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EURECA

Enabling information re-Use by linking clinical Research and CAre

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0 DOCUMENT INFO

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V0.2	18.06.2012	Definition of ToC
V0.3	12.10.2012	First complete draft
V0.4	09.11.2012	Integrated version (send to WP members)
V0.5	16.11.2012	Updated version (send PCP)
V0.6	20.11.2012	Updated version (send to project internal reviewers)
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0.4 Distribution list

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Table of Contents

1 Introduction

Whereas deliverable D1.1[1] deals with interviews of potential stakeholders for the identification and prioritisation of the user needs – as well as a first iteration of the definition of scenarios based on the answers and needs from users – the current version of this deliverable includes a consolidation of the user needs, with a reorganisation of the scenarios and definition of technical use cases.

For that matter this document proposes a more refined iteration for the scenarios that have been previously submitted. The purpose of this new design of scenarios is to be challenging while remaining realistic regarding to the possibility of development of these tools. The philosophy of this reorganisation is to present logical and chronological links between all the scenarios, to be both more comprehensive and be of use for their technical implementation and coordination.

The use cases that are presented in this document are written from a technical point of view, in a way that will provide us to design the initial EURECA architectural decomposition in D2.2[2], as these use cases are the logical interface between clinical needs and technical development. Indeed their normal flow are very close to a graphical user interface (GUI) in their expression, as it focuses on the different step of interaction that could be realised by the final user (e.g. clinicians, investigators, patients).
Figure 1 illustrates the pipeline of interaction between different deliverables of both WP1 and WP2 about use cases and architecture.

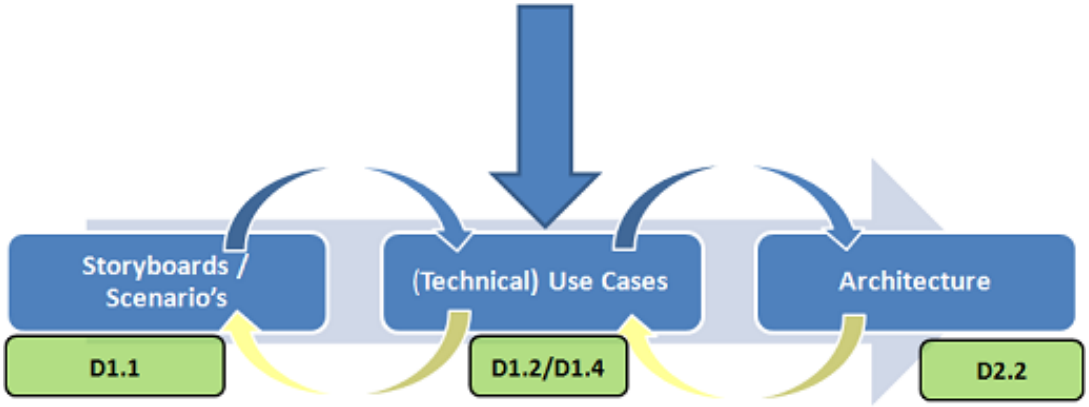


Figure 1 - Interaction between deliverables on use cases and architecture

In addition this document gives an overview of legal and ethical requirements applied to the use cases. For that matter, a more precise analysis will be explained in more details in D7.1[3].

[1] EURECA project, "User needs and specifications for the EURECA environment and software services," due date: August 2012.
[2] EURECA project, "Initial architecture," due date: February 2013.
[3] EURECA project, "Initial EURECA legal and ethical requirement," due date: January 2013.

2 Scenarios

2.1 New scenarios from partners

As we are facing an iterative process, new scenarios are still welcomed to be considered and developed within the project, so that we can take into account new expressions of user needs and requirements which have not already been covered by the scenarios that have been previously defined in the first round.

2.1.1 Universität des Saarlandes: Microbiology SAE

Description of the tool:
In case of chemotherapy for a malignancy fever, infectious complications are important and sometimes life threatening SAEs.
To get an early knowledge about infectious agents and their resistance profile, an oncology ward will help to choose pre-emptively the correct antibiotic treatment for a patient. Meaning if a new patient enters the ward with fever of unknown origin, one can compare his data with the data stored of other patients and to check which treatment was given to similar patients and what was their outcome.
This use case will also help to analyse the use of antibiotics on a ward and compare the distribution of infectious agents on a specific ward with other wards of a hospital as well as with other oncology centres, if they use the same tool.

Problem(s) to solve:
Early correct treatment for infectious complications (SAE) under chemotherapy for cancer.

Challenges:
To get data from different databases as the hospital information system (HIS) for clinical data, CTC grade, laboratory data, the microbiological databases about the infectious agents and from which material (blood, CSF, urine, etc.) they were isolated, the antibiotic resistance profile, etc. In addition the antibiotics given to a patient on the ward on a daily basis is needed.

Expected benefits:
Better antibiotic treatment for infectious complications.

The use cases for that new scenario are available in *Section 3.4.1*.

2.2 The EURECA scenarios

Scenarios that were proposed by clinical partners and that have been presented in D1.1 have been grouped into general scenarios (see *Figure 2):*

1. Information
2. Investigation (a. Guidelines investigation / b. Protocol and research investigation)
3. Selection and recruitment (a. Choice of treatment / b. Patient recruitment into a trial)
4. Reporting
5. Long-term follow-up
6. Economic analysis

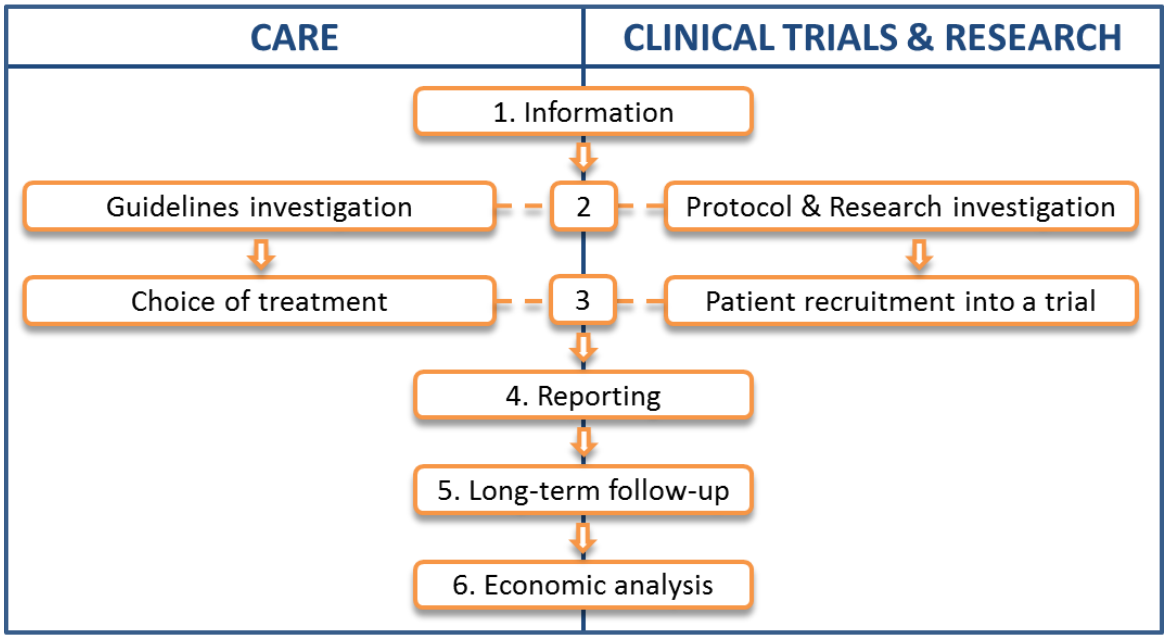


Figure 2 - General schema for the scenarios

	Final scenarios (Sub-scenarios)		Partners	Scenarios from partners	Technical use cases	Responsible partner
1	Information		SIT 2	Medical information recommender	Personal medical information recommender	StoneRoos
			VUA 2	Contextualized discovery		
			UdS 3	Extract patient data from EHR and PHR	Export from EHR to PHR	FORTH
			UdS 2	Data mining on consultation data	Data mining of consultation	FhG IAIS
			VUA 1	Contextualized overview	Contextualized overview	VUA
			C-P 1	Similarity of datasets to combine		
2	Investigation	Guidelines investigation	UdS 4	Guideline development	Update of guidelines	VUA
			Maastro 1	Rare case literature		
			UOXF1	Diagnostic sarcoma classifier	Training a diagnostic classifier	UOXF
		Protocol & Research investigation	UdS 5	Opt-out solution for further research	Broad consent	Custodix
			UdS 6	Hypothesis generation	Hypothesis generation	UOXF
			VUA 3	Design of trial conditions	Supporting design of new trials	Philips
			UdS 7	Trial/Protocol feasibility	Protocol feasibility	
3	Selection & Recruitment	Choice of treatment	UdS 8	Microbiology SAE	Microbiology SAE	FhG IBMT
			Maastro 2	Rapid learning	Outcome prediction	UOXF
			Maastro 3	Outcome prediction		
			UOXF 1	Diagnostic sarcoma classifier	Use a diagnostic classifier	UOXF
			Maastro 4	Rare case experience		
		Patient recruitment into a trial	Maastro 5	Guideline protocol selection	Find trials for patient	Custodix
			Maastro 6	Trial selection		
			IJB 1	Suggest clinical trials for a patient		
			BIG 1	Trial-enrolment advice to clinicians attending the MDT, based on clinical trials protocol eligibility criteria		
			BIG 2	Ranking clinical trials		
			UOXF 2	Clinical trials finder and patient matcher	Alert service	
			UdS 9	Select patients for a trial	Find patients for trial	
4	Reporting		IJB 2	Identify episodes of febrile neutropenia	Reporting episodes of febrile neutropenia	IJB
			IJB 3	Identify incident tumours and report to cancer registry	Cancer registry reporting	
			IJB 4	Identify recurrent tumours and report to cancer registry		
			IJB 5	Extract EHR data to fill cancer registry and eCRF	Pre-filling of CRF and AE reports	UPM
			Maastro 7	Clinical data reuse		
			Maastro 8	"GGO": Using DNA sequencing in Oncology (for clinical trials & daily health care) to identify patients that have a non-synonymous mutation in a gene that is related to drug or radiation sensitivity	Automatic dectection of SAEs/SUSARs	FhG IBMT
			UdS 10	Detection and prediction of SAEs and SUSARs		
			UdS 11	Pharmacovigilance - Reporting SAEs and SUSARs automatically	Automatic reporting of SAEs/SUSARs	
5	Long-term follow-up		IJB 7	Safety reporting of specific adverse reactions after study treatment completion	Long-term follow-up & Patient diary	FORTH
			IJB 8	Primary and key secondary outcome measures		
			UOXF 3	Access and integrate information from primary care and other clinical databases in patients undergoing clinical trial in Sarcoma		
			IJB 9	Survival follow-up		
			FhG IBMT 1	Long-term-follow-up of patients from clinical trials by linking PHR data to clinical trial management systems		
			UdS 12	Patient diary		
6	Economic analysis		UdS 13	Analyse economic data between different procedures	Economic analysis of different procedures	FhG IAIS

Figure 3 - Summary table of the scenarios and technical use cases

These scenarios have been design in a logical and chronological way in order to take into account the links between all scenarios and the assignments of all use cases (see *Figure 3*). Scenarios are then divided between Care and clinical Trials Systems.

2.3 Update of the ranking interest for clinical partners and on available data for the scenarios

Together with the reorganisation of the scenario and the development of the technical use cases comes an update of the ranking of them by clinical partners (See *Figure 4*) whose ranking numbers are defined as:

- 4: the most interesting
- 3: very interesting
- 2: interesting
- 1: little interest
- 0: no interest

	Final scenarios (Sub-scenarios)		Partners	Scenarios from partners	Ranking from clinical partners						AVERAGE RANKING	Technical use cases
					IJB	UdS	UOXF	BIG	Maastro	GBG		
1	Information		SIT 2	Medical information recommender	1	1	2	2	1	2	1.50	
			VUA 2	Contextualized discovery	1	1	2	2	1	2	1.50	Personal medical information recommender
			UdS 3	Extract patient data from EHR and PHR								Export from EHR to PHR
			UdS 2	Data mining on consultation data	1	3	2	1	3	2	2.00	Data mining of consultation
			VUA 1	Contextualized overview	1	1	4	2	2	2	2.00	Contextualized overview
			C-P 1	Similarity of datasets to combine								
2	Investigation	Guidelines investigation	UdS 4	Guideline development	2	2	3	3	3	2	2.50	Update of guidelines
			Maastro 1	Rare case literature								
			UOXF1	Diagnostic sarcoma classifier	1	1	4	1	4	1	2.00	Training a diagnostic classifier
		Protocol & Research investigation	UdS 5	Opt-out solution for further research	1	4	2	3	1	2	2.17	Broad consent
			UdS 6	Hypothesis generation	2	3	4	3	3	3	3.00	Hypothesis generation
			VUA 3	Design of trial conditions								Supporting design of new trials
			UdS 7	Trial/Protocol feasibility	4	4	1	3	4	4	3.33	Protocol feasibility
3	Selection & Recruitment	Choice of treatment	UdS 8	Microbiology SAE								Microbiology SAE
			Maastro 2	Rapid learning	1	1	4	1	4	1	2.00	Outcome prediction
			Maastro 3	Outcome prediction								
			UOXF 1	Diagnostic sarcoma classifier								Use a diagnostic classifier
			Maastro 4	Rare case experience								
		Patient recruitment into a trial	Maastro 5	Guideline protocol selection	4	2	4	4	4	4	3.67	Find trials for patient
			Maastro 6	Trial selection								
			IJB 1	Suggest clinical trials for a patient								
			BIG 1	Trial-enrolment advice to clinicians attending the MDT, based on clinical trials protocol eligibility criteria								
			BIG 2	Ranking clinical trials								
			UOXF 2	Clinical trials finder and patient matcher								Alert service
			UdS 9	Select patients for a trial	1	1	4	4	2	4	2.67	Find patients for trial
4	Reporting		IJB 2	Identify episodes of febrile neutropenia	4	4	4	4	4	3	3.83	Reporting episodes of febrile neutropenia
			IJB 3	Identify incident tumours and report to cancer registry								
			IJB 4	Identify recurrent tumours and report to cancer registry								Cancer registry and tumour bank reporting
			IJB 5	Extract EHR data to fill cancer registry and eCRF								
			Maastro 7	Clinical data reuse								Pre-filling of CRF and AE reports
			Maastro 8	"GGO": Using DNA sequencing in Oncology (for clinical trials & daily health care) to identify patients that have a non-synonymous mutation in a gene that is related to drug or radiation sensitivity	3	4	2	2	1	3	2.50	Automatic dectection of SAEs/SUSARs
			UdS 10	Detection and prediction of SAEs and SUSARs								
			UdS 11	Pharmacovigilance - Reporting SAEs and SUSARs automatically	3	3	2	2	2	3	3.00	Automatic reporting of SAEs/SUSARs
5	Long-term follow-up		IJB 7	Safety reporting of specific adverse reactions after study treatment completion	4	4	4	3	3	3	3.50	Long-term follow-up & Patient diary
			IJB 8	Primary and key secondary outcome measures								
			UOXF 3	Access and integrate information from primary care and other clinical databases in patients undergoing clinical trial in Sarcoma								
			IJB 9	Survival follow-up								
			FhG IBMT 1	Long-term-follow-up of patients from clinical trials by linking PHR data to clinical trial management systems								
			UdS 12	Patient diary	1	3	3	1	2	2	2.00	
6	Economic analysis		UdS 13	Analyse economic data between different procedures	1	1	1	1	1	1	1.00	Economic analysis of different procedures

Figure 4 - Ranking of scenarios by clinical partners

This ranking is informative, but it remains important to keep in mind the interest of clinical partners for the tools that will be developed and which will be the core of the project. It also assures that the whole project, and in particular the technical use cases that are presented in this document, remain clinically-driven.

3 Technical use cases development

3.1 Actors

In the EURECA scenarios 17 main actors were identified. *Table 1* lists these actors together with the use cases in which they interact.

Actor Name	Description	Interacts with
Patient		**Patient Diary**
Clinical investigator	An oncologist, or a person working with an oncologist and who is in charge of collecting data on patients for the clinical trial (e.g. a research nurse)	**Data mining of consultation** **Training a diagnostic classifier** **Protocol feasibility** **Microbiology SAE** **Find trials for a patient** **Find patients for a trial** **Reporting episodes of febrile neutropenia** **Cancer registry and tumour bank reporting** **Automatic detection of SAEs/SUSARs** **Automatic reporting of SAEs/SUASRS** **Long-term follow-up**
Trial chairman		**Data mining of consultation** **Microbiology SAE** **Automatic detection of SAEs/SUSARs** **Automatic reporting of SAEs/SUASRS** **Long-term follow-up**
Researcher	Person that investigates new trials	**Supporting design of new trials** **Protocol feasibility**
Pharmaceutical company		**Find patients for a trial**
Guideline developer		**Update of guideline**
Local trainer	The person using the tool locally	**Training a diagnostic classifier**
Local study group	The support team for the local trainer	**Training a diagnostic classifier**
Over-viewing study group	The co-investigators	**Training a diagnostic classifier**
Statistician/ bioinformatician/ IT		**Training a diagnostic classifier**
System administrator		**Find patients for a trial** **Automatic reporting of SAEs/SUSARs**

Table 1 - List of use case's actors

3.2 "Information" related use cases

USE CASE: Personal medical information recommender

This use case will be implemented in D1.4.

USE CASE: Export from a EHR to a PHR

This use case will be implemented in D1.4.

USE CASE: Data mining of consultation

This document describes the uses cases for the scenario of data mining of consultation data. The goal is to help a trial chairman to answer frequently asked questions in consultations posed by clinicians.

This scenario comprises the following use cases:

Use Case ID	UC.CD.CR.01	**Priority**	REQUIRED
Use Case name	**Entering a consultation request**		
Date created	10/10/2012	**Last updated**	31/10/2012
Brief description	A local physician asks for consultation by filling in a consultation request form.		
Relates to Scenario	Data mining of consultation		
Includes use case	-		
Actors Involved	Investigator		
Trigger			
Pre-conditions	Local physician is authenticated to use the consultation tool and is authorized to enter a new consultation request. Trial chairman has sufficient rights to process data in a tool at his own institution		
Post-conditions			
Successful End condition	Consultation request is stored successfully in system.		
Fail End Condition	Consultation request is incomplete and cannot be processed by system		
Normal Flow	1. Local physician opens the application for entering a consultation request. A consultation request screen is shown in which all relevant information can be entered. 2. Local physician inputs the relevant information into the data fields and clicks "submit". Structured clinical data is mandatory. Additional Images, free text and documents, which might be uploaded, are optional. 3. The trial chairman is notified by e-mail that a new consultation request has been submitted and is waiting for a reply. 4. Local physician is informed that the trial chairman has		

	been informed about the consultation request.
Alternative Flow 1	
Usage Frequency	Medium
User interfaces	T.b.d., dependent on format of consultations.
Business Rules	
Assumptions	
Notes and Issues	The system is installed at each Eureca client site and runs as a local service integrated in the local ObTiMa.

