the following pop-up screen will be displayed:

Figure 30 : Case Subsetting Administration



By default a PV247 system is NOT enabled for case subsetting. Before any subsets are defined the administrator must switch this function on. To do this click on the Enable button in the top right hand corner of the screen, taking note that this operation is irreversible:

The workflow for creating a case subset is:

a) Add the name of the customer as a location (see configuration option described in section 3.2.

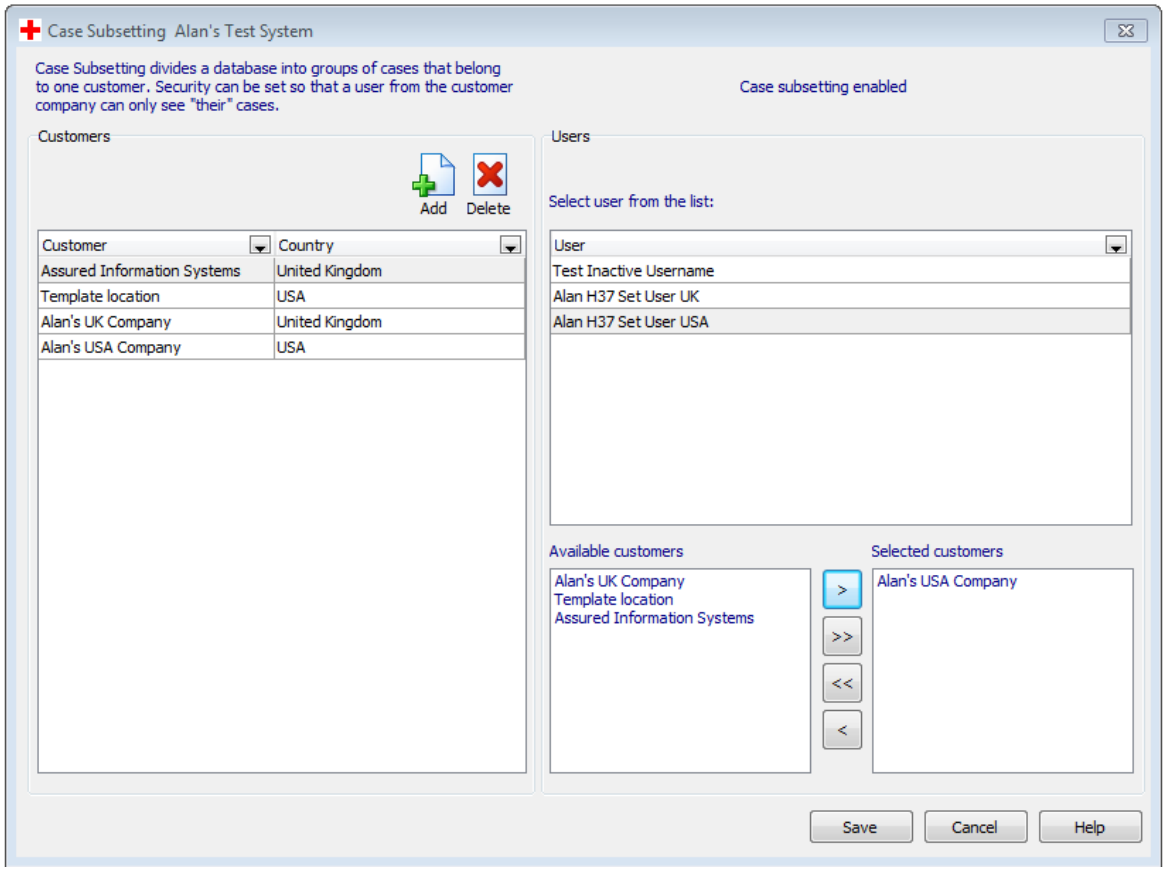
b) Add the customer as a "subsetted customer". Note that a CROS would only do this for customers who require access to the PV-Works system

c) Select a user from the list of all users (see section 3.3 regarding the addition of user accounts in a PV247 system)

d) Grant access to cases for a particular company / companies for this user

A sample subset is defined in Figure 31 which shows two companies (one is UK and one in USA). The selected user (Alan H37 User USA) has been granted access to cases from the USA company but denied access to the cases from UK.

