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Compliance and Inspections

Functional specifications for the EU portal and EU database to be audited

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*Hyperlink added to page 12 to link to document EMA/228383/2015 - Appendix, on disclosure rules, to the “Functional Specifications for the EU portal and EU database to be audited – EMA/42176/2014”, plus correction of acronym EUTCT on page 3.

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1. List of abbreviations

EC	European Commission
AR	Assessment report
Art	Article
ASR	Annual safety report
CET	Central European time
CT	Clinical trial
EEC	European Economic Community
EMA	European Medicines Agency
EU	European Union
EUTCT	European Union telematics controlled terms
EudraCT	European clinical trials database
EudraVigilance	European Union drug regulating authorities pharmacovigilance
Euratom	European Atomic Energy Community
EVCTM	EudraVigilance clinical trial module
ID	Identification
IMP	Investigational medicinal product
IMPD	Investigational medicinal product dossier
MAH	Marketing authorisation holder
MP	Medicinal product
MPD	Medical product dictionary
MS	Member State
MSC	Member State concerned
N	No
PDF	Portable document format
Req	Requirement
RMS	Reporting Member State
SUSAR	Suspected unexpected serious adverse reactions
UI	User interface
VHP	Voluntary harmonisation procedure
XML	Extensible mark-up language
Y	Yes

2. Introduction

The new Clinical Trial Regulation (EU) No 536/2014 (hereinafter "the Regulation") establishes a harmonised approach to submission, assessment and reporting of clinical trials (CTs) with the implementation of consistent rules throughout the Member States (MSs). These processes are to be supported by a EU portal and EU database which will ensure a centralised workflow with monitoring by the relevant parties. This Regulation repeals the Directive on Clinical Trials 2001/20/EC (hereinafter "the Directive") implemented in 2004 and which was the initial European legislation that aimed to simplify and harmonise the administrative requirements for clinical trials across the EU, whilst ensuring the safety of clinical trial participants, the ethical soundness of trials and the reliability and robustness of data generated. While achieving some of its aims, the Directive has also increased the administrative burden, costs and approval process of conducting clinical trials in the EU.

The application of the new Regulation is conditional on the conduct of an audit of the EU portal and the EU database showing that the system has achieved full functionality. The aim of this document is to draw up the functional specifications to be audited as specified in Article 82 of the Regulation.

3. Legal basis

In accordance with the Regulation, the European Medicines Agency has the following obligations:

- In accordance with Article 80, the Agency shall, in collaboration with the Member States and the Commission, set up and maintain a portal at Union level as a single entry point for the submission of data and information relating to clinical trials in accordance with this Regulation. The portal shall be technically advanced and user-friendly so as to avoid unnecessary work. Data and information submitted through the EU portal shall be stored in the EU database referred to in Article 81.
- In accordance with Article 81, the Agency shall, in collaboration with the Member States and the Commission, set up and maintain a database at Union level. The Agency shall be considered to be the controller of the EU database and shall be responsible for avoiding unnecessary duplication between the EU database and the EudraCT and EudraVigilance databases. The EU database shall contain the data and information submitted in accordance with this Regulation. The agency shall ensure that hyperlinks are provided to link together related data and documents held on the EU database and other databases managed by the Agency.
- In accordance with Article 82, the Agency shall, in collaboration with the Member States and the Commission draw up the functional specifications for the EU portal and the EU database, together with the timeframe for their implementation.

The Management Board of the Agency shall, on the basis of an independent audit, inform the Commission when the EU portal and the EU database have achieved full functionality and meet the functional specifications drawn up pursuant to the third paragraph.

The Commission shall, when it is satisfied that the Union portal and the EU database have achieved full functionality, publish a notice to that effect in the Official Journal of the European Union. Six months after the publication of this notice the Regulation shall apply, but in any event no earlier than 28 May 2016.

4. Scope

The Regulation clearly states that all information that is submitted through the EU portal is stored in the EU database (Article 80).

According to Article 81(4), the EU database shall be made publicly available unless, for all or part of the data and information contained therein, confidentiality is justified on the grounds outlined in that article.

Table 1 include the articles of the Regulation which explicitly specify the information that goes via the portal to the EU database and, as consequence, potentially publicly available as outlined above. These articles guide on the requirements for the functional specifications to be drawn up in accordance with Article 82(1) of the Regulation.

However, in order for the EU portal and the EU database to function correctly certain other technical features are essential and these are provided by the workspace. The workspace is required in order to support activities such as the preparation and compilation of the clinical trial application by the sponsor, the drafting of the assessment reports (ARs) by the Member States (Articles 6(5), 14(6) and 18(4)) prior to submission via the EU portal, as well as other features essential to track and control these activities. Whilst the workspace is essential to the functioning of the EU portal and EU database, and is therefore included in the scope of the audit, its content is outside of the EU portal and the EU database as defined by the Regulation.