Use Case ID	UC.CD.CR.02	**Priority**	REQUIRED
Use Case name	**Viewing a consultation recommendation**		
Date created	10/10/2012	**Last updated**	31/10/2012
Brief description	A trial manager receives a recommendation of existing consultations and the answers that might be relevant for the new consultation.		

Relates to Scenario	Data mining of consultation
Includes use case	-
Actors Involved	Trial chairman
Trigger	Trial chairman has received an e-mail notification from UC.CD.CR.1 Entering a consultation request
Pre-conditions	UC.CD.CR.1 has been executed successfully. Trial chairman is authenticated to use the consultation tool and is authorized to enter consultation replies.
Post-conditions	UC.CD.CR.3 giving feedback on consultation recommendations is called
Successful End condition	Consultation recommendation is shown to trial chairman
Fail End Condition	No recommendation matching the request found. Trial chairman is redirected to UC.CD.CR.4 Entering a new consultation reply
Normal Flow	1. The system computes the similarities between the current CRF and all CRFs in the system. 2. A list of previous consultation requests and answers that were given to them is shown to the trial chairman. The list is ranked according to its relevance to the current case.
Alternative Flow 1	Trial chairman is informed that database of consultations is empty. Trial chairman is redirected to UC.CD.CR.4 Entering a new consultation reply.
Alternative Flow 4	If recommendations shown in step 1. do all not fit the current case the trial chairman can click on a button to show more consultation suggestions.
Usage Frequency	Medium
User interfaces	T.b.d., dependent on format of consultations.
Business Rules	

Assumptions	
Notes and Issues	Data protection: Only in case the local physician got informed consent from the patient, the local physician can give the trial chairman the right to see the personal data. Else the trial chairman will see only pseudonymous data.

Use Case ID	UC.CD.CR.03		**Priority**	REQUIRED
Use Case name	**Giving feedback on consultation recommendations**			
Date created	10/10/2012	**Last updated**	31/10/2012	
Brief description	Trial chairman gives feedback on the relevancy of the consultation he has received in UC.CD.CR.2			
Relates to Scenario	Data mining of consultation			
Includes use case	-			
Actors Involved	Trial chairman			
Trigger	UC.CD.CR.2 is successfully executed			
Pre-conditions				
Post-conditions				
Successful End condition	recommendation model is updated			
Fail End Condition	-			
Normal Flow	1. Trial chairman views all recommendations from UC.CD.CR.2 and marks cases as relevant or not relevant to his case in a checkbox. 2. Trial chairman clicks “submit feedback” to store feedback in system 3. System internally updates recommendation model			
Alternative Flow 1	Optionally, after Step 3 UC.CD.CR.2 may be executed again to display a new set of recommendations.			
Alternative Flow N				
Usage Frequency	Medium			
User interfaces	Checkboxes for consultation recommendations in UC.CD.CR.2			
Business Rules				
Assumptions				
Notes and Issues				

Use Case ID	UC.CD.CR.04		**Priority**	REQUIRED
Use Case name	**Entering a consultation reply**			
Date created	10/10/2012	**Last updated**	31/10/2012	
Brief description	A trial manager writes a consultation reply (FAQ) and stores it in the system for future usage.			
Relates to Scenario	Data mining of consultation			
Includes use case	-			
Actors Involved	Trial chairman			

Trigger	UC.CD.CR.3 is successfully executed.
Trigger 2	UC.CD.CR.2 has been unsuccessful.
Pre-conditions	Trial chairman is authorized to enter new consultation replies into the system.
Post-conditions	
Successful End condition	Consultation reply is stored successfully in the ObTiMa system and linked to the consultation request.
Fail End Condition	
Normal Flow	1. Trial chairman clicks on “enter reply”. 2. Trial chairman selects one answer from the system and copies it to the answer section of the consultation request form. 3. Trial chairman modifies the answer as required and clicks “submit”. 4. Confirmation is shown, user is re-directed to home screen. 5. Local physician is notified by email that his request has been answered.
Alternative Flow 1	If no matching answer was found the trial chairman enters all data manually into structured data and free text fields and clicks “submit”
Alternative Flow N	
Usage Frequency	Medium
User interfaces	T.b.d., dependent on format of consultations.
Business Rules	
Assumptions	
Notes and Issues	

Use Case ID	UC.CD.CR.05	**Priority**	REQUIRED
Use Case name	**Viewing a consultation reply**		
Date created	12/11/2012	**Last updated**	12/11/2012
Brief description	A local physician views a consultation reply from a trial chairman.		

Relates to Scenario	Data mining of consultation
Includes use case	-
Actors Involved	Investigator
Trigger	Local physician has received an e-mail notification from UC.CD.CR.4
Pre-conditions	
Post-conditions	
Successful End condition	Consultation recommendation is shown to local physician
Fail End Condition	
Normal Flow	1. Consultation reply is shown to local physician
Alternative Flow 1	
Alternative Flow N	

Usage Frequency	Medium
User interfaces	T.b.d., dependent on format of consultations.
Business Rules	
Assumptions	
Notes and Issues	

USE CASE: Contextualized overview

This use case will be implemented in D1.4.

3.3 "Investigation" related use cases

The following table summarises the use cases which have goals related to investigation of new guidelines for treatment of patients, new proposals for protocols and new research, which are part of the investigation scenario.

Use Case ID	Use Case Description
UC.RD.UG.01	Update of guidelines
UC.CD.SC.01	Training of a diagnostic classifier
UC.TS.PF.01	Define a new clinical trial proposal
UC.TS.PF.02	Define a new eligibility criterion for a trial proposal
UC.TS.PF.03	Request execution of a trial feasibility
UC.TS.PF.04	View trial feasibility verification request
UC.TS.PF.05	Execute trial feasibility request on data source
UC.TS.PF.06	Delete a trial feasibility verification request
UC.TS.PF.07	Edit a clinical trial proposal
UC.TS.PF.08	Define trial path options
UC.TS.PF.10	Define eligibility criterion - probability
UC.TS.PF.11	Compute eligibility criterion probability
UC.TS.PF.12	Define trial path probability
UC.TS.PF.13	Compute trial path probability
UC.TS.PF.14	Determine required sample size
UC.TS.PF.15	View patient data for trial feasibility verification

3.3.1 Guidelines investigation

USE CASE: Update of guidelines

Use Case ID	UC.RD.UG.01		**Priority**	REQUIRED
Use Case name	**Update of guidelines**			
Date created	07/09/2012	**Last updated**	24/09/2012	
Brief description	Support the updating process of a guideline by identifying relevant literature (evidence) for this guideline.			
Relates to Scenario	• **Develop or update of guidelines from clinical trial data and literature mining.**			
Includes use case	N/A			
Actors Involved	• Guideline developer (e.g. Dutch Institute of Health improvement CBO)			

Trigger	• A developer wants (or is requested) to check the availability of new relevant literature for items of an existing guideline
Pre-conditions	• Guidelines with links to evidence are available. For instance those that are developed based on the AGREE method from the Guideline International Network (G-I-N-network). (guideline repository) • Access is provided to papers on PubMed and clinical trials repository. • The guideline developer has sufficient access rights and is authenticated to the EURECA platform • The guideline developer is authenticated to the system and has sufficient access rights. • Guidelines and literature are in the same languages, i.e. with English guidelines
Post-conditions	N/A
Successful End condition	New evidence or counterevidence is found for one or more items of the selected guideline, in literature linked as “potentially relevant”.
Fail End Condition	N/A

Normal Flow	1. The guideline developer starts the guideline system.
	2. The guideline developer can make a choice between:
	  • A search for relevant literature (incl. Clinical trials) for a specific goal (e.g. an update of a guideline of a specific disease)
	  • to get all possibly relevant literature for a set of guidelines that he/she is interested in which lead possibly to an update of the guideline (push)
	3. A list of Guidelines is presented with evidences and the level of evidence.
	4. The guideline developer can find new and relevant evidences from papers in PubMed or clinical trial repositories based on the evidences of a guideline.
	  • This is based on a set of keywords from the evidence description, keywords of the papers, and the references of the papers to identify the relevance. The system shows the potentially relevant literature.
	5. (S)he can examine the newly found evidences manually or semi-automatically by filtering and ranking the new evidence (by the system) if possible.
	6. The system shows two types of examination:
	  • increasing/ decreasing the existing evidence of a conclusions of a guideline,
	  • specialisation of the conclusions by new evidence for a new treatment, by combination of the treatment of multiple diseases for more personalized guidelines (comorbidity), or specialisation by splitting a patient group
	7. The guideline developer can then make suggestions for update of the guidelines in two ways:
	  • update of the level of evidence
	  • an update of the conclusions together with identifying the evidence and level of evidence.

Alternative Flow 1	• In **step 2**: the guideline developer can choose or control the method for searching relevant literature. Examples are that the guideline developer gives particular keywords (e.g. one of key questions of the guideline that have to be updated), only recently updated guidelines of other countries, only search for USA-trials.
Usage Frequency	Pull: when a guideline needs an update. The update frequency of guideline is rather low 2-5 years. Push: when relevant literature is found for a particular (set of) guidelines. The final goal is to have "living guidelines" which are guidelines that are updated as soon new evidence is available. The tool will only contribute to the direction of this final goal.
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	N/A

USE CASE: Training a diagnostic classifier

Use Case ID	UC.CD.SC.01	**Priority**	REQUIRED
Use Case name	**Training of a diagnostic classifier**		
Date created	16/10/2012 **Last updated**		05/11/2012
Brief description	Initial training and every time a new data is available train the sarcoma classifier again.		
Relates to Scenario	Diagnostic Classifier		
Includes use case	N/A		
Actors Involved	• Investigator • Local trainer • Local study group • Over-viewing study group • Statistician/bioinformatician/IT		
Trigger	Clinician receives a notification that new data are available		
Pre-conditions	• An over-viewing study group is composed by the clinician, who will design the study and agree on the Quality Control. • A study group is present at each clinical site • The toolbox for distributed training is installed at various clinical locations • Toolboxes for data pre-processing are installed at various sites (e.g. image processing tools). • The local installation of the tool has access to integrated data from: EHR and PHR, genomic databases, imaging databases, pathology databases, clinical trial databases as needed by the classifier. • [if needed] The tool has access to current guidelines • [if needed] The tool has access to PUBMED • [if needed] The tool has access to NCBI databases • [if needed] The tool has access to public clinical trials databases		

	• [if needed] The tool has access to web based ontologies (e.g. http://bioportal.bioontology.org)
Post-conditions	The model is initialised at different institutions and the models are combined into a summary model
Successful End condition	Diagnostic classifier is trained
Fail End Condition	N/A
Normal Flow	1. The chair clinician receives a notification that initial or new data are available. 2. The chair clinician notifies the over-viewing study group to plan and design the training. 3. Study design, data pre-processing and quality control (QC) guidelines are set by the over-viewing study group 4. The chair clinical is notified by the study group 5. The local trainers are contacted at each institution by the chair to start the training; they receive the study design, data pre-processing guidelines and the QC guidelines 6. The local trainer at each site works with the local study group to finalize the requirements for data use and access (e.g. consent, institution research board and ethics committee approvals) 7. The local trainer retrieves the data according to the requirements 8. The local trainers at each site initialize the pre-process of the data as required by the data pre-processing guidelines (e.g. image segmentation and processing, genomic data summarization and normalization) 9. Pre-processed data and QC statistics are generated at each site; this is anonymous data 10. The QC is approved locally and reviewed by the over-viewing study group for general consensus. 11. The study group notifies consensus on the QC to the chair 12. The chair clinician notifies the local trainers to initiate the training of the statistics models 13. At each institution/local site a model is trained/obtained by using the distributed data mining toolbox 14. Each site returns a trained model (or several if different algorithms are used) qualified by a set of statistics (e.g. AUC, calibration). This model contains no personal data. 15. A summary model is obtained to form the base of the Diagnostic classifier 16. The Diagnostic classifier is ready for later independent evaluation (see Validation Scenario)
Alternative Flow 1	If no general consensus is achieved in step 9, then back to 6
Alternative Flow N	N/A
Usage Frequency	Low
User interfaces	N/A
Business Rules	Not yet clear
Assumptions	N/A
Notes and Issues	N/A

3.3.2 Protocol and research investigation

USE CASE: Broad consent

This use case will be implemented in WP7.

USE CASE: Hypothesis generation

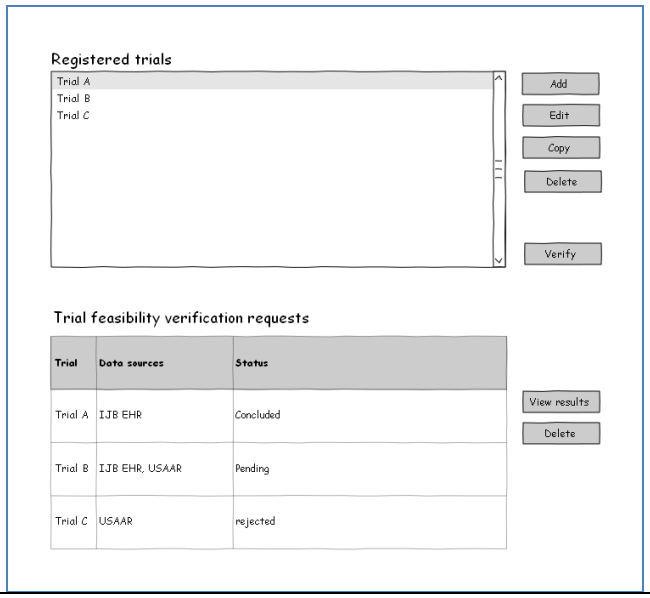
This use case will be implemented in D1.4.

USE CASE: Supporting design of new trials / Protocol feasibility

In this section, the use cases for the Protocol Feasibility scenario are described (see Figure 5). The use cases can be divided into 3 rough groups: defining a trial proposal, requesting an evaluation of the recruitment potential of a trial for selected data sources, and viewing of the results of the evaluation.

Figure 5 - Protocol feasibility use cases diagram

Use Case ID	UC.TS.PF.01		**Priority**	REQUIRED
Use Case name	**Define a new clinical trial proposal**			
Date created	05/09/2012	**Last updated**	1/11/2012	
Brief description	A researcher defines a new clinical trial proposal			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Includes use case	• **UC.TS.PF.02** Define a new criterion for a clinical trial proposal • **UC.TS.PF.08** Define trial path options • **UC.TS.PF.14** Determine required sample size			
Actors Involved	• Researcher			
Trigger	The researcher wants to define a new clinical trial proposal			
Pre-conditions	• The researcher is authenticated to the system and is authorized to use the trial feasibility application			
Successful End condition	A new clinical trial has been defined			
Normal Flow	1. The researcher opens the (web)application for trial feasibility verification. A screen is shown containing a “registered trials” list and a “trial feasibility verification requests” list (see UI1). 2. The researcher clicks on the “add” button situated next to the “registered trials” list in order to create a new trial. 3. A new screen is shown, presenting several trial specific entry fields: • The trial name • The trial description • A list to contain eligibility criteria • A tree structure to contain the trial paths (see notes) • A date range (see notes) 4. The researcher fills in the correct trial name, description and date range. 5. He can optionally add, define or delete (eligibility) criteria for the trial (see **UC.TS.PF.02**) 6. He can optionally add, define or delete trial paths for the trial (see **UC.TS.PF.08**) 7. He can optionally determine the required sample size for the trial (see **UC.TS.PF.014**) 8. He can optionally estimate the percentage of patients that decide to not enroll into the trial though they are eligible for enrollment 9. He can optionally estimate the percentage of patients that will be enrolled into a competitive trial though they are eligible for enrollment 10. He can optionally estimate the percentage of patients that will quit the trial after inclusion (“drop-out rate”) 11. The researcher clicks on a “save trial” button. 12. The researcher is redirected back to the main trial screen where a “successful saved trial” message is displayed. The new trial is visible in the “registered trials” list.			
Alternative Flow 1	• In **step 2** the researcher can chose to copy an already existing trial proposal by selecting a trial in the “registered trials” list and clicking on the “copy” button. This will redirect him to step			

	3 where the entry fields are already filled in with the copied data.
Usage Frequency	Low
User interfaces	UI1: 
Notes and Issues	• The date range in which observations should fall is set to assess enrolment rates (Returning only patient counts as encountered in the data sources is not sufficient to assess feasibility). • One might imagine working collaboratively on the trial proposals. • The trial paths are displayed in a tree format, where each path from the root to a leaf represents a trial path.

Use Case ID	UC.TS.PF.07		**Priority**	RECOMMENDED
Use Case name	**Edit a clinical trial proposal**			
Date created	17/09/2012	**Last updated**	17/09/2012	
Brief description	A researcher wants to edit a clinical trial proposal			
Notes and Issues	• This is a placeholder for the case where a researcher wants to edit an existing clinical trial proposal. The steps followed in the use case will be very similar to **UC.TS.PF.01**			

Use Case ID	UC.TS.PF.02		**Priority**	REQUIRED
Use Case name	**Define a new eligibility criterion for a trial proposal**			
Date created	05/09/2012	**Last updated**	27/09/2012	
Brief description	A researcher defines a eligibility criterion for a trial proposal			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Actors Involved	• Researcher			
Trigger	The researcher wants to define a new criterion			
Pre-conditions	• The researcher is authenticated to the system, • The researcher is authorized to use the trial feasibility application			

	• A trial is selected
Post conditions	
Successful End condition	The new eligibility criterion has been defined
Normal Flow	1. A screen is shown containing an entry field for a textual description of the criterion 2. The researcher can specify logics of the criterion. The researcher can use concepts from the ontology and use these to build a criterion. • The exact functionality is topic of research, but it will allow indicating the required presence/absence of codes, support various comparison operators for the values of observations (e.g. lab test results), and allow for specification of temporal constraints (e.g. "no prior …"). 3. The researcher selects the "save criterion" button. 4. The researcher is redirected to the previous screen, which shows the addition of the criterion to the trial proposal
Usage Frequency	Low
Notes and Issues	• A library of already defined criteria can be incorporated at a later stage. • Step 2 is merely a placeholder until the required functionality (and behavior) is specified

Use Case ID	UC.TS.PF.10		**Priority**	OPTIONAL
Use Case name	**Define eligibility criterion - probability**			
Date created	05/09/2012	**Last updated**	27/09/2012	
Brief description	A researcher defines a criterion for a selected trial, he defines the probability of a successful outcome of the criterion			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Includes use case	• **<<alternative>> UC.TS.PF.02** Define a new eligibility criterion for a trial			
Actors Involved	• Researcher			
Successful End condition	The probabilities are added to the criterion			
Normal Flow	1. **Alternate step 2:** The researcher can specify the probability of a successful outcome of the criterion.			
Notes and Issues	• This UC is merely a placeholder until the required functionality (and behavior) is specified • Normally, this alternative path for UC2 should be included in the description of UC2. It is however specified separately as the expected impact on the system design is high			

Use Case ID	UC.TS.PF.11		**Priority**	OPTIONAL
Use Case name	**Compute eligibility criterion probability**			
Date created	05/09/2012	**Last updated**	26/09/2012	

Brief description	A researcher defines a criterion for a selected trial proposal; he uses external sources to determine the probability of a successful outcome of the criterion.
Relates to Scenario	• Support design of new trials • Protocol feasibility
Extends use case	• **<<alternative>> UC.TS.PF.10** Define eligibility criterion - probability
Normal Flow	1. **Alternative step 1 for UC.TS.PF.10:** The researcher can select sources of public data which will be used to automatically determine the probability of a successful outcome of the criterion.
Notes and Issues	• This UC is merely a placeholder until the required functionality (and behavior) is specified • The sources of public data can be population information, other trials, literature, and cancer registries.

