20 November 2015
EMA/659146/2014
Compliance and Inspection

Overview of comments received on 'Draft functional specifications for the EU portal and EU database to be audited' (EMA/42176/2014)

Comments received from public consultation (10-31 October 2014)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	Viorica Cursaru, Myeloma Euronet Romania
2	Freie und Hansestadt Hamburg, Germany Ministry of Health and Consumer Protection, Pharmaceutical Inspectorate
3	Barry Corbett, Guild of Healthcare Pharmacists
4	William Cragg
5	LTS Lohmann Therapie-Systeme AG (for compilation by BPI)
6	Medac GmbH, Germany
7	German Pharmaceutical Industry Association
8	Ipsen Pharma
9	Association of Clinical Research Organizations (ACRO)
10	Mihaela David, Head Regulatory & Matrix Services, PSI CRO AG
11	Arbeitskreis Medizinischer Ethik-Kommissionen in der Bundesrepublik Deutschland e.V., Germany
12	GYEMSZI ,Directorate General of National Institute of Pharmacy, Clinical Trial Department, Hungary
13	Dr. med. Monika Nothacker, The Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Stakeholder no.	Name of organisation or individual
	Fachgesellschaften e.V., AWMF)
14	Hessen, Germany, Regierungspräsidium Darmstadt (Regional Council Darmstadt), Pharmaceutical Inspectorate
15	PhUSE
16	vfa – German Association of Research-Based Pharmaceutical Companies
17	Gilead Sciences International Ltd.
18	German Society of Pharmaceutical Medicine
19	LYSARC
20	European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)
21	Federal Ministry of Health (BMG), Germany Federal Institute for Drugs and Medical Devices (BfArM), Germany Paul-Ehrlich-Institute (PEI), Germany
22	Research Quality Association (RQA)
23	Clinical Research Department, Public Health Institute, French National Institute of Health and Medical Research (Inserm)
24	EGAN (Patients' Network for Health and Medical Research)
25	The Danish Health & Medicines Authority
26	European Network of Research Ethics Committees (EUREC)
27	Clinical trials committee of the ADKA (association of German Hospital Pharmacists)
28	Cancer Research UK
29	European Organisation for Research and Treatment of Cancer (EORTC)
30	European Society for Medical Oncology (ESMO)
31	European Society for Paediatric Oncology - SIOPE
32	Medicinal Product Agency, Sweden
33	Hans-Juergen Stellbrink
34	Lori J. McKenney
35	Ina B. Kopp - Association of the Scientific Medical Societies in Germany, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)

Stakeholder no.	Name of organisation or individual
36	EuropaBio
37	European CRO Federation (EUCROF)
38	Walter Marrocco
39	Quotient Clinical Limited, United Kingdom
40	State Institute for Drug Control, Czech Republic
41	Sini Eskola, EFPIA
42	Júlia Savarijová, State Institute for Drug Control
43	Swedish Society of Medicine, Section for Pharmacology and Therapeutics
44	Agence Nationale de Sécurité des Médicaments et des produits de santé (ANSM)
45	Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)
46	AESGP
47	International Plasma Fractionation Association (IPFA)