Figure 31 : Completed Sub-setting example

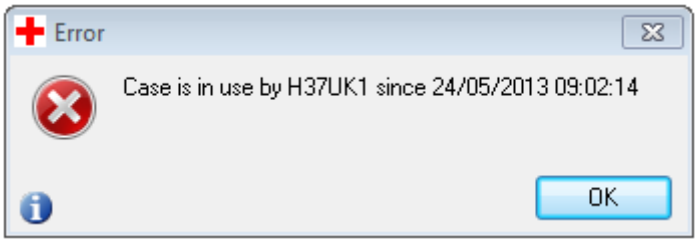


3.11 Re-activate Cases

When a user opens a case for edit, PV-Works places a lock on it such that other users may not amend it at the same time. Occasionally this lock is not released correctly when the case is closed. This is most likely to occur with a network / system issue. In this situation the user is presented with a message such as Figure 32 where the user that PV-Works thinks has the case open is actually themself. In this situation it is not possible to open the case.

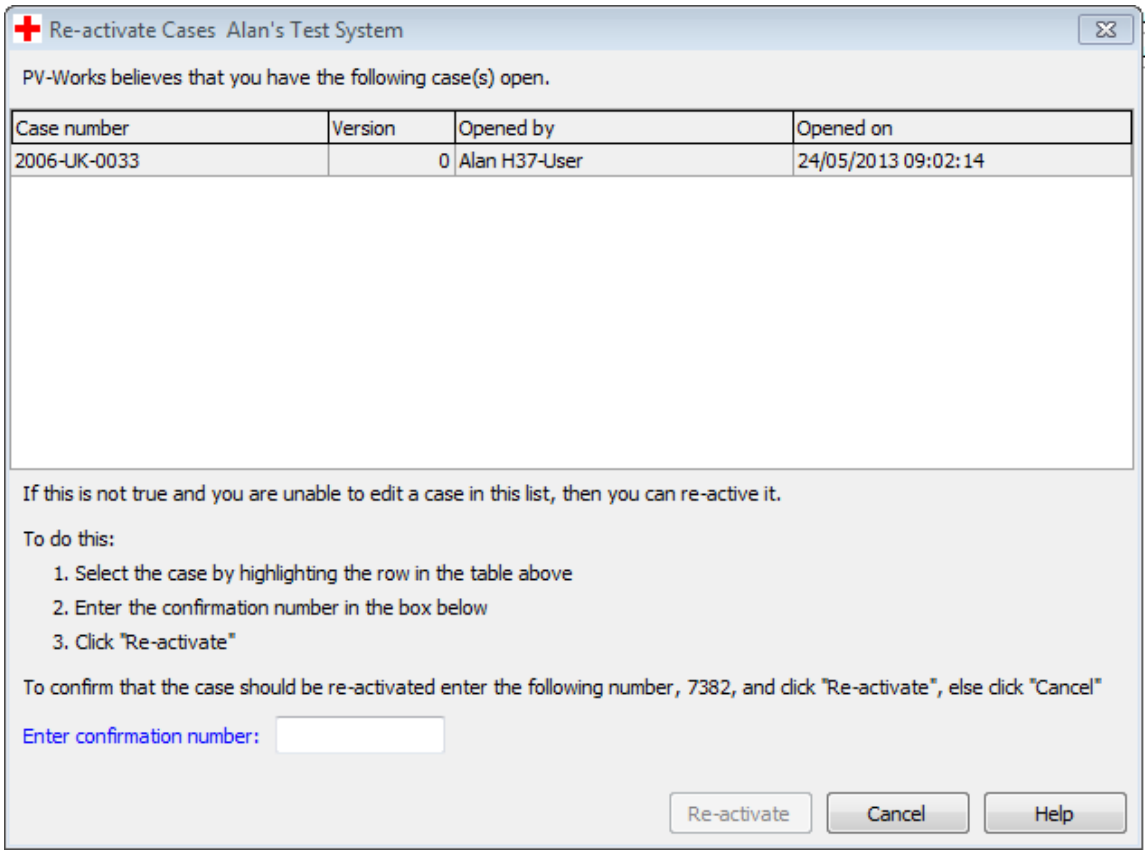
The "Re-activate Cases" function allows the administrator to free the lock.

Figure 32 : Case open by another user message



On clicking the Configuration | Reactivate Cases option, the following pop-up screen will be displayed listing all cases currently open for all users.