Use Case ID	UC.TS.PF.08		**Priority**	OPTIONAL
Use Case name	**Define trial path options**			
Date created	24/09/2012	**Last updated**	26/09/2012	
Brief description	A researcher introduces different treatment paths.			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Actors Involved	• Researcher			
Trigger	The researcher wants to define different treatment paths			
Pre-conditions	• The researcher is authenticated to the system • The researcher is authorized to use the trial feasibility application • A clinical trial has been selected			
Post-conditions				
Successful End condition	Different treatment paths have been added to the trial			
Normal Flow	1. A window is shown to the researcher displaying a tree structure which defines all the possible treatment paths (see notes for further elaboration). 2. The researcher selects a leaf node 3. The researcher selects the “Branch” option. 4. The researcher is requested to input the number of treatment path alternatives (say *k*), resulting in the addition of the same number (*k*) of child nodes to the originally selected node. 5. The researcher can specify a dataquery to retrieve for instance an observation to base the treatment path for a patient on. The researcher can use concepts from the ontology and use these to build a criterion. The exact functionality is topic of research, but it will allow indicating the required presence/absence of codes, retrieve observations (e.g. lab test results), and allow for specification of temporal constraints (e.g. “no prior …”). 6. For each of the child nodes, the researcher specifies the permissible outcomes of the data query or probability (representing the treatment path alternatives.) 7. The researcher saves the treatment path tree			

Usage Frequency	Low
Notes and Issues	• Each node of the tree structure represents a situation where the possible treatment path branches. This can for instance be due to a particular clinical criteria (e.g. one branch for HER+ and one branch for HER- patients) or external events like Randomization. • If necessary, different ways of manipulating the tree can be added

Use Case ID	UC.TS.PF.12		**Priority**	OPTIONAL
Use Case name	**Define trial path probability**			
Date created	05/09/2012	**Last updated**	27/09/2012	
Brief description	A researcher defines the probabilities for the outcomes of the trial path options.			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Includes use case	• **<<alternative>> UC.TS.PF.08** Define trial path options			
Actors Involved	• Researcher			
Successful End condition	The probabilities are added to the criterion			
Normal Flow	1. **Alternate step 5:** The researcher can specify a probability function (modeling the distribution of the different trial paths).			
Notes and Issues	• This UC is merely a placeholder until the required functionality (and behavior) is specified			

Use Case ID	UC.TS.PF.13		**Priority**	OPTIONAL
Use Case name	**Compute trial path probability**			
Date created	05/09/2012	**Last updated**	27/09/2012	
Brief description	A researcher defines the probabilities for the outcomes of the trial path options, he uses external sources to determine the probabilities.			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Includes use case	• **<<alternative>> UC.TS.PF.12** define trial path probabilities			
Actors Involved	• Researcher			
Successful End condition	The probabilities are added to the criterion			
Normal Flow	1. **Alternate step 1:** The researcher can select sources of public data which will be used to automatically determine the probabilities (modeling the distribution of the different trial paths).			
Notes and Issues	• This UC is merely a placeholder until the required functionality (and behavior) is specified			

Use Case ID	UC.TS.PF.14	**Priority**	OPTIONAL
Use Case name	**Determine required sample size**		

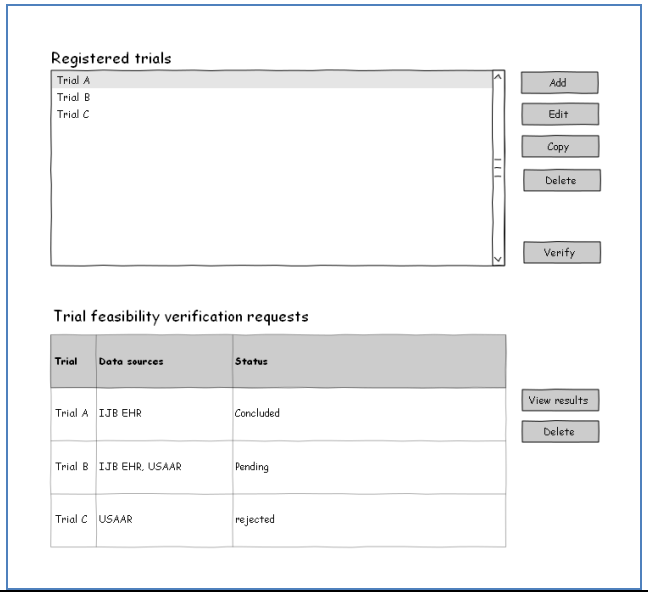
Date created	01/11/2012	**Last updated**	02/11/2012
Brief description	A researcher determines the required minimum number of patients for the treatment paths in order to have a statistically relevant outcome of the protocol.		
Relates to Scenario	• Support design of new trials • Protocol feasibility		
Actors Involved	• Researcher		
Trigger	• A researcher determines the required minimum number of patients for the treatment paths in order to have a statistically relevant outcome of the protocol.		
Pre-conditions	• The researcher is authenticated to the system • The researcher is authorized to use the protocol feasibility application • A clinical protocol has been selected • The treatment path options have been defined		
Post-conditions	The required sample size has been determined		
Successful End condition	The required sample size has been determined		
Normal Flow	1. A window is shown to the researcher displaying the defined treatment paths. 2. The researcher selects the statistical model which will be used to assess the required minimum number of patients for the treatment paths in order to have a statistically relevant outcome of the protocol. 3. The researcher fills in the (model dependent) parameters 4. The required sample size is calculated and shown.		
Usage Frequency	Low		
Notes and Issues	• The researcher can iterate over step 3 and 4		

Use Case ID	UC.TS.PF.03	**Priority**	REQUIRED
Use Case name	**Request execution of a trial feasibility study**		
Date created	17/09/2012	**Last updated**	26/09/2012
Brief description	A researcher requests the execution of an assessment of the feasibility of a new clinical trial (according to the estimations of recruitment potential).		
Relates to Scenario	• Support design of new trials • Protocol feasibility		
Actors Involved	• Researcher		
Trigger	A researcher wants to assess the feasibility of running a clinical trial with certain criteria when enrolling patients contained in different data sources (e.g. EHR's of various hospitals).		
Pre-conditions	• The researcher is authenticated to the system and is authorized to use trial feasibility application • A trial has been defined • At least one data source is available in the EURECA platform		
Post-conditions			
Successful End	The trial feasibility study request has been submitted for execution		

condition	
Normal Flow	1. The researcher opens the (web)application for trial feasibility verification (see UI1 for an impression). A screen is shown containing a “registered trials” list and a “trial feasibility verification requests” list 2. The researcher selects a trial from the “registered trials” list and click on a “verify” button. A new “request” screen is shown containing a list of available data sources in the EURECA platform, a comment field and a “request” button. 3. The researcher selects the data sources (see notes) which (s)he wants to use to verify the trial feasibility • The data sources are registered in the meta data repository of the trial feasibilty 4. [optionally] The researcher indicates that patient data needs to be returned. 5. [optionally] The researcher can explain the request to the clinical investigators of each data source in a comment field 6. The researcher executes the request (triggering **UC.TS.PF.05** for all selected data sources) by clicking on the “request” button. 7. The researcher is sent back the main screen, where a “request successful” message is displayed. • The request is added to the “trial feasibility verification” list. While executing, the status of the verification is “pending”. When **UC.TS.PF.05** finishes (for all data sources), the status becomes “concluded” or “rejected” (see notes).
Usage Frequency	Low
User interfaces	UI1: 
Business Rules	N/A
Assumptions	N/A
Notes and Issues	• The request status can be either rejected, pending or concluded. “Rejected” means that at least one clinical investigator did not allow execution of the request on his/her managed data source, “pending” means that at least one clinical investigator didn’t execute UC.TS.PF.05 yet, and

	"concluded" means that all clinical investigators have executed the request and results have been obtained. • The data sources can be the data sources of the hospitals (e.g. EHRs) and relevant clinical data warehouses (to which patient data is typically exported (pseudo-)anonymised). • Auditing will be necessary in order to ensure that no individual patients may be traced from the given out aggregated data. Questionable, whether besides this auditing procedure contractual obligations on the researcher not to attempt to re-identify will be a necessity. The legal WP will investigate this matter.

Use Case ID	UC.TS.PF.04		**Priority**	REQUIRED
Use Case name	**View trial feasibility verification request**			
Date created	17/09/2012	**Last updated**	1/11/2012	
Brief description	A researcher views a trial feasibility verification request.			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Includes use case	• **UC.TS.PF.15** View patient data for trial feasibility verification			
Actors Involved	• Researcher			
Trigger	A researcher wants to view a trial feasibility request.			
Pre-conditions	• The researcher is authenticated to the system and is authorized to use trial feasibility application • A trial feasibility verification request has been submitted for execution			
Successful End condition	The researcher has viewed the trial feasibility verification request			
Normal Flow	1. The researcher opens the (web)application for trial feasibility verification (see UI1 for an impression). A screen is shown containing a list of trial feasibility verification requests. • Each request has a request status. The request status can be either rejected, pending or concluded. Rejected means that at least one clinical investigator did not want to execute the request on his/her managed data source, pending means that at least one clinical investigator did not execute **UC.TS.PF.05** yet, and concluded means that all clinical investigators have executed the request. 2. The researcher selects the request he wants to view and clicks on a "view results" button. 3. The researcher can now examine the results in a new window. This window will contain: a. The date range b. The overall status c. For each criterion: the count of patients that satisfied the criterion (taking all data sources with status "concluded" into account) d. The count of patients that satisfied all criteria (taking all data sources with status "concluded" into account)			

	e. The counts of patients per trial path (taking all data sources with status “concluded” into account) f. Optionally: Whether the patient counts satisfy the minimum sample size. (taking all data sources with status “concluded” into account) g. Optionally: if patient data is returned, **UC.TS.PF.15** can be started (taking all data sources with status “concluded” into account) h. For each data source: i. The status of the request for that data source ii. [the status is concluded for that data source] For each criterion: the count of patients that satisfied the criterion iii. [the status is concluded for that data source]The count of patients that satisfied all criteria iv. [the status is concluded for that data source] The counts of patients per trial path v. [the status is rejected for that data source] the reason why the request is rejected (if available).
Usage Frequency	Low
User interfaces	UI1: 
Notes and Issues	• The data sources can be the data sources of the hospitals (e.g. EHRs) and relevant clinical data warehouses (to which patient data is typically exported (pseudo-)anonymised). • Auditing will be necessary in order to ensure that no individual patients may be traced from the given out aggregated data. Questionable, whether besides this auditing procedure contractual obligations on the researcher not to attempt to re-identify will be a necessity. The legal WP will investigate this matter.

Use Case ID	UC.TS.PF.15		Priority	OPTIONAL
Use Case name	**View patient data for trial feasibility verification**			
Date created	01/11/2012	**Last updated**	01/11/2012	
Brief description	View patient data for trial feasibility verification. This use case should aid the researcher in exploring the returned patient data in order to better articulate the required query.			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Actors Involved	• Researcher			
Notes and Issues	• This UC is merely a placeholder until the required functionality (and behavior) is specified • This UC will require further legal investigation.			

Use Case ID	UC.TS.PF.06		Priority	REQUIRED
Use Case name	**Delete a trial feasibility verification request**			
Date created	17/09/2012	**Last updated**	26/09/2012	
Brief description	The researcher deletes a trial feasibility verification request.			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Actors Involved	• Researcher			
Trigger	A researcher wants to delete to a trial feasibility verification request.			
Pre-conditions	• The researcher is authenticated to the system and is authorized to use trial feasibility application • A trial feasibility study has been submitted for execution			
Post-conditions	The trial feasibility result has been deleted from the result list and this deletion is alerted to the site(s) to which the request was sent			
Successful End condition	The trial feasibility result has been deleted from the result list and this deletion is alerted to the site(s) to which the request was sent			
Normal Flow	1. The researcher opens the (web)application for trial feasibility verification. A screen is shown containing a list of verified trial studies. 2. The researcher selects a trial feasibility verification request and clicks on a “delete” button 3. A “deleted” message is shown on the screen after successful deletion.			
Usage Frequency	Low			
Notes and Issues				

Use Case ID	UC.TS.PF.05		Priority	REQUIRED
Use Case name	**Execute trial feasibility request on data source**			
Date created	05/09/2012	**Last updated**	26/09/2012	
Brief description	A designed trial is executed on a data source and results are returned			
Relates to Scenario	• Support design of new trials • Protocol feasibility			
Actors Involved	• Clinical investigator			

Trigger	The clinical investigator receives a trial feasibility verification request (for example by mail), containing the identity of the requester (researcher), the trial name, the trial description, the (optional) comment field, the (optional) patient data, the criteria, the trial paths and the date range
Pre-conditions	• The clinical investigator is authenticated to the system and is authorized to use trial feasibility application
Successful End condition	The feasibility results (consisting of the patient count satisfying all criteria, counts per criterion, and counts per trial path, given the specified time period) for this data source are returned to the requester
Normal Flow	1. The clinical investigator opens the trial feasibility application and enters the screen showing a list of requests. 2. The clinical investigator selects the incoming request from the list 3. A new screen is shown with the auto-generated results of the trial feasibility verification on the data source (total patient counts, and patient counts per criterion, counts per trial path, and (optionally) the patient data) • How this auto-generation will work, is a research topic 4. [the clinical investigator agrees] The clinical investigator selects the request and clicks on an “Accept” button and returned to the requester is: a. Patient counts: For each criterion: the count of patients that satisfy the criterion. (Satisfaction is determined by the eligibility criteria matcher (**UC.TS.CM.01**)) b. The count of patients that satisfy all criteria c. The count of patients for each treatment path d. (optionally) the patient data 5. The clinical investigator is redirected to the main screen where a “successful send result to requester” message is shown.
Alternative Flow 1	• In **step 4** [if the clinical investigator does not agree] the clinical investigator selects the request, optionally enters a reason why the request is rejected, and clicks on a “Reject” button. The reject status and reason are sent back to the requestor.
Alternative Flow 2	• In **step 4** the clinical investigator can delegate the access approval to the access control management service (This can either be on a per data source level, or on a per patient level (e.g. using a consent management service)).This means that the trial is executed automatically when the access control management service give authorization.
Usage Frequency	Low
Notes and Issues	• Trial feasibility is assessed by estimating the enrolment rate that the hospital can provide). • All counts are constraint by the specified time period. • Auditing will be necessary in order to ensure that no individual patients may be traced from the given out aggregated data. Questionable, whether besides this auditing procedure contractual obligations on the researcher not to attempt to re-identify will be a necessity.

	• Patient data is pseudo-anonymized.

3.4 "Selection and recruitment" related use cases

The following table summarises the use cases which have goals related to investigation of new guidelines for treatment of patients, new proposals for protocols and new research, which are part of the investigation scenario.

Use Case ID	Use Case Description
UC.TS.PS.01	Suggest eligible clinical trials for a patient
UC.TS.PS.02	Print a detailed summary of the screening ranked trials
UC.TS.TR.01	Suggest patients for a trial
UC.TS.AS.01	Alerting service for patient recruitment
UC.TS.AS.02	Alerting service for when a patient's data is added/modified
UC.TS.PM.01	List all the patients registered on a site
UC.TS.PM.02	Register a patient to a site
UC.TS.PM.03	Launch a query on the registered patients on a site
UC.TS.TM.01	List the trials running on a site
UC.TS.TM.02	Launch a query on the registered trials on a site
UC.TS.CM.01	Run the criteria matcher on a patient for a selected trial

3.4.1 Choice of treatment

USE CASE: Microbiology SAE

Use Case ID	UC.TS.MS.01	**Priority**	required
Use Case name	**Create Microbiology CRF**		
Date created	09/10/2012	**Last updated**	05/11/2012
Brief description	The trial chairman defines in one or more specific CRFs which specific information have to be documented in order to get an early knowledge about infectious agents and their resistance profile for patients in a chemotherapy. Common Toxicity Criteria can be specified in order to detect SAE events automatically. These CRFs are summarized in a Microbiology Module (observational trial). There are three main CRFs: - Clinical Data; entries like general values, patient's diagnoses, lab values, admission date, discharge date (linked to HIS, see UC.TS.MS.02) - Microbiology Data; entries spectrum of pathogens, infectious agents, antibiogram (linked to Microbiology database, see UC.TS.MS.03) - Antibiotic treatment		
Relates to Scenario	Microbiology SAE		
Includes use case	No other use cases included		
Actors Involved	Trial chairman		
Trigger	Trial chairman selects "create new CRF" in the Microbiology Module		

Pre-conditions	• Microbiology Module exits (observational trial) • The trial chairman is logged in on the CT system • The trial chairman is authorized to create CRFs and to operate with the related CT • hospital ward(s) exist in the CT system • Patients are linked to the hospital ward
Post-conditions	
Successful End condition	CRF for Microbiology Module
Fail End Condition	Microbiology Module could not be created
Normal Flow	1. The trial chairman opens the CT system. 2. A screen containing all of his registered trials is presented to him. 3. The trials shown to the chairman are possible restricted by access control 4. The chairman selects the Microbiology Module. 5. The chairman selects “create new CRF” 6. A screen that enables the trial chairman the creation of the CRF is shown. There are three main CRFs, which have to be created for the Microbiology Module • Clinical Data; entries like general values ,patient’s diagnoses, lab values, admission date, discharge date (linked to HIS, see UC.TS.MS.02) • Microbiology Data; entries spectrum of pathogens, infectious agents, antibiogram (linked to Microbiology database, see UC.TS.MS.03) • Antibiotic treatment 7. The chairman creates a CRF. He defines beside the specific parameters (see 6.) Common Toxicity Criteria in order to detect a SAE event automatically. (The SAE parameters and its Common Toxicity Criteria are defined by literature) a. In order to avoid the creation of similar items twice, an existing item of an existing CRF can be linked the new CRF (or the item should be marked as already covered by another CRF) 8. The chairman clicks on a “save” button. 9. The chairman is redirected to the Microbiology Module overview. The successfully created CRF is listed (and can be selected). 10. Repeat step 5-9 as far as needed 11. The trial chairman selects “link ward” 12. A new screen is displayed containing the of available hospital wards. 13. The chairman selects the ward for which he wants to link the Microbiology Module 14. The chairman selects “add Microbiology Module”. All registered patients form the ward are linked automatically. 15. The chairman is redirected to the Microbiology Module overview. The linked hospital ward is displayed.
Alternative Flow 1	