1. General comments – overview

Stakeholder no.	General comment
2	After having the chance to review the Draft Functional Specification for the above mentioned portal/database we strongly recommend the implementation of a general system of ´automatic notifications´, not only for the application part but for the inspection part as well. Automatic notifications/alerts will ensure a timely response by the concerned authorities for all the different types of actions (information/requests/patient safety related actions), which is in the interest of all stakeholders. The introduction of such functionality will allow the efficient handling of incoming information and as a result it will contribute significantly to the user friendliness of the portal/database.
3	We believe the proposals appear to be a very reasonable way to proceed. The main issue would be further down the line when the system is functioning i.e. how easy will it be for anyone to obtain user access? How full will publication be? What loopholes will still exist?
4	The functional specifications document mention avoidance of duplication several times. While I completely accept that it is beyond the scope of the project to have any sort of interactions with country-specific systems, e.g. the Integrated Research Application System in the UK, it would be a good start if the EU portal and database allowed a good deal of flexibility in terms of data export. For example, it would be good if users could extract certain data fields for their projects on an ad hoc basis, and also save certain queries for future use. These data extracts could then in theory be used (eventually) with other systems, thereby reduce duplication.
4,14	I have appreciated the opportunity to review and comment on the functional specifications document. However, I feel it is crucial that this engagement with the system users should continue, and that it should be formalised by inclusion in this document. In particular, I feel that users should be further involved in testing and, if possible, development of the systems, although I appreciate the timelines are short. I also think it would be extremely beneficial to have a prominent 'feedback' feature with the portal, database and any related systems, with a commitment to reviewing all feedback on a regular basis. Development of these new systems, while it forms a mandatory part of the new clinical trial regulations, also presents a great opportunity to produce modern systems that could facilitate clinical trials in the EU. It would be an opportunity wasted if we end up with inflexible, unchangeable systems.
7	It is absolutely necessary and basic requirement that functional specifications of the EU database and EU portal listed in mentioned draft ensure a perfect, user friendly, at any time functioning of the EU database and the EU

Stakeholder no.	General comment
	portal. In case of a malfunction of database and/or portal it is absolutely necessary and basic requirement that immediately appropriate communication, data submission and flow of information will be maintained between sponsors, national authorities, Ethics committees, EMA, Commission, member states, national contact points and CTAG to ensure all deadlines and time limits mentioned in the regulation will be met at any time.
8	It would be good to have clarifications on how the Ethics Committee(s) of each MS will be included in the review of Part II. Will they get access to this portal or should they go through the MSs?
11, 26	It should be part of the audit that the system works stable and with short reaction times even under full load (maximum number of users and user accesses to be determined, number of active trials to be determined). The European Commission/EMA should provide a test environment for both, member states and sponsors, to get used to the portal and to test interfaces.
13	We are looking forward to comment on the “underlying principles to support the … transparency requirements” for the EU Portal as outlined in Line 113-127. in Good defined criteria for public accessibility of data in fair balance to the wish/need of confidentiality are essential Therefore (referring to p. 9, “public”): The portal should give a statement describing the procedures adopted for ensuring data protection/confidentiality/privacy including duration of storage of personal data for the user of the EU portal and the EU database. The sentence: “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”: This sentence gives much room for interpretation and the official path and the entitled personnel to justify an overriding public interest in disclosure should be announced. Commercially information on interventional trials with medicinal products with marketing authorisation shall be publicly accessible in any case.
13	As the Functionality of the Portal is so important we strongly suggest to realise a period of testing for all stakeholders including the public!
14	For supervision and inspection of the clinical trials in Hessen (federal state/Bundesland of Germany) is the „Regierungspräsidium Darmstadt” (Regional Council Darmstadt) the competent authority, federal state authority. As one of the affected competent authorities the requirements 5, 6, 8, 15, 16 are concerned and the following comments should to be considered:
15	The group welcomed the opportunity to review this document and would like to continue to participate in review in

Stakeholder no.	General comment
	the future.
15	The review group felt that this document needs greater detail, especially with the direction taken with regard to the standards used.
15	It is also felt that there needs to be more Granularity in section 5 as there is little here that could actually be tested against.
15	Will there be a piloting of the EU portal/EU database before the functional specification is finalised and signed-off? If so, when will that be?
16	From the position of the vfa the following basic principles should apply to the Portal: 1. Interface Solution - Clear definition of data standards 2. The archiving requirements, definition of individual documents in terms of public or private 3. Clearly define the responsibilities of the roles 4. Acknowledgement of the documents submitted - split documents vs. packages 5. Each process step has to be linked with the appropriate timeline. Avoid manual entries. 6. Report record functions in the general requirements Part 1 – define what regulatory necessary is.
16, 41	A successfully passed user acceptance test (including sponsors from academic institutions, industry and CROs; also stakeholders form MS level – NCA(s) and EC(s)) should be – in addition to the successful audit of the system – another prerequisite before publication in the Official Journal.
16, 41	It seems that the draft misses to clearly address also the process regarding the assessment report part I as foreseen in article 6, para 5 a) to c) of the regulation 536/2014. The process steps (draft AR from rMS after 26 days, comments by cMS within 12 days, finalization by rMS within 7 days) are not mentioned or respected in this draft. This is a clear deficit in the present wording of the draft on the functional specifications for the EU portal as this is an important aspect of the whole process for multinational application.
16, 41	It is crucial that the new portal/database has a 24/7 robust technical and scientific support that allows sponsors and MS to troubleshoot any problems effectively. We further recommend that some kind of backup system is foreseen in case the system breaks down. This is needed as the - positive - experience with clinicaltrials.gov shows.
16	It is important to respect also global data standards. The proposed requirements relating to secure transfer and secure electronic submission to avoid unauthorised access including non-repudiation of message dispositions should be in line with ICH M2 recommendations (http://www.ich.org/products/electronic-standards.html).
17	Gilead proposes that it may be beneficial to set up the database so that a “living IMPD”, akin to the IND system that the US FDA adopts, could be used in the EU. Having an IMPD, possibly in eCTD format, that Sponsors could keep