Schematic representation of the clinical trial systems is provided in figure 1:

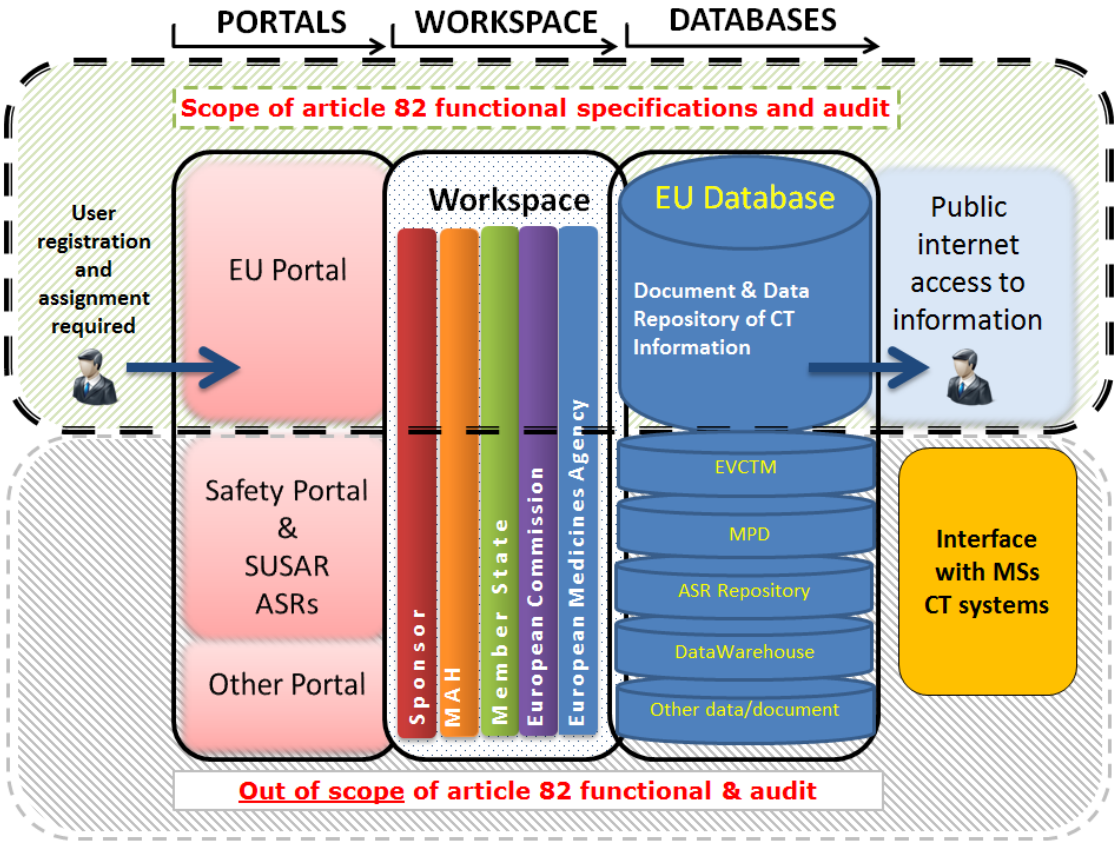

Figure 1: High level overview of the clinical trial systems

The legal requirements that set out the data and information to be submitted through the EU portal to the EU database are presented in section 5. The functional specifications identified in line with those legal requirements are presented in section 6.

5. Overview of the activities required in the Clinical Trial Regulation

5.1. Legal requirements of the EU portal and EU database

The EU portal and EU database and associated workspace are to provide sponsors and applicants to a marketing authorisation (including individuals, companies, institutions or organizations to whom any or all tasks have been delegated by the sponsor or by the applicant to a marketing authorisation) the same as MSs, the Commission and the Agency with an effective network tool to streamline and facilitate the flow of information for the authorisation and supervision of clinical trials in the EU and to support publication of information on clinical trials. The information stored in the EU database will be accessible to the public through a public interface. An overview of the legal requirements for the submission of data and information through the EU portal to the EU database and the key actors is provided in table 1.

Table 1: EU clinical trial portal and EU database activities and requirements

EU clinical trials portal and EU database activities and requirements				
Stakeholder	Role (high level)	Requirement	Requirement ID No.	Legal basis (Art.)
Sponsor	Submit an initial CT application, substantial modification or an additional MS in a CT/conduct of the trial, supervision by the sponsor.	Request of a unique EU trial number to identify each CT	Req. 1	Art. 81(1)
		Record and submission of medicinal products and substances to the medicinal product dictionary, including the request of the EU medicinal product number and EU active substance code	Req. 2	Art. 81(3)
		Submission of application related to CT (initial with the proposal on the RMS, additional MS and substantial modifications)	Req. 3	Art. 5(1), 11, 14(1), 16
		Submission of the requested additional information by the reporting Member State (RMS) or Member State concerned (MSC), as applicable	Req. 4	Initial application: Art. 5(5) for validation, Art. 6(8) for Part I and Art. 7(3) for Part II. Additional MS: Art. 14(6) Part I and Art. 14(8) Part II.

