Deliverable No. D6.2

Evaluation report of the usability of p-medicine tools within the ECRIN infrastructure

Annex 1: Completed Questionnaires

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ABSTRACT:

Developers of p-medicine tools were surveyed to evaluate the usability of p-medicine tools using requirements for GCP compliance, quality management, sustainability / business plan and process conformance. This attachment contains the completed questionnaires.

KEYWORD LIST: requirements, regulations, GCP, tools, quality management, agile development, data security, pseudonymization, system validation, evaluation, ECRIN

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[1] **R**=Report, **P**=Prototype, **D**=Demonstrator, **O**=Other

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Content

1 Requirements for a CDMS / EDC system for the data collection in GCP compliant clinical trials (ObTiMA)

1.1 Part 1 Technical requirements for GCP compliant data management

I. General aspects and system limitations

No	Requirement ObTiMA	categories	Commentary (Yes, no, in development, n/a (not applicable), specifics, description, …)
1	Is your system completely web-based? Completely web-based means that all modules (e.g. user administration, study setup and maintenance, data entry) can be configured and used with full functionality via a web browser).	Specification and design	For end user complete web based; new user in web, Admin, and DB admin is local
2	If no: please list the web-based modules and describe the functionality provided.	Specification and design	-
3	Does your system allow conducting multiple studies at the same time (e.g. manage different user accounts across different studies)?	Specification and design	y
5	Is there a limit to the number of studies that can be conducted simultaneously?	Specification and design	Theoretically, n
6	Is there a limit to the number of patients that can participate in a study?	Specification and design	Theoretically, n
7	Is there a limit to the number of users who can use the system (total or simultaneously)?	Specification and design	Theoretically, n
9	Is there a limit to the number of	Specification and	n

	validity rules that can be defined for a study?	design	
10	Is there a limit to the number of data fields per eCRF?	Specification and design	n

II. Aspects data quality during data collection

18	Does your system support repeating data items (1 to n entries of element groups, e.g. concomitant medication, within a single form, an additional 'row' will be displayed when the last 'row' is filled in)?	Specification and design	y
19	Does your system support repeating forms, meaning that the number of a form depends on the occurrence of an event (e.g. Adverse Event form)?	Specification and design	y
20	Does your system support **repeating study events**, meaning that the number of a "study event" depends on the occurrence of a previous event?	Specification and design	ObTiMA is form based system Study event is not implemented, goes through CRF → extension
21	Does your system support conditional forms, which are opened automatically in case a pre-defined condition is met (e.g. an AE is categorized as SAE)?	Specification and design	planned
22	Does your system support the definition of data items or data item groups that become editable or visible only if a predefined condition is met?	Specification and design	y
23	Is the creation of eCRFs graphically oriented (design by mouse), or tabular oriented (table of data items)? Exists the possibility for modification of eCRF after the creation of the	Specification and design	Y Y, audit trail,

	eCRF?		versions
	Does the creation of eCRFs has different steps (e.g. draft, test, validation)?	Specification and design	?, versioning exists, 2 states: revision and running No flags for e.g. validation
24	During designing the eCRF, is it possible to define a header for each form? Can the header contain: Text objects *y (commentary field)* Dynamic objects (e.g. Subject ID*=earlier) warning* pops up	Specification and design	Y, no calculation of questions
25	Is the versioning of eCRFs supported?	Specification and design	y
26	Is it possible to establish a library with eCRF elements with: - CRF pages - CRF modules - variables - other objects	Specification and design	Y Repository for CRF exists
27	CRFs can be assigned to a visit.	Specification and design	planned study event
	Sample collection can be assigned to a visit?	Specification and design	planned
28	Repeating visits are possible.	Specification and design	planned
29	Support of CDASH standard for data collection elements?	Specification and design	n
30	Is the creation of CRFs for international trials supported? For example: - Multilingual CRFs - Multilingual help functions of	Specification and design	Planned, at present only in English N

	eCRF - Consideration of different time zones, time specifications, etc. (MEZ, summer time, etc.)		Relevance? (web based CRFs= only one time point: server time), components are given, user interface is simple, calendar is localised, time is part of audit trail: server time is indicated
31	Consideration of different time zones (e.g. during data input or CRF update)?	Specification and design	n/a release on server, multi-lingual CRFs are language-agnostic, localising is easy
32	Lab data are shown in eCRF (e.g. as table)?	Specification and design	n
33	Is there a limit to the number of parameters per eCRF, i.e. the number that can be collected and stored?	Specification and design	n
34	Is there a limit to the number of studies that can be managed simultaneously?	Specification and design	Theoretically, n
35	Is there a limit to the number of validity rules that can be defined for a study?	Specification and design	Theoretically, n
36	Is there a limit to the number of users who can use the system (total or simultaneously)?	Specification and design	n
37	Does your system allow the use of different date formats (e.g. for date	Specification and design	y

	German/ US)?		
38	Does your system support the handling of incomplete date information?	Specification and design	Interruption is possible
39	Does your system support derived data items, meaning that the value of these data items are calculated based on the values of other data items which are distributed over a set of forms / study events of the same subject?	Specification and design	n
39	Is the change/update of eCRFs during study conduct based on an amendment of the study protocol possible and how can this be achieved in international trials?	Specification and design	y
40	Does your system provide the possibility to deny ***recruitment*** of a subject if given conditions is not met?	Specification and design	Eligibility criteria are not re-checked
41	Can the following environments for data entry be established and managed within the application: - development - testing - training - production / operation	Specification and design	y
42	Does your system offers integrated help functions? If yes: Is it possible to define study related help features e.g. tooltips for data items, context sensitive help?	Specification and design	Y, but Actual functionality is limited Commentary texts can be linked to data items
43	Is an automatic monitoring of input for consistency with a defined field type (e.g. data field) available? - Use of parameter-related	Specification and design	Is part of CRF design Type of question, e.g. date, check for date, ranges

	selection lists *y* - Use of parameter-related value ranges *y* - Use of standardised selection lists (e.g. diagnoses, medicines) *coding lists*		CRF designer, creating new
47	Is the uniform use of international units (e.g. cm, inch) is supported?	Specification and design	N, measurement units can be attached
48	Which of the following supplementary functions for data monitoring and / or processing are available in the eCRFs of the software? - Spell checking of entered text *n* - Automatic conversion of parameters (e.g. transformation of lab value unit into other unit) *n* - Possibility of annotations at the document level - Display of protocol violations during data input *n, eligibility*	Specification and design	Is planned For investigator? Field for commentary Query → give commentary
49	Are the following options for data input supported in eCRFs? - Saving incomplete eCRFs *y* - Saving invalid eCRFs *n, with explanation/reason* - Collection and display of all error messages in list format after data input *y, audit trail, abnormal values, e.g.=y; list is not indicated; wrong input=immediate correction* - Recording of errors = *audit trail* - Others	Specification and design	What is invalid? depends on design of validity checks, dependent on operations Abnormal values=y

III. Training and support

50	Can support and training for CRA, investigator, data manager and data entry personal provided?	training	n
51	Does a user support for forgotten pass words exist?	Specification and design	y
52	Is a help desk for users provided?	Specification and design	y/n procedure available, at present no support for running phase
53	What is the average training requirement in employee-days for introduction to the software?	training	
54	Can you offer training for system administrators?	training	
55	Training for monitors is offered?	training	Is possible, e.g. through STaRC, persons must be assigned for support
56	Training for study managers is offered?	training	
57	Is an additional training offered?	training	
58	Which of the following support and / or hotline services are you able to offer? - Hotline in German, other languages - Hotline in English - Telephone hotline - 24-hour hotline availability - Email hotline - Training by consultant	support	At present, not yet offered, is done by developers, assignment of staff necessary! Dedicated infrastructure required, e.g. dedicated telephone

	- Training by p-medicine? *Training=y, by p-medicine =n* - Video courses		number
59	Which forms of documentation do you provide for training - Printed documentation (manuals, etc.) - Media-based documentation (e.g. video) *n* - Online documentation	training	In preparation
60	What type of support do you offer for **eCRF design**? - eCRFs can be prepared in collaboration with p-medicine *CRFs are not programmed, should be as easy as MS Word. Assignment of personal for training, customer care, hotline* - Collection of sample eCRFs is available *y* - Training is provided by p-medicine	support	N, should be done by externals Available, CRF repository Is done ad hoc, no process defined
61	What type of support do you offer for the **installation** of your software updates? - Technical support available for installation - Technical support available for update process - Update can be installed without additional aid from the company - Automatic update of the software - Audit trail for upgrades is available	support	Hosting Core as Open Source MS SQL Platform → buy support Must be done, in a regulated way

	- Test scripts for updates - Manual for updates		
62	What type of support do you offer for the expansion and programming of the software? - new interfaces created upon request - new functionalities created upon request - CDISC support *y ODM export exist, import in programmed*	support	Y, e.g. biobank add-on
63	Which of the following services do you offer? - Support for error correction in the software - Regular updates of the software - Regular meeting - User groups - Access to websites with news, problem-solving tips,…	Specification and design	In future Two business models (Open Clinica=Open Source), Support costs STaRC? Services, SaaS What is needed for this? Keep open, what means Open Source?: when local installation, somebody must do this

IV. eCRF administration

64	eCRFs can be tracked/depicted/searched for according to: - patient *y* - site / investigator *n, is planned* - visit / time *n* - investigator *n*	Specification and design	(see answers left)

	- country *n* - total number of CRFs is shown *n*		
65	In the eCRF incomplete eCRFs are indicated, flag lists of incomplete eCRFs can be generated	Specification and design	y
66	The investigator should be able to sign an eCRF for approval? Can this eCRF approval function be modified for different countries?	validation	N, goes through log-in authorisation CRF lock, valid Special role / during log-in, doesn't need to input password Approved field?
67	The system should support the import of lab data into the corresponding eCRF.	Specification and design	Through biobanking module possible, still prototype Other lab data =n HIS connector, still proof-of-concept
68	Does your system support the management of laboratory reference ranges? If yes: Does your system provide the possibility to manage laboratory reference ranges per laboratory, including: - assignment of one or more laboratories to **a site** - possibilities for changes **of site assignment** during study execution	Specification and design	For biobanks =y
69	Does the system support the definition of ranges for each laboratory parameter depending on laboratory, sex and age?	Specification and design	y

70	Does your system provide a status for data items / forms / study events / subjects marking (e.g. **data entry status=*y*),** query status, SDV status, recruitment status=*n*	validation	y/n
71	Does the system display graphic status icons for data items, forms, study events, subjects?	Specification and design	y
72	Does your system support plausibility checks during data entry ("edit checks")?	validation	y
73	Does your system support plausibility checks in batch mode ("batch checks")?	validation	n

V. Audit trail and query system

	An **Audit Trail** records per item all: - data input actions *y* - data changes (including value before and after change) *y* - data deletions *n* - date/time stamp and username of action *y* - "Reason for change" *y*	validation	Y, no deletion possible, only overwrite
	The "Reason for Change" of the audit trail is - always required *y* - optional for defined variables *y* - "change due to query" ? - "Reason for Change" is logged *y*	validation	Y, but ObTiMA has no query system

	The characterisation as „Self Evident Corrections /Obvious Corrections“ is possible	validation	N, not for text Typing error or out of range, not in audit trail
	Is a query system for data cleaning available in the tool?	validation	n
	Queries can be listed according to: - patient - site/investigator - country - total number of queries	validation	n
	The creation of manual queries is possible; the creation of queries in batch modus is possible?	validation	n
	A query can be indicated as “resolved”, when - Released by data manager - Released by monitor	validation	n
	Data query system: - Unequivocal query number is assigned - Specific query text is indicated - Query text can be modified	validation	n
	Identical queries are not generated during repeated query run in batch modus	validation	n
	Which options for eCRF validity checks does your software offer? - Setting mandatory fields *y* - Definition of conditional branches (if-then rule) *y* - Definition of validity checks for	validation	Sub-questions are possible e.g. range checks

	individual parameters *y* - Definition of tests for logical consistency between parameters within documents (e.g. gender and pregnancy) *y* - Definition of tests for logical consistency between parameters of different documents (e.g. diagnosis and therapy) *y*		to a certain degree possible e.g. date/operation; if-then is not possible, no scripting
	Are unresolved queries flagged?	validation	n
	To the Investigator information that new queries exists is indicated: - when the investigator connects to the system - by e-mail	validation	n
	Does your system support the automatic generation of queries by checking for discrepancies?	validation	n
	Exists a link between the query and its discrepancy, so that a correction of the value will set the query status to “responded” or “corrected”?	validation	n
	Is it possible to link manually raised queries to a data item? Is it possible to link manually raised queries to a set of data items?	validation	n
	When resolving a query: is it possible to correct the value of a data item and to answer the query in a single step?	validation	n
	Does your system support query numbers (unique numbers for queries and query lists)?	validation	n
	Does your system provide the possibility to print a list of queries sorted site, country, subject, study	validation	n

	event, related data items and date the queries were raised?		