Stakeholder no.	General comment
	updated and could serve as the basis for all CTAs that refer to it, would greatly diminish the burden of updating multiple CTAs where the same IMP is being used. It would also reduce the review burden for the Agencies since the IMPD would be reviewed extensively upon first submission and could then be reviewed again only if substantial amendments were submitted to it. This would ensure consistency and transparency across CTAs.
17	Gilead proposes that the portal have an area where Sponsors can search for their trials that require results posting which appear on the EU Clinical Trials Register (EU-CTR). Currently, the only method for obtaining this information is to search the public search engine and sift through results. The proposed approach would help sponsors comply with results posting requirements.
17	Gilead proposes that the portal have an interface where Sponsors can propose modifications to information appearing in a study EU-CTR record prior to results posting, which could improve the accuracy of the record during its life cycle, and that a version that is more understandable to a lay reader interested in finding a study for treatment of their disease and site information so they can inquire further.
18	In principle the idea of a unique data portal and database for clinical trials (CT) is appreciated. But the draft needs some clarification to minimize time and effort of the stakeholders.
19	An access to the portal by Ethics Committees would help the transmission of documents and the communication with the National Competent Authority in order to facilitate the legal deadlines respect and the harmonization of documentation.
20	We recommend that some kind of backup system is foreseen in case the portal breaks down. Would it be perhaps be possible to submit via Eudralink in such an instance?
22	Why is the safety portal with all related features not within the scope of the audit? The safety portal is one crucial part of the database and thus functionality should be confirmed through audit. Is there an additional audit planned for this part? It is important that this EU Portal continues to work efficiently. Should there be a section for Disaster Recovery Plans and Business Continuity Plans so that these can be audited? It had been stated that investigators unable to store their TMFs, will be able to add these to the EMA database, but this is not discussed here under the specification for the portal. Is this covered elsewhere? The term “validation/validated” could be confused with the term shorten term of Computerised System Validation (CSV). Suggest the term is defined as “verification step”. Whereas, Computerised System Validation is proof of system fit for purpose.

Stakeholder no.	General comment
	As the portal and database contain GxP records, shouldn't the system be validated (CSV) to ensure it is fit for purpose and ensure data integrity? It seems that the legal requirements were used as user requirements and then the functional specifications were used to also demonstrate a traceability matrix (how the legal/user requirements will be delivered).Maybe clarify this in the preamble text of the document (pages 1-4) for those people that are not as familiar with CSV?
24	The value of data sharing to the rare disease patient community: Many rare diseases are severe and life-limiting. For individuals or families affected by most rare diseases, the day-to-day challenges of managing a severe condition are made worse by the absence of an effective treatment or cure. These patients look to research as the source of new therapies to address their unmet health need. In order for progress to be made, patients recognise that the rarity of their conditions means that research relies on the effective sharing and use of their medical data, nationally and internationally. Patients are generally very willing to share their medical data in order to drive research. It is therefore essential that there are clear, functional systems in place to facilitate the sharing of data for these purposes whilst reassuring those that participate that their data will be stored and shared safely and accountably. EGAN therefore considers the specifications set out for the EU portal and database in this consultation to be generally reasonable. We speak on behalf of patients when we welcome greater sharing of clinical trial data throughout the union due to opportunities this will provide to improve our understanding of rare diseases and therefore our ability to develop new treatments. To ensure rare disease patients are able to benefit from the opportunities that such data sharing can provide there should not be unnecessary onerous restrictions on data access.
25	We would like to thank you for the opportunity to comment on the functional specifications, and we kindly urge that our comments be taken into consideration during the future process. As a general remark, we welcome that workspace is deemed essential to the functioning of the EU portal and the EU database, and that it has therefore been included in the scope of the audit. We would like to emphasize the need to strike a sound balance between on the one hand the legitimate need to protect sensitive commercial data and on other hand transparency towards the public at large. We kindly refer to our letter of 9 September 2014 in which we have provided you with our more specific comments on the matter.
26	There is one functionality related to the national competent authorities (page 27, "Automated two-way exchange of documents and related data held in the EU portal/EU database between NCS systems and the EU portal/EU database to reduce administrative burden for NCAs") that is required to be included in the EU clinical trial systems. The