EU clinical trials portal and EU database activities and requirements				
Stakeholder	Role (high level)	Requirement	Requirement ID No.	Legal basis (Art.)
				Substantial modification: Art. 17(4) for validation, Art. 18(6) for Part I, Art. 20(6) for Part II, Art. 22(3) for Part II.
		Submission of inspection reports of third country authorities concerning the clinical trial	Req. 5	Art. 53(2)
		Notifications	Req. 6	Reasons for withdrawal- Art. 12. Start of the clinical trial in each MSC - Art. 36(1). First visit of the first subject in each MSC - Art. 36(2). End of the recruitment in each MSC - Art. 36(3). Re-start of recruitment in each MSC - Art. 36(3). End of trial- Art. 37(1) (in relation to each Ms concerned), Art. 37(2) (within the EU), Art. 37(3) (global end). Temporary halt - Art. 37(5) (for reasons not affecting benefit-risk balance) and Art. 38 (for reasons affecting benefit-risk balance). Restart of the trial after temporarily halt - Art. 37(6) and Art. 38(2) Early termination - Art. 37(7) (for reasons not affecting benefit-risk balance) and Art. 38 (for

EU clinical trials portal and EU database activities and requirements				
Stakeholder	Role (high level)	Requirement	Requirement ID No.	Legal basis (Art.)
				reasons affecting benefit-risk balance). Serious breaches- Art. 52(1). Unexpected events which affect the benefit-risk balance- Art. 53(1). Urgent safety measures – Art. 54.
		Submission CT summary results (including lay summary)	Req. 7	Art. 37(4) (after the end of trial), Art. 37(8) (after the intermediate analysis date)
	Update of information	Update any changes to the clinical trials which are not substantial modification but are relevant for the supervision of the CTs by the MSs	Req. 8	Art. 81(9) Art. 55, investigator's brochure.
Applicant for marketing authorisation		Submission clinical study report	Req. 9	Art. 37(4)
MSC and RMS where applicable	Authorisation and supervision of clinical trials	Selection and notification of RMS	Req. 10	Art. 5(1)
		Submission of considerations relevant to the application by the additional MSC	Req. 11	Art. 14(5)

EU clinical trials portal and EU database activities and requirements				
Stakeholder	Role (high level)	Requirement	Requirement ID No.	Legal basis (Art.)
		Request for additional information	Req. 12	Initial application- Art. 5(5) for validation, Art. 6(8). for Part I and Art. 7(3) for Part II. Additional MS- Art. 14(6) for Part I and Art. 14(8) for Part II. Substantial modification- Art. 17(4) for Part I validation, Art. 18(6) for Part I, Art. 20(6) for Part II, Art. 22(2) for Part II. Request for translation of the third country inspection report (Art. 53(2))
		Submission of final ARs (Part I and Part II) and its conclusions	Req. 13	Initial application- Art. 6(4) for Part I, Art. 7(2)for Part II Additional MS- Art. 14(7) Substantial modification- Art. 18(3) for Part I, Art. 20(5) for Part II, Art. 20(6), Art. 22.1 for Part II
		Notifications (validation outcome, decision, disagreement on Part I, revoke , suspend a CT, surveillance)	Req. 14	Validation - Art. 5(3), 17(2), 17(4), 20(1), 20(3). Decision - Art. 8.1, 14(3), 19(1), 20(5), 23(1). Disagreement on Part I together with a detailed justification - Art. 8(2), 14(4), 19(2), 23(2). Corrective measures

EU clinical trials portal and EU database activities and requirements				
Stakeholder	Role (high level)	Requirement	Requirement ID No.	Legal basis (Art.)
				(revoke/suspend/request for modification) - Art. 77(3).
		Supervise compliance with the Regulation: inspection planned/outcome inspections conducted	Req. 15	Art. 78(3)
		Submission inspection reports	Req. 16	Art. 78(6)
Commission	Supervision of regulatory systems in EU and outside EU	Submission Union control reports	Req. 17	Art. 79(2)
Public	View the clinical trial related information	The EU database shall be publicly accessible unless, for all or parts of the data and information contained therein, confidentiality is justified on any of the following grounds: – protecting personal data in accordance with Regulation (EC) No 45/2001; – protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product unless there is an overriding public interest in disclosure; – protecting confidential communication between Member States in relation to the preparation of the assessment report; – ensuring effective supervision of the conduct of a clinical trial by Member	Req.18	Art. 81(4)