Usage Frequency	medium
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.TS.MS.02	**Priority**	required
Use Case name	**Update infection/medication information from HIS system**		
Date created	09/10/2012	**Last updated**	05/11/2012
Brief description	A service collects data from the Hospital Information system (HIS) for a specific patient in order to get specific information as defined in the CRFs oft he Microbiology Module. These data will be automatically included in the corresponding CRF. As far as Common Toxicity Criteria are defined, a SAE event can be automatically detected and reported. (see use case UC.CD.AD.01, UC.CD.AR.01)		
Relates to Scenario	Microbiology SAE		
Includes use case	UC.TS.MS.01 Create Microbiology Module		
Actors Involved	• Clinical investigator • Trial chairman		
Trigger	Configured Service that requests the HIS system frequently (e.g. every night)		
Pre-conditions	• UpdateMicrobiologyFromHIS service is a registered and configured service • Linkage between patient in the CT system and the HIS • Microbiology Module exits and is linked to the hospital ward (and its patients)		
Post-conditions			
Successful End condition	Updated Microbiology information		
Fail End Condition	Not updated Microbiology information		
Normal Flow	1. The CT system triggers a service “UpdateMicrobiologyFromHIS” automatically (e.g. every night) 2. The service builds a request 3. This request summarizes all parameters of the Clinical data CRF of the Microbiology Module (for the patients of the linked hospital ward) 4. The service requests and returns data from the integrated HIS. 5. The corresponding data are saved in the database of the CT system. 6. As far as Common Toxicity Criteria are defined, a SAE event can be automatically detected and reported (see use cases UC.CD.AD.01, UC.CD.AD.02) 7. The user logs in the CT system. 8. An information “HIS data are updated” is displayed 9. The data are displayed in the Clinical Data CRF of the Microbiology Module (for each patient of a linked hospital ward).		
Alternative Flow 1	Alternative trigger: The user selects a Button “Update HIS		

	information" in the Microbiology Module in order to trigger the service manually.
Alternative Flow 2	When the service does not update the data automatically, the data can be entered manually in the corresponding Clinical data CRF of the Microbiology Module.
Usage Frequency	High, every day
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.TS.MS.03		**Priority**	required
Use Case name	**Update infection information from microbiological databases**			
Date created	09/10/2012	**Last updated**	05/11/2012	
Brief description	A service collects data from the Microbiology database for a specific patient in order to get specific information as defined in the CRFs oft he Microbiology Module. These data will be automatically included in the corresponding CRF. As far as Common Toxicity Criteria are defined, a SAE event can be automatically detected and reported (see use case UC.CD.AD.01, UC.CD.AR.01).			
Relates to Scenario	Microbiology SAE			
Includes use case	UC.TS.MS.01 Create Microbiology Module			
Actors Involved	• Clinical investigator • Trial chairman			
Trigger	Configured Service that requests the Microbiological database (e.g. every night)			
Pre-conditions	• UpdateMicrobiologyFromMicrobiology service is a registered and configured service • Linkage between patient in the CT system and the Microbiology DB • Microbiology Module exits and is linked to patients			
Post-conditions				
Successful End condition	Updated Microbiology information			
Fail End Condition	Not updated Microbiology information			
Normal Flow	1. The CT system triggers a service "UpdateMicrobiologyFromMicrobiology automatically (e.g. every night) 2. The service builds a request 3. This request summarizes all parameters of the Microbiology Data CRF of the Microbiology Module (for the patients of the linked hospital ward) 4. The service requests and returns data from the integrated Microbiology database.			

	5. The corresponding data are saved in the database of the CT system. 6. As far as Common Toxicity Criteria are defined, a SAE event can be automatically detected and reported (see use cases UC.CD.AD.01, UC.CD.AD.02) 7. The user logs in the CT system. 8. An information “Microbiology data are updated” is displayed 9. The data are displayed in the Microbiology Data CRF of the Microbiology Module (for each patient of a linked hospital ward).
Alternative Flow 1	Alternative trigger: The user selects a Button “Update Microbiology information” in the Microbiology Module in order to trigger the service manually.
Alternative Flow 2	When the service does not update the data automatically, the data can be entered manually in the corresponding Microbiology CRF of the Microbiology Module.
Usage Frequency	High, every day
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.TS.MS.04	**Priority**	required
Use Case name	**Documentation of medication**		
Date created	09/10/2012	**Last updated**	29/10/2012
Brief description	The nurse/local physician documents the medication (in particular Antibiotics) of a patient in the hospital level. This will be carried out by scanning of the patient’s and the medication’s barcode.		
Relates to Scenario	Microbiology SAE		
Includes use case	No other use cases included		
Actors Involved	Clinical investigator		
Trigger	Medication of a patient		
Pre-conditions	• Barcode for patient exists • Barcode for medication exists • Patient exists in the microbiology database		
Post-conditions			
Successful End condition	Stored medication for the patient in the microbiology database		
Fail End Condition	Not stored medication for the patient in the microbiology database		
Normal Flow	1. The nurse scans the barcode of the patient and the barcode of the drug. 2. A screen which displays the patient and the drug is shown. 3. The nurse enters the dose. 4. The nurse selects the save button. 5. The data are saved in the microbiology database.		
Alternative Flow 1	Entering of patient and drug manually.		
Alternative Flow 2	Entering of medication in the corresponding Microbiology CRF in		

	the CT system manually.
Usage Frequency	High, every day
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.TS.MS.05	**Priority**	recommended
Use Case name	**Statistical analyses of specific infection/medication based parameters**		
Date created	09/10/2012	**Last updated**	24/10/2012
Brief description	The CT system enables an export function in order to carry out statistical analyses. Exported statistical parameters can be - Summary of the SAE of the patient - Summary of all infections of a specific patient with all infectious agents, their source and resistance profile, usage of antibiotics for each infectious disease - Summary of infectious agents, their source and resistance profile of a ward, or of a specific infection (e.g.: pneumonia) and a list of antibiotics used - Comparison of the above generated data with other oncology wards or other wards in the same hospital or outside.		
Relates to Scenario	Microbiology SAE		
Includes use case	• UC.TS.MS.02 Update Microbiology information from HIS • UC.TS.MS.03 Update Microbiology information from Microbiology database • UC.TS.MS.04 Documentation of medication • UC.CD.AD.01 Automatic detection of SAEs/SUSARs		
Actors Involved	• Trial chairman • Clinical investigator		
Trigger	A registered user selects “Export for statistical analysis” in the CT system		
Pre-conditions	• Export function exits in the CT system • The user is authorized to use the export function • The user is logged in on the CT system		
Post-conditions			
Successful End condition	Export file within the corresponding information for statistical analysis		
Fail End Condition	Export not successful Export file erroneous		
Normal Flow	1. The user selects “export for statically analyses” in the CT System 2. An export file with the corresponding details is generated		
Alternative Flow 1			
Usage Frequency	medium		
User interfaces	N/A		
Business Rules	N/A		

Assumptions	N/A
Notes and Issues	

USE CASE: Outcome prediction

This use case will be implemented in D1.4.

USE CASE: Use a diagnostic classifier

This use case will be implemented in D1.4.

3.4.2 Patient recruitment into a trial

USE CASE: Patient recruitment into a trial

Patient screening

Use Case ID	UC.TS.PS.01		**Priority**	REQUIRED
Use Case name	**Suggest eligible clinical trials for a patient**			
Date created	07/08/2012	**Last updated**	23/10/2012	
Brief description	Suggest a list of eligible clinical trials to an investigator for a selected possible trial candidate.			
Relates to Scenario	• **Selection of trials for patient enrolment**			
Includes use case	• **UC.TS.PM.01** List all the patients registered on a site • **UC.TS.PM.02** Register a patient on a site • **UC.TS.TM.01** List the trials running on a site • **UC.TS.TM.02** Launch a query on the registered trials of a site • **UC.TS.PS.02** Print a detailed summary of the screening ranked trials • **UC.TS.TM.03** Enrol a patient to a trial			
Actors Involved	• Treating physician			
Trigger	A patient has been identified[4] as a possible trial candidate (process out of scope). The treating physician will use the EURECA platform to check eligibility of a selected patient for one or more of the trials.			
Pre-conditions	• The treating physician is authenticated to the system and is authorised to use the patient trial screening service. ○ This scenario runs over a longer period of time, in which the treating physician would logout and log-in again to continue this use case. This has however been abstracted from the use case. • A trial management component (trial registry) is available where all trials running on the site are registered together with their Inclusion/Exclusion criteria (in processable form).			

[4] **NOTE:** There are several possibilities: 1. A physician has a patient for whom he is searching for a clinical trial; 2. A patient wants to know if there is trial available for him; 3. The system itself checks for clinical trials for all registered patients (research question)

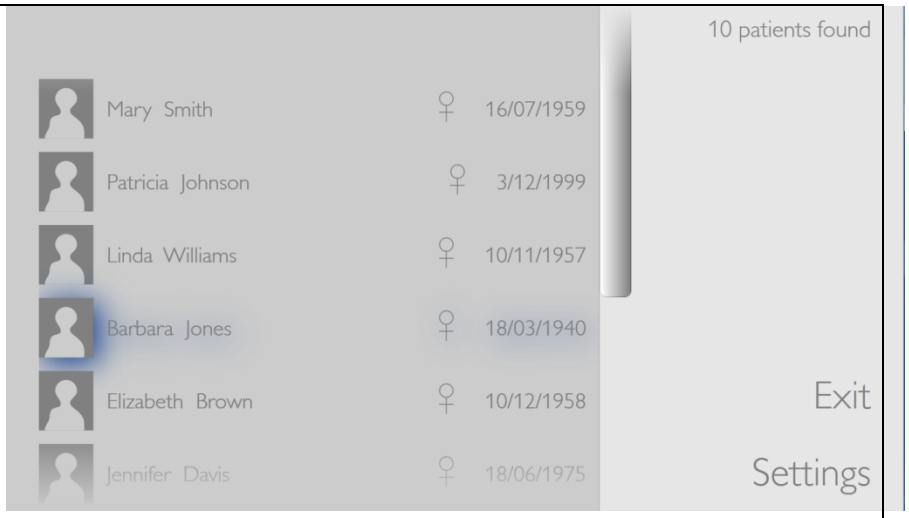
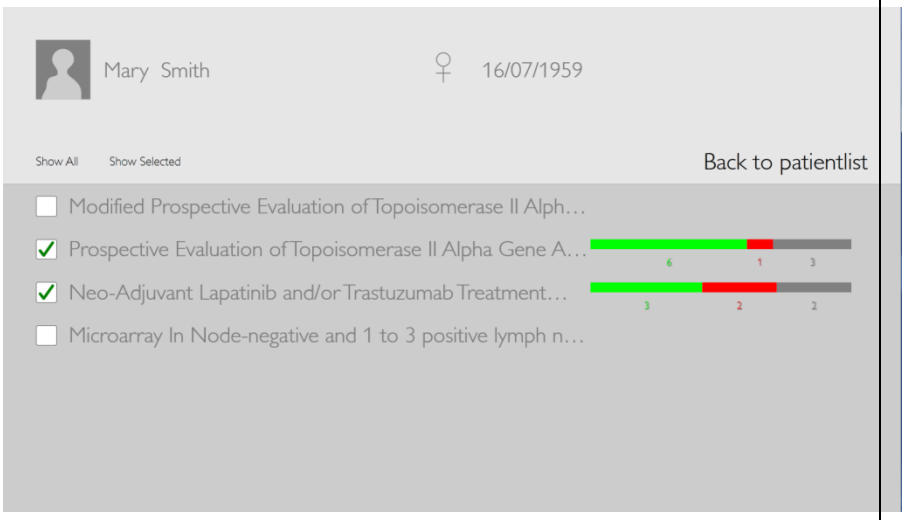
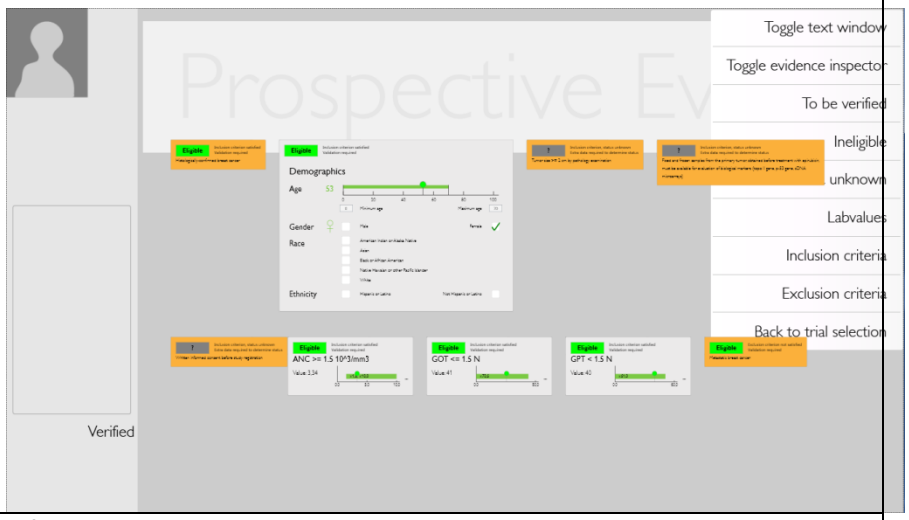
	• A patient management component is available containing a list of patients that are registered on the site where the screening is done. • All patients listed in this use case have given consent for screening.
Post-conditions	N/A
Successful End condition	A ranked list of eligible trials for a patient is shown according to quality criteria[5]
Fail End Condition	
Normal Flow	1. The treating physician opens the patient screening client. 2. A window is shown where the investigator can select the patient who he wants to screen for enrolment from a list (**UC.TS.PM.01**). If the patient is however not yet registered, the treating physician will need to register the patient first (**UC.TS.PM.02**) • Note that this screening step requires complex interaction with a patient identity management component ("patient lookup & selection"). • Access to this patient list is limited; depending on the access rights of the treating physician (usually a treating physician can only see his own patients). • In the first iteration of this use case we will only return the patients that are located on the site where the screening is done. Other possibilities need to be examined (clustering). • Each registered patient has a EURECA screening number, which is used as reference during the next screening steps. 3. After a patient is selected, a new page is displayed where the treating physician sees which informed consents are required to continue to the next screening steps. • The informed consent forms that are already entered in the EURECA platform, are marked as fulfilled. • The informed consent forms that are missing, need to be registered on the EURECA platform (**UC.TS.IC.1**, **UC.TS.IC.2**) • As long as the necessary informed consents are not present (**UC.TS.IC.3**), the next screening steps cannot be executed. 4. After all necessary informed consent forms are submitted for the patient to the platform, the treating physician is presented a new screen containing the list of available trials found in the set of trial databases[6] (**UC.TS.TM.01**) 5. The treating physician can browse and search through the trials (**UC. TS.TM.02**) and select the trials he is interested in. • Which trial(s) are selected is the responsibility of the treating physician.

[5] **NOTE:** these quality criteria need to be defined

[6] **NOTE:** this is slightly different from the scenarios where the investigator selects the trial databases he wishes to include. In the use cases we move this responsibility to the trial management component which will have a discovery service to work with these databases.

	• It is also possible to check and select all trials at once by clicking the “check all“ button. • It is possible to have a set of trials pre-selected by the system (e.g. based on preferences on a per organisation or per user level) • This searching and browsing can depend on an advanced indexing mechanism 6. Once all preferred trials are selected, the eligibility of the selected patient is checked for each of these selected trial(s). • This eligibility checking is done by the eligibility criteria matcher • The matcher matches the criteria of the trials with the patient information and determines for each of the criteria an outcome result: ○ Match: the patient satisfies the criteria ○ Non-match: the patient fails to satisfy the criteria ○ Undetermined: the matcher cannot generate a result for the criteria (see note) 7. When the matching is finished, the trials on the screen are ranked according to quality criteria[7] [8] 8. The treating physician clicks on a trial of interest in the ranked list. 9. A new screen is rendered giving a visualisation of all the defined criteria for the selected trial together with their accompanying matching result. 10. The treating physician can now investigate, accept and possibly overrule the outcomes of the matcher for each criterion. 11. 11. If the patient is found eligible for the selected trial, the treating physician can decide to enrol the patient in the selected trial (**UC.TS.TM.03**).
Alternative Flow 1	• In step 7 when no matching trial is found for a patient, the treating physician can decide to: ○ Go back to step 4 and select a new set of trials. ○ Refer the patient to conventional treatment
Alternative Flow 2	• In step 7 the investigator can decide to print a summary with details about the ranked trials (**UC.TS.PS.02**) by clicking on a “print” button.
Alternative Flow 3	• In step 11 if the patient is not found eligible for the selected trial, the treating physician can go back to step 7
Usage Frequency	High

[7] **NOTE:** These quality criteria need to be defined , this is possibly another use case
[8] **NOTE:** This can be an automated ranking or the user can select ranking rules manually

User interfaces	  
Business Rules	N/A
Assumptions	N/A
Notes and Issues	**NOTE**: the “a questionnaire online that defines selection criteria from the perspective of the patent and his psychological profile”

	step in the scenario will be moved to another use case **NOTE**: the "The list of hospitals that are registered for the selected trial can be requested by the investigator" is not part anymore of this use case. **NOTE**: The outcome "undetermined" can have different gradations

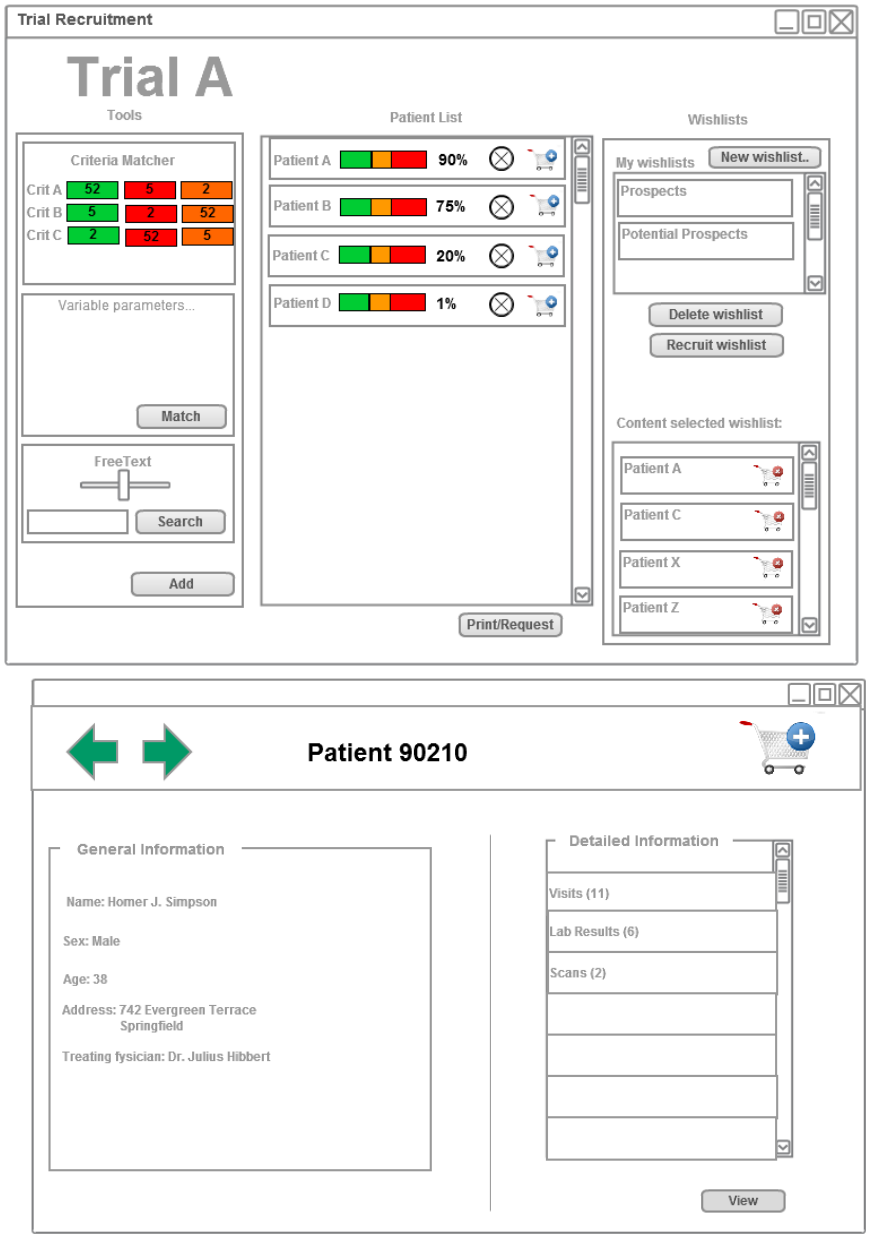
Use Case ID	UC.TS.PS.02		**Priority**	OPTIONAL
Use Case name	**Print a detailed summary of the screening ranked trials**			
Date created	13/09/2012	**Last updated**	13/09/2012	
Brief description	Print a detailed summary of the screening ranked trials			
Notes and Issues	• This is out of scope for the current scenarios.			