Stakeholder no.	General comment
	existence of this functionality in the draft functional specification document automatically presupposes that national competent authorities will surely have access to the EU clinical trial systems. Meanwhile this document lacks any specification whether national ethics committees involved in the clinical trial assessment process will have access to EU clinical trial systems. We believe that despite the fact that there may be different national models on how ethics committees and competent authorities will cooperate in the clinical trial application assessment procedure in EU countries, the draft functional specification document should explicitly include that the EU clinical trial systems will provide national ethics committees involved in clinical trial assessment procedure with the access to these systems. The access is crucial for ethics committees in order to ensure their independence from national competent authorities when following clinical trial assessment process as well as their easier compliance with the short timelines for the clinical trial authorisation that are set out in Clinical Trial Regulation.
26	The portal and the database must be established for the use of be RECs too. The perspective of the ethical evaluation must be taken into account in parallel with any other elements when constructing these tools. Otherwise RECs role will be endangered for the technical reasons only.
26	RECs should be involved with the assessment of both of the assessment procedure, Part I and Part II of the Regulation.
26	The European Medicines Agency should guarantee effective communication between National Regulatory Authorities (RAs) and Ethics Committees (ECs), including the proper method/tool for it. Ethics Committees should be considered stakeholder as they are key in the global process. As a consequence, ECs should have access to share point repository areas. The above method/tool to be used for effective communication between RAs and ECs should include an EC validation process to the report RA is finally uploading to ensure alignment between EC input and RA report. EC input requirements to part I of the dossier should be standardized globally.
26	Related to the issue “Reporting of clinical trials: Publication of the results”. It’s recommended to introduce a section where sponsor could send publications.
26	In Table 1 (activity and requirements) many of the requirements included, for example those in columns 6 and 7, are to be evaluated and approved by an EC. Participation of ECs, which have not been taken into account, is required. If it is expected that the opinion of the ECs is mediated by the RAs or by their "super-users", ethical results could became be very poor. The same applies to requirements 10-18. There are also other issues that could affect vulnerable populations that have not been taken into account. For example the Plans Paediatric Research (PIP), involving economic privileges and advantages for developers provided