VI. Additional functions (data sharing / coding / analysis and reporting)

	Does your system support the transfer of a study subject with all data from one site to another site?	Specification and design	y
	Does your system support data sharing with patient registers by providing an interface to integrate patient register data with clinical trial data?	Specification and design	N, no interface
	Does your system provide the possibility to lock and unlock a study allowing only read access when locked?	Specification and design	N, for CRFs
	Is it possible to input data from medical records into the eCRF? Can electronic source documents be used?	Specification and design	For HIS is planned
	Is guaranteed that the sponsor does not have exclusive control of source documents and eCRF data?	validation	Print out of CRFs
	Is a copy of the completed eCRFs (site specific patient data) stored independently from the study database at the corresponding site under control of the investigator?	validation	Print out of CRFs
	Is it possible that in a clinical study the medical record may be the first place in which trial related data is recorded (source document) with later transfer of data to the eCRF?	Specification and design	For HIS is planned
	Is a notification system integrated in your system that can trigger a notification of study related events	Specification and design	Y, planned

	(e.g. Adverse Event form, state of an eCRF “ready for review”)?		
	Does your software offer the following options for the management of patient study data? - Issuing of an ID for study subject *y* - Control of unequivocal assignment of ID *y* - Customisation of patient IDs / study subject ID *y* - Creating pseudonyms for subject IDs *y* - Rendering primary data anonymous / pseudonymous *y* - Storage of primary patient data in a separate database - Selection of patients according to personal data (age, gender, place of residence, etc.)	validation	Pseudonym eCRF data n, but database is encrypted, identifying data is treated with Custodix system (TTP), are encrypted n, what are the criteria for what is allowed? Stored together
	Which of the following parameters for the administration of eCRFs does your software utilise? - Date-, time stamp *y* - Author logging *y* - Indication of status parameters (e.g. cleaning status, Quality Assurance status, completeness) - Source data **verification code** for monitor	validation	Partly n
	Which options does the software offer for status types of eCRFs (e.g. document stored, document incomplete, data erroneous, and document complete and checked)?	validation	-

	Is a fully automatic status checking supported? (e.g. automatic status checking with confirmation and user modification options or status checking via manual user input)?	validation	Y Y eCRF
	Does your system support the planning of monitoring visits?	validation	n
	Does your system support the conduct of source data verification (e.g. remote monitoring)?	validation	Y, but: no querying, no monitoring
	Does your system support randomization?	validation	n
	Does your system provide an interface for the integration of randomization services?	Specification and design	n
	Does your system support medical coding of terminology utilizing: - MedDRA - WHO Drug Dictionary - CTCAE (CTC) - ATC - ICD	Specification and design	Planned SNOMED is planned, is ongoing ICD is planned, LOINC is planned
	Can your system manage different coding releases of the same coding dictionary?	Specification and design	n
	Does your system manage different language versions of the same coding dictionary?	Specification and design	n
	Does your system support	Specification and design	n

	auto-coding?		
	Are coding decisions recorded?	Specification and design	n
	Does your system allow the printing of “annotated CRFs”? (The annotated CRF provides the variable name and the coding for each CRF item). e.g. weight is WEIG	Specification and design	N, but DB automatically generates eCRFs, one variable per question, DB entry gets ID. DB export in ODM, has reference to patient data, or export as CRF-CSV file Coding-Questions, coding, ID plus the questions But coding is missing ODM has code list definitions
	Does your system allow to print filled out/saved and empty eCRFs of a subject or a site?	Specification and design	Y, through export
	Does the system generate reports? (e.g. query status report, database structure report, plausibility check -report, **audit trail reports=y, others=n**, user reports).	Specification and design	y/n
	Is it possible to sort or filter reports by e.g. site, subject, form, data item, and/or status?	Specification and design	n
	Does your system allow the import of data?	Specification and design	Planned, with ODM

	Does your system support the following import formats: - CSV - XML **=ODM** - HL7-**HIS import** - LAB - other	Specification and design	HIS system is SAP, HL7-Connector for Push/Sync service But manual adjustment of generic interface, Proof of concept Each hospital has own HIS, data definitions may be different, use of own definitions, different sub-systems are involved
	Does your system provide the possibility to export study data and metadata (including the audit trail) for the purpose of migration, application, and analysis?	Specification and design	y
	Is it possible to filter data for export?	Specification and design	y
	Is your system **CDISC certified** for: - Import (Data) - Import (Metadata) - Export (Data) - Export (Metadata)	Specification and design	n
	Reports can be generated for: - Edit checks - Derivations - Database plausibility/ integrity checks	Specification and design	n
	Report can be printed or exported concerning:	Specification and design	N, CRFs print

	- visits - eCRFs items		out
	Is Change Management of CRFs (Version Control) supported? (e.g. control if in different centres in different countries different versions of an eCRFs are used for data entry).	validation	N Is cleared per study, not country specific
	Does the system generate country-specific reports for international trials, e.g. data quality reports?	Specification and design	n
	Which types of analyses does your study-related software offer: Are standardised analyses according to centre, time, etc. (e.g. **recruitment lists**) possible? Is data quality analysis possible?	Specification and design	N, task of Tanaka's tool
	Is a free configuration of analyses by centres, period, patient parameters, etc. possible? - Single-variable analyses - Two-variable (two-dimensional) analyses	Specification and design	n
	Are standard reports provided by the tool? - Interim reports - Billing reports - Recruitment reports - Insurance reports - Study progress reports / status reports	Specification and design	n

VII. Electronic documents

	Which of the following study related documents (eDocuments) can the software generate, show, reference	Specification and design	N (no electronic documents involved)

	and/or manage: - Patient identification - Patient consent declarations - Storage of emergency medicines - Documents for specimen processing - Patient-related info sheets - Documents for specimen storage - Patient-related labels - Notification of patients regarding an examination - Patient warning letters - Research schedules for test physicians - Documents for exam scheduling - Release tickets for patients - Scheduling for therapy - Therapy-related documents - Scheduling / Planning of medicine(s) - Chemotherapy records - Radiotherapy records - Documents for medicine optimisation (e.g. dosage) - Documentation of toxicity criteria - Documents regarding parallel therapies - Incident reports		Master protocol, PDF generated An SAE/SUSAR reporting module is planned, next year

	- Patient-care documents - Examination results / reports - Physicians' letters - Others		
	Which of the following options does your software offer for the management of eDocuments? - Date-time stamp - Audit-trails / Author tracking - Setting of multiple status parameters - Version control	validation	n
	Which selection options are available for the access to eDocuments? - Selection according to various criteria (e.g. centre, addressee, date) - Direct retrieval by input of name or number - Restriction of accessibility according to the user's status and access rights	Specification and design	n

VIII. Platform requirements

	The Platform on which the server runs is: - UNIX/Linux *y* - Windows Server *y* - Other	Specification and design	
	The database system for the study database is: - Oracle - Microsoft SQL	Specification and design	Adoption of another DB is simple

	- PostgreSQL *y* - Other		
	What web browsers can be used?	Specification and design	All, IE from 9, all Firefox/Chrome
	Is the data transfer encrypted?	security	y
	Are specify browser features mandatory, like **Flash** or **Java Script**?	Specification and design	Both, Flash is used by Custodix for encryption
	Which web server is used: - Microsoft - Apache *y* - Tomcat *y* - Other	Specification and design	
	Can the system be hosted? - Internally at ECRIN data centre - Externally by p-medicine - Externally by an independent hosting provider	Specification and design	Y, is a political decision
	Does your system offer a well-defined and stable application interface (API), which can support interoperability with ***other systems=n****?* *What for? Biobank module exists, similarly it is possible to develop other moduls*	Specification and design	ODM export/import OpenClinica Security framework
	Does your system support the setup of an extended data protection scheme?	security	y
	A step-by-step database lock is possible (e.g. soft lock): - per patient	Specification and design	n/y

	- per site - per eCRF= *y, lock of all CRFs*		
	A step-by-step database unlock is possible: - per patient - per site - per eCRF = *y, lock of all CRFs*	Specification and design	n
	Any database lock or unlock is automatically recorded	Specification and design	y
	Can a report about locked data be generated?	Specification and design	Y, from audit plan
	The complete database can be exported as: - XML - ODM *=y* - SDTM - Other format */SQL*	Specification and design	
	Is it possible to export from study data base only the eCRFs / collected study data per site?	Specification and design	n
	Is **study archiving** supported? - Database export as ODM/XML *=y* - eCRFs export as PDF *=y per patients* - References exist to documents that exists as paper documents (e.g. signed informed consent)	validation	As commentary
	Is personal patient data be separated from medical study data?	Security, validation	-
	Is information available about system stability and system available during	support	Planned, load

	operation (e.g. Load test / Stress test) / Performance)?		testing by ObTiMA, partly developed, for server, usability of ObTiMA is tested
	Are trivial administration issues performed automatically; e.g. triggered by a user in case of a forgotten pass word?	support	y/n, partly automation, for admin, bottom: automatic password included in security infrastructure of Custodix, own tools
	Password and log-in features cover: - minimal password length *=y* - forced password change after 1st login *=n* - forced password change after defined time *=n* - defined complexity of password*=y* - recording of password history *=n* - minimum of changed characters*=n* - restricted number of failed logins*=y, usability?*	security	Mechanism is available
	Possible definition of **user roles** *(=free)* with assignment of specific rights possible for - Data Entry - Data Manager - Monitor - Investigator	security	y

	- Patient - System administrator - Other self-defined roles		
	Is the definition of User Groups with assignment of specific rights (e.g. study group) possible?	security	Y, roles define groups (=rights)
	Are e-mails sent by the system in encrypted form?	security	Secure mechanisms are available, e.g. lost password, but no notification system
	Which of the following procedures are integrated into the software? - Encrypted sending of usernames and passwords *=n (secure mechanism)* - Encrypted saving and storage of data and documents*=y* - Backup-Restore system (e.g. secondary hard disk, CD-ROM) *=y* - Crash protection (hard-disk imaging) *=y* - Loss of connection triggers automatic log-off - *=y, connection time off is configurable*	security	

IX. Implementation support

	Is an **Installation Guidance** including scripts for installation provided? *How? Hosted?*	Support, QA	In development
	Can the installation be performed by	Support, QA	Y, see above

	ECRIN data centre personal?		
	User manuals are provided for - Data managers *in dev.* - Investigators = *trail chairman* - system administrators - monitors - Others	support	In development
	Will p-medicine support installation of the system in an ECRIN centre?	support	n/y-is political decision
	Will p-medicine support **system validation** of the system in an ECRIN centre, by: - **Providing validation documents** (requirements, test results, QA documents) - **Providing test scripts** - **Joint conduct** of validation	Support, validation	Go in this direction
	Will p-medicine support **maintenance** of the system in an ECRIN centre?	support	?, n is political decision: p-medicine is a project, only 2 years on-going, is question of sustainability when official, we need these documents, task of Starc

1.2 Part 2: Requirements for development QA / generic GCP

X. Module 1: Software development planning, code writing and use of standards

Question	**Comment**
Description of developer group	Academic environment, software as a project
Composition of group, number of developers, number of supporting staff	2 core full time 1 part-time together with IBMP: 3 positions splitted 1/2
Lead of developer group (name)	H.S
Organisation/Institution	USAAR
Experience	5 years in company (HS)
Prior projects	ACGT

No.	**Question**	**category**	**Comment** **(if answer "yes", please specify)**
1	How is software development planned and conducted?	QA	
2	Is a conventional or agile approach used for software development?	QA	Agile approach, often meetings
3	In case of an agile approach, how is it organized (product owner, scrum master, meetings)?	QA	nearly daily meetings of group
4	Does a software development plan	QA	y

	(SDP) exist?		
5	Do developers participate in training?	training	Not lately
6	Are members of the software group trained to perform their development activities?	training	internally
7	Do SOPs for the development activities exist?	Controlled documents	N, Based on good practices, conventions that developers used and that are trained
8	Are the activities for managing the requirements reviewed by management?	QA	n
9	Does an information security policy exist?	QA	y. For development
10	Do information security awareness, education and training exist?	QA	y. Internally, IBMT, control
11	Do developers have knowledge/experience with testing and validation of computer systems (e.g. previous audits, inspections)?	training	Y/n. Testing is done
12	Are there reports of previous audits or inspections available?	validation	n
13	Are developers familiar with the regulatory background for software for clinical research (e.g.	Validation, training	y ECRIN standard

	GCP)?		
14	Are developers familiar with the evaluation of patient risks during development planning?	Validation, training	y
15	Is software developed /maintained/adapted according to SDLC (Systems development life-cycle)?	QA	y Bug tracking, feature requests, audit
16	Are there programming standards available for each programming language that is used?	QA	y
17	Is good technical documentation for the tool available?	QA	y
18	Do the standards cover the following details - Naming conventions for files y - Naming conventions for variables y - Log-out conventions y - Versioning (which tools), including documentation history y - Error handling y - Rules for writing code y - Rules for lines with comments n - Conventions concerning platform y - Conventions concerning user interface y	QA	(answers see left)
19	Is the compliance with development standards and data standards assessed?	QA	y
20	Do you support the CDISC standard?	Data consistency	y
21	Do you support ISO2701?	Data consistency	?