Figure 33 : Re-activate cases screen



Warning note that this list will also include cases that are open and not just a case that is locked. "Re-activating" a case that is not actually locked could mean that another user opens that case at the same time as the current user. The likely consequence of this is lost data changes.

In order to re-activate a case, the administrator should:

a) Highlight the case by clicking its row

b) Enter the randomly generated confirmation code in the box at the foot of the screen (this is a simple security measure to make the administrator slow down and confirm that the correct case is selected). Once entered, the “re-activate” button will become active

c) Click re-activate

Once re-activated the case will disappear from the list on this screen and may be re-opened by a user.

4 Security

4.1 Introduction

All PV247 users are allocated a default set of pools that allow them to access all aspects of the PV-Works application. In addition users may also be granted access to the configuration module by an administrator setting having the relevant field on the user management screen.

Security rights to use PV-Works are assigned when a user successfully logs on to the system. Outside of PV-Works the user has no rights to the database, thus preventing use of third-party tools to access or amend the database, unless these permissions have been granted by the Database Administrator. This restriction applies to the use of third party products running alongside PV-Works, ie when PV-Works is open and rights have been granted to the user, these only apply to the PV-Works application itself.

PV-Works includes two other features related to security:

1. Case Lock – the ability to lock a case at a certain point in its processing to prevent further amendment.

2. Single user update – PV-Works can be configured so that only one user may update a particular case at any one time. See section 4.3for further details.

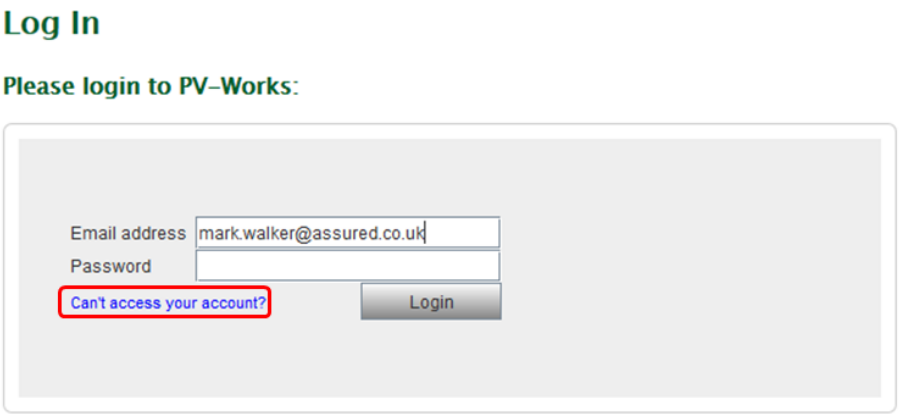
4.2 User Passwords

PV247 uses a dual authentication system to restrict access to the service

- A user name and password are created automatically for each user at the time the PV-Works account is created by the administrator. The username is by default the email address that is registered at the time of account creation. The password is an alphanumeric string which is none-expiring.

- A new password can be requested at any time either at an interval specified by the company's internal process or if the user cannot access the system. The new password request is made from the main login screen by entering a valid username and then clicking on the link shown below.

Figure 34 : Password Reset



- A new password will be sent to the users email address.

- The second level of authentication is provided by a memorable word which is required to access the PV-works application. Where a user has access to multiple PV-Works systems either Production and Test or Human and Vet, then a separate memorable word is required for each system.

- User is required to register a memorable word the first time they access a particular system and there after every 100 days. A new memorable word is set using the popup screen shown in Figure 35.

Figure 35 : Change User memorable word

4.3 Single user update

PV-Works is configured so that two users can not update the same case at the same time.

When a user starts a function that could update the database such as data entry, assessment and translation, PV-Works checks whether another user is already working in a similar function on the same case. In this situation the new user is prevented from starting the function and is informed which user has the case open. If no other user is accessing an update function, PV-Works assigns the case to the new user.