Stakeholder no.	General comment
	by the RAs are agreed directly between sponsors and EMA without the supervision by ECs. This could be even more serious because their procedures and designs are established before they are performed; fixing errors that could very difficult to amend once the clinical trial have the agencies authorization. All this information should be in the database and be affordable in the evaluation process, particularly for ECs.
26	To comply with the spirit and the wording of Regulation (EU) No 536/2014 and in particular with art. 2,4,8,10,14,19,20,23,42-44 and annex 1, it is necessary that MSs: Guarantee ethics committees full and direct access to the application and data-base (including downloads) through the EU portal, from the time the application is submitted. This will ensure effective review by independent ethics committees and avoid undesired scenarios such as tacit approvals. The necessary access could be achieved via the existing portal functionalities.
27	A crosslink between the EU-Portal and the EudraGMP database would be useful to be able to directly upload necessary MIA documents for the manufacturer of the IP from the database.
27	The timeline of 12 days for preparation and submission of additional information in assessment of part one is extremely short, therefore a delegation of certain tasks to other persons – in case of absence of main responsible person – must be possible and quick. If at all possible a longer period of time would be better.
27	Will review function of ethics committees in part one be restricted to the study protocol? If ethics committees also start reviewing manufacturing and quality aspects of IPs it may lead to more dissent between reviewing member states.
28	The Clinical Trials Regulation, if implemented appropriately, will represent a significant improvement on the Clinical Trials Directive introduced in 2004. The academic community, in particular, welcomes the risk proportionate approach the Regulation has taken on matters such as safety reporting, approvals and monitoring. The sooner these changes are fully introduced, the sooner researchers and patients will experience the benefit to the trials environment.
28	We are aware that there is still some confusion in the academic clinical trials community over the legal basis of the EU portal and database. We would like the EMA to do more to communicate the content of the Regulation to all stakeholders, especially the academic clinical community, so that there is a clear understanding of what will be required of trial sponsors and coordinators once the Regulation is in place.
28	It is vital that the Regulation is implemented as early as possible, providing the systems supporting it are fully functional. Given that the application of the Regulation is conditional on a fully functional EU portal and database, it is extremely important that the EMA continues to drive forward the development of the portal and database to

Stakeholder no.	General comment
	ensure that the implementation of the Regulation is not delayed.
28	The EMA should set out its plans for how users of the EU portal and database will be trained. It is important that the EMA facilitates effective training to ensure that users are fully equipped to use the system. This will be necessary to guard against delays in the submission, assessment and approval of applications, when the system is launched. We recommend that the EMA considers providing online training modules similar to that provided for the Integrated Research Application System (IRAS) in the UK. Information on this module can be found here: http://www.myresearchproject.org.uk/ELearning/introducing_iras_menu.html.
28	Cancer Research UK welcomes the opportunity to respond to the EMA's draft functional specifications for the EU portal and database. As the EMA's plans for implementing the Regulation progress, it is important that all stakeholders are fully engaged with, and help to shape developments. To this end, the EMA should hold full and timely public consultations on functionalities of the EU portal and database that are outside of the scope of this audit, including system performance, scalability and security, as well as the functional specifications and underlying principles to support the transparency requirements of the Regulation.
28	Assessment of system performance, scalability and security will be crucial for the success of the EU portal and database. The EMA will need to provide assurance that the system will be able to cope with the volume of data submitted through the portal and to be stored in the database, and with the volume of users. We understand that these functionalities will be audited separately from the functionalities outlined in the current document (line 128-130). However, we would recommend that the EMA begins to develop and consult on these functionalities in parallel, especially given that these are referred to in the current functionalities (line 134, 1.4). This would ensure that flexibility and growth of the system are planned for and built in at an early stage.
28	The EMA should hold a full public consultation on the functional specification and underlying principles to support the transparency requirements of the Regulation, at the earliest opportunity. In particular, it is important that greater clarification is provided on public access to clinical trial data and information and we welcome the EMA's recognition of this in the detail of function 4.3. It is important that the EMA considers the impact of public access to data such as CT results intermediary data analysis, which could unblind the trial. The EMA should also ensure that Terms of Use are in place for any user who downloads data from the EU database. As well as the additional text and additions to Table 2 that will be developed through the planned consultation on functionalities to support the transparency requirements of the regulation, it will be important for the EMA to remain flexible and allow other sections of the functional specifications to be amended if appropriate. This would be in line with Section 4.2 of the document, lines 105-108, which acknowledges: 'the current functionalities need to be maintained, adapted or further developed