22	Are written policies in place and employed for document review?	Controlled doc	n Code review, but no corresponding SOP
23	Is there a unique definition, which documents underlie a review process?	Controlled doc	n
24	How is the review process organized?	Controlled doc	y Is done on an ad hoc basis, process is defined, but not fixed in writing
25	Are processes for deviations specified?	QA	Processes exist, implicitly spcified. Error → bug tracking → not paper based
26	Is system documentation that covers system architecture, individual modules / classes and their inputs, outputs, and purposes developed that can be provided?	QA	y partly
27	Is "In line Commenting" employed?	QA	y
28	Does a reference installation for the p-medicine tool exist?	QA, training	y
29	Does the reference installation represent a functionally equivalent testing environment?	QA, training	y Is used for testing
30	Does a demo installation of the p-medicine tool for ECRIN user training ~~exist~~?	QA, training	N, y Would be doable, test server exist that could be used by ECRIN
31	Can the reference installation be used for testing configuration changes?	QA	y

32	Can the reference installation be used by ECRIN users for the assessment of the tool?	QA, training	y
33	Does the **reference installation** consists of separate phases: e.g. initial installation, then test phase use and routine use?	QA	y Several reference installations exist
34	Are written policies in place and employed for integrity tests, security checks, patches and updates that are security relevant?	Controlled doc	n Policies are conventional, agreements
35	Are written policies in place for emergency precautions?	Controlled doc	n conventions

1.2.1.1 Module 2: Quality management during development

No	Question	categories	Comment (If answer "yes", please specify)
1	What is your quality management system (QMS)?	QA	y
2	What **Software Quality Assurance (SQA)** activities exist in your group?	QA	Bug tracking, SVN, nightly installations are run, bibliothecs are used
3	The Software Quality Assurance (SQA) activities are reviewed with management on a periodic basis n	QA	From time to time code checking, no QM handbook, Holger with double role, also as reviewer
4	Are software quality assurance activities trained?	QA	Y, by peer review
5	Does SQA review the activities and development products of the group?	QA	y
6	Follows the group a **written policy** for managing requirements?	QA, specifications	Y (n)feature request
7	Follows the group a **written policy** (n) for managing the software project?	QA	n Java feature request / bug tracking User level, requirements enter afterwards, No written policy for e.g. feature handling Requests in different directions / core, REST, SOAP,

			All: conventions
8	Follows the group a written policy for software configuration management?	QA	n
9	Follows the group a written policy for employing and maintaining a standard software development process?	QA	n
10	Follows the group a written policy for training?	QA	n
11	Can written policies be provided for a developer audit by ECRIN?	QA, validation	n
12	Are adequate resources provided for quality management activities?	QA	n
13	Are adequate resources provided for tracking reviewing the software project progress?	QA	y
14	Are adequate resources provided for the software development process?	QA	? What is required? No separate testing department, core functionalities: all tested
15	Are adequate resources provided for training and dissemination of tool usage?	training	? Modules, documentation by author, training by taking part
16	Does the quality management system include a **quality plan** for the p-medicine project, covering: - Roles and responsibilities - Documentation standards - Measures of quality assurance - Tools, methods and standards for	QA, controlled doc	y/n Plan exist, but no contract, everybody knows, by arrangement

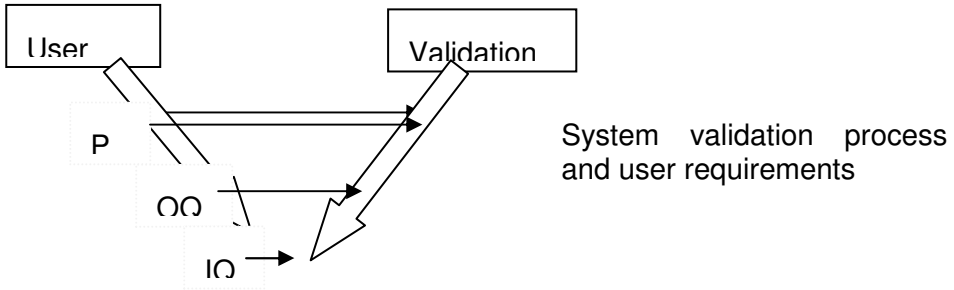
	development - Code review - Traceability		
17	Are **written instructions (e.g. SOPs)** employed for: - Software development - Change control - Configuration management - Review and approval of documents - Support of software problems - Supervision of project plans - Storing and archiving of quality relevant documents - Archiving of software (source code) - Management of problems - User access and physical/logical security - Handling of complaints - Performance of audits by customers?	controlled doc	n Descriptions exist for checks, testing, configuration management, but not with written SOPs
18	Are there standards for the technical and user documentation (e.g. user manual)?	QA	n
19	What Quality Control Activities are performed? For example: - Check for transcription errors in data input and reference - Check the integrity of database - Check for consistency of data - Check for uncertainties in data, database files, etc - Review of internal documentation *n no standard*	QA	y Document configuration, installation of development

	- Check methodological and data changes resulting in recalculations n - Undertake completeness checks - Compare new results to previous results y		environment = no SOPs
20	How does the group perform the testing of the software tools?	QA	Test classes, manuals GUI testing, each test has its own code
21	Is testing done by a dedicated and independent person/group?	QA	n
22	Are written policies in place and employed for the test activities?	Controlled doc	n Test documents, but no policies, this concerns all
23	Do you perform: - Functional tests y - Non-functional tests y - Acceptance tests y - Regression tests y - System tests y - Software tests y - Integration tests y - Unit tests y - Database tests y	QA	y
24	Do you conduct risk-based testing? (Risk based testing uses risk to prioritize the appropriate test cases)	QA, validation	n
25	Do you test according to risks of GCP relevance (e.g. risks for patient's wellbeing)?	QA, validation	y
26	Do the standards cover the following details - Naming conventions for files y - Naming conventions for variables y	Controlled doc	y/n =test

	- ~~Log-out conventions~~ - ~~Versioning (which tools), including documentation history~~ - ~~Error handling~~ - ~~Rules for lines with comments~~ - ~~Conventions concerning platform/screen?~~		
27	Is the compliance with standards assessed?	QA	y
28	Are there standards used for planning, performing and reporting of tests?	QA	y Java unit, use of standardize test tools
29	Exists a Software Quality Control / Testing Plan and how is it implemented?	QA	y Unit tests/classes, GUI tests
30	Is the testing done in a systematic way?	QA	y
31	Does separation of development, test and operational activities exist?	QA	? partly
32	Are the tests structured with respect to different phases? Is it possible to differentiate and allocate the tests (white-box testing, black-box testing, user acceptance testing)?	QA	y Unit tests, user testing, Too few users, external results are useful
	Does the **test plan** cover the following points - System characterization, incl. status of development y - Objectives of testing/relationship to	Controlled doc, specifications	y Partly, no dedicated test plan

	risk analysis - Test cases y - Test data, including acceptance criteria y - Performance, amount of testing - Results of tests, including descriptions of deviations - Assessment of results, if applicable changes dependent on the development phase (SDLC) and repeated testing? - others		
	Is there a systematic approach to the specification of the amount of testing?	QA, specifications	n
	Are the evaluators/reviewers different persons than the developers?	QA	n
	Are test tools used?	QA	y
	Is there a documented procedure for **change control** for the: - SDLC y - Source code y - Hardware specification and operational qualification n → not necessary - Configuration data y	Controlled doc	y
	Is there a clear definition, from which change on a re-testing, completely or partly, is necessary?	QA	n But, testing is always done when software is implemented
	Are responsibilities for change	QA	y Ticket is assigned,

	management defined (release of change, implementer, reviewer)?		bug report
	Are there procedures to prevent that an update or change of a software module is performed undetected or simultaneously by several persons?	QA	y
	Is assured that after changes to the system have been done, tests (preferably the same tests, regression tests) have to be performed?	QA	y
	Is it possible to audit changes from the proposal to the implementation?	QA	y
	Is it possible to uniquely identify each version of each configuration element?	QA, controlled doc	y
	Are delivered versions of hard- and software systems, including documentation, somehow archived?	QA	y Source code versions, milestones, version definitions



XI. Module 3: Generic requirements for GCP compliance of the tool

No.	Requirements for GCP compliance	categories	Comment (if answer "yes", please specify)
1	Plays GCP compliance aspects	validation	y

	during the planning of the programming of p-medicine tools a role?		
2	Is all clinical trial information be recorded, handled, and stored in a way that allows for accurate reporting, interpretation and verification?	validation	y
3	Is the confidentiality of records that could identify subjects protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements?	Validation, security	y
4	Are the tools implemented with **procedures** that assure quality?	Validation, QA	y Procedures? Evidence for procedures?
5	Allows the tool that the investigator can ensure the accuracy, completeness, legibility, and timeliness of the data reported in the CRFs (or other records)?	Validation, security	y
6	Supports the tool that data reported in the CRF that are derived from source documents, are consistent with the source documents?	validation	y
7	Supports the tool that any change or correction to a CRF is being dated, initialled, and explained (if necessary); is an audit trail maintained?	validation	y
8	Does the tool support that all data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable	Validation, security	y

	regulatory requirements?		
9	Does the tool ensure that the electronic data processing system conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended **performance**: is the tool **validated**?	Validation, QA	? validation
10	Are SOPs for using the tool (system) available and maintained?	Validation, controlled doc	n In development
11	Is the tool designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. audit trail, data trail, edit trail)?	validation	y
12	Is a security system maintained that prevents unauthorized access to the data? *Designed to*	Validation, security	y Applies to reference installation; dependent on final installation
13	Is a list maintained of the individuals who are authorized to make data changes?	Validation, security	y
14	Is adequate backup of the data maintained? *Is a local problem*	Validation, security	y Depends upon the installation
15	Exist safeguards for the **blinding** (e.g. maintain the blinding during data entry and processing)? *TOB allocation*	Validation, security	y/n Identity, allocation, not necessarily in CRF

16	Is it possible to always be able to compare the original data and observations with the processed data in the system (tool)?	Validation, security	y
17	Is the use of an unambiguous subject identification code supported that allows identification of all the data reported for each subject?	Validation, security	y
18	Allows the tool **direct access** to source data/documents for trial-related monitoring, audits, IRB/IEC review, and regulatory inspection?	validation	y Meaning is unclear? eSource from HIS; access to eSource data?
19	Can requirements documentation (e.g. functional requirements) be provided to support system validation?	Specifications, validation	partly
20	Can test documentation be provided to support system validation?	Validation, QA	partly
21	Can test reports be provided to support system validation?	validation	partly
22	Are test reviews, including document reviews, performed in the different phases of tool development (IQ, OQ, PQ)?	Validation, QA	y Will be done when necessary
23	Does the developer or another p-medicine group perform **system validation** of the developed software?	validation	y works for deployment?
24	Do test reports exist that can become part of the validation plan?	validation	partly
25	Does the developer or another p-	Validation, QA	y

	medicine group support the user conduct of IQ, OQ, PQ?		
26	How is **data security** in p-medicine tools guaranteed?	Validation, security	y p-medicine framework, roles/rights/ anonymised data, encryption of data
27	Does protection against malicious and mobile code exist?	Validation, security	y
28	Is information back-up implemented?	Validation, security	y
29	Does an access control policy exist?	Validation, security	? No document exists; convention
30	Does user access management and user registration exist?	Validation, security	y
31	Does a policy for user password management exist?	Validation, security	y/? Exists, but freely definable
32	Does secure log-on procedure exist?	Validation, security	y Secure?
33	Does user identification and authentication exist?	Validation, security	y
34	Does a password management system exist?	Validation, security	y

35	Is the sensitive part of the system isolated from the other parts?	Validation, security	y Depends on interpretation, end user configuration exist, Separated server / DB
36	Does input data validation exist?	Validation, security	y
37	Does a policy for the use of cryptographic controls exist?	Validation, security	y
38	Does access control to source code exist?	Validation, security	y
39	Does a control of technical vulnerabilities exist?	Validation, security	y DB backup, security control
40	Is risk management applied throughout the lifecycle of the computerized system (taking into account patient safety, data integrity and product quality)?	validation	y No written policies, work with tools, backups
41	Are decisions on the extent of validation and data integrity controls based on a justified ***(y)*** and documented risk assessment of the system?	validation	n Justified?
42	Can close cooperation between all relevant personnel such as Process Owner, System Owner, Qualified Persons and IT personal be shown?	validation	y Not written, photos?