Trial Recruitment

Use Case ID	UC.TS.TR.01		**Priority**	REQUIRED
Use Case name	**Suggest patients for a trial**			
Date created	23/08/2012	**Last updated**	23/10/2012	
Brief description	Suggest a list of eligible patients for a trial			
Relates to Scenario	• **Selection and inclusion of patients into trials**			
Includes use case	• **UC.TS.PM.01** List all the patients registered on a site • **UC.TS.TM.01** List the trials running on a site • **UC.TS.TM.02** Launch a query on the registered trials of a site • **UC.TS.TM.03** Enrol a patient to a trial			
Actors Involved	• Clinical investigator • Pharmaceutical company			
Trigger	A pharmaceutical company wants to recruit a cohort of patients for a specific trial. For this they contact the sites (hospitals) on which this trial is running. Investigators on these sites will start locally the recruitment tool.			
Pre-conditions	• An investigator member is authenticated to the system and is authorised to use the patient recruitment service. • A trial management component (trial registry) is available where all trials running on the site are registered together with their Inclusion/Exclusion criteria (in processable form). • A patient management component is available containing a list of patients that are registered on the site • There is an agreement to start recruitment for this trial on this site • All the patients used in this use case have given consent for screening.			
Post-conditions	N/A			
Successful End condition	A cohort of eligible patients is requested to give consent for the selected trial.			

Fail End Condition	N/A
Normal Flow	1. The investigator opens the patient recruitment tool. 2. A window is shown containing a list of available trials that are running on the site(**UC.TS.TM.01**, **UC.TS.TM.02).** • It is possible that not all the trials are to be accessed by the investigator, so this may need some filtering by access control 3. The investigator selects the trial specified by the pharmaceutical company 4. A new screen is shown, that displays the list of the available patients on the site (**UC.TS.PM.01**), who have given consent for screening, together with one or more widgets that offer services to easily query patients. • The list of patients will be pseudonymised. • Querying patients will be plug-in system where easily new functionality can be added. • The query widgets can re-use existing EURECA services ○ The criteria query service ○ The expanded free-text query service ○ ... • The investigator is only allowed to see patients that have given consent for screening. 5. The investigator uses the widgets to filter/group/ order patients until a desirable[9] cohort of patients is displayed. 6. The investigator clicks on a patient for more information. • A new window is displayed with detailed patient information. 7. The investigator can add the patient to the list of prospects via an "add to wishlist"-button. • A 'wishlist ' is a collection of selected patients. There is a possibility to create multiple wishlists. The content of a wishlist can be viewed or modified at any time. This scenario is out of scope. 8. The investigator can decide to recruit the patients in a wishlist, by pushing the "Recruit wishlist"-button. • For every patient in the wishlist, the treating physician receives a request to recruit this patient (**UC.TS.TM.03**). This request also contains information on the trial protocol.
Alternative Flow 1	• In step 5 no matching cohort is found, the investigator provides this as feedback to the pharmaceutical company and ends the recruitment.
Alternative Flow 2	• Step 6 can be skipped; a patient can also be added to a wishlist directly without viewing detailed patient information
Usage Frequency	High

[9] **Note: "**Desirable" depends on the needs of the pharmaceutical company

User interfaces	
Business Rules	N/A
Assumptions	
Notes and Issues	○ This scenario runs over a longer period of time, in which an investigator member would logout and log-in again to continue this use case. This has however been abstracted from the use case.

Recruitment Alerting Service

Use Case ID	UC.TS.AS.02	**Priority**	REQUIRED
Use Case name	**Patient screening alerting service**		
Date created	10/09/2012	**Last updated**	24/09/2012
Brief description	When a patient's data is updated or a new patient is added to the		

	system, this patient is checked for eligibility in running trials		
Relates to Scenario	• **Selection and inclusion of patients into trials**		
Includes use case	• **UC.TS.TM.02** Launch a query on the trial database of a site		
Actors Involved			
Trigger	1. The data of a patient is updated. 2. A new patient enters the system.		
Pre-conditions	1. A trial management component (trial registry) is available where all trials are registered together with their Inclusion/Exclusion criteria (in processable form). 2. All the patients used in this use case have given consent for screening.		
Post-conditions			
Successful End condition	An alert is given when a patient is eligible for a registered trial.		
Fail End Condition			
Normal Flow	1. The eligibility of this patient is checked for all available trials found in the set of trial databases[10] (**UC.TS.TM.01**). • This eligibility checking is done by the eligibility criteria matcher • The matcher matches the criteria of the trials with the patient information and determine for each of the criteria an outcome result: o Match: the patient satisfies the criteria o Non-match: the patient fails to satisfy the criteria o Undetermined: the matcher cannot generate a result for the criteria (see note) 2. If a match is found, the treating physician is alerted. The alert can happen in several ways, e.g.: • The treating physician receives an email with the name of the patient and the trial id. • When the treating physician logs in to the system, he is notified that his patient is eligible for this trial (pop-up/message box).		
Alternative Flow			
Usage Frequency	High		
User interfaces	N/A		
Business Rules			
Assumptions			
Notes and Issues	**NOTE**: The way the suggested trials are ranked is still to be decided **NOTE**: The outcome "undetermined" can have different gradations		
Use Case ID	UC.TS.AS.01	**Priority**	REQUIRED
Use Case name	**Trial recruitment alerting system**		

[10] **NOTE:** this is slightly different from the scenarios where the investigator selects the trial databases he wishes to include. In the use cases we move this responsibility to the trial management component which will have a discovery service to work with these databases.

Date created	10/09/2012	**Last updated**	24/09/2012
Brief description	When a trial is added/modified, an alert is given when an eligible patient is found		
Relates to Scenario	• **Selection and inclusion of patients into trials**		
Includes use case	• **UC.TS.PM.03** Launch a query on the registered patients of a site		
Actors Involved			
Trigger	• A trial has been modified/added to the trial database.		
Pre-conditions	• A trial management component (trial registry) is available where all trials are registered together with their Inclusion/Exclusion criteria (in processable form). • A patient management component is available containing a list of patients that are registered on the site. • All the patients used in this use case have given consent for screening.		
Post-conditions			
Successful End condition	An alert is given when a patient is eligible for the added/modified trial.		
Fail End Condition	No alert is given when an eligible patient is present.		

Normal Flow	1. On every site registered to the EURECA platform, a list of patients who have given consent for screening is retrieved. (**UC.TS.PM.03**)
	2. The eligibility of each patient on this list is checked for the added/modified trial.
	  • This eligibility checking is done by the eligibility criteria matcher
	  • The matcher contains scripts that try to match the criteria of the trial with the patient information and determine for each of the criterion an outcome result:
	  ○ Match: the patient satisfies the criterion
	  ○ Non-match: the patient fails to satisfy the criterion
	  ○ Undetermined: the matcher cannot generate a result for the criteria (see note)
	3. If a match is found for all criteria, the treating physician is alerted. This alert can happen in two ways:
	  • The treating physician receives an email with the name of the patient and the trial id.
	  • When the treating physician logs in to the system, he is notified that his patient is eligible for this trial (pop-up/message box).		

Alternative Flow			
Usage Frequency	Medium		
User interfaces	N/A		
Business Rules			
Assumptions			
Notes and Issues	**NOTE**: The outcome "undetermined" can have different gradations		

Patient identity Management

Use Case ID	UC.TS.PM.01	**Priority**	REQUIRED
Use Case name	**List all the patients registered on a site**		
Date created	07/08/2012	**Last updated**	12/09/2012
Brief description	List the patients available on a site		
Relates to Scenario	• **Selection and inclusion of patients into trials** • **Selection of trials for patient enrolment**		
Includes use case	• No other use cases included		
Actors Involved	• No actors involved		
Trigger	A component of the EURECA platform sends a patients list request to the patient identity management component of a site		
Pre-conditions	• A requesting component needs to have sufficient access rights in order to retrieve the list of available patients on a site		
Post-conditions			
Successful End condition	• A list is returned, containing all the available patients registered on the site.		
Fail End Condition			
Normal Flow	1. A list request enters the patient identity management component 2. The patient identity management component searches for the available patients in the patient meta data database situated on the site • The patient meta data that is returned, depends on the needs of the requesting component. (this will be probably the patient ID and the name) 3. A list is generated of the found patients • If no patients were found, an empty list is returned 4. This list is sent back to the requesting component • The returned list can still be filtered by access control restrictions		
Usage Frequency	High		
User interfaces	N/A		
Business Rules			
Assumptions	• A patient meta data database is available		
Notes and Issues			

Use Case ID	UC.TS.PM.02	**Priority**	REQUIRED
Use Case name	**Register a patient to a site**		
Date created	07/08/2012	**Last updated**	12/09/2012
Brief description	The steps that needs to be followed to enter a new patient on a site		
Relates to Scenario	• Selection and inclusion of patients into trials • Selection of trials for patient enrolment		

Includes use case	• No other use cases included
Actors Involved	• Administrator
Trigger	• A new patient needs to be registered on the site
Pre-conditions	• The administrator is authenticated to the system and is authorised to use the patient registration service.
Post-conditions	
Successful End condition	• The patient is registered onto the site, this should allow his/her data on the site to be linked.
Fail End Condition	
Normal Flow	1. The administrator browses to the site's patient management portal 2. In the menu (s)he selects: "Register new patient" 3. A screen is shown where the administrator is requested to enter the unique ID number of the patient • This can be the EHR number of the patient 4. The system will check if the patient is not already registered in order to prevent double entry of the patient 5. If the patient has not already been registered, a new screen is shown where the administrator is requested to add administrative info about the patient • This administrative info will be the information relevant for the EURECA platform that is not included in the EHR of the patient 6. The system validates the input 7. The administrator is presented with a new screen where the message "successfully added patient X" is shown, the new patient is stored in the patient meta data database.
Alternative Flow 1	• In step 5 if the patient is already registered, a screen is shown to the administrator with message "patient already registered". This means the end of the use case.
Alternative Flow 2	• In step 6 if the input contains incorrect information, the administrator is sent back to step 5 to correct the invalid input
Usage Frequency	Medium
User interfaces	N/A
Business Rules	
Assumptions	• A patient meta data database is available
Notes and Issues	• Patients can also come through the eHR (also nominative) or through already de-identified datasets. • The easiest solution to this problem would be to use the PIMS solution for patient identity management; this however will need a legal verification.

Use Case ID	UC.TS.PM.03		Priority	OPTIONAL
Use Case name	**Launch a query on the registered patients of a site**			
Date created	24/09/2012	**Last updated**	24/09/2012	
Brief description	Enable to send a query to the patient management, in order to retrieve a filtered list of patients that were registered for this site			
Notes and Issues	• This use case is very similar to **UC.TS.PM.01** . Here not the whole list of available patients is returned but a filtered version depending on the query that comes with the request. • This is more a nice to have at the moment, if needed this use case can be worked out in a later iteration.			

Trial Management

Use Case ID	UC.TS.TM.01		Priority	REQUIRED
Use Case name	**List the trials running on a site**			
Date created	07/08/2012	**Last updated**	12/09/2012	
Brief description	Return the list of the available trials found in the trial meta database registered on a site			
Relates to Scenario	• **Selection and inclusion of patients into trials** • **Selection of trials for patient enrolment**			
Includes use case	• No other use cases included			
Actors Involved	• No actors involved			
Trigger	A component of the EURECA platform sends a trial list request to the trial management component of a site			
Pre-conditions	• A requesting component needs to have sufficient access rights in order to retrieve the list of available trials on a site			
Post-conditions				
Successful End condition	• A list is returned, containing all the available trials registered on the site.			
Fail End Condition				
Normal Flow	1. A list request enters the trial management 2. The trial management component requests the available trials of the trial meta data database situated on the site • The trial meta data that is returned, depends on the needs of the requesting component. (this will be probably the trial ID and the trial name) 3. A list is generated from the found trials • If no trials were found, an empty list is generated 4. This list is sent back to the requesting component • The returned list can still be filtered by access control restrictions			
Usage Frequency	High			
User interfaces	N/A			
Business Rules				

Assumptions	• A trial meta data database is available
Notes and Issues	

Use Case ID	UC.TS.TM.02		**Priority**	OPTIONAL
Use Case name	**Launch a query on the registered trials of a site**			
Date created	07/08/2012	**Last updated**	12/09/2012	
Brief description	Enable to send a query to the trial management, in order to retrieve a filtered list of trials that were registered for this site			
Notes and Issues	• This use case is very similar to **UC.TS.TM.01** . Here not the whole list of available trials is returned but a filtered version depending on the query that comes with the request. • This is more a nice to have at the moment, if needed this use case can be worked out in a later iteration			

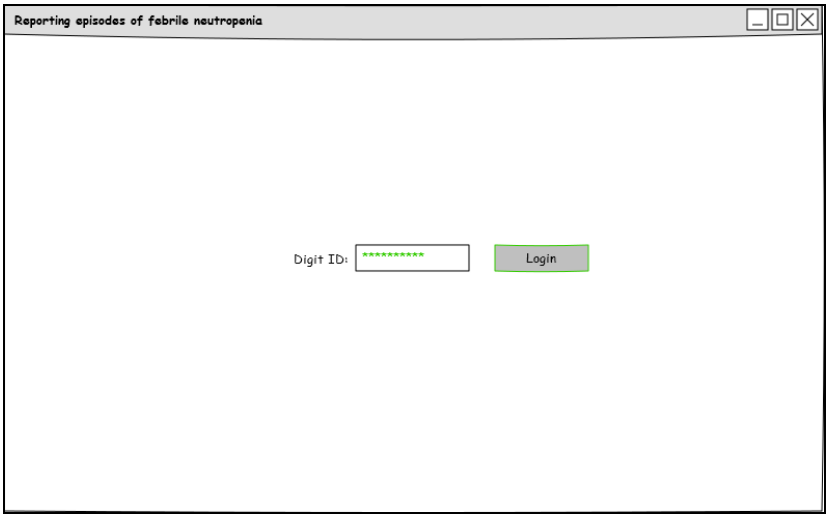
Use Case ID	UC.TS.TM.03		**Priority**	OPTIONAL
Use Case name	**Enrol a patient to a trial**			
Date created	13/09/2012	**Last updated**	13/09/2012	
Brief description	Enrol a patient to a selected trial			
Notes and Issues	• This is out of scope for the current scenarios.			

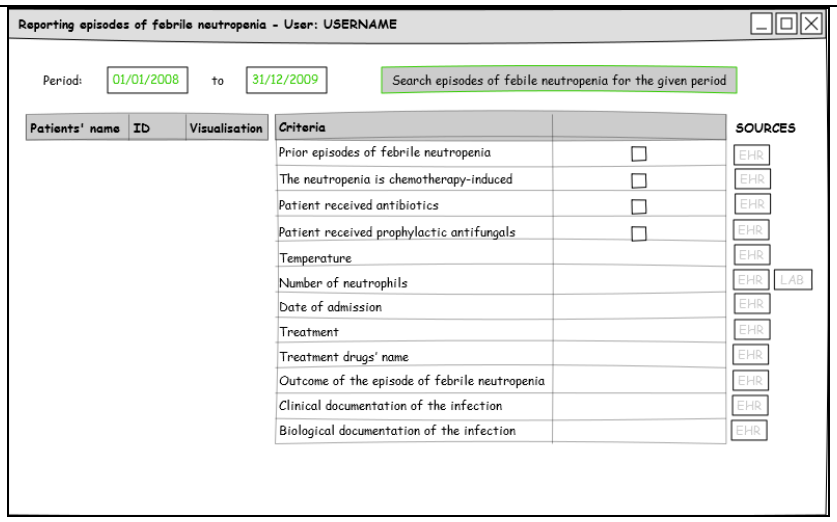
3.5 "Reporting" related use cases

Use Case ID	Use Case
UC.RE.FN.01	Reporting episodes of febrile neutropenia
UC.RD.CR.01	Cancer registry reporting
UC.RD.TB.01	Tumour bank reporting
UC.TS.PF.01	Pre-filling of Case Report Form (CRF)
UC.TS.PF.02	Pre-filling of Adverse Event (AE) Report

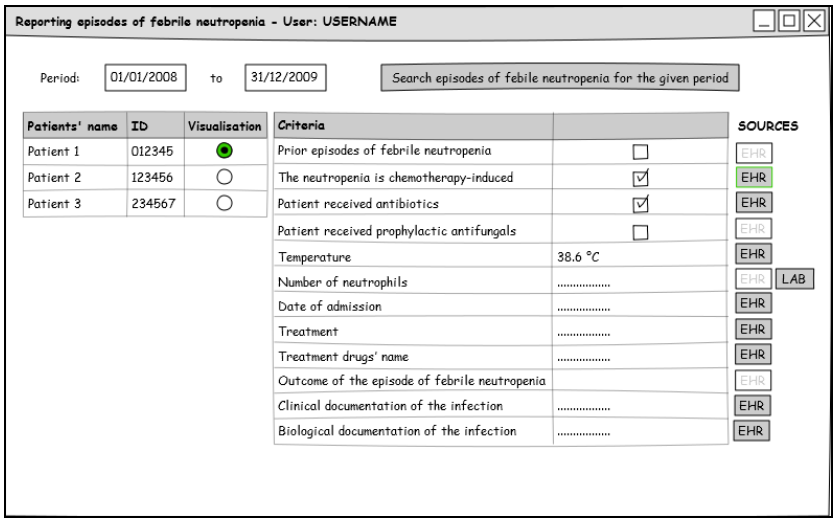
USE CASE: Reporting episodes of febrile neutropenia