EU clinical trials portal and EU database activities and requirements				
Stakeholder	Role (high level)	Requirement	Requirement ID No.	Legal basis (Art.)
		States.		
The Agency	Database controller	Compliance with applicable data protection framework Administrative and maintenance of the database Integration of data and documents held in the EU database and other databases managed by the Agency.	Req. 19	Art. 81(1)

5.2. Systems overview

The functional specifications have to address the following systems requirements:

- secure electronic submission system by the stakeholders listed in table 1 (except public);
- user access management system to enable the stakeholders listed in Table 1 (except public) to log on with their credentials (username and password), administer their own user group, assign roles, enable single sign on to the clinical trial systems of the EU portal and database etc.;
- a secure document management system of clinical trial information to facilitate the capture, titling, retrieval, maintenance and nullification of records of clinical trial information (data and documents);
- the system should enable MSs to have access to documents/data related to all clinical trials in the EU database where applicable legal requirements provided for by Regulation (EU) 536/2014 and Regulation (EC)1049/2001;
- a management platform/dashboard for the users, to be accessed and/or configured by authorised users only and with a workflow control tool to track activities (submissions, notifications, validations/assessment activities etc.) and the timelines required in the legislation including the possibility to shorten the timelines but also whenever required as per the assessment procedure extend the timelines within the limits set by the Regulation. The calendar solution will take into account the requirements of Regulation (EEC, Euratom) No 1182/71 of the Council of 3 June 1971;
- a publication module/system to make publicly available clinical trial information allowing search and download functionalities.

In accordance with the legal requirements as set out in Article 81 of the Clinical Trials Regulation, the functionalities of the EU portal and database need to be maintained, adapted or further developed where necessary to adequately support the EU clinical trial activities and processes of the Agency and the EU regulatory network.

6. Functional specifications to be audited

The functional specifications of the EU portal and the EU database and associated workspace are outlined below and are considered necessary to enable the EU portal and the EU database to be fully functional.

In accordance with the Regulation, the EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the grounds outlined in Article 81(4).

Table 2 section 4.3 sets out the technical features to support publication of the information on clinical trials. The rules and criteria on what data and documents are to be made public, and on the timing of that publication, will be included in an appendix to these functional specifications. That appendix will be prepared following review of the responses to the public consultation that has taken place (21 Jan-18 Feb 2015) and preparation and agreement of the rules and criteria by the Agency with the EU clinical trial information system expert group in collaboration with the Member States and the European Commission. The final text will be submitted for endorsement to the EMA Management Board and published following their endorsement and sign-off by the Agency Deputy Executive Director. This process should be completed by October 2015.

In addition to the functionalities outlined in this document, system performance, scalability and security are to be audited taking into account the need to support multiple users and an increase in volume of data over time.

Additional requirements to be made available in the workspace but outside of the scope of the functional specifications and audit as described in Article 82 are provided in annex 1 for information.

Table 2- Functional specifications

1- General functional specifications					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA**	**Details**	**Link to the legal requirements presented in table 1**
1.1	User registration and authentication	Y	Y	Allows users to register and to log on to access to the EU portal and EU database. The system will limit access and rights to authorised users only. Allow authorised users to log on with their credentials to access the systems according to their user's role(s) (user rights and access). The users of the EU portal will have access to workspace functionalities according to their user's role(s), so the system will display the appropriate data, as well as, to make available the appropriate activities to be executed according to their user's role(s) in the system. Enable the identification of a super user for each trial at the sponsor level and for each MS. The super user can designate other super users if required. Enable the sponsor super user for a given clinical trial to be linked to the sponsor details (name and address) provided at the time of trial submission and to any subsequent update of the sponsor information. Enable the unique EU trial number to be linked to the sponsor details (name and address) provided at the time of trial submission and to any subsequent update of the sponsor information. Allow single sign on for users from MS, sponsor and applicant of marketing authorisation (according to their roles)	Req. 1 to 17 and 19

1- General functional specifications					
No	**Functional specification**	**Sponsor/ Applicant**	**MS/ EC/ EMA**	**Details**	**Link to the legal requirements presented in table 1**
				for accessing the EU portal, the clinical trial workspace, the EU database and to enable the selections of products from the medicinal product dictionary (if applicable), and the reporting tool of the EU portal and EU database.	
1.2	Security control and levels	Y	Y	EMA to assign and administer super users for the regulatory network. MS super user will be designated by the MS via the Pharmaceutical Committee. Enable user to self-register and enable user management to be performed by a super user. Enable all super users to administer and manage their group of users and assign roles/work packages to users either per trial or per group(s) of trials including all trials they administer if necessary. The assignment may be done by assigning several roles/work packages to a user. Users may be part of the same sponsor organisation or from individuals, companies, institutions or organisations to which any or all tasks have been delegated by the sponsor. Enable the sponsor super user to update the sponsor information during the life cycle of the trial (e.g. address, contact details) and ensure traceability at all time. EMA to assign and administer their own users and identify system administrator super users.	Req. 1 to 17 and 19
1.3	Audit trail	Y	Y	The system should have audit trail to trace the activities and any change to data/documents that are performed/submitted during the lifecycle	Req.1 to 17 and 19