43	Do all personnel have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties?	Validation, training	y “Qualification file”? not Internal training
44	Is it assured that the competence and reliability of a supplier are key factors when selecting a product or service provider?	Validation, training	? Use of external libraries for code, database Reliable provider, final version
45	Is it assured that quality system and audit information relating to suppliers or developers of software and implemented systems are being made available to inspectors on request?	validation	? No policies, system exists, Can be shown, processes demonstrate
46	Can developers and manufacturers justify their standards, protocols, acceptance criteria, procedures and records based on their risk assessment?	validation	y
47	Does a **listing** of all relevant systems / components and their GXP functionality exist?	validation	y No lists
48	Does for critical systems a description of the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and security measures exist?	Validation, specifications	partly In p-medicine deliverables documents exist
49	Do the User Requirements Specifications describe the required functions of the computerised system and are	Validation, specification	y/n URS exist as use cases in p-medicine

	they based on a documented risk assessment of GXP impact.		
50	Are user requirements traceable throughout the life-cycle of the tool?	Validation, specification	partly No matrix, requirements are included in tools Requirements are abstract, connection, more detailed
51	Is it ensured that the tool has been developed in accordance with an appropriate quality management system?	Validation, QA	y
52	Is the customised computerised system **formally** assessed and are quality and performance measures for all the life-cycle stages of the system reported?	Validation, QA	n Not formally
53	Is evidence of appropriate test methods and test scenarios demonstrated? Are particularly, system (process) parameter limits, data limits and error handling should considered?	Validation, QA	y data limits=n error handling=y test cases exist, not 100% for everything, resource limit
	If data are transferred to another data format or system, validation checks conducted that data are not altered in value and/or meaning during this migration process?	validation	ODM/other n If necessary scripts for external data format can be written, compare with database
	Do computerised systems **exchanging data electronically with other systems** have appropriate built-in checks for the correct and secure entry and	Validation, security	y exchanging data=n/a data entry possible ODM data entry is in development

	processing of data, in order to minimize risks?		
	For critical data entered manually, does an additional check on the accuracy of the data exist?	validation	y
	Does **risk management** of the tool cover the criticality and the potential consequences of erroneous or incorrectly entered data?	validation	? Correctness of data is tested CRFs ObTiMA allows checks, problem of the implementation of CRFs, creation of CRFs=task
	Is data secured by both physical and electronic means against damage?	Validation, security	y For test environment, is problem of implementation → ObTiMA makes available
	Is stored data checked for accessibility, readability and accuracy? Can the access to data be ensured throughout the retention period?	validation	y problem of implementation
	Can regular back-ups of all relevant data be conducted?	Validation, security	y problem of implementation
	Is the integrity and accuracy of back-up data and the ability to restore the data checked?	Validation, security	y problem of implementation
	Is it possible to obtain clear printed copies of electronically stored data?	validation	y

	For records supporting batch release, is it possible to generate printouts indicating if any of the data has been changed since the original entry?	validation	n Is possible but not yet implemented
	Is it considered during development that, based on a risk assessment, the creation of a record of all GXP-relevant changes and deletions (a system generated "audit trail") is built into the system?	validation	y
	Are audit trails available and convertible to a generally intelligible form and regularly reviewed?	validation	y Capable of development
	Are any changes to a computerised system including system configurations only possible in a controlled manner in accordance with a defined procedure?	Validation, QA	y implementation
	Are computerised systems evaluated periodically to confirm that they remain in a valid state and are compliant with GXP? (Such evaluations should include, where appropriate, the current range of functionality, deviation records, incidents, problems, upgrade history, performance, reliability, security and validation status reports).	Validation, QA	? n/a

	Are physical and/or logical controls in place to restrict access to computerised system to only authorised persons?	Validation, security	y implementation
	Does the extent of security controls depend on the criticality of the computerised system?	Validation, security	y implementation
	Are the creation, change, and cancellation of the access authorizations recorded?	Validation, security	y For ObTiMA = Audit trail Server access is local
	Do the management systems for data and for documents record the identity of operators entering, changing, confirming or deleting data including date and time?	Validation, security	y
	Are all **incidents**, not only system failures and data errors, reported and assessed?	Validation, security	?
	Are electronic records signed electronically (e.g password)?	validation	n Indirectly (during log-in)
	Does the electronic signatures have the same impact as a hand-written signature; is it permanently linked to its record, and includes the time and date that it was applied?	validation	y/n No field, audit trail is link Who does change what and how
	Are provisions in place for the availability of computerised systems supporting critical processes, to ensure continuity of support for those processes in the	validation	y Implementation Reference installation =y

	event of a system breakdown?		
	Is archived data checked for accessibility, readability and integrity?	validation	Server is daily backup, proof of concept Checked initially
	If relevant changes are made to the system, is the ability to retrieve the data ensured and tested?	validation	proof of concept Checked initially

2 Requirements for imaging in GCP compliant clinical trials (Dr.Eye)

2.1 Part 1: Technical requirements for compliant imaging in clinical trials (Dr.Eye)

A second version of the questionnaire with comments and explanations was sent to the developers.

XII. General aspects and system limitations

No	Requirement	Commentary (Yes, no, in development, not applicable, n/a, specifics, description, …)
1	What components of your imaging system are web-based modules (please describe the functionality provided).	Query, browse, view and manage DICOM images (in development)
2	Does your system support image handling during the conduct of clinical trials?	Yes
3	Does your system allow image handling during multiple trials at the same time (e.g. manage different user accounts across different trials)?	Yes
4	Is there a limit to the number of trials that can be conducted simultaneously?	No
5	Is there a limit to the number of images that is supported?	No
6	Is there a limit to the number of users who can use the system (total or simultaneously)?	Not applicable
7	Is there a limit in the size of the images?	No
8	What are the components of your imaging system? - a picture archiving system (PACS), a web-based picture archive system - a connection to a clinical data management system (CDMS, EDC) - an imaging amendment tool	- DICOM Viewer - an image processing unit - a portal or web entrance (a single access unit for all study participants)

	- DICOM viewer - an image processing unit - a portal or web entrance (a single access unit for all study participants) - an image review unit - an image analysis unit - an data extraction unit - an image transfer system - others	**(in development)** - an image analysis unit - an data extraction unit - an image transfer system **(in development)**
	If your system has no PACS as a component, does your system interact with a PACS?	In development

XIII. Quality aspects of imaging in clinical trials

9	Does your system checks quality of incoming images?	Yes
10	Does your system support the use of validated standardized image analysis techniques?	Yes
11	Does your system support the standardized extraction of quantitative image information?	Yes
12	Are validated and standardized image processing techniques used?	Yes
13	Is the PACS system that is part of your tool marked as a medical product (CE certificate)?	Not applicable
14	Is your tool marked as a medical product (CE certificate)?	No
15	Is the loss-less transfer of information (imaging data) guaranteed?	Yes
16	Does your system generate transfer protocols?	Yes
17	Is a centralized analysis of imaging data supported?	No

18	Are validated DICOM protocols used to ensure a lossless transfer of images via internet	Yes
19	Is the upload of an image data set accompanied by a quality check that assures that the data set fulfils the trial rules, e.g. regarding patient anonymity of the image meta information	In development
20	Can the user define generic quality specifications, e.g. Base Clinical, Clinical CT, De-identification, etc.	In development
21	Are measures performed on the image bitmap itself, such as checking for burned-in identifying information, evaluating of contrast, or checking that the correct anatomy has been imaged?	No

XIV. Process aspects of imaging and standards in clinical trials

22	Is the electronic transmission of imaging data between different sites and the central repository supported?	Could be implemented if needed
23	The combined management of imaging and numerical and other data by linking image storage with the clinical data management system is supported	Could be implemented if needed
24	Is high availability (site independent) and well-structured access to data, images and trial results provided?	No
25	Is it possible to specify rules to be set up for individual studies, for example to ensure a consistent use of information in DICOM tags?	Could be implemented if needed
26	Does your system support the definition of data items or data item groups that become editable or visible only if a predefined condition is met?	Yes
27	Are numerical analysis results automatically exported into a CRF?	No
28	Is it possible that the investigator can input own clinical trials images / clinical imaging data?	No

29	Is it possible to send/receive images by the investigator from any personal computer?	In development
30	Does the imaging system exchange data with a data management system for clinical trials (e.g. import image number in CRF, link between CRF and image)?	No
31	Is a central image repository for the clinical trial supported? Are local image repositories used?	Yes (if it is a PACS), Yes
32	Are transfer, up-/down-load and viewing of imaging data via internet from a local personal computer to/from a central PACS possible?	In development
33	Is it possible to send/receive images by the investigator from the local PACS to be used by your tool?	In development
34	Is it possible to define parameter of the study protocol in your tool to support the workflow of image handling?	No
35	Is it possible to clean data / correct/edit data? Is any correction/change of data accompanied by an audit trail?	Yes, No
36	Does your tool support image post-processing and analysis? When yes, what kind of processing?	Yes Histogram & PDF diagrams, statistics, Surface & volume measurements
37	Does your tool support the joint usage of CDMS/EDC, PACS and image processing tools?	No
38	Allows your tool searches in the imaging data bases?	In development
39	Does your system generates reporting forms related to image acquisition and analysis (e.g. presence of image artefacts or patient compliance)	No
40	Does your tool support DICOM and DICOM protocols? Is a DICOM dictionary included?	Yes
41	Are analysis results of your tool send back to the PACS	In development

	in the format of DICOM and DICOM Structured Reports.	
42	Can Image analysis results be queried and retrieved? Can they be queried through DICOM interface?	No
43	Exists the option to call PACS and the image processing unit from the clinical data management system (e.g. EDC system) for cross-linking of data and for enabling semantic searches in the database?	No
44	Can the following environments for image handling be established and managed within the application: - development - testing - validation - training - production / operation	Development (There is an API available for creating tools as plugins in order to extend the application's capabilities)
45	Can your tool provide imaging data with expert annotations?	Yes
46	Can metadata be managed by the imaging tool?	Yes
47	Can images be tracked/depicted/searched for according to: - patient / PID - site - visit / time - investigator - country - total number of images uploaded is shown	Yes
48	Are corrupted images flagged?	No
49	Does your tool support imaging review, does it provide image approval functions during image review?	No
50	Does your system assign a status to images (e.g. image reviewed, image analysed)? Does the system display graphic status icons for the images?	No