Use Case ID	UC.RD.FN.01		**Priority**	REQUIRED
Use Case name	**Reporting episodes of febrile neutropenia**			
Date created	04/10/2012	**Last updated**	07/11/2012	
Brief description	Detect and report an episode of febrile neutropenia by extracting some specific symptoms and clinical relevant characteristics from EHR on a given period of time for retrospective study			
Relates to Scenario	• **Reporting**			
Includes use case	N/A			
Actors Involved	• Investigator			
Trigger	One wants to check some specific symptoms and clinical characteristics of febrile neutropenia side effect for a given period of time			

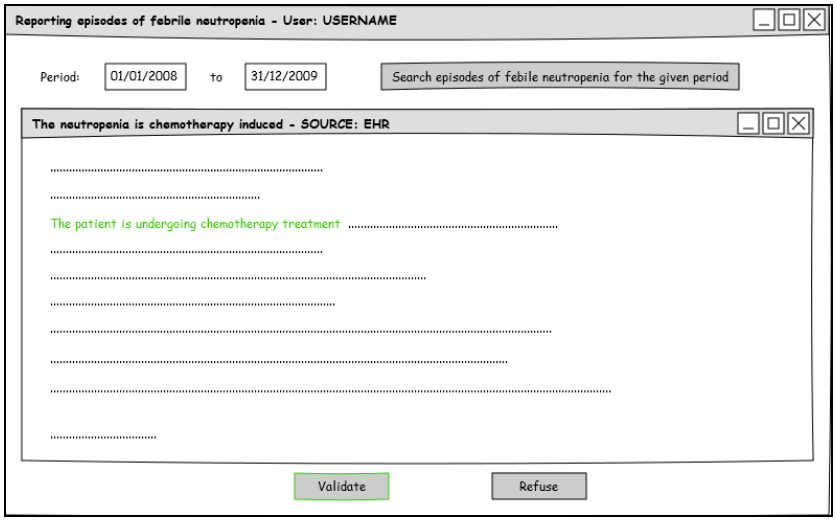
Pre-conditions	• An investigator member is authenticated to the system and is authorised to use the service. (See Ui1) • Interoperability layer to retrieve data from EHR and other clinical data systems.
Post-conditions	N/A
Successful End condition	Patients that suffered an episode of febrile neutropenia for a given period of time are detected
Fail End Condition	Patients that suffered an episode of febrile neutropenia for a given period of time are not found
Normal Flow	1. The investigator opens the patient screening client. 2. A window is shown where the investigator can select a given period of time for which s/he wants to detect the episodes. (See Ui2) 3. The investigator is presented a new screen containing the list of patients who suffered an episode of febrile neutropenia, and the list of found criteria within the patient's data that brought to the conclusion. This functinoality is topic of research. (See Ui3) 4. The investigator can visualise the data source where the information has been extracted. (See Ui4) • Information successfully retrieved is waiting for investigator validation.
Alternative Flow	N/A
Usage Frequency	Medium
User interfaces	Ui1:  Ui2:



Ui3:



Ui4:

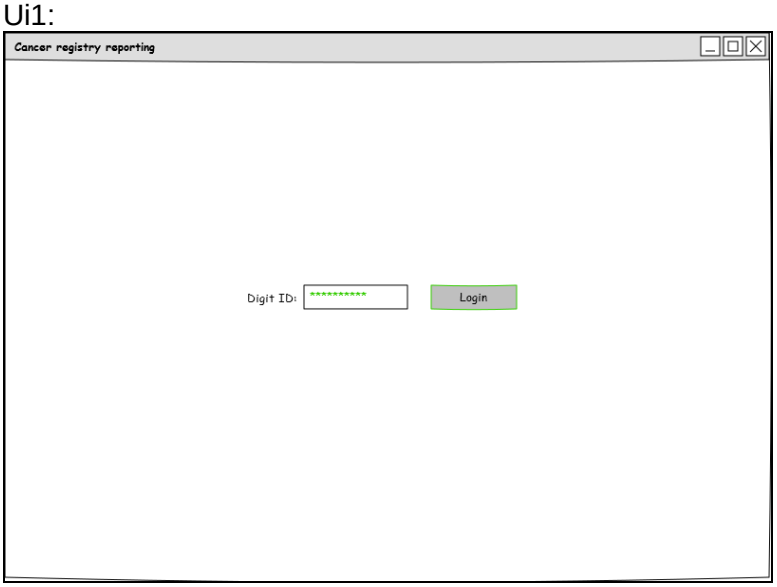
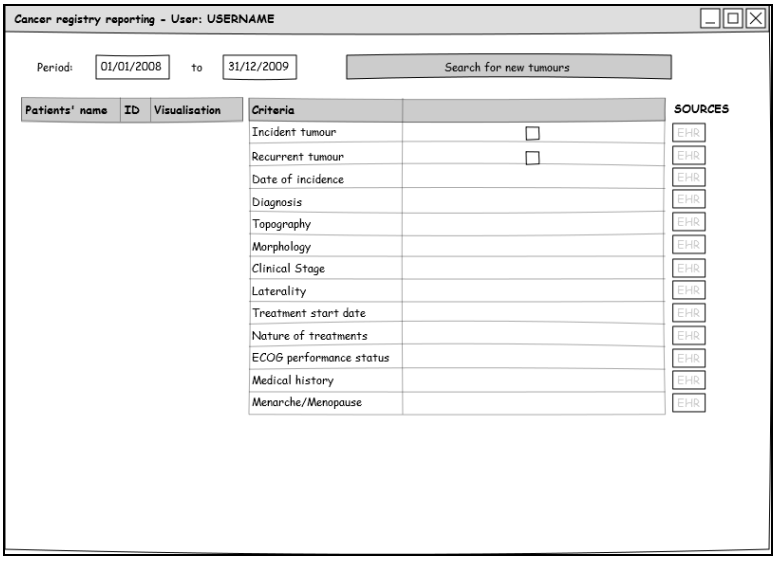


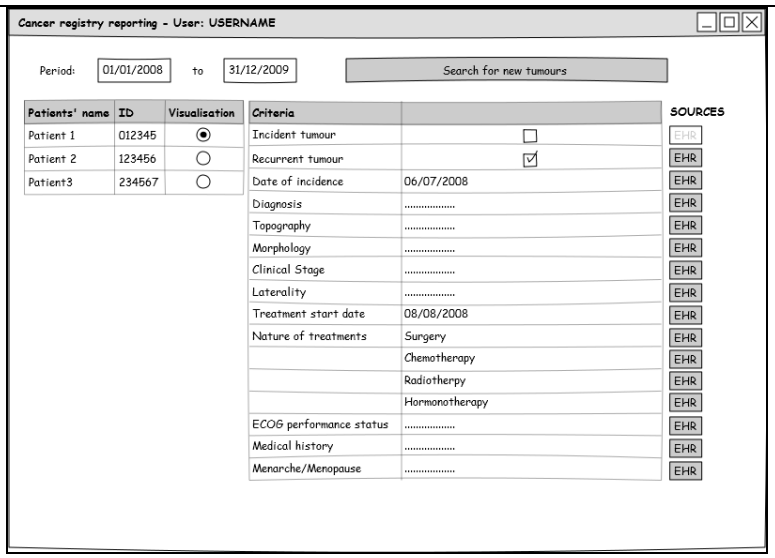
Business Rules	N/A

Assumptions	N/A
Notes and Issues	**QUESTION:** N/A **NOTE:** N/A

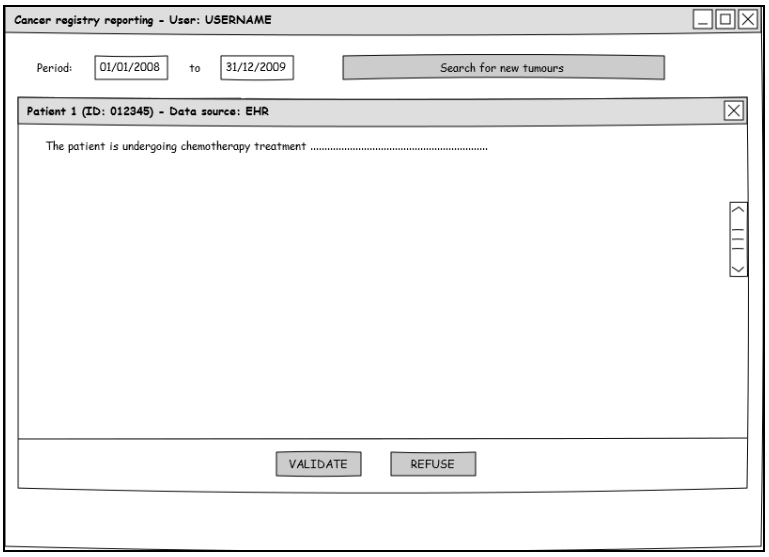
USE CASE: Cancer registry reporting

Use Case ID	UC.RD.CR.01		**Priority**	REQUIRED
Use Case name	**Cancer registry reporting**			
Date created	04/10/2012	**Last updated**	11/11/2012	
Brief description	Cancer registry reporting			
Relates to Scenario	• **Reporting**			
Includes use case	N/A			
Actors Involved	• Investigator			
Trigger	An investigator is filling the local cancer registry.			
Pre-conditions	• An investigator is authenticated to the system and is authorised to use the patient screening service. (See Ui1) • A system that can manage the local cancer registry system should be available. • Interoperability layer to retrieve data from EHR and other clinical data systems			
Post-conditions	N/A			
Successful End condition	A report is generated in the local cancer registry including all the patient information found about a specific tumour.			
Fail End Condition	Information about patient is not found, no information is filled in the local cancer registry report.			
Normal Flow	1. The investigator opens the patient screening client. 2. A window is shown where the investigator can select a given period of time for which s/he wants to register a tumour (incident/recurrent) into the cancer registry. (See Ui2) 3. The investigator is presented a new screen containing the list of patients for whom has been detected an incident or a recurrent tumour for the given period. The investigator can then select the patient s/he wants to screen for generating the cancer registry report from a list. (See Ui3) • Note that this screening step requires complex interaction with a patient identity management component (“patient lookup & selection”). 4. The investigator can visualise the data source where the information has been extracted. (See Ui4) • Information successfully retrieved is waiting for investigator validation.			
Alternative Flow 1	N/A			

Usage Frequency	High
User interfaces	Ui1:  Ui2:  Ui3:



Ui4:



Business Rules	N/A
Assumptions	N/A
Notes and Issues	**QUESTION:** N/A **NOTE:** N/A

USE CASE: Tumour bank reporting

Use Case ID	UC.RD.TB.01	**Priority**	REQUIRED
Use Case name	**Tumour bank reporting**		
Date created	04/10/2012	**Last updated**	05/11/2012
Brief description	Tumour bank reporting		
Relates to Scenario	• **Reporting**		
Includes use case	N/A		

Actors Involved	• Investigator
Trigger	An investigator is filling the tumour bank report.
Pre-conditions	• An investigator is authenticated to the system and is authorised to use the patient screening service. • A system that can manage the tumour bank system should be available. • Interoperability layer to retrieve data from EHR and other clinical data systems
Post-conditions	N/A
Successful End condition	A report is generated in the tumour bank system including all the patient information found about a specific tumour.
Fail End Condition	Information about patient is not found, no information is filled in the tumour bank report.
Normal Flow	1. The investigator opens the patient screening client. 2. A window is shown where the investigator can select a given period of time for which s/he wants to register a tumour (incident/recurrent) into the tumour bank. 3. The investigator is presented a new screen containing the list of patients for whom has been detected an incident or a recurrent tumour for the given period. The investigator can then select the patient s/he wants to screen for generating the tumour bank report from a list. • Note that this screening step requires complex interaction with a patient identity management component ("patient lookup & selection"). 4. The investigator can visualise the data source where the information has been extracted. • Information successfully retrieved is waiting for investigator validation.
Alternative Flow 1	N/A
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	**QUESTION:** N/A **NOTE:** N/A

USE CASE: Pre-filling of CRF and AE reports

Use Case ID	UC.TS.PR.01	**Priority**	REQUIRED
Use Case name	**Pre-filling of Case Report Form (CRF)**		
Date created	03/09/2012 **Last updated**		07/10/2012
Brief description	Pre-filling of electronic Case Report Form (eCRF)		
Relates to Scenario	• **Reporting**		
Includes use case	N/A		
Actors Involved	• Investigator		
Trigger	An investigator wants to fill in an electronic Case Report Form (eCRF)		

Pre-conditions	• All patients included in data have given informed consent. • An investigator (or an authorized team member) is authenticated to the system • A system that can manage and store the eCRFs for CT should be available.
Post-conditions	N/A
Successful End condition	The case report form has been pre-filled with relevant patient information where possible.
Fail End Condition	N/A
Normal Flow	5. The investigator opens the trial execution client. 6. The investigator is presented a new window containing the list of trials in which s/he is involved, and the investigator selects the correct trial. 7. Then, a window new is shown where the investigator can select a set of patients from the list of patients that are enrolled in selected CT. • Access to this patient list is limited; depending on the access rights of the investigator (usually an investigator can only see the patients s/he owns). 8. Once a trial and a set of patients are selected, a new screen loads the list of eCRF of the selected trial. The user selects one or more of the eCRFs: • Where possible, eCRF fields are pre-filled with patient data. i. Each field that has been filled provides a link to inspect the source clinical evidence. 9. Information successfully retrieved is included in eCRFs is saved for **investigator validation** (for each eCRF generated). ○ NOTE : Interaction with eCRF system has to be defined.
Alternative Flow 1	N/A
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	**QUESTION:** N/A **NOTE:** N/A

Use Case ID	UC.TS.PR.02	**Priority**	REQUIRED
Use Case name	**Pre-filling of Adverse Event (AE) reports**		
Date created	03/09/2012	**Last updated**	20/09/2012
Brief description	Pre-filling of Adverse Event (AE) Report		
Relates to Scenario	• **Reporting**		
Includes use case	N/A		
Actors Involved	• Investigator		
Trigger	An investigator is searching for patient information.		
Pre-conditions	• All patients included in data have given informed consent.		

	• An investigator (or an authorized team member) is authenticated to the system and is authorised to use the patient trial screening service. • A classification of AE about patients has to be defined (CTCAE as initial candidate).
Post-conditions	
Successful End condition	An AE report is generated including relevant patient information from the selected CT.
Fail End Condition	If not AE information is found, no report is generated.
Normal Flow	5. The investigator opens the trial execution client. 6. The investigator is presented a new window containing the list of trials in which s/he is involved, and the investigator selects the correct trial. 7. Then, a window new is shown with the list of patients that are enrolled in selected CT, and an alert icon is shown nearby that CT that contains information about an adverse event of the patient. • Access to this patient list is limited; depending on the access rights of the investigator (usually an investigator can only see the patients s/he owns). • Information about AE is retrieved from the EURECA interoperability layer, and when it is found, the CT which this information belongs to is marked with an icon. 8. The investigator selects the AE icon and a new screen is showed, containing AE report pre-filled with patient AE information.
Alternative Flow 1	N/A
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	**QUESTION:** N/A **NOTE:** N/A

USE CASE: Automatic detection of SAEs/SUSARs

Use Case ID	UC.CD.AD.01	**Priority**	required
Use Case name	**Detection of an SAE/SUSAR event**		
Date created	23/10/2012	**Last updated**	12/11/2012
Brief description	The CT system detects an SAE/SUSAR event automatically based on the defined Common Toxicity Criteria in the CRFs. The local physician checks the pre-filled CRF. He decides if it a real SAE/SUSAR or not. If yes, the trial chairman will be informed (UC.CD.AD.02).		
Relates to Scenario	Automatic Detection of SAEs/SUSARs		
Includes use case			
Actors Involved	Local physician		
Trigger	Data is saved in the CRF (manually entered or automatically by		

	services)
Pre-conditions	• Common Toxicity Criteria are defined in CRFs of the CT system • Local physician is allowed to check and complete SAE/SUSAR events • Email service is configured in the CT system • SAE/SUSAR CRF exists in the CT system and is linked to a study
Post-conditions	
Successful End condition	The detected SAE/SUSAR event is reported to the trial chairman
Fail End Condition	SAE/SUSAR events are not reported
Normal Flow	1. The CT system checks the entries of CRFs against the Common Toxicity Criteria (service returns and/or manual entered) 2. CT system detects an SAE/SUSAR event 3. CT system informs the local physician by email automatically 4. The local physician logs in the CT system 5. A screen shows the detected SAE/SUSAR events directly. 6. The local physician checks these data and decides if it is a SAE/SUSAR event or not. 7. If no – The CRF is saved with a comment from the local physician 8. If yes –The local physician completes the CRF by entering the empty parameters manually. 9. The local physician selects “save” in order to save the SAE/SUSAR CRF. 10. The trial chairman is informed about a detected SAE/SUSAR event by email automatically. 11. -> UC.CD.AD.02
Alternative Flow 1	1. The local physician fills in the specific SAE/SUSAR CRF manually without any information from the CT system. 2. He informs the trial chairman about that event (telephone, email, …).
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.CD.AD.02	**Priority**	required
Use Case name	**SAE/SUSAR confirmation of the trial chairman**		
Date created	23/10/2012	**Last updated**	12/11/2012
Brief description	The trial chairman is informed about an SAE/SUSAR event (see UC.CD.AD.01). The trial chairman has to decide, if that event has to be reported to the local authorities and the European Medicines Agency (EMA) or not.		
Relates to Scenario	Automatic Detection of SAEs/SUSARs		
Includes use case			

Actors Involved	Trial chairman
Trigger	The local physician detects an SAE/SUSAR event in the CT system. This event is reported to the trial chairman
Pre-conditions	• Trial chairman is allowed to confirm SAE/SUSAR events • Email service is configured in the CT system • Completed SAE/SUSAR CRF exits in the CT system
Post-conditions	
Successful End condition	Confirmed the SAEs/SUSARs events
Fail End Condition	Not Confirmed the SAEs/SUSARs events
Normal Flow	1. The trial chairman is informed about an SAE/SUSAR event. 2. The trial chairman logs in the CT system 3. A screen shows the SAE/SUSAR CRF directly. There are also two buttons visible: “confirm” and “not confirm” (these buttons are only visible for the trial chairman) 4. The trial chairman checks if this event has to be reported (local authorities/EMA) or not. 5. If no – The CRF is saved with a comment from the trial chairman (status “not confirmed”). 6. If yes – The CRF is saved with a comment from the trial chairman (status “confirmed”). 7. -> UC.CD.AR.01
Alternative Flow 1	
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

USE CASE: Automatic reporting of SAEs/SUSARs

Use Case ID	UC.CD.AR.01	**Priority**	required
Use Case name	**Preparation for electronic exchange of SAE/SUSARs with the EMA**		
Date created	12/11/2012	**Last updated**	12/11/2012
Brief description	Before the European Medicines Agency (EMA) allows an automatic reporting of SAE/SUSAR, a registration procedure is required (see http://eudravigilance.ema.europa.eu/human/TenSteps.asp)		
Relates to Scenario	Automatic reporting of an SAEs/SUSARs event		
Includes use case			
Actors Involved	trial chairman/system administrator		
Trigger			
Pre-conditions	• SAE/SUSAR data exits in the local system • The CT system can communicate with the internet		
Post-conditions			
Successful End	CT system is able to report SAE/SUSAR events to the EMA		

condition	automatically
Fail End Condition	CT system is not able to report SAE/SUSAR events to the EMA automatically
Normal Flow	Steps as required at http://eudravigilance.ema.europa.eu/human/TenSteps.asp 1. Register with the EMA 2. Obtain EudraVigilance Gateway certification (for Internet communication) 3. Communication test (to assure successful Gateway to Gateway communication) 4. Development and Validation testing 5. XML test phase with submission of 10 sample cases 6. Production phase
Alternative Flow 1	
Usage Frequency	low, one time
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.CD.AR.02	**Priority**	required
Use Case name	**Automatic reporting of SAEs and SUSARs**		
Date created	24/10/2012	**Last updated**	12/11/2012
Brief description	The CT system reports an Sudden Adverse Event (SAE) and Sudden Unexpected Serious Adverse Reaction (SUSAR) automatically to the European Medicines Agency (EMA) and the local authorities		
Relates to Scenario	Automatic reporting of an SAEs/SUSARs event		
Includes use case	• SAE/SUSAR confirmation of the trial chairman (UC.CD.AD.02) • Preparation for electronic exchange of SAE/SUSARs with the EMA (UC.CD.AR.01)		
Actors Involved	trial chairman		
Trigger	The trial chairman confirms a SAE or SUSAR in the CT system		
Pre-conditions	• SAE/SUSAR CRF has status confirmed in the CT system • The CT system is authorized to report an SAE event to the involved authorities automatically. • Local eureca-DW and a setSAESUSAR service exists		
Post-conditions	If the trial chairman confirms the SAE/SUSAR, it has to be reported within a time period of 24 hours.		
Successful End condition	SAE or SUSAR is automatically reported		
Fail End Condition	SAE or SUSAR is not automatically reported		
Normal Flow	1. The trial chairman confirms a SAE/SUSAR in the CT system 2. The CT system reports the SAE/SUSAR to the involved authorities automatically.		