Stakeholder no.	General comment
	where necessary to adequately support the EU clinical trial activities and processes of the Agency and the EU Regulatory Network'. We would therefore remove 'and will not change the existing text in this document' page 11, line 121.
28	We welcome the functionalities outlined in Annex 1 and hope that the EMA's plans to develop these functionalities will be considered as soon as possible and, ideally, in parallel to the functionalities to be audited in this document. In particular, we believe that the success of the EU portal and database will hinge on its interface with Member State's IT systems and we would like the EMA to prioritise the development of an automated two-way exchange of documents and related data between National Competent Authorities (NCAs) systems and the EU portal and database.
28	Throughout the functional specifications document there are terms that are not defined. We are concerned that this lack of clarity makes it difficult to interpret the functionalities and we strongly recommend that the EMA produces a glossary to go with this document.
28	Many of the specifications lack the necessary level of detail to be able to determine the likely effectiveness of the functions. As the EU portal and database is developed, we strongly recommend that the EMA invites users to stress test the system as soon as possible to ensure it evolves to be effective and user friendly.
28	We supported the formal introduction of co-sponsorship in the Regulation and believe it will facilitate academic trial conduct within Europe. Co-sponsorship currently takes place in the UK and other European countries; it allows allocation of the sponsors' responsibilities between two or more institutions (co-sponsors) or joint responsibility shared by institutions. Sharing responsibility allows institutions and organisations which are not capable of taking on the full liability of sponsoring a trial to participate and share responsibility with other organisations. We do not think that the situation of co-sponsoring has been fully considered in the development of the functional specifications and would like the EMA to rectify this. For example, in Table 2, function 1.1, it is unclear how super users will be assigned in the situation of trial co-sponsorship.
28	For applications involving more than one Member State (MS), it is crucial that communication between MSs is adequately supported to assist the assessment process. Although functions to support communication between Sponsors and MSs are outlined for the EU portal (2.3), currently, functions to support communication between MSs are only described for the workspace (3.3). Such functions are within the scope of the EU portal as defined by the Regulation and outline in Table 1 of this document, for example, requirement ID numbers 11 and 14. We would therefore like the EMA to more fully describe functions to support communication between MSs and to include these in the functional specifications for the EU portal, in addition to the workspace.

Stakeholder no.	General comment
29	Functional specification does not clearly describe roles of users and super users (as far as the role of sponsor is concerned). EORTC understanding is that user is the one performing the task (and there may be several users working on the same trials from different organisations and there may be different groups of users working on different trials from the same sponsor). On the other hand, super user is the sponsor. The document has been analysed with this assumption.
29	The possibility of co-sponsorship (art 72) is not at all described / touched to in the text. It is not at all clear how this possibility will match roles of “user” and “super user”; it is not clear how and who within the co-sponsors will have access to the sponsor’s workspace etc…
29	System shall facilitate more informal communication between sponsor and RMS or CMS for seeking clarifications on requests, either by providing a message system (48h reply) or by making available and maintaining up to date in collaboration with MSs through the portal appropriate contacts (phone, fax, mail) for such a communication with MSs.
29	The system shall indicate automatically, based on the list of MSs if a legal rep. is required. It shall be able to update the status with addition of new MSs in a course of the trial with a visual alarm in case of change of status.
29	The system shall enable clear visual distinction between the current version of the documents and previous (not anymore applicable), e.g. old versions of the protocol shall be clearly visually separated from the current one.
29	Possibility to re-use the same Portal number in case of re-submission shall be clearly mentioned. Guideline shall be provided when a re-submission will need the new number (e.g. if done later than 2 years after withdrawal or rejection).
29	System shall enable individuals whose name is mentioned in the system to contact directly the Agency to ask to delete their information (e.g. in case of the end of contract with the sponsor if sponsor do not update the system spontaneously).
30	ESMO welcomes this initiative from EMA, which intends to simplify and harmonize the process of submission, assessment and reporting of clinical trials in Europe. ESMO is supporting EMA’s recently announced policy (as of 2/10/2014) to publish clinical reports that underpin the decision-making on medicines already by 1 January 2015, ahead of the implementation of the new EU Clinical Trials Regulation which will come into force not before May 2016. This act of transparency goes beyond previous intentions of EMA and will allow even the download or printing of clinical trial reports followed by the option to make available even individual patient data in the future. Final judgment from the side of ESMO will depend on the detailed content of the rules still to be defined in section 4.3, Table 2. of the draft.