51	Can different types of images be handled (e.g. MRI, CT, PET, or ultrasound)?	Yes
52	Is it possible to integrate a third party for image evaluation / review?	No
53	Is it for an analysis core lab possible to log in, submit, and retrieve data / images?	No
54	Are open standards in accordance with the Integrating the Healthcare Enterprise (IHE) supported? Are established standards such as DICOM, HL7, and XDS supported?	Yes
55	Does your system support image retention? Do policies, especially security policies, exist?	No
56	Can the system generate automated alerts, e.g. for outliers or according to specified criteria? Are the alerts send via email, text, system messages?	No
57	Can the PACS or another database be used for long-term archiving of study images after the end of the study?	In development
58	Is Source Data Management supported? Are the eSDI requirements / recommendations for managing electronic source data applied to imaging?	No

XV. Data security and data protection aspects

No	**Requirement**	**Commentary (Yes, no, in development, not applicable, n/a, specifics, description, …)**
59	Is the access to the data base /imaging repository controlled? Has each user of the tool to register a user account before using the system?	Yes
60	Can all privileges and access rights be controlled via user accounts, e.g. who is allowed to upload and download data/images, access certain images?	No
61	Is data protection (privacy) guaranteed? Are different national laws for Data Protection considered?	No
62	Does the system support following security relevant methods: - https, secure web-protocol - eligibility check of users - each user has only access to assigned data	Some in development

	- during the image up-load, all private header information will be automatically removed and replaced by a pseudonymous patient identifier (PID) - does your tool generate pseudonyms or does it interact with a tool to generate pseudonyms (e.g. PID generator) - imaging data is transferred through the internet only in pseudo-anonymous form - storage of all data/images is done pseudo-anonymously - it is possible to encrypt the pseudonym (PID) during transfer via internet and during storage - it is possible to integrate a TTP in the operations - the tool to generate pseudonyms (PID) will be located and operated by a trusted party (TTP)	
63	Is image generation, transfer and storage tracked? Is a tracking report provided?	No
64	Is the access to the PACS subject to concepts of access rights (e.g. each research group / site has its own secured environment and the access to data is strictly regulated according to the specifications of each group)?	Yes
65	Does your system provide the possibility to deny registration of a subject if given conditions is not met?	No

XVI. Training and support

66	Can support and training for CRA, investigator, image reviewer, image analyser and data managers be provided?	yes
67	Does a user support for forgotten passwords exist?	Yes
68	Is a help desk for users provided?	Yes
69	Does your system offer integrated help functions?	No
70	What is the average training requirement in employee-days for introduction to your tool?	4 hours

71	Can you offer training for system administrators?	Yes
72	Which of the following support and / or hotline services are you able to offer? - Hotline in German, other languages - Hotline in English - Telephone hotline - 24-hour hotline availability - Email hotline - Training by consultant - Training by p-medicine - Online documentation	Email hotline
73	Which forms of documentation do you provide for training - Printed documentation (manuals, etc.) - Media-based documentation (e.g. video) - Online documentation	All three
74	What type of support do you offer for the parameterisation of your tool / image analysis validation? - Image validation in collaboration with p-medicine - Image analysis in collaboration with p-medicine - Training provided by p-medicine	Training
75	What type of support do you offer for the installation of software updates? - Technical support available for installation - Installation Guidance including scripts - Technical support available for update process - Update can be installed without additional aid from the company - Automatic update of the software	Technical support & manual

	- Audit trail for upgrades is available - Test scripts for updates - Manual for updates	
76	What type of support do you offer for the expansion and programming of the software? - new interfaces created upon request - new functionalities created upon request - new analysis algorithms - image analysis validation	• SDK available for extending the tool • Any modification/extension of the tool can be done, after discussion
77	User manuals / SOPs are provided for - Data managers - investigators - image reviewers - image analysts - system administrators - monitors - others	Image analysts and system administrators
78	Will p-medicine support system validation of the imaging system in an ECRIN centre?	If needed
79	Will p-medicine support installation of the imaging system in an ECRIN centre?	If needed
80	Can you support an ECRIN centre, by: - Providing validation documents (requirements, test results, QA documents) - Providing test scripts - Providing image validation scripts - Joint conduct of validation	If needed
81	Will p-medicine support maintenance of the system in an ECRIN centre?	

XVII. Platform requirements

82	What web browsers can be used?	Not applicable
83	Is the image data transfer encrypted?	Not applicable
84	Are specify browser features mandatory, like Flash or Java Script?	HTML5 support
85	Can the system be hosted? - internally at ECRIN data centre - by p-medicine - externally by an independent hosting provider	Not applicable
86	Does your system offer a well-defined and stable application interface (API), which can support interoperability with other systems?	No
87	Password and log-in features cover: - minimal password length - forced password change after 1st login - forced password change after defined time - defined complexity of password - recording of password history - minimum of changed characters - restricted number of failed logins	Partly
88	Which of the following procedures are integrated into the software? - Encrypted sending of usernames and passwords - Encrypted saving and storage of data and images - Backup-Restore system (e.g. secondary hard disk, CD-ROM) - Crash protection (hard-disk imaging) - Loss of connection triggers automatic log-off	Encryption

2.2 Part 2: Requirements for development QA / generic GCP

(to be answered by developers and quality managers)

XVIII. Module 1: Software development planning, code writing and use of standards

Question	**Comment**
Description of developer group	Computational Medicine Laboratory (CML) of Institute of Computer Science (ICS) of Foundation for Research & Technology – Hellas (FORTH)
Composition of group, number of developers, number of supporting staff	Head: Konstantinos Marias, 22,31
Lead of developer group (name)	Konstantinos Marias
Organisation/Institution	Institute of Computer Science (ICS) of Foundation for Research & Technology – Hellas (FORTH)
Experience	• biomedical informatics in support of individualized medicine • ambient intelligence eHealth environments
Prior projects	• EURECA • YPERTHEN • CHIC • E-NO FALLS • MyHealthAvatar • P-MEDICINE • INTEGRATE • ENCCA • EDGE • NEREIDs • TUMOR • REACTION • iCARDEA • GEN2PHEN

	• VPH NoE • Contra Cancrum • POSEIDON • ACGT • EHR-IMPLEMENT • Rural Wings • HEARTFAID • Technical Educational Institution of Athens • LOCCANDIA • Action-Grid • MIMP • HEALTHWARE • eHealth Survey • D.Y.P.E. Western Greece • D.Y.P.E. 3rd Regional Health System of Attica • D.Y.P.E 2nd Regional Health System of South Aegean • 1st Regional Health System of Attica • Venizelio-Pananio Hospital • Venizelio-Pananio Hospital • University Hospital of Patras • PHC of Harakas • PHC of Kandanos • TWISTER • eu-DOMAIN • SYMBIOmatics • Venizelio-Pananio Hospital • Venizelio-Pananio Hospital • SAFE • PHC of Spili • INFOBIOMED • PROGNOCHIP • WS-TALK • University Hospital of Patras • Attiko Hospital • INCO-HEALTH • HYGEIA' S PROTYPON • OPENECG • EMISPHER • ADOL

	• I-EHR • RemoteCare • e-Health Network • JUST • PICNIC • CORAS • IRAIA • ATTRACT • HYGEIANET • RETRANSPLANT • DNASequence • IntelCoronary • BreastCancer • INTERCARE • HEALTHNET • TEMeTeN • INTOURISME • HECTOR • ET-ASSIST • TEN-TELEMED • IHIS • TelePACS • EuriPACS • IRHIS • TELEMEDICINE • HIPACS

No.	Question	Answer (yes, no, not rel.)	Comment (if answer "yes", please specify)
1	How is software development planned and conducted?		
2	Is a conventional or agile approach used for software development?	Agile	
3	In case of an agile approach, how is it organized (product owner, scrum master, meetings)?	Yes	
4	Does a software development plan (SDP) exist?	Yes	

5	Do developers participate in training?	Yes	
6	Are members of the software group trained to perform their development activities?	Yes	
7	Do SOPs for the development activities exist?	No	
8	Are the activities for managing the requirements reviewed by management?	Yes	
9	Does an information security policy exist?	Yes	
10	Do information security awareness, education and training exist?	Yes	
11	Do developers have knowledge/experience with testing and validation of computer systems (e.g. previous audits, inspections)?	Yes	
12	Are there reports of previous audits or inspections available?	????	
13	Are developers familiar with the regulatory background for software for clinical research (e.g. GCP)?	Yes	
14	Are developers familiar with the evaluation of patient risks during development planning?	Yes	
15	Is software developed /maintained/adapted according to SDLC (Systems development life-cycle)?	?????	

16	Are there programming standards available for each programming language that is used?	Yes	
17	Is good technical documentation for the tool available?	Yes	
18	Do the standards cover the following details - Naming conventions for files - Naming conventions for variables - Log-out conventions - Versioning (which tools), including documentation history - Error handling - Rules for writing code - Rules for lines with comments - Conventions concerning platform - Conventions concerning user interface	Yes	
19	Is the compliance with development standards and data standards assessed?	Yes	
20	Do you support the CDISC standard?	No	
21	Do you support ISO2701?	No	
22	Are written policies in place and employed for document review?	No	
23	Is there a unique definition, which documents underlie a review process?	No	
24	How is the review process organized?	Not rel	
25	Are processes for deviations specified?	Yes	

26	Is system documentation that covers system architecture, individual modules / classes and their inputs, outputs, and purposes developed that can be provided?	Yes	
27	Is “In line Commenting” employed?	Yes	
28	Does a reference installation for the p-medicine tool exist?	No	
29	Does the reference installation represent a functionally equivalent testing environment?		
30	Does a demo installation of the p-medicine tool for ECRIN user training exist?		
31	Can the reference installation be used for testing configuration changes?		
32	Can the reference installation be used by ECRIN users for the assessment of the tool?		
33	Does the reference installation consists of separate phases: e.g. initial installation, then test phase use and routine use?		
34	Are written policies in place and employed for integrity tests, security checks, patches and updates that are security relevant?	No	
35	Are written policies in place for emergency precautions?	No	

XIX. Module 2: Quality management during development

No	Question	Answer (yes, no, not rel.)	Comment (If answer "yes", please specify)
1	What is your quality management system (QMS)? Do you have a quality manager?	No	
2	What Software Quality Assurance (SQA) activities exist in your group? Do you have a Quality Handbook?	No	
3	The Software Quality Assurance (SQA) activities are reviewed with management on a periodic basis	No	
4	Are software quality assurance activities trained?	No	
5	Does SQA review the activities and development products of the group?	No	
6	Follows the group a written policy for managing requirements?	No	
7	Follows the group a written policy for managing the software project?	No	
8	Follows the group a written policy for software configuration management?	No	
9	Follows the group a written policy for employing and maintaining a standard software development process?	No	
10	Follows the group a written policy for training?	No	
11	Can written policies be provided for a developer	No	

	audit by ECRIN?		
12	Are adequate resources provided for quality management activities?	?????	
13	Are adequate resources provided for tracking reviewing the software project progress?	Yes	(svn)
14	Are adequate resources provided for the software development process?	Yes	>>
15	Are adequate resources provided for training and dissemination of tool usage?	No	
16	Does the quality management system include a quality plan for the p-medicine project, covering: - Roles and responsibilities - Documentation standards - Measures of quality assurance - Tools, methods and standards for development - Code review - Traceability	No	
17	Are written instructions (e.g. SOPs) employed for: - Software development - Change control - Configuration management - Review and approval of documents - Support of software problems - Supervision of project plans - Storing and archiving of quality relevant documents - Archiving of software (source code) - Management of problems - User access and physical/logical security - Handling of complaints - Performance of audits by customers?	No	
18	Are there standards for the technical and user documentation (e.g. user manual)?	Yes	
19	What Quality Control Activities are performed? For example: - Check for transcription errors in data input and reference - Check the integrity of database	Yes	