	3. If the data are transferred correctly the involved authorities, the CRF will be marked as “reported”. 4. The SAE or SUSAR will also be saved in the local eureca – DW (saveSAESUSAR service).
Alternative Flow 1	1. The trial chairman confirms an SAE/SUSAR CRF in the CT system 2. The trial chairman prints the SAE/SUSAR CRF in order to send it paper based sent to the authorities. 3. The trial chairman sets the status of the SAE/SUSAR CRF to “reported”. 4. The SAE or SUSAR will also be saved in the local eureca – DW (saveSAESUSAR service).
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.CD.AR.03		**Priority**	required
Use Case name	**Update of a reported SAE/SUSAR event**			
Date created	05/11/2012	**Last updated**	12/11/2012	
Brief description	The outcome of a SAE/SUSAR is often uncertain at the reporting date. Therefore it is important to update this parameter in the CT system afterwards. These updates have to be reported to the involved authorities. All updates have to be attached to the original SAE/SUSAR report (including the date) in the CT system.			
Relates to Scenario	Automatic reporting of an SAEs/SUSARs event			
Includes use case	• SAE/SUSAR confirmation of the trial chairman (UC.CD.AD.02) • Automatic reporting of SAEs and SUSARs (UC.CD.AR.02) • Preparation for electronic exchange of SAE/SUSARs with the EMA (UC.CD.AR.01)			
Actors Involved	trial chairman/local physician			
Trigger	• Trial chairman updates the outcome in the SAE/SUSAR CRF • Local physician updates the outcome in the SAE/SUSAR CRF, trial chairman confirms this update.			
Pre-conditions	• SAE/SUSAR CRF has status “reported” in the CT system • The outcome of the SAE/SUSAR is uncertain at the reporting date • The CT system is authorized to update an SAE/SUSAR event to the involved authorities • Local eureca-DW and a updateSAESUSAR service exists			
Post-conditions				
Successful End condition	SAE/SUSAR event is updated and reported			
Fail End Condition	SAE/SUSAR event is not updated			
Normal Flow	1. The trial chairman logs in the CT system 2. The trial chairman selects the SAE/SUSAR event he wants to update			

	3. The SAE/SUSAR report is displayed 4. The trial chairman selects “update outcome” at the SAE/SUSAR CRF 5. The trial chairman enters the outcome and its date in the CT system 6. The trial chairman selects “save and report” 7. The SAE/SUSAR report is displayed within the updated outcome and its date. 8. The CT system reports the SAE/SUSAR event to the involved authorities 9. If these data are transferred correctly the involved authorities, the CRF will be marked as “updated” 10. If the SAE/SUSAR CRF will have no further updates, the trial chairman can set the status to “finalized”. The SAE/SUSAR CRF is marked as “finalized”. 11. The SAE or SUSAR will be update in the local eureca – DW (updateSAESUSAR service).
Alternative Flow 1	1. The trial chairman confirms an SAE/SUSAR CRF in the CT system 2. The trial chairman prints the SAE/SUSAR CRF in order to send it paper based sent to the authorities. 3. The trial chairman sets the status of the SAE/SUSAR CRF to “updated”. 4. If the SAE/SUSAR event is closed and consequently no further updates, the trial chairman can set the status to “closed”. The SAE/SUSAR CRF is marked as “finalized” 5. The SAE or SUSAR will be update in the local eureca – DW (updateSAESUSAR service).
Usage Frequency	High
User interfaces	N/A
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

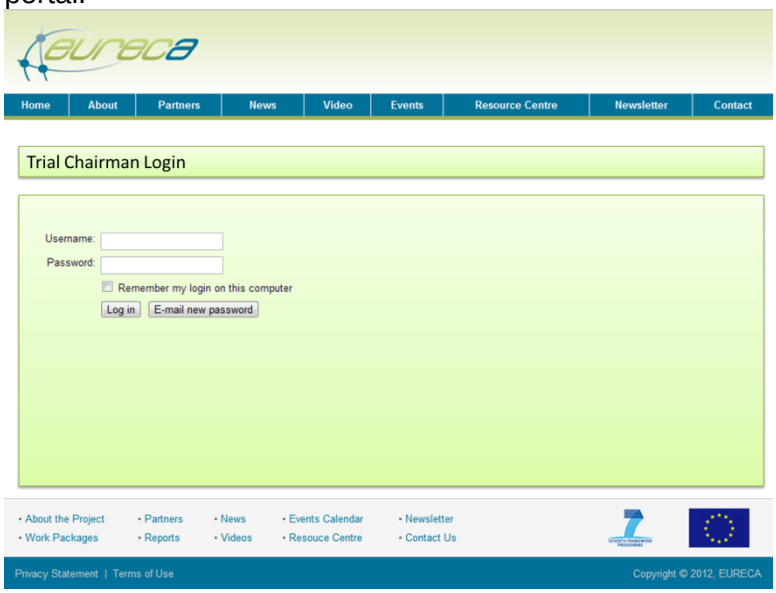
3.6 “Long-term follow-up” related use cases

Use Case ID	Use Case
UC.CD.LT.01	Create eCRF
UC.PD.TS.01	Patient diary
UC.PD.TS.02	Collect data from PHR and link it to CRF
UC.CD.LT.04	Survival follow-up EURECA platform

USE CASE: Long-term follow-up & Patient diary

Use Case ID	UC.CD.LT.01		**Priority**	REQUIRED
Use Case name	**Create eCRF**			
Date created	20/08/2012	**Last updated**	18/09/2012	
Brief description	The trial chairman defines in one or more specific CRFs which health related information is of interest for follow-up of a clinical trial.			

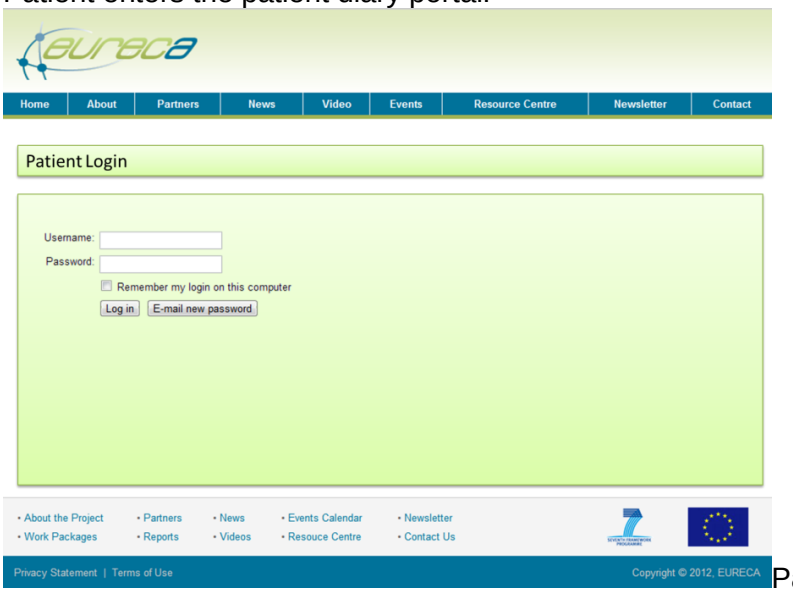
	These CRFs can include entries like - patient status (alive or deceased) - primary and secondary outcome measures - Safety reporting of specific adverse reactions after study treatment completion
Relates to Scenario	• Long-term follow-up
Includes use case	• No other use cases included
Actors Involved	• Trial chairman
Trigger	Trial chairman selects “create follow up CRF” for a corresponding Clinical Trial (CT) in the CT system
Pre-conditions	• Clinical trial exists in the CT system – CRFs might be created at the same time the other CRFs of a clinical trial are created. • The trial chairman is logged in on the CT system • The trial chairman is authorized to create CRFs and to operate with the related CT • The CT system is linked to the local DWH
Post-conditions	
Successful End condition	Long-term follow-up CRF that includes the specific parameters for a specific CT and a corresponding patient.
Fail End Condition	Long-term follow-up CRF could not be created
Normal Flow	16. The trial chairman opens the CT system of his choice. Each CT system works with its own database and connects to the local DW in order to receive further information 17. The CT system connects to the local DWH to retrieve the Clinical trial data and the corresponding CRFs already created. 18. A screen containing all the registered trials is presented to him. 19. The trials shown to the chairman are potentially restricted by access control 20. The chairman selects the trial he needs for creating the follow up CRF. 21. The chairman selects “create follow-up CRF” 22. A screen that enables the trial chairman the creation of the follow up CRF is shown. 23. The chairman creates a follow-up CRF. He formulates specific questions in order to follow the patients’ health status after the end of a trial. These questions can summarize information like 24. survival follow up (patient alive or deceased) 25. primary and secondary outcome measures 26. safety reporting of specific adverse reaction 27. The chairman clicks on a “save” button 28. The created CRF is saved in the CT system and can be uploaded to the local DWH 29. The chairman is redirected to the trial overview. The successfully created follow up CRF is listed.
Alternative Flow 1	The chairman links an existing follow up CRF form the repository of the CT system.

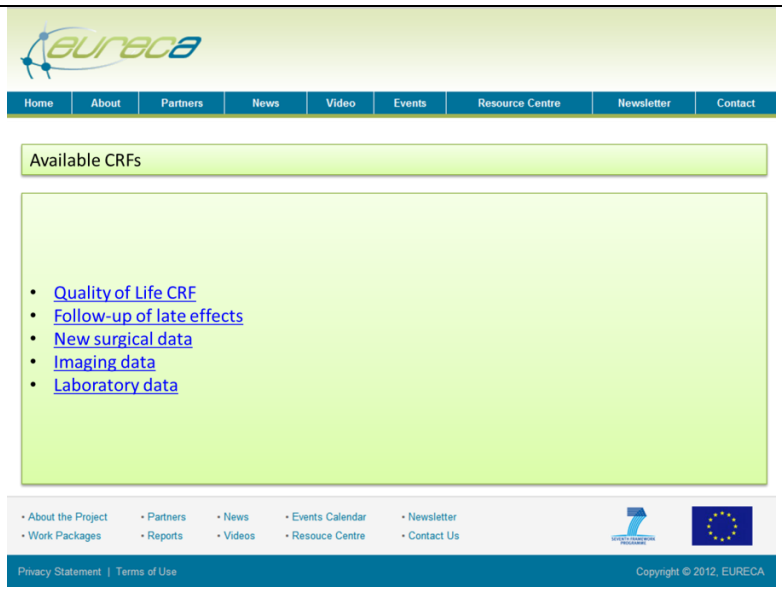
Alternative Flow 2	1. The CT system connects to the local DWH to retrieve the Clinical trial data and the corresponding follow up CRFs already created. 2. He selects an adequate CRF and link it to the trial in the CT system
Usage Frequency	Moderate
User interfaces	1. Trial Chairman enters the CT portal.  2. Selection of the appropriate CT to create eCRF  3. Create eCRF question

4. Final eCRF created

Business Rules	N/A
Assumptions	N/A
Notes and Issues	

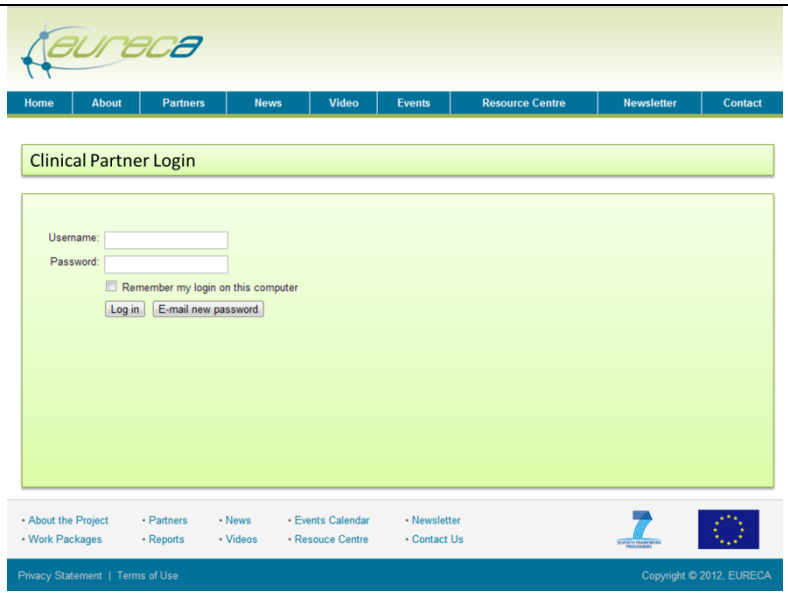
Use Case ID	UC.PD.TS.01		**Priority**	REQUIRED
Use Case name	**Patient diary**			
Date created	10/09/2012	**Last updated**	10/09/2012	
Brief description	A patient fills in an eCRF in his patient diary. Those eCRFs can be filled using ObTiMA, OpenClinica or IndivoX which are used as data management systems for such eCRFs. The collection of the information from these eCRFs builds the patient diary.			
Relates to	• Long-term follow-up			

Scenario	
Includes use case	• UC.CD.LT.01
Actors Involved	• Patient
Trigger	• A patient wants to fill in his eCRFs
Pre-conditions	• eCRFs should be available generated by trial chairman • A system should be available that will manage/store the eCRF • The local DWH should be available • A mechanism should be available to push data from filled eCRFs to the warehouse. • The patient has sufficient access rights and is authenticated to the platform
Post-conditions	
Successful End condition	An eCRF is filled by the patient
Fail End Condition	Failure on filling eCRFs or loading data to the local DWH
Normal Flow	1. The patient enters the patient diary portal or his PHR system 2. A list is shown of all available eCRF available to the patient. 3. Patient selects the eCRF to fill-in. 4. Patient fills-in the eCRF. • The data that needs to be filled in is determined by the trial chairman that generated the eCRF 5. After filling and saving the eCRF a report is presented to the patient about the submitted eCRF. 6. As soon as the eCRF is submitted a “Push” service uploads the data to the local DWH with a “Pending Validation” status. a. An expert should validate the pushed data.
Alternative Flow 1	
Usage Frequency	High
User interfaces	Patient enters the patient diary portal.  Patient Selects appropriate CRF

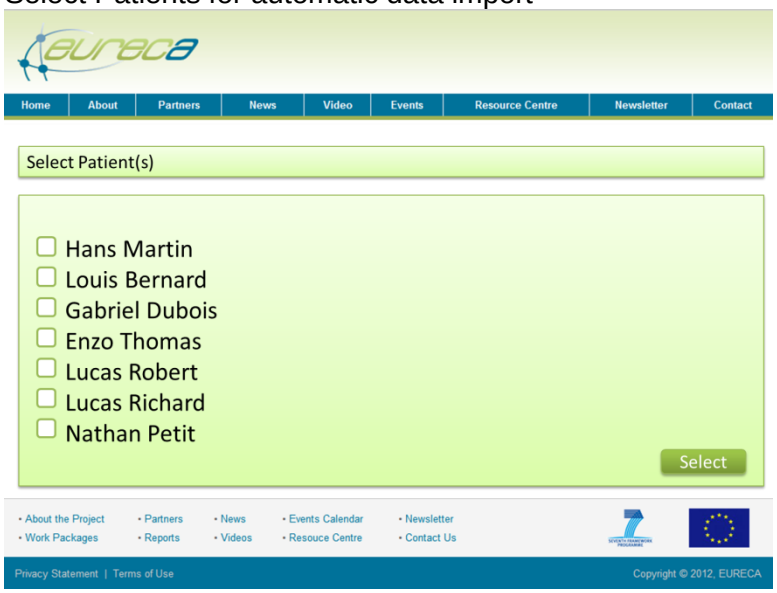
	 Patient fills CRF 
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

Use Case ID	UC.PD.TS.02		**Priority**	REQUIRED
Use Case name	**Collect data from PHR and link it to CRF**			
Date created	10/09/2012	**Last updated**	20/09/2012	
Brief description	Collect data from PHR and link it to CRF			
Relates to Scenario	• Long-term follow-up			

Includes use case	• UC.CD.LT.01
Actors Involved	• Doctor • Trial Chairman
Trigger	A Doctor /Trial Chairman wants to automatically fill eCRFs in CT/EHR/PHR from data already available and stored at the local DWH (possibly coming from a patient PHR system)
Pre-conditions	• A EURECA compatible DWH should be available locally • A service (“Sync”) will match data from the DWH with eCRF in CT/EHR/PHR • Informed consent should have been signed from the patients that their data are going to be accessed • The “Sync” service should have access to the DWH • eCRF available in CT//EHR/PHR • The Doctor / Trial Chairman has sufficient access rights and is authenticated to the platform.
Post-conditions	
Successful End condition	eCRF in CT/HIS/EHR/PHR successfully filled from data already stored in PHR
Fail End Condition	
Normal Flow	1. Doctor/Trial Chairman logs-in to the CT/EHR/PHR. 2. Doctor/Trial Chairman browses to the CT/EHR/PHR. 3. Doctor/Trial Chairman selects the patient(s) that their data should be automatically imported to the CT/EHR/PHR. 4. The “Sync” service accesses the local DWH and identifies relevant data for the patient(s). 5. The imported field are marked as imported data that should be validated before they are used
Alternative Flow	-
Usage Frequency	High
User interfaces	1. Doctor/Trial Chairman enters the CT/EHR/PHR.