1- General functional specifications					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA**	**Details**	**Link to the legal requirements presented in table 1**
				of a CT from application to end of reporting and at any time thereafter. The system use cases should indicate the point at which the audit records are created.	
1.4	System performance and scalability	Y	Y	Performance and scalability to be defined during the preparation of the detailed requirements.	Req. 1 to 19

2- EU portal					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC**	**Details**	**Link to the legal requirements presented in table 1**
2.1	Support the recording and submission to the medicinal product dictionary, contained in the EudraVigilance database, of all the data on medicinal products without a marketing authorisation in the Union and substances not authorised as part of a medicinal product in the Union, that are necessary for the	Y	N	Sponsor to be able to submit information related to a new IMP and/or a new substance through the EU portal and obtain a provisional EU MP number and a provisional substance code until the final EU MP number or substance code can be granted. The request for an EU MP number should be linked to a specific EU CT number and to the submission of the IMPD quality part. For an IMP with a marketing authorisation, for the preparation of the clinical trial dossier, the sponsor should refer to the product and active substance numbers recorded in the medicinal product dictionary. The EU MP number for product in development and the product number for marketed product to be used to link clinical trials and medicinal products.	Req. 2

2- EU portal					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC**	**Details**	**Link to the legal requirements presented in table 1**
	maintenance of that dictionary				
2.2	Submission of documents/data	Y	Y	Allow submission by sponsors (e.g. CT dossier, notifications) or by MSC (e.g. decision on which MSC is RMS, final assessment report Part I and/or Part II, validation outcome etc.) of validated packages/documents/data, as applicable, that comply with the validation rules. An overview of all the information submitted through the portal is provided in annex 2. Acknowledge receipt of submitted packages/documents/data as applicable. In those cases where a duplicate dossier has been submitted, enable the MSs to notify the sponsor of this error in order to trigger a withdrawal of the application by this sponsor. In some circumstances where notifications may be incorrectly submitted (e.g. a serious breach submitted to the wrong trial), enable a mechanism to correct this information by the sponsor (e.g. by submitting a second notification that nullifies the first one).	Req. 1 to 17
2.3	Communication between sponsor and Member States	Y	Y	Functional specification 2.3 refers to the communication between the sponsor and the MSC and details the submissions previously highlighted in the functional specification 2.2: MSC to put request for information to the sponsors and for the sponsor to communicate back to the MSC in relation to these requests. Allow MS to notify to sponsor the outcome of decision.	Req. 4, 6, 12, 13 and 14

2- EU portal					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC**	**Details**	**Link to the legal requirements presented in table 1**
				Allow MSC to request correction to an application dossier and for the sponsor to communicate back to the MSC in relation to these requests.	
2.4	Withdrawal of an application	Y	N	Allow the sponsor to withdraw an application at any time until the reporting time and to submit reason for withdrawal.	Req. 3 to 4
2.5	Planning and reporting on MS inspection	N	Y	Allow MS to notify inspection dates (planned and conducted) to the EU database through the EU portal in relation to one or several clinical trials performed in its territory or in a third country. Allow MS to report on inspection findings to the EU database through the EU portal. Allow for validation of the structured data field before submission to the EU database. Allow for the submission of inspection report to the EU database.	Req. 15
2.6	Portal interface	Y	Y	The portal interface is to be in English initially at the time of the audit with the technical capability for the user interface to be displayed in the official EU languages when the system is launched.	Req. 18
2.7	Dependencies on other systems	Y	Y	To avoid duplication of entry, the portal will allow for data stored in the other EMA systems to be readily available for selection in the portal. This feature applies to user access management tools and master data (e.g. substances, products, organisations, referential, other master data` source) to be made available in the portal. Enable the transition from using current	Req. 1 to 19

2- EU portal					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC**	**Details**	**Link to the legal requirements presented in table 1**
				master data system (e.g. EUTCT) to future master data management (e.g. substance and product management systems, organisation management system and referential management system). Enable the request and entry of new master data terms. To be able to use master data in such a way that it can be linked to future versions of those terms.	