	- Check for consistency of data - Check for uncertainties in data, database files, etc - Review of internal documentation - Check methodological and data changes resulting in recalculations - Undertake completeness checks - Compare new results to previous results		
20	How does the group perform the testing of the software tools?	?????	
21	Is testing done by a dedicated and independent person/group?	Yes	
22	Are written policies in place and employed for the test activities?	???	
23	Do you perform: - Functional tests - Non-functional tests - Acceptance tests - Regression tests - System tests - Software tests - Integration tests - Unit tests - Database tests	Yes	
24	Do you conduct risk-based testing? (Risk based testing uses risk to prioritize the appropriate test cases)	No	
25	Do you test according to risks of GCP relevance (e.g. risks for patient's wellbeing)?	?????	
26	Do the standards cover the following details - Naming conventions for files - Naming conventions for variables - others	Yes	
27	Is the compliance with standards assessed?	Yes	
28	Are there standards used for planning,		

	performing and reporting of tests?		
29	Exists a Software Quality Control / Testing Plan and how is it implemented?		
30	Is the testing done in a systematic way?		
31	Does separation of development, test and operational activities exist?		
32	Are the tests structured with respect to different phases? Is it possible to differentiate and allocate the tests (white-box testing, black-box testing, user acceptance testing)?	????	
33	Does the test plan cover the following points - System characterization, incl. status of development - Objectives of testing/relationship to risk analysis - Test cases - Test data, including acceptance criteria - Performance, amount of testing - Results of tests, including descriptions of deviations - Assessment of results, if applicable changes dependent on the development phase (SDLC) and repeated testing? - others	Yes	
34	Is there a systematic approach to the specification of the amount of testing?		
35	Are the evaluators/reviewers different persons than the developers?	Yes	
36	Are test tools used?	No	

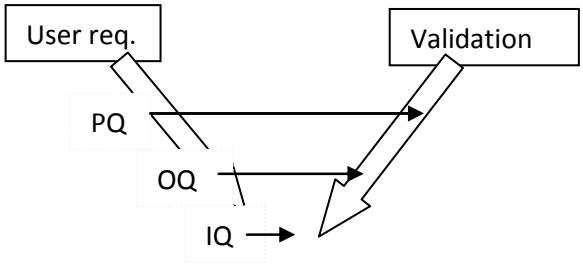
37	Is there a documented procedure for change control for the: - SDLC - Source code - Hardware specification and operational qualification - Configuration data	No	
38	Is there a clear definition, from which change on a re-testing, completely or partly, is necessary?	No	
39	Are responsibilities for change management defined (release of change, implementer, reviewer)?	No	
40	Are there procedures to prevent that an update or change of a software module is performed undetected or simultaneously by several persons?	No	
41	Is assured that after changes to the system have been done, tests (preferably the same tests, regression tests) have to be performed?	No	
42	Is it possible to audit changes from the proposal to the implementation?	Yes	
43	Is it possible to uniquely identify each version of each configuration element?	Yes	
44	Are delivered versions of hard- and software systems, including documentation, somehow archived?	Yes	

XX. Module 3: Generic requirements for GCP compliance of the tool

No.	**Requirements for GCP compliance**	**Answer (yes, no, not rel.)**	**Comment (if answer "yes", please specify)**
1	Plays GCP compliance aspects during the	Not rel	

	planning of the programming of p-medicine tools a role?		
2	Is all clinical trial information be recorded, handled, and stored in a way that allows for accurate reporting, interpretation and verification?	Yes	
3	Is the confidentiality of records that could identify subjects protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements?	????	
4	Are the tools implemented with procedures that assure quality? Can evidence for quality implementation be provided?	?????	
5	Allows the tool that the investigator can ensure the accuracy, completeness, legibility, and timeliness of the data reported in the CRFs (or other records)?	Not rel	
6	Supports the tool that data reported in the CRF that are derived from source documents, are consistent with the source documents?	Not rel	
7	Supports the tool that any change or correction to a CRF is being dated, initialled, and explained (if necessary); is an audit trail maintained?	Not rel	
8	Does the tool support that all data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements?	Not rel	
9	Does the tool ensure that the electronic data processing system conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance: is the tool validated?	Yes	
10	Are SOPs (standard operating procedures) for using the tool (system) available and maintained?	Yes	

11	Is the tool designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. audit trail, data trail, edit trail)?	Yes	
12	Is a security system maintained that prevents unauthorized access to the data?	Yes	
13	Is a list maintained of the individuals who are authorized to make data changes?	No	
14	Is adequate backup of the data maintained?	Not rel	
15	Exist safeguards for the blinding (e.g. maintain the blinding during data entry and processing, pseudonyms)?	Not rel	
16	Is it possible to always be able to compare the original data and observations with the processed data in the system (tool)?	Yes	
17	Is the use of an unambiguous subject identification code supported that allows identification of all the data reported for each subject?	No	
18	Allows the tool direct access to source data/documents for trial-related monitoring, audits, IRB/IEC review, and regulatory inspection?	?????	
19	Can requirements documentation (e.g. functional requirements) be provided to support system validation?	Yes	
20	Can test documentation be provided to support system validation?	Yes	
21	Can test reports be provided to support system validation?	Yes	

22	Are test reviews, including document reviews, performed in the different phases of tool development (e.g. unit tests, integration tests, IQ, OQ, PQ)?	No	
23	Does the developer or another p-medicine group perform system validation of the developed software?	????? Graf?	
24	Do test reports exist that can become part of the validation plan?		
25	Does the developer or another p-medicine group support the user conduct of IQ, OQ, PQ?		
	Explanation: Validation process 		System validation process and user requirements IQ=installation qualification OQ=operational qualif. PQ=performance qualif.
26	How is data security in your tools guaranteed?		
27	Does protection against malicious and mobile code exist?		
28	Is information back-up implemented?	No	
29	Does an access control policy exist?	Yes	
30	Does user access management and user registration exist?	Yes	
31	Does a policy for user password management exist?	Yes	

32	Does secure log-on procedure exist?	Yes	
33	Does a procedure for user identification and authentication exist?	Yes	
34	Does a password management system exist?	Yes	
35	Is the sensitive part of the system isolated from the other parts?	No	
36	Does a validation procedure for the input of data exist?	Not rel	
37	Does a policy for the use of cryptographic controls exist?	Not rel	
38	Does access control to source code exist?	No	
39	Does a control of technical vulnerabilities exist?	No	
40	Is risk management applied throughout the lifecycle of the computerized system (taking into account patient safety, data integrity and product quality)?	?????	
	Are decisions on the extent of validation/verification and data integrity controls based on a justified and documented risk assessment of the system?		
	Can close cooperation between all relevant personnel such as Process Owner, System Owner, Developers, Qualified Persons and IT personal be shown?	Yes	
	Do all personnel have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties?	Not rel	
	Is it assured that the competence and reliability of a developer/supplier are key factors when selecting a product or service provider?	Yes	
	Is it assured that quality system and audit	Not rel	

	information relating to supplier or developers of software and implemented systems are being made available to inspectors/auditors on request?		
	Can developers justify their standards, protocols, acceptance criteria, procedures and records based on their risk assessment?	Not rel	
	Does a listing of all relevant components of the developed tool and their GXP functionality exist?	No	
	Does for critical tools a written description of the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and security measures exist?	Not rel	
	Do Requirements Specifications describe the required functions of the tool and are they based on a risk assessment of GXP impact.	No	
	Are user requirements traceable throughout the life-cycle of the tool?	Yes	
	Is it ensured that the tool has been developed in accordance with an appropriate quality management system?	Not rel	
	Is the customized computerised system/tool formally assessed and are quality and performance measures for all the life-cycle stages of the system reported?	?????	
	Is evidence of appropriate test methods and test scenarios demonstrated? Are particularly, system (process) parameter limits, data limits and error handling considered?	Yes	
	If data are transferred to another data format or system, are validation checks conducted	Not rel	

	that data are not altered in value and/or meaning during this migration process?		
	Do computerised systems/tools exchanging data electronically with other systems/tools have appropriate built-in checks for the correct and secure entry and processing of data, in order to minimize risks?	Not rel	
	For critical data entered manually, does an additional check on the accuracy of the data exist?	Yes	
	Does risk management of the tool development exist and does it cover the criticality and the potential consequences of erroneous or incorrectly entered data?	No	
	Is data secured by both physical and electronic means against damage?	Not rel	
	If data is stored by the tool, is stored data checked for accessibility, readability and accuracy? Can the access to data be ensured throughout the storage period?	Yes	
	Are regular back-ups of all relevant data conducted?	No	
	Is the integrity and accuracy of back-up data and the ability to restore the data checked?	Not rel	
	Is it possible to obtain clear printed copies of electronically stored data?	Yes	
	Is it possible to generate printouts indicating if any of the data has been changed since the original data entry?	No	
	Is it considered during development that, based on a risk assessment, the creation of a record of all GXP-relevant changes and deletions (a system generated "audit trail") is built into the system?	No	

	Are audit trails available and convertible to a generally intelligible form and regularly reviewed?	Not rel	
	Are any changes to a computerised system/tool including system configurations only possible in a controlled manner in accordance with a defined procedure?	Not rel	
	Are physical and/or logical controls in place to restrict access to computerised system/tool to only authorised persons?	Yes	
	Does the extent of security controls depend on the criticality of the computerised system/tool?	Not rel???	
	Are the creation, change, and cancellation of the access authorizations recorded?	Not rel	
	Do the management systems for data and for documents record the identity of operators entering, changing, confirming or deleting data including date and time?	No	
	Are all problems, system failures and data errors reported and assessed?	No	
	Are electronic records, when used for clinical trials, signed electronically (e.g. by password)?	Yes/????	
	Does the electronic signature has the same impact as a hand-written signature; is it permanently linked to its record, and includes the time and date that it was applied?	Not rel	
	Are provisions in place to ensure continuity of support for critical processes (e.g. data entry) in the event of a system breakdown?	No	
	If relevant changes are made to the system, is the ability to retrieve all data ensured and tested?	Yes	

3 Requirements for a system to support biobanking in clinical trials

3.1 Part 1 Technical requirements for GCP compliant Biosample Manager

No	Requirement	Commentary (Yes, no, in development, n/a not applicable, specifics,…)
26	User, centres, institutions, can be created	Yes
27	Biosampling is integrated with clinical data management system (e.g. EDC system)	Yes
28	The input of biosamples information in eCRF is possible	Yes
29	Institutions should be able to assign in the system centres (sites)	Yes
30	The system must be able to capture automatically the current date and time.	yes
31	The system must be able to generate unique identifiers (pseudonyms) for patients.	Yes
32	Samples should be managed, employing: - Centre details - Analysis / extraction lists - Addition of extraction - Deactivation of extractions - Destruction notification	Possible to manage samples, but extraction list, analysis and destructions not possible.
33	System should support study controlling processes: - Audit trail - Data history - Audit results - Notification list about process controlling	Yes

	- List of assigned centres - List of studies - List of study access	
	System should be possible to set up of a new clinical study. In each study the number of collected samples as well as the complete storage time of samples is indicated.	Clinical studies and virtual biobanks can be set up. In biobank number of collected samples and storage time is indicated. Future work: Number of collected samples in trial not yet displayed but can be easily added.
34	System should be able to consider sites of a trial, containing information about: - leading investigator - study number - study start - study end - participating countries - participating sites - date of last update - site ID - telephone number - number of enrolled patients - date of first patient, first visit - date of last patient, last visit	Yes
35	Management of centres (sites) should be possible containing information about: - number of participating sites - number of planned patient recruitment - status of study - number of collected samples	Yes, but currently not possible to view number of collected samples

	- storage duration of samples - location of samples	
36	Management of central sample repository (CSR). It should be possible to assign each CSR an own admin role with following data: - name - role - collaborator ID / employee ID - telephone number - mail address - authorisation date	Yes, ObTiMA supports the creation of virtual biobanks, for each biobank a biobank manager can be assigned, who has admin roles for the biobank and can assign rights to other users for the biobank (collaborator ID/employee ID not stored).
37	Set up of new institutions, labs or clinics must be possible. A list per institution with assigned centres can be generated.	Yes
38	Each CSR can have assigned any number of study sites	Yes each virtual biobank can have assigned any number of trials.
39	Each institute can be set up with following data: - name of institute - type - name of responsible person - address - country - telephone - mail - authorisation date	Yes

XXI. Sample acquisition /check in requirements

No	**Requirement**	**Commentary (Yes, no, in development, n/a not applicable, specifics,…)**
41	Sample Acquisition: The system must allow users to upload and associate signed informed patient consent forms with biological sample records.	Not yet developed, could be implemented easily.
42	The system should have a link/reference to the patient informed consent	Patient Informed consent can be stored in patient

		metadata.
43	The system should support the creation of informed patient consent form templates which: - are in a language understandable to the subject or their representative - list the research projects for which the biological samples given by the subject will be used - address the future use of the samples (including commercial use and unspecified use) - provide information about the release of individual research results - provide information about consent withdrawal or later modification	Not yet implemented, will be considered in future.
44	The system must support the withdrawal of patient consent by the patient or their legal representative	Not yet implemented, will be considered in future.
45	The system must allow authorized users to alter the scope of patient consents according to the patient's or their legal representative's requests.	Not yet implemented, will be considered in future.
46	The system must allow authorized users to enter new biological sample records.	Yes
47	In addition to compulsory sample data, the system should allow users to enter the following data when importing biological samples: - identifier - depositor's name and address - source, substrate or host from which the biological material was isolated - geographical origin of material - growth media and conditions, cell preservation or storage conditions where known; - hazard information, e.g. in the form of a safety data sheet.	Yes, can be added to biobanking specimen CRF
48	The system should be able to store the shipping records (shipping log) which document biological sample arrival	Not yet possible, but will be considered in the future
49	The system must support the anonymization of samples in the following ways: - removal of identifying data - two-way coding by double pseudonymisation.	Not applicable. Samples are shown pseudonymized to users who have no rights to see personal information.