Stakeholder no.	General comment
	With regard to the “Functional Specifications for the European Union Portal and European Union Database”, ESMO is focusing on the following suggestion to EMA: To guarantee the scalability of the demanding process of submission and reporting of clinical trials via the portal also for academia. The reduction of the frequency of clinical trials up to 25% during the era of the Directive was mainly due to a dramatic decrease in the segment of academic clinical trials, whereby less concerning the operation of multi-national/global pharmaceutical enterprises. Since ESMO wishes to make Europe more competitive not only on the large scale/pharmaceutical industry dominated sector, but also in the world of academia, EMA should facilitate that the use of the EU portal is made operable also by dedicated physicians/scientists and not only by professionals. According to ESMO, the process has to be made as user-friendly (announced on page 3/28) as to allow academicians to get familiar therewith without the need of professional help. Necessary explanations, which have to be also downloadable, have to be provided by EMA once the portal will be operative.
31	SIOPE, on behalf of the European Paediatric Oncology Clinical Research community welcomes the opportunity to comment on the draft specifications for the EU Portal and EU Database in preparation for the implementation of the Clinical Trials Regulation. Whilst it is crucial that the implementation of the Clinical Trial Regulation is not delayed, SIOPE would like to reiterate the importance of ensuring robust functionality of the EU Portal and EU Database and appreciate this public consultation on the auditable functionality. Some specific comments are included below, however greater detail on both the specifications for the auditable functionality and the broader functionality. For this reason, we feel that it is essential that further consultations will be incorporated into the on-going development of the full functionality of the EU Portal and EU Database, including those not included in the audit. We strongly support full testing of the system by stakeholders, including academic sponsors ahead of the system going live. We are pleased that as a result of the Clinical Trial Regulation there will be a uniform EU portal for submission of clinical trials but we remain concerned that there will still be a requirement to satisfy multiple national requirements in order to secure approval.
31	There needs to be a function to add a member state to the application retrospectively.
32	We thank the European Medical Agency and the European Commission for taking the views expressed by several Member States into consideration when drafting the functional specifications for the EU Portal and EU database to be audited (EMA/42176/201§4 corr), in particular regarding two issues Sweden considers critical for a correct and well-

Stakeholder no.	General comment
	functioning implementation of the Clinical Trials Regulation 536/2014. The first one regards communication between Member States being part of the audited functional specifications of the EU Portal and EU database mentioned in Art 82 of the Regulation. The other issue regards the principles of Regulation 1182/1971[1] on how to calculate timelines. It is important that this Regulation is respected taking the calendar of all Member States concerned into consideration both during the early validation procedure, i.e. in situations before a Reporting Member State has been selected, and later for all timelines regarding national decision procedures specified in the regulation text. Once a Reporting Member State has been selected for a multinational clinical trial, it can be argued that sufficient protection for timelines regarding required actions to be taken should only take Regulation 1182/1971 into consideration for that Reporting Member State alone. Some further views on these aspects are presented as an addendum to this document, in order to further promote fruitful discussions on how to keep timelines in Regulation 536/2014 both short and competitive while avoiding the necessity to work on weekends and official public holidays, leading to unacceptable additional costs for Member States.
32	Some further views on how to take regulation 1182/1971 into consideration in order to further promote fruitful discussions on how to implement timelines in Regulation 536/2014 regarding early validation procedures selecting a Reporting Member State. Although we must ensure that the timelines in the Regulation 536/2014 are kept short and competitive, it is not acceptable that public holidays and weekends make them impossible to fulfill, particularly not since the Regulation includes the principle of tacit approval and does not allow considerations from Member States concerned if actions are not taken within the stipulated time frames. To shorten the timelines below what is possible to achieve will jeopardize the safety of trial subjects and could lead to additional costs for Member States. An automated function of the EU Portal/Database taking Regulation 1182/1971 into account would make specified maximum timeframes for all sub-processes defined in the Regulation predictable and acceptable to both Member States and Sponsors. Thus, for all Member States Concerned the first three calendar days should be protected to secure sufficient time for a Member State Concerned to express willingness to serve as Reporting Member State (Art 5.1) for a multinational clinical trial. Also, the following three days resulting in a notification to the sponsor specifying which Member State concerned is the Reporting Member State (day 6, Art 5.1) needs a similar protection of calendar days from situations where the deadline falls on weekends or official national holidays to make it possible for all Member States concerned to follow the procedure outlined in the Regulation 536/2014, i.e. to agree on the selection of a Reporting