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
3.1	Dashboard	Y	Y	Have a dashboard that meets the user requirements for navigation, data/document entry/upload, maintenance, reporting and enable the tracking of the flows in relation to the processes that the users monitor. Enable the timelines of the procedure to be viewed from the date of submission up until notification on the decision. Enable the timelines to be expressed in days and hours (hours according to CET). Have the features to enable the functional specifications presented in this table (e.g. preparation of application and notification, e.g. submission) and according to the user's roles enable read, write, search and edit.	Req. 1 to 17

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
3.2	Preparation of documents/ data	Y	Y	Initial clinical trial application to be uniquely identified by a unique EU CT number. Each application to be assigned a sequence number in numeric order to maintain a chronological order of submission within the life cycle of a clinical trial. The EU CT number format will be: yyyy-xxxxxx-zz including an extension to differentiate initial submissions from re-submissions. For those years where EudraCT and Portal are both operational the following formats should apply: • Portal: yyyy-5xxxxx-zz • EudraCT: yyyy-0xxxxx-zz Allow sponsors to prepare CT application form, dossier, notifications and update information as foreseen by the Regulation. Allow sponsors to modify or delete any information that is under preparation and before it is submitted to MSC. Allow sponsors to prepare application dossier using a dossier builder including the upload feature for documents formats including PDF and commonly available document formats and documents consisting of structured data (e.g. XML for the EU CT form). The application dossier should be customised to the nature of the application (initial application, substantial modification, Part I submission only) performed by the user. Allow sponsor users to cross refer to information previously submitted for the preparation of a new application.	Req. 1 to 17

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
				Enable MSC to discuss and agree upon the selection of the RMS, prepare their validation, assessment (e.g. assessment report, request for information) and decision tasks. This functionality is covered under the functionality described below “collaboration between Member States in the context of assessment and supervision of clinical trials”. Allow sponsors to copy fully or partially information from an application previously prepared for another trial in their workspace.	
3.3	Collaboration between Member States in the context of assessment and supervision of clinical trials	N	Y	The workflow is to be supported with communication features (structured and un-structured) essential for the operation of the EU portal and the EU database. These features are to address the MSC collaboration in the event that more than one MS is concerned by the application and the features are to enable: 1. reporting Member State to manage the initial assessment phase; 2. a coordinated review phase involving all Member States concerned; 3. (reporting Member State to manage the consolidation phase. These features revolve around the assessment and would lead to: • selection of the RMS; • preparation for validation outcome; • generation and review of requests of additional information; • preparation, review and consolidation of the assessment report including communicate disagreement with conclusion of Part I; • preparation, review and consolidation of assessment of clinical trial related	Req. 10 to 16

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
				information during the life cycle of a trial including sponsor responses; • preparation of MSC decision. The gathering of the detailed requirements will enable to identify the structured and unstructured data to be collected in the systems to enable the assessment and supervision of trials by Member States.	
3.4	Communication between sponsor and Member States	Y	Y	Allow MS to request additional information in relation to the notifications made by the sponsors (Articles 36, 37, 38, 42, 43, 44, 52, 53, 54, 55, 77) or to address informal requests in those cases where the Regulation does not define a validation phase like in the case of Articles 11 and 14. Allow the sponsor to communicate back to the MSC in relation to these requests.	Req. 6 and 12
3.5	Assessment report (AR) templates	N	Y	Make available AR template for the MS to prepare the assessment report for Part I and Part II.	Req. 12
3.6	Upload/download	Y	Y	Allow users to upload or download different document format (e.g. pdf). The gathering of the detailed business requirements will facilitate the identification of the kinds of document file format that enable word search within a document and the choice of document file format for the key documents (e.g. protocol, Investigator's brochure) will be further defined in the detailed requirements. Allow users to upload or download data as an XML (or similar technology). Enable the possibility to download or upload several documents and data at	Req. 2 to 17

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
				the same time. Ability to download the whole trial dossier.	
3.7	Technical validation of application before submission of documents/ data	Y	Y	The system must perform certain validation checks, in order to ensure compliance with the system specifications. Validation checks to validate the correctness of specific fields or documents, number of documents attached to ensure completeness (e.g. of the application dossier) or prior to confirm the submission to the EU database. Users to be able to validate the information that they intend to submit at any time during the course of the preparation of the information and receive feedback on the validation errors.	Req. 1 to 17
3.8	Workflow control	Y	Y	Automated tracking and alerting functionalities for the user to assist the assessment procedure: • The system should be able to predict the timelines based on the MSC calendar solution adopted for the application which will include an informally agreed clock stop[1] between 23rd December to 7th January (for all clinical trials i.e. national and multinational) and the reference time zone adopted for the system (the CET). The calendar solution will consider the requirements of Regulation (EEC, Euratom) No 1182/71 of the Council	Req. 1 to 16

[1] The clock stop, even if does not have a legal basis in the Regulation and therefore cannot be legally enforced, is based on the informal agreement between the users of the Portal comparable to the solutions adopted now in the VHP.

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
				of 3 June 1971. • The system should be able to track the timelines based on the MSC calendar solution adopted. • The system should be able to track activities (submissions, notifications, validations/assessment activities etc.) and inform users that a new pending task has arrived or a deadline is coming. • Alerts with direct link to the task (e.g. additional request for information). • User should also be able to reassign/redirect tasks if they cannot handle them (people on leave for instance). • Allow for user to enter information structured and unstructured data in the UI through the workflow and in relation to the pending task • MS user with the appropriate role/work package to be able to extend or shorten the deadlines within limits set by the Regulation. • MS user with the appropriate role/work package to have the administrative right to update MS information already submitted to the sponsor and to enter a reason. • Allow MS user with the appropriate role/work package to revert a decision & to provide reason (e.g. appeal).	