50	The system should support the review of the anonymization. It should allow a suitably authorized user to confirm the anonymisation procedure.	Not applicable (s. 49)
51	The process of anonymization and its review must be logged by the system	Not applicable (s. 49)
52	Generation of a pseudonym for a barcode (BC1)should be possible	Yes
53	The system should be possible to generate a second pseudonym for a second barcode (BC2)	Currently not possible, but will be considered
54	The system should manage the check-in of patients, including following information: - informed consent is available - BC1 search - BC1 as well as BC2 is checked for validity - following information is checked: date of visit in centre, type of sample (blood, serum, tissue, others... - sex of patient - BC1 and BC2	? Obtima supports enrolment of patients into a trial.
55	Creation of a new trial; system should guarantee that for each study the number of samples to be taken out of the storage as well as the complete storage time is indicated. Following steps should be managed: - Pseudonymisation of barcode 1 - check-in of patient - check: informed consent is available - BC1 search - BC1 as well as BC2 is checked for validity	Obtima supports creation of new trial.
	It should be possible to check-in patients	Yes.
	System must guarantee that samples of studies are coded threefold: 1. Study participant number (patient number) 2. First pseudonym (BC1, barcode 1) 3. Second pseudonym (BC2, barcode 2). The sample is stored only with BC2.	Not yet implemented, but can be considered.
	After the check-in of new samples: BC2 is generated BC2 replaces BC1	s. 53

	Generation of an unequivocal patient number: every patient study ID is used only once in the system, this is checked when a new ID is assigned	Yes
	Check-in of patients without IC entry should be possible	Yes
	It should be guaranteed that every sample can be identified only by its BC2 (second pseudonym)	Not yet implemented, but can be considered.
	The system can generate an inventory list of all samples collected for a study, in a country, per site or patient.	Not yet possible, but can be considered.
	There should be no limit on the number of BC codes possible	Not yet possible, but can be considered.
	The system should be able to read BCs	Yes
	The system should make it possible that a patients withdraws from a study, inclusive the deletion of patient number and corresponding samples	Not yet possible, will be considered in future
	The system should allow the change of centres	? The virtual biobanks can be associated to a localization (institution). That can be changed.
	The system should allow a patient audit	?
	BC2 should have a length of at least 14 characters	Not yet implemented, will be considered in future.
	Pseudonymisation BC2: the system checks that BC2 has been assigned to a sample before the sample is being stores in the biobank	Not yet implemented, will be considered in future.
	During patient check-in the system checks the validity of the informed consent	Not yet implemented, will be considered in future.
	System may request informed consent information	Not yet implemented, will be considered in future.
	During patient check-in the system checks that all patients of a study have been assigned to a site	Yes
	The system supports the pseudonymisation of patient's informed consent A patient's informed consent can be deposited in the system	Yes
	Pseudonymisation of BC1 scan; it is guaranteed that the assigned BC is not used again in the study	Yes

	BC1 verification: a scanned BC is checked according to given validity criteria	No
	A patient identification number (study-ID) is generated; an already assigned study ID can be imported	Yes
	The system allows double input of patient study numbers to avoid typing errors.	No, could be considered in the future
	The system must be able to track the physical location of samples by allowing users to associate the following data with samples: - location - container	Yes
	If the sample container's metadata include information about the container's location, the system is not required to store the location of the sample separately.	?
	The system must allow users to track the movement of samples by recording the following data: - current location - a predefined number of previous locations - date moved from last location - date received at current location - person responsible for the move	Not yet implemented, but will be considered in the future
	The system should support the validation of biological samples by allowing users to record details of the validation process, including the following data: - location of the validation - list of items validated - customer name and address - date of receipt of items to validate - date of validation - type of action carried out on the sample (e.g. purity check, quality check, identity check) - reference to sample plans and procedures where relevant - validation results with units of measurement - any abnormalities observed - person responsible for the validation results	Not yet implemented, but will be considered in the future

XXII. Selection / Requests for samples / Retrieval

Note: a query interface for the biobank module will be implemented in the next year.

	A process for request and selection of samples should be possible	Implemented in p-BioSPRE, but also considered to implement in Obtima
	Sample request should be possible. Upon request a list with following information is generated: - study - CSR - number of samples - name of analysis / extraction - due date	Not yet implemented, but will be considered in future
	After sample request, a list is generated covering all samples of the request with following information: - SGN - BC2 - material - amount - units used - status of sample - status of process	Not yet implemented, but will be considered in future
	For a request a list with selected BC2s is send to the sample manager The sample manager finds and checks out the requested samples from the biobank	Not yet implemented, but will be considered in future
	Request of sample status should be possible. Samples with following status are depicted, but not selected: - destruction requested - destroyed - lost - empty - shipped	Not yet implemented, but will be considered in future
	Request for sample selection. Right samples are selected on the basis of BC2 and made available	Yes
	The trustee should be able to search for patients, but only for patient number or BC1	Yes

	The system should support sample retrieval. It should track all requests for sample retrieval. This includes recording the following data: - date of request - list of samples requested - person who requested samples (investigator) - purpose of retrieval (study)	Not yet implemented, but will be considered in future
	The system should allow authorized users to approve, partially approve or reject sample requests.	Not yet implemented, but will be considered in future

XXIII. General system requirements and interoperability

	An interface with a biobank management system should be supported	Not yet implement, could be considerd in future, but not planned
	What steps of Biosampling is supported by your tool, what by the biobank?	
	It should be possible to create new users Only the administrator can activate and deactivate users	Yes
	Only the administrator can assign following roles: 1. Clinic (site): data manager, process controller, auditor 2. Lab: administrator, sample registrar, sample manager	Yes
	The system can create a list of all users	Yes
	The Trustee can make changes in the system concerning the informed consent of patient, only when patient expresses wishes to change in written form	Not yet implemented, but will be considered
	Only process controller and auditor can see all processes in the system, about a study, or about a single sample	Not yet implemented, but will be considered
	The system must allow authorized users to export - sample records, and - a catalogue of sample records	Not yet implemented, but will be considered
	The system should log all export operations.	Yes
	The system should be able to import - sample records, and - records of other entity types	Yes

	- imported records are subject to data validation	
	The system should use an open or a well-document proprietary data interchange format to support the interaction of the system with external software products	Yes, CDISC-ODM is used
	The system should support a graphical user interface.	Yes
	The system can display text elements of the user interface (e.g. button text, tool tips, error messages) in the local language. The system should be able to display the text elements of the user interface in English	Yes
	The system must be documented in sufficient detail: - functions - fields in data entry forms - errors and possible solutions	Not yet, but will be implemented
	The system must provide online help: - context sensitive; - provide visual guidance	Not yet, but will be implemented
	The system should assist data entry by following measures: - suggest possible text values - drop down menus when possible - provide default values	Yes
	The system should be possible to generate error messages or alerts	Yes
	Error messages produced by the system must be meaningful, so that users can decide how to correct the error or cancel the process.	Yes
	System recovery must be possible	Yes
	The system must provide an automatic backup feature	Yes
	The system must provide a recovery feature for restoring entities from backup files.	Yes
	The capability of data backup by the system must be checked regularly.	Yes

XXIV.Security issues

No	Requirement	Commentary (Yes, no, in development, n/a,

		specifics,…)
	The system must record the following data per log: - action - entities involved - user undertaking action - date and time of action	Yes
	The system must record automatically all critical actions in an log: - actions which result in the deletion of entities - anonymization / pseudonymisation - data modifications - user management actions - user authentication attempts - access violation attempts - changes to log settings	Yes
	The system must not allow users to access the tool without authentication	Yes
	The system must support authentication by user ID and password.	Yes
	The system must ensure that the data entered by the user during authentication cannot be intercepted by third parties	Yes
	The system must log both successful and unsuccessful user authentication attempts.	Yes
	If the system receives an unsuccessful user authentication attempt, the system must not reveal any information about the validity of the user ID.	Yes
	If the system registers more than a predefined number of consecutive unsuccessful user authentication attempts from the same IP address, the system may refuse to accept further attempts from that address	Same as for Obtima
	The system should not allow users to have unsecure passwords, i.e. character strings which: - are less than 8 characters long - can be found in dictionaries	Same as for Obtima

	- are not made up of a combination of letters, numbers and punctuation marks - are on a list of prohibited character strings (e.g. “password”, “123456”)	
	To protect health information of patients, the system adheres to privacy laws with respect to information systems.	Same as for Obtima
	The logistics for a withdrawal of consent must be clearly defined and conveyed to all subjects at the time of consent.	Same as for Obtima
	Anonymization should be verified by an appropriate review procedure.	Same as for Obtima
	The system must support the management of information related to the following sample lifecycle processes: - sample acquisition, including sample collection and receipt of samples - storage of samples and associated data - processing of samples - disposition, selection, retrieval of samples	Yes, but disposition of samples currently not possible
	The system must not allow users to associate identifying data with non-identifiable biological samples	Only for authorized persons with appropriate rights
	The system guarantees that no role except „sample registrar“ or „code exchanger“ has access to patient number or BC1	Roles in Obtima are called differently
	The system should be able to send and receive encrypted messages.	?
	The system should store passwords and similar credentials in an encrypted form.	Yes
	The system should store protected health information and users’ personal data in an encrypted form.	Yes
	The system must test whether the input value matches the format specified for the given field	Yes

	The system must ensure that the input value satisfies metadata constraints (e.g. age).	Yes
	The system must check the spelling of text field inputs.	No
	The system should allow authorized users (users have the required permission) to access: - sample records - procedure records - documents (e.g. informed consent) - storage unit records - user records	Yes

3.2 Part 2: Requirements for development QA / generic GCP

(to be answered by developers and quality managers)

XXV. Module 1: Software development planning, code writing and use of standards

Question	**Comment**
Description of developer group	Gabriele Weiler (Gabriele.weiler@ibmt.fraunhofer.de) Fatima Schera (fatima.schera@ibmt.fraunhofer.de)
Composition of group, number of developers, number of supporting staff	2 main developers, supporting staff is the Obtima team
Lead of developer group (name)	Gabriele Weiler
Organisation/Institution	Fraunhofer IBMT
Experience	Senior Developers
Prior projects	ACGT, Ensure, Eureca, Chronious

No.	**Question**	**Answer (yes, no, not rel.)**	**Comment (if answer "yes", please specify)**
1	How is software development planned and conducted?		
2	Is a conventional or agile approach used for software development?		Agile
3	In case of an agile approach, how is it organized (product owner, scrum master, meetings)?		Scrum like, with monthly sprint meeting
4	Does a software development plan (SDP) exist?		No

5	Do developers participate in training?		No
6	Are members of the software group trained to perform their development activities?		Yes
7	Do SOPs for the development activities exist?		No formal ones
8	Are the activities for managing the requirements reviewed by management?		yes
9	Does an information security policy exist?		no
10	Do information security awareness, education and training exist?		no
11	Do developers have knowledge/experience with testing and validation of computer systems (e.g. previous audits, inspections)?		yes
12	Are there reports of previous audits or inspections available?		no
13	Are developers familiar with the regulatory background for software for clinical research (e.g. GCP)?		yes
14	Are developers familiar with the evaluation of patient risks during development planning?		yes
15	Is software developed /maintained/adapted according to SDLC (Systems development life-cycle)?		no
16	Are there programming standards available for each programming language that is used?		yes
17	Is good technical documentation for the tool available?		Not yet, but planned
18	Do the standards cover the following details - Naming conventions for files - Naming conventions for variables - Log-out conventions - Versioning (which tools), including documentation history - Error handling - Rules for writing code - Rules for lines with comments - Conventions concerning platform - Conventions concerning user interface		no
19	Is the compliance with development standards and data standards assessed?		no
20	Do you support the CDISC standard?		yes