[1] describing rules on how to handle situations where the timeline falls on a weekend or an official public holiday

Stakeholder no.	General comment
	Member State (Art 5.1). Exactly how Regulation 1182/1971 should be applied for all Member States Concerned for the first three + three days during the validation procedure needs further analysis. In order to facilitate the discussion when designing the EU Portal /EU Database respecting the final functional specifications to be audited drawn up by the European Medicines Agency, the European Commission and Member States in collaboration, we here briefly present our interpretation how Regulation 1182/1971 article 3.4 and 3.5 could be taken into consideration for these two early timelines. In brief, if a *deadline falls on a weekend or public holiday* for the Member States concerned, it should be moved to the following working day. Also, timelines longer than two calendar days should always include *at least two working days*. Since the first three days of Art 5.1 (expression of willingness to serve as Reporting Member State) does not involve necessary interaction between the Member States concerned, a way to solve this would be to use the "day of the last Member State Concerned" as the deadline for all Member States Concerned using an IT system solution ticking a box as a way to express willingness to serve as Reporting Member State. The next three days must however also allow interaction between the Member States concerned before they select a Reporting Member State, why the IT solution for the EU Portal would need a tool to facilitate such a selection procedure if several Member States Concerned are willing to serve as Reporting Member State. Although general principles, may be applied (See Art 85), it is the Member States Concerned in a particular multinational trial that should agree on the selection of a Reporting Member State, not a computer-based tool or general principle.
33	Let me please express my deep concerns at this point: to me as a clinical investigator involved in clinical research since more than 25 years the portal represents yet another bureaucratic hurdle to investigator-initiated clinical research. Pharmaceutical companies involved in drug development are able to cope with the bureaucratic requirements with their specialized staff. Following the current definition of the sponsor of a clinical study, however, all these requirement would have to be met by the principal investigator of a trial in the context of very limited financial resources. Moreover, all these procedures have to be followed in a continuous manner. This by far exceeds the "once in a life-time" effort of just registering a trial, and will cause significant additional cost. I think that this will further diminish investigator-initiated and academic clinical research and reduce its independence from industry support.
34	These comments may be more appropriate for a detailed functional specification, but should be considered as part of the basis for determining when the EU Portal and EU Database are actually ready for launch. 1. There is no mention of a parallel test platform for sponsors or other users, such as MSs. A test platform provided in advance of the formal launch, or at least at the same time as launch would be a tremendous advantage to

Stakeholder no.	General comment
	your users. 2. Please don't limit to just a few UAT users or only EFPIA members. Consider allowing access to software testers and developers. 3. The test platform functionality and code should be at the same level or newer, than the production platform. It should always be the same or one step ahead for evaluating new features. It should never lag production; otherwise, it becomes useless as a training platform. 4. Consider providing a preview version of the public website both for the production and test submission platforms, so that sponsors and regulatory users can see the resultant public fields and public view, based on their actions. This could be via "preview publication" screens and/or files, or a test version of the public website, similar to what RoPR provides. 5. A dedicated team of professionals should always be available and funded to implement new features and/or fix problems rather than waiting for a new tender to allocate funds and resources to address issues. 6. Will there be a History of Changes feature to show prior versions of public data? 7. There is no mention of the timing for when each of the different types of information/data will become public. Isn't this critical to determining if the platform is performing correctly and thus needed to confirm fully functional audit conditions? 8. Please include specifications for updating the platform so it stays current with internet browsers and operating systems. EudraCT was built for, and is only maintained for, compatibility with IE 8, which was released in 2009 (five years ago). IE 8 support stopped in April 2014 on Windows XP, and will end completely in January 2016.
35	The EMA's announcement on the publication of clinical reports is a major step forward and represents a real shift in favour of ensuring research data is shared routinely and re-used effectively in the public interest. However, with the aim to ensure full transparency and access, we still are concerned about how clinical study reports are made available not only prospectively (starting January 2015) but for all of those drugs that are in use EMA's attitude towards the possibility for redacting information by trial sponsors – it still may never become clear which information is being kept hidden sponsors still