2. Select Patients for automatic data import

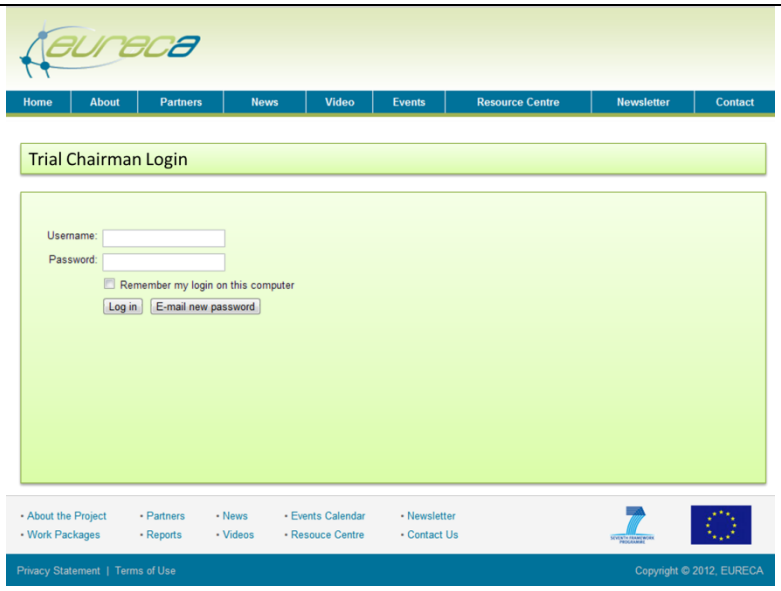


3. Filled eCRF with patient data

	
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

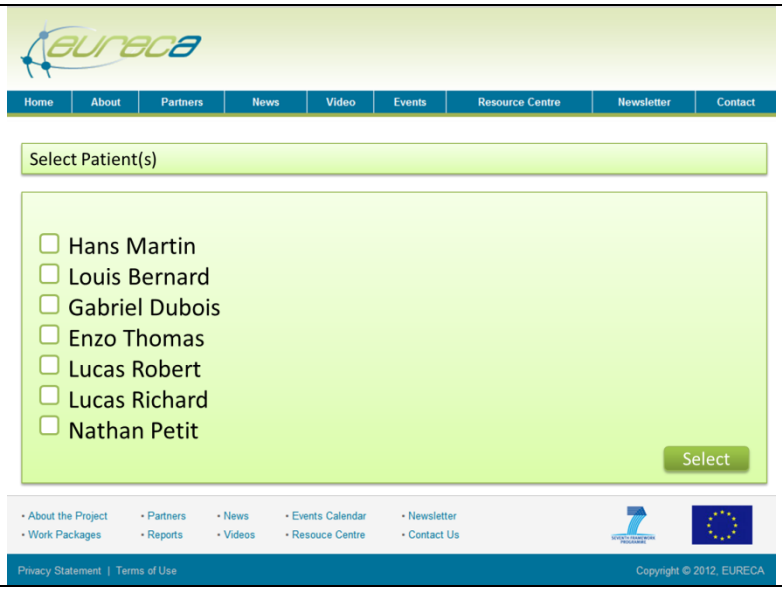
Use Case ID	UC.CD.LT.04	**Priority**	REQUIRED
Use Case name	**Survival follow-up EURECA platform**		
Date created	20/08/2012	**Last updated**	20/09/2012
Brief description	A service collects follow up information from National Registries for a specific patient after the end of a clinical trial. These data will be automatically included in the corresponding follow up CRF.		
Relates to Scenario	• Long-term follow-up		
Includes use case	• UC.CD.LT.01		
Actors Involved	• Trial chairman • Doctor		
Trigger	Select “Update NR Follow Up”		
Pre-conditions	• UpdateFollowUpFromNR service is a registered and configured service in EURECA infrastructure • Informed consent should have been signed from the patients that their data are going to be accessed • National Registries must be linked to EURECA infrastructure. • A “Pull” service should be available and authorized to access the national registries • A local DWH should be available • The trial chairman is authorized to use the service • Patient from National Registries must be linked to the EURECA patient • Follow up CRF exits for the specific clinical trial • The trial chairman is logged in on the CT system		

Post-conditions	
Successful End condition	Updated follow-up information in the corresponding CRF
Fail End Condition	Not updated follow-up information
Normal Flow	1. The trial chairman/doctor logs-in to the CT system. 2. A screen containing all the registered trials is presented to him. 3. The trials shown to the chairman are possible restricted by access control 4. The trial chairman/doctor selects a trial from the list 5. The trial chairman/doctor selects “patients in trial” 6. A new screen is displayed containing the list of available patients of a specific trial. a. This list is protected by access control, only the patients that the chairman is allowed to see, is shown. 7. The trial chairman/doctor sees the information collected from National Registries. a. A service automatically periodically checks the National Registries and updates the relevant patient data at the DWH. b. The data are marked as “imported from external registries” in order to be validated before they are used c. The imported data are pushed to the CT/EHR/PHR.
Alternative Flow 1	In step 6, the trial chairman/doctor can select all patients in a trial for checking the national registries.
Alternative Flow 2	In step 7a if relevant information is not stored at the local DWH a “pull” service is used to check the registered national registries for the aforementioned patients. It “pulls” the relevant information at the DWH
Usage Frequency	
User interfaces	1. Trial Chairman enters the CT portal.



2. Selection of the appropriate CT

3. Select Patients to search national registries

	
Business Rules	N/A
Assumptions	N/A
Notes and Issues	

3.7 “Economic analysis” related use cases

USE CASE: Analyse economic data between different procedures

This use case will be implemented in D1.4.

4 Use cases and legal requirements

Use cases are the specific applications of the EURECA project. These applications greatly vary in relation to their potential impact on data protection issues. Some use cases, for example, work with non-personal anonymous data, whilst other use cases include personal patient data processing. Some use cases are carried out for care purposes. Others are carried out for research purposes. Due to this variety in purpose and scope, three data processing domains can be separated from each other, in which different use cases are run that, from a legal perspective, are similar in relation to their data privacy sensitivity: the care, research and trial-support domain. Use cases are grouped together within these different domains and legally analysed. The following abstract will only give an overview over the legal requirements that have to be met in the care, the research and the trial support domain. A closer legal analysis of the specific use cases will follow.[11]

4.1 Care Domain

Within the clinical care domain sensitive personal patient data in the understanding of Art 2 (a) of the Data Protection Directive[12] will be processed. Fair and lawful processing of sensitive health data, Art 6 (1a) of the Directive[13], requires that all possible measures are applied to ensure safety and security of this information. Therefore, the safe havens approach is conducted in the care domain. The safe havens approach ensures safe handling of confidential patient information by efficiently working and effective access controls.[14] Only a closed project user group with specific characteristics[15] may access personal patient data. Authentication and authorisation procedures will be put in place to ensure that patient privacy rights are preserved. As the care domain covers all data processing for care, or care supportive purposes, no further legal requirements have to be met. This is owed to the fact that the lawmaker privileged data processing for care purposes in Art 8 (3) of the Directive[16]. This derogation only covers 'processing of personal data for the specific purpose of providing health-related services of a preventive, diagnostic, therapeutic or after-care nature and for the purposes of

[11] This will be part of Deliverable 7.1; due in 31.12.2012.
[12] Data Protection Directive 95/46/EC. Art 2 (a) of the directive reads: Personal data shall mean any information relating to an identified or identifiable natural person ('data subject'); an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity.
[13] Art 6 (1a) of the Directive reads: Member States shall provide that personal data must be processed fairly and lawfully.
[14] Pseudonymisation Implementation Project (PIP), Guidance on Business Processes and Safe Havens, Reference Paper 2, p.8, found at: http://www.connectingforhealth.nhs.uk/systemsandservices/pseudo/ref2busprosh.pdf; last accessed on 08.10.2012.
[15] eg. a patient's treating physician.
[16] Art 8 (3) of the Directive reads: Paragraph 1 shall not apply where processing of the data is required for the purposes of preventive medicine, medical diagnosis, the provision of care or treatment or the management of health-care services, and where those data are processed by a health professional subject under national law or rules established by national competent bodies to the obligation of professional secrecy or by another person also subject to an equivalent obligation of secrecy.

management of these health-care services, eg invoicing, accounting or statistics'.[17] Obtaining explicit informed consent, Art 8 (2a) of the Directive[18], is not a necessity in this domain, if data is strictly processed for care or care related purposes. The Art 29 Working Party stressed that processing of data for such purposes must be carried out by medical or other staff subject to professional medical secrecy or an equivalent obligation to secrecy.[19] Furthermore, data processing must be a necessity and may not exceed the purpose to enable patient care.[20] Art 8 (3) of the Directive must be interpreted in a restrictive way.[21] Any data processing that is not carried out for strict care purposes requires informed consent of the patient involved or any other legitimate legal ground.[22] Non personal medical research information may be reused for preventive care purposes.
The use case 'personal medical information recommender' falls in this domain, as data processing is carried out solely for care purposes (evaluating the best possible treatment for a particular patient).[23]

4.2 Research Domain

The research domain lies outside of the care domain. Data processing in the research domain can be distinguished from data processing in the care domain, as information is usually processed for medical research purposes to establish general rules relating to a specific disease. These rules may be applied in the clinical care context to improve the effectiveness and efficiency of care processes. Within the research domain medical literature is mined to obtain information about specific diseases. As this is not personal data processing according to Art 2 (a) of the Data Protection Directive, the scope of the Directive does not cover data processing within the research domain in the EURECA-context. The legal restrictions of the Directive do not apply. Therefore, data processing within the EURECA-research domain does not require specific legal safeguards, such as informed consent or strict access controls.
The use case 'guideline update' falls into the research domain, as medical literature is mined to detect information which potentially helps to cure specific diseases most efficiently.[24]

4.3 Trial Support Domain

The trial support domain covers data processing for recruitment purposes such as patient screening but also follow up data processing in the context of clinical trials. Data collected within the clinical care domain is reused for trial support purposes.
Use cases included in this domain are[25]:

[17] Art. 29 Working Party, Working Document on the processing of personal data relating to health in electronic health records (EHR), p.10.
[18] Art 8 (2a) of the directive reads: Paragraph 1 (Member states shall prohibit the processing of (...) data concerning health (...)) shall not apply where the data subject has given his explicit consent to the processing of those data (...).
[19] Art. 29 Working Party, Working Document on the processing of personal data relating to health in electronic health records (EHR), p.10.
[20] Art. 29 Working Party, ibid.
[21] Art. 29 Working Party, ibid.
[22] Art. 29 Working Party, ibid.
[23] For closer analysis see D7.1.
[24] For closer analysis see D7.1.
[25] For closer analysis see D7.1.

- patient screening
- protocol and trial feasibility
- patient recruitment
- alerting service (selection and inclusion of patients into trials
- long term follow up
- pre – filling of case report form
- pre – filling of adverse events report
- patient fills eCRF
- collect data from PHR and link it to CRF.

These use cases fall in the trial support domain as they facilitate the realization of clinical trials. It is questionable which legal requirements trial support services have to meet when data collected in the care domain is reused for trial support services. Art 6 (1b) of the Data Protection Directive[26] allows secondary data processing of clinical care data for medical research purposes if 'suitable safeguards' to protect patient privacy are implemented. Generally speaking, as data processing for trial support purposes is closely linked to the execution of a trial, it falls outside of the care domain, just like the execution of a clinical trial itself. Data processing within a clinical trial is usually carried out to investigate the effects of medicinal products, Art 2 (a) of the Clinical Trials Directive[27]. Findings can potentially help to cure individual patients. As they are fed back to patients via general rules, data is not being processed solely for care purposes. On the other hand, trials are not executed in the trial support domain of the EURECA infrastructure. Data is rather being processed to offer support services to clinical trials. The trial support domain falls outside of the scope of the research domain. As trial support services are not carried out to conduct research, but are run in preparation of research, data processing for support services has to be considered as being incompatible to the purpose of prior collection of such data in the care domain. The general principles outlined in the Data Protection Directive restricting patient data processing have to be adhered to. The legal requirements that have to be met in the trial support domain will consist in 1) informed consent 2) de-identification of data 3) auditing and 4) conclusion of Data Protection Contracts. Special legal requirements therefore have to be adhered to when offering trial support services. These requirements vary from case to case so that an in depth analysis of the use cases in EURECA has to be carried out.[28] The legal requirements ensuring patient privacy in the trial support domain shall therefore be generally introduced here.

4.3.1 Informed Consent

Obtaining informed consent will be a necessity when processing patient data for trial support services, (pursuant to Art 8 (2a) of the Directive). Informed consent ensures that a patient can make a voluntary decision whether his or her personal patient data may be

[26] Art 6 (1b) of the Data Protection Directive reads: 'Member States shall provide that personal data must be collected for specified, explicit and legitimate purposes and not further processed in a way incompatible with those purposes. Further processing of data for historical, statistical or scientific purposes shall not be considered as incompatible provided that Member States provide appropriate safeguards.'

[27] Clinical Trials Directive 2001/20/EC. Art 2 (a) reads 'Clinical trial': any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.

[28] For closer analysis see D7.1.

processed for a particular purpose at a particular time and which conditions have to be adhered to when processing this information. In the case of offering trial support services the patient can decide freely whether his personal information may be screened for trial enrolment purposes. Furthermore, a patient may also decide freely to take part in particular trial or not and that collected follow up medical information may be linked to his patient information collected during the execution of a trial or not.
For this reason the EURECA consent forms entail clauses which allow a patient to consent to specific of the diverse processing activities relating to trial support within the project. Furthermore, a patient may withdraw his consent at any time, disallowing data processing for trial support services.

4.3.2 De-Identification

Whenever possible and senseful, data will be de-identified to ensure privacy. De-identification entails anonymisation and pseudonymisation of data using the 'state of the art' pseudonymisation tool CATS supplied by CUSTODIX or any other equivalent pseudonymisation tool ensuring a high de-identification standard. When anonymising personal data, direct identifiers such as the name and address of a patient will be stripped of a patient's medical information and stored in a separate database. When pseudonymising patient data, these direct identifiers are replaced by a code. The link between the name of a patient and the code will be stored in a database which is again safeguarded by strict access controls. Data will be further processed under the code, allowing the data processor to process data without knowledge of the data subject standing behind the pseudonym, eg in case of recruiting patients for a trial. The investigator (trial chairman) may select, at a first stage, suitable patients from a pseudonymised database. Identification of patients will only be necessary at a later stage, when they are individually contacted (possibly through the treating physician) to take part in a particular trial.
By de-identifying personal and sensitive patient data, data is used frugally and in compliance with Art 6 of the Data Protection Directive. Conversely, de-identification itself is data processing. For this reason, within all use cases in the trial support domain that require de-identification of personal patient data informed consent needs to be obtained from participating patients.
In a number of use cases data is de-identified by giving out query results in aggregated form, eg. in the use case 'a researcher views a protocol feasibility verification request'. Whether and under which conditions aggregated data can be regarded as anonymous data is a highly controversial legal question.[29] To ensure data privacy, aggregation of data shall be backed by two other privacy preserving mechanisms: internal and external audit controls as well as the conclusion of data protection contracts, obliging the data end user not to re-identify any patient from aggregated data.[30]

4.3.3 Internal / External Auditing

Internal (or external) audits shall be run before aggregated data is given out to a project end user. This is relevant in the use cases: 'a designed protocol is executed on a data source and results are returned' and 'a researcher views a protocol feasibility verification request'. The audit procedures can be carried out by the specific hospitals returning aggregated data to an end user as a requester. This audit can be run manually or automatically. The purpose of the audit procedure is to ensure that no patient is

[29] See Ohm, Broken promises of privacy: responding to the surprising failure of anonymization, p.1715.
[30] See below: 4.3.3 and 4.3.5.

identifiable from the returned aggregated data. Furthermore, an effective audit makes sure that also a variety of requests by the same end user does not allow patient identification. This audit procedure could potentially be run by an external independent third party. It is a suitable safeguard to ensure data privacy. The conclusion of data protection contracts can serve as an additional safeguard which obliges end users not to identify patients from aggregated data.[31]

4.3.4 Access Control

Access control will play a major role in the trial support domain. Patient data may only be processed by a limited user group. For this reason, the EURECA applications offering trial support services may be run by persons with sufficient access rights. Users have to authenticate themselves to the EURECA system before running trial support applications. This is relevant in the use cases: 'create follow up CRF, update follow up information from EHR, update follow up information from PHR, update follow up information from national registries, pre-filling of case report form, pre-filling of adverse event report, suggest eligible clinical trials for patient, suggest a list of eligible patients for a trial, collect data from PHR and link to CRF'.
Usually only the trial chairman has sufficient access rights to run the trial support applications. Due to access control the number of persons who can process data is greatly reduced and patient privacy is enhanced.

4.3.5 Data Protection Contracts

Data protection contracts can be concluded between a central data controller, the EURECA Center for Data Protection (CDP[32]) and all project partners processing sensitive patient data when running trial support applications. Within these contracts partners running specific trial applications shall oblige themselves not to attempt to reidentify individual patients from processed data as well as not to disclose personal data to third persons. This obligation may be backed up by a penalty clause. The penalty kicks in if an end user attempts to re-identify a particular patient from project data. This economic sting will effectively safeguard patient privacy.[33]
Contracts could be concluded eg in the use cases 'a designed protocol is executed on a data source and results are returned' and 'a researcher views a protocol feasibility verification request' to ensure patient privacy when aggregated data is given out to project end users.

4.4 Summary

Personal patient data within the care domain needs to be safeguarded by valid access controls. If access controls are in place, data may be processed for care or care supportive purposes without adhering to further legal requirements. Non personal medical research information may be reused for preventive care purposes in the care domain. Within the research domain, personal data with regard to Art 2 (a) of the Data Protection Directive will not be processed. As the Directive is not applicable, data may be processed without legal restrictions. Things lie different within the trial support domain. Five different legal safeguards will be enacted to ensure patient privacy:

[31] See 4.3.5.
[32] The CDP is a non-profit legal entity established under Belgian Law and responsible for ensuring patient privacy throughout the project. For further information on the CDP see: http://www.privacypeople.org/.
[33] WP Opinion 05/2012, p.11.

- Informed consent
- De-Identification
- Internal/External Audits
- Access Control
- Data Protection Contracts

Depending on the specific use cases, one or a variety of safeguards will need to be applied. This mix of requirements will ensure that patient privacy is preserved and, on the other hand, medical research (or medical research support) is not further restricted than necessary.

5 Conclusion

This deliverable presents the more advanced use cases whose first iteration has been finalised and reviewed, according to the user needs and the scenarios that were proposed by clinicians. Nevertheless the provided use cases are not to be considered as final in their current form, but have to be considered in regard with constraints that we have for the first implementation of the EURECA platform.
Indeed the first iteration of these use cases will then be used for the first technical implementation of platform architecture, which will be presented in deliverable D2.2 (due in month 12). Then the final iteration of the use cases, together with a formal consolidation of the user needs, will be presented in deliverable D1.4 (due in month 18).