21	Do you support ISO2701?		no
22	Are written policies in place and employed for document review?		no
23	Is there a unique definition, which documents underlie a review process?		no
24	How is the review process organized?		no
25	Are processes for deviations specified?		No
26	Is system documentation that covers system architecture, individual modules / classes and their inputs, outputs, and purposes developed that can be provided?		Not yet
27	Is “In line Commenting” employed?		yes
28	Does a reference installation for the p-medicine tool exist?		yes
29	Does the reference installation represent a functionally equivalent testing environment?		yes
30	Does a demo installation of the p-medicine tool for ECRIN user training exist?		yes
31	Can the reference installation be used for testing configuration changes?		yes
32	Can the reference installation be used by ECRIN users for the assessment of the tool?		yes
33	Does the reference installation consists of separate phases: e.g. initial installation, then test phase use and routine use?		no
34	Are written policies in place and employed for integrity tests, security checks, patches and updates that are security relevant?		yes
35	Are written policies in place for emergency precautions?		yes

XXVI.Module 2: Quality management during development

No	Question	Answer (yes, no, not rel.)	Comment (If answer "yes", please specify)
1	What is your quality management system (QMS)? Do you have a quality manager?	no	
2	What Software Quality Assurance (SQA) activities exist in your group? Do you have a Quality Handbook?	no	
3	The Software Quality Assurance (SQA) activities are reviewed with management on a periodic basis	no	
4	Are software quality assurance activities trained?	No	
5	Does SQA review the activities and development products of the group?	No	
6	Follows the group a written policy for managing requirements?	no	
7	Follows the group a written policy for managing the software project?	no	
8	Follows the group a written policy for software configuration management?	no	
9	Follows the group a written policy for employing and maintaining a standard software development process?	no	
10	Follows the group a written policy for training?	no	
11	Can written policies be provided for a developer audit by ECRIN?	no	
12	Are adequate resources provided for quality management activities?	no	
13	Are adequate resources provided for tracking reviewing the software project progress?		
14	Are adequate resources provided for the software development process?		
15	Are adequate resources provided for training and dissemination of tool usage?		

16	Does the quality management system include a quality plan for the p-medicine project, covering: - Roles and responsibilities - Documentation standards - Measures of quality assurance - Tools, methods and standards for development - Code review - Traceability		
17	Are written instructions (e.g. SOPs) employed for: - Software development - Change control - Configuration management - Review and approval of documents - Support of software problems - Supervision of project plans - Storing and archiving of quality relevant documents - Archiving of software (source code) - Management of problems - User access and physical/logical security - Handling of complaints - Performance of audits by customers?		
18	Are there standards for the technical and user documentation (e.g. user manual)?		
19	What Quality Control Activities are performed? For example: - Check for transcription errors in data input and reference - Check the integrity of database - Check for consistency of data - Check for uncertainties in data, database files, etc - Review of internal documentation - Check methodological and data changes resulting in recalculations - Undertake completeness checks - Compare new results to previous results		
20	How does the group perform the testing of the software tools?		
21	Is testing done by a dedicated and independent person/group?		

22	Are written policies in place and employed for the test activities?		
23	Do you perform: - Functional tests - Non-functional tests - Acceptance tests - Regression tests - System tests - Software tests - Integration tests - Unit tests - Database tests		
24	Do you conduct risk-based testing? (Risk based testing uses risk to prioritize the appropriate test cases)		
25	Do you test according to risks of GCP relevance (e.g. risks for patient's wellbeing)?		
26	Do the standards cover the following details - Naming conventions for files - Naming conventions for variables - others		
27	Is the compliance with standards assessed?		
28	Are there standards used for planning, performing and reporting of tests?		
29	Exists a Software Quality Control / Testing Plan and how is it implemented?		
30	Is the testing done in a systematic way?		
31	Does separation of development, test and operational activities exist?		
32	Are the tests structured with respect to different phases? Is it possible to differentiate and allocate the tests (white-box testing, black-box testing, user acceptance testing)?		
33	Does the test plan cover the following points - System characterization, incl. status of development - Objectives of testing/relationship to		

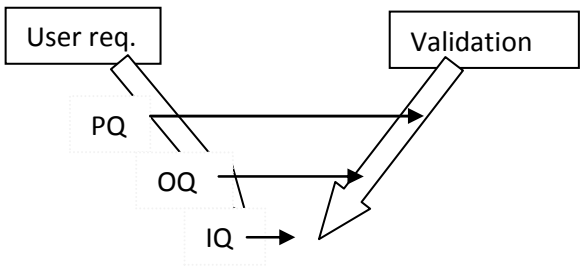
	risk analysis - Test cases - Test data, including acceptance criteria - Performance, amount of testing - Results of tests, including descriptions of deviations - Assessment of results, if applicable changes dependent on the development phase (SDLC) and repeated testing? - others		
34	Is there a systematic approach to the specification of the amount of testing?		
35	Are the evaluators/reviewers different persons than the developers?		
36	Are test tools used?		
37	Is there a documented procedure for change control for the: - SDLC - Source code - Hardware specification and operational qualification - Configuration data		
38	Is there a clear definition, from which change on a re-testing, completely or partly, is necessary?		
39	Are responsibilities for change management defined (release of change, implementer, reviewer)?		
40	Are there procedures to prevent that an update or change of a software module is performed undetected or simultaneously by several persons?		
41	Is assured that after changes to the system have been done, tests (preferably the same tests, regression tests) have to be performed?		

42	Is it possible to audit changes from the proposal to the implementation?		
43	Is it possible to uniquely identify each version of each configuration element?		
44	Are delivered versions of hard- and software systems, including documentation, somehow archived?		

XXVII. Module 3: Generic requirements for GCP compliance of the tool

No.	Requirements for GCP compliance	Answer (yes, no, not rel.)	Comment (if answer "yes", please specify)
1	Plays GCP compliance aspects during the planning of the programming of p-medicine tools a role?		
2	Is all clinical trial information be recorded, handled, and stored in a way that allows for accurate reporting, interpretation and verification?		
3	Is the confidentiality of records that could identify subjects protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements?		
4	Are the tools implemented with procedures that assure quality? Can evidence for quality implementation be provided?		
5	Allows the tool that the investigator can ensure the accuracy, completeness, legibility, and timeliness of the data reported in the CRFs (or other records)?		
6	Supports the tool that data reported in the CRF that are derived from source documents, are consistent with the source documents?		

7	Supports the tool that any change or correction to a CRF is being dated, initialed, and explained (if necessary); is an audit trail maintained?		
8	Does the tool support that all data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements?		
9	Does the tool ensure that the electronic data processing system conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance: is the tool validated?		
10	Are SOPs (standard operating procedures) for using the tool (system) available and maintained?		
11	Is the tool designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. audit trail, data trail, edit trail)?		
12	Is a security system maintained that prevents unauthorized access to the data?		
13	Is a list maintained of the individuals who are authorized to make data changes?		
14	Is adequate backup of the data maintained?		
15	Exist safeguards for the blinding (e.g. maintain the blinding during data entry and processing, pseudonyms)?		
16	Is it possible to always be able to compare the original data and observations with the processed data in the system (tool)?		
17	Is the use of an unambiguous subject identification code supported that allows identification of all the data reported for each subject?		

18	Allows the tool direct access to source data/documents for trial-related monitoring, audits, IRB/IEC review, and regulatory inspection?		
19	Can requirements documentation (e.g. functional requirements) be provided to support system validation?		
20	Can test documentation be provided to support system validation?		
21	Can test reports be provided to support system validation?		
22	Are test reviews, including document reviews, performed in the different phases of tool development (e.g. unit tests, integration tests, IQ, OQ, PQ)?		
23	Does the developer or another p-medicine group perform system validation of the developed software?		
24	Do test reports exist that can become part of the validation plan?		
25	Does the developer or another p-medicine group support the user conduct of IQ, OQ, PQ?		
	Explanation: Validation process 		System validation process and user requirements IQ=installation qualification OQ=operational qualif. PQ=performance qualif.
26	How is data security in your tools guaranteed?		
27	Does protection against malicious and mobile code exist?		
28	Is information back-up implemented?		

29	Does an access control policy exist?		
30	Does user access management and user registration exist?		
31	Does a policy for user password management exist?		
32	Does secure log-on procedure exist?		
33	Does a procedure for user identification and authentication exist?		
34	Does a password management system exist?		
35	Is the sensitive part of the system isolated from the other parts?		
36	Does a validation procedure for the input of data exist?		
37	Does a policy for the use of cryptographic controls exist?		
38	Does access control to source code exist?		
39	Does a control of technical vulnerabilities exist?		
40	Is risk management applied throughout the lifecycle of the computerized system (taking into account patient safety, data integrity and product quality)?		
41	Are decisions on the extent of validation/verification and data integrity controls based on a justified and documented risk assessment of the system?		
42	Can close cooperation between all relevant		

	personnel such as Process Owner, System Owner, Developers, Qualified Persons and IT personal be shown?		
43	Do all personnel have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties?		
44	Is it assured that the competence and reliability of a developer/supplier are key factors when selecting a product or service provider?		
45	Is it assured that quality system and audit information relating to supplier or developers of software and implemented systems are being made available to inspectors/auditors on request?		
46	Can developers justify their standards, protocols, acceptance criteria, procedures and records based on their risk assessment?		
	Does a listing of all relevant components of the developed tool and their GXP functionality exist?		
47	Does for critical tools a written description of the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and security measures exist?		
48	Do Requirements Specifications describe the required functions of the tool and are they based on a risk assessment of GXP impact.		
49	Are user requirements traceable throughout the life-cycle of the tool?		
50	Is it ensured that the tool has been developed		

	in accordance with an appropriate quality management system?		
51	Is the customized computerised system/tool formally assessed and are quality and performance measures for all the life-cycle stages of the system reported?		
52	Is evidence of appropriate test methods and test scenarios demonstrated? Are particularly, system (process) parameter limits, data limits and error handling considered?		
53	If data are transferred to another data format or system, are validation checks conducted that data are not altered in value and/or meaning during this migration process?		
54	Do computerised systems/tools exchanging data electronically with other systems/tools have appropriate built-in checks for the correct and secure entry and processing of data, in order to minimize risks?		
55	For critical data entered manually, does an additional check on the accuracy of the data exist?		
	Does risk management of the tool development exist and does it cover the criticality and the potential consequences of erroneous or incorrectly entered data?		
	Is data secured by both physical and electronic means against damage?		
	If data is stored by the tool, is stored data checked for accessibility, readability and accuracy? Can the access to data be ensured throughout the storage period?		

	Are regular back-ups of all relevant data conducted?		
	Is the integrity and accuracy of back-up data and the ability to restore the data checked?		
	Is it possible to obtain clear printed copies of electronically stored data?		
	Is it possible to generate printouts indicating if any of the data has been changed since the original data entry?		
	Is it considered during development that, based on a risk assessment, the creation of a record of all GXP-relevant changes and deletions (a system generated "audit trail") is built into the system?		
	Are audit trails available and convertible to a generally intelligible form and regularly reviewed?		
	Are any changes to a computerised system/tool including system configurations only possible in a controlled manner in accordance with a defined procedure?		
	Are physical and/or logical controls in place to restrict access to computerised system/tool to only authorised persons?		
	Does the extent of security controls depend on the criticality of the computerised system/tool?		
	Are the creation, change, and cancellation of the access authorizations recorded?		
	Do the management systems for data and for documents record the identity of operators entering, changing, confirming or deleting data including date and time?		
	Are all problems, system failures and data errors reported and assessed?		

	Are electronic records, when used for clinical trials, signed electronically (e.g. by password)?		
	Does the electronic signature has the same impact as a hand-written signature; is it permanently linked to its record, and includes the time and date that it was applied?		
	Are provisions in place to ensure continuity of support for critical processes (e.g. data entry) in the event of a system breakdown?		
	If relevant changes are made to the system, is the ability to retrieve all data ensured and tested?		