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
3.9	Reporting features	Y	Y	Possibility to create reports for the users to monitor the processes governed by the workflow.	Req. 1 to 17
3.10	Search functionalities	Y	Y	The system should allow the users to search and filter specific topics based on basic search criteria (e.g. CT EU number, product number, product name, RMS, MSC…). Authorised users should be able to query the system from their workspace by use of metadata based on fields present in the information stored in the EU database and be able to retrieve the information requested.	Req. 1 to 17
3.11	Training and help for users	Y	Y	Allow for online help and tooltips to be made available to the users to assist in the use of the system features, understand the navigation and explain the user interface.	Req. 1 to 17
3.12	Dependencies on other systems	Y	Y	Link to the master data available at the Agency as defined in the EU portal functional specification 2.7 to be made available in the workspace.	Req. 1 to 17
3.13	Workspace database	Y	Y	The workspace database should enable the storage and retrieval of documents and data as being saved in the workspace. The document and data store should allow: • Metadata elements associated with all documents and data to be captured. • Support multiple aggregations without duplication. • Every record and associated aggregation must have a unique identifier persistently linked to it. This allows to the user to locate records	Req. 1 to 17 and 19

3- Workspace					
No	**Functional specification**	**Sponsor / Applicant**	**MS / EC / EMA ***	**Details**	**Link to the legal requirements presented in table 1**
				and helps them to distinguish between versions. • Establish a classification scheme that can facilitate the capture, titling, retrieval, maintenance and disposal of records by defining the way in which individual electronic records are grouped together (aggregated). • In relation to any action taken by the system administrator as described in the functionality 4.1, the system administrator will retain the possibility of deleting corrupted or incorrect or unlawfully processed data; issue a notice in the system that processed information has been removed from the user's view, highlight that processed information may not be valid in view of GCP non-compliance, or, where necessary for reasons of factual accuracy or compliance with regulatory requirements. A process should be in place to ensure that the system administrator has documented approval before such actions are implemented.	

* In relation to the workspace and the EU database, functional specifications 3.13 and 4.1 only will apply to the EMA users.

4- EU database			
No	**Functional specification**	**Details**	**Link to the legal requirements presented in table 1**
4.1	Document store and database	The EU database should enable the storage and retrieval of documents and data specified by the legislation as being saved in the EU database. The document and data store should allow: • Metadata elements associated with all documents and	Req. 1 to 17 and 19

4- EU database			
No	**Functional specification**	**Details**	**Link to the legal requirements presented in table 1**
		data to be captured. • Support multiple aggregations without duplication. • Every record and associated aggregation must have a unique identifier persistently linked to it. This allows to the user to locate records and helps them to distinguish between versions. Establish a classification scheme that can facilitate the capture, titling, retrieval, maintenance and disposal of records by defining the way in which individual electronic records are grouped together (aggregated). The system administrator will retain the possibility of deleting corrupted or incorrect or unlawfully processed data; of removing information from the public view, highlighting that the clinical trial related information may not be valid in view of GCP non-compliance, or adding a notice to the public record, where necessary for reasons of factual accuracy or compliance with regulatory requirements, including personal data protection. A process should be in place to ensure that the system administrator has documented approval before such actions are implemented.	
4.2	Document and data retention	Retention period to be unlimited and readability of data to be ensured for the entire retention period.	Req. 1 to 17
4.3	Publication of CT data and information	*The following text of Table 2 Section 4.3 was revised following the EMA Management board decision on 19 March 2015.* The clinical trial data and information is to be made publicly available through a publication module of the database according to detailed rules to be defined taking into consideration the workflow of the trial. The rules are to be automated and implemented through the publication module of the database. The publication of clinical trial related documents and/or information will be an automatic process based on technical features set out here in section 4.3 and operated in accordance with predefined rules and criteria for publication, to be included as an appendix to this document. The rules and criteria for publication will be defined in such a way that in general manual intervention is not required. A manual override will be made available to enable publication	Req. 18