A case remains unavailable until the user who is editing it moves to another case, moves to a non-updating function in the same case or closes the system. To prevent cases being left unavailable permanently due to system crashes:

- every time a case is made unavailable to other users, this action is time-stamped and will become invalid at mid-night on the day it was set

- as part of the log-on process all cases that were made unavailable from previous days are cleared

- a systems administration function allows a privileged manager to make unavailable cases available again (See section 3.11)

4.4 Access to Database Subsets (Not applicable to PV247 vet systems)

From version 3.4 onwards a more comprehensive case sub-setting function is introduced where filter rules may be introduced that are applied to the database BEFORE any pool assignments are considered. In principle the System Administrator may create subset rules that refer to any database field. However, it is expected that a small list of fields will be used commonly. These are:

- Customer name (eg in a CRO setting)
- Country of occurrence of the case
- Country of product registration
- Product family
- Study protocol

Examples of rules that might be created:

- All cases where the product is marketed in France.
- All cases for products owned by 'MyPharma Ltd'
- All cases which occurred in Scandinavia
- All cases which contain the product 'Sludgo'

In parallel with sub-set definitions for cases, it is possible to sub-set dictionary data so that a filtered list of products, locations and clinical trials is presented to a user who views a sub-set of cases. Four dictionaries are subject to subset filters:

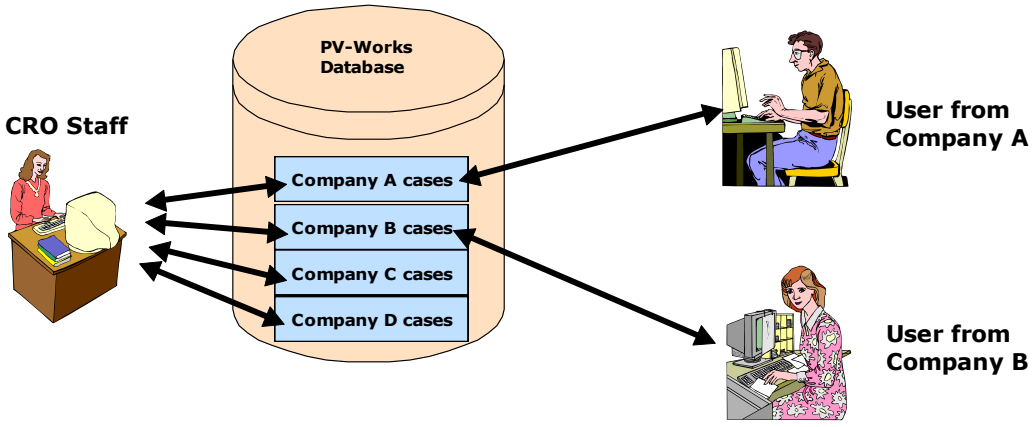
- Product dictionary – so that the subset only sees products relevant to its definition
- Contact dictionary – so that company names are filtered
- Clinical trial dictionary – so that studies are filtered
- User security dictionary – so that users within a subset can only see colleagues of their subset

Each rule is defined by the System Administrator and users are assigned to a rule or to a number of rules. For customers using the PV247 implementation it is possible to administer case subsetting rules at a customer level from within PV-Works (see section 3.10).

Within a subset the standard PV-Works security rules of local versus foreign cases and "per study" access rules are still applicable. In other words a sub-set can be seen as a mini-database.

A typical case-subsetted arrangement is illustrated in Figure 36

Figure 36 : Case Subsetting of a PV-Works Database



Over-riding the whole function is a system option that determines whether any case sub-setting rules apply to the user or not. 'Restricted' users and 'Unrestricted' users may co-exist in the same database.

A user who is not restricted by any rules will see the whole database, subject to their pool membership and the access rights of each pool. A user who is restricted by one or more rules will only see a case if its data passes one or more of the rules to which they are assigned – and then this set of cases is subject to the permissions granted through pool membership.

It is possible to mix restricted users and non-restricted users in the same database. An example of this would be a CRO implementation where CRO staff would be unrestricted so that they can view all cases while client staff would be restricted to a database subset that represents their cases.

The rules are applied across all functions of PV-Works – data entry, queries and reporting.

WARNING : It would be inadvisable to allow a user subject to case subsets to run PSUR reports unless the case included in the line listing should be restricted to those visible in the user's subset.

This could lead to an incomplete PSUR.

If a user is assigned to multiple rules then a case will be visible if any of the rules make it visible. That is this function applies OR logic to the rules, ie

"case is visible in rule A" OR "case is visible in rule B"

This can be used to advantage in the rule "all cases which occurred in Scandinavia". To deliver this subset it is necessary to create four rules:

- All cases which occurred in Denmark
- All cases which occurred in Finland
- All cases which occurred in Norway
- All cases which occurred in Sweden

and then assign each of these rules to the users responsible for Scandinavia.