4- EU database			
No	**Functional specification**	**Details**	**Link to the legal requirements presented in table 1**
		in exceptional circumstances where an overriding public interest applies, as provided in the Regulation. The override may also be used to remediate errors where an item is required to be removed from the public domain for example when information has been published contrary to the established rules, or where data processing errors have occurred. The system should identify all data and documents in the EU database regarding their public or non-public status and any timeframe/event to trigger that publication, and include the necessary rules to ensure their public availability at the required time. For each data field (or set of related fields) or document the system will have metadata and rules to support their publication status and timing publication. The system should display the current and anticipated public status and timing of publication of each field and document. This information should be clearly flagged to sponsors, Member States and public users, alongside the relevant documents and data of each clinical trial. For each of these sets of information the database will have a structure to contain a document (or data such as names and addresses in the case of the investigator/trial sites list, sponsors etc.), but the content of the related documents should be defined outside of the design of the database and taking into account whether or not the information should be made public. The appropriate expert group of the EU should develop guidance and/or templates for the content of documents to be included in the database. The IMPD should be structured to enable each section (Q, S, E) to be separate and have different publication rules applied to each. The protocol synopsis and protocol should be separate and have different publication rules applied to each. The application form, and related assessment and conclusion on parts I and II will contain questions, and their corresponding answers, that will provide data points on which to base certain of the publication rules, which are not driven by other actions or data in the database. These questions (to be adjusted based on the predefined rules and criteria for publication, to be included as an appendix to this document) will include items such as: 1. Does the trial have a therapeutic (or prophylactic) intent? 2. Does the active substance appear in any marketing	

4- EU database			
No	**Functional specification**	**Details**	**Link to the legal requirements presented in table 1**
		authorisation already granted in the EU? 3. Does the indication(s) under study in this trial appear in any marketing authorisation already granted in the EU for that active substance? 4. Does the formulation(s) appear in any marketing authorisation already granted in the EU for that active substance? 5. Does the route(s) of administration appear in any marketing authorisation already granted in the EU for that active substance? 6. What is the phase of the trial? 8. Is this a low interventional trial? 9. Does the sponsor request a deferral of the publication of the registration data until the publication of the summary results (for phase I trial only)? The examples above do not pre-empt any final decision on the actual rules and criteria for publication. The specific questions will be adjusted once the rules and criteria for publication have been agreed and finalised.	
4.4	Search functionality	The public user interface to allow querying the clinical trial information by use of metadata based on fields present in the application dossier, MSC notification and decision and to have download functionalities. Ability to have bookmarks associated with the search and possibility to subscribe.	Req. 18
4.5	Presentation of the information	Allow related information to be grouped together by way of the EU trial number with links or display of data and document of relevance. Allow content of the application dossier to be displayed in the language in which it was submitted.	Req. 18
4.6	Download option	The public user interface to enable the download of document and data as XML and other document format (e.g. pdf, word, excel etc.).	Req. 18
4.7	Public interface	The public interface of the EU database is to be in English initially at the time of the audit with the technical capability for the user interface to be displayed in the official EU languages when the system is launched.	Req. 18

4- EU database			
No	**Functional specification**	**Details**	**Link to the legal requirements presented in table 1**
4.8	Help and training features	Allow for online help and tooltips to be made available to the public to assist in the understanding of the information published.	Req. 18
4.9	Dependencies with other systems	The data terms in the EU database to use the master data list available at the Agency. Enable the transitions from using current master data system (e.g. EUTCT) to future master data management (e.g. substance and product management systems, organisation management system and referential management system). To be able to use master data in such a way that it can be linked to future versions of those terms.	Req. 1 to 17 and 19

Annex 1: Additional requirements to be made available in the workspace (not to be audited)

The following additional requirements are identified which are not part of the functional specifications to be audited as set out in the Article 82. Taking into account the provisions set out in Article 82 of Regulation (EU) No 536/2014, the functionalities to be audited are those outlined in section 5.

The following additional key functionalities were requested to be included in the EU clinical trial systems. The detailed requirements will be collected for these features:

1. Allowing communication features to be made available to MS for general discussion related to clinical trials and not necessarily related to a unique trial (e.g. communication where a substantial modification concerns more than one clinical trial, supervision of clinical trials etc.).
2. Automated two-way exchange of documents and related data held in the EU portal/EU database between MS systems and the EU portal/EU database to reduce administrative burden for MSs.
3. Additional reporting capabilities linking the clinical trial systems allowing a full range of statistics reports (per year, per month, per user, per MS, per IMP etc.).
4. Without prejudice to the legal role and responsibilities of the RMS, an execution of that role may be delegated to another MSC.
5. Option to initiate ad hoc-workflow/case management for the assessment of clinical trial related notifications, safety information or other issues.
6. Integration of cooperation in assessment and surveillance of safety (e.g. ASR, SUSAR, other safety relevant information/notification) of a CT during its life time.
7. Enable a link to the EudraVigilance database from the workspace for MS for surveillance.
8. Possibility to upload a CTA dossier that has been prepared outside of the workspace.

These additional functionalities, beyond those to be audited, are to be provided in future post-audit releases of the EU portal for which further business requirements will be developed with Member States in consultation with the Commission.

Based on the initial implementation experience, an iterative approach will be followed allowing for improvement of functionalities if necessary.

Annex 2: Submission through the EU portal to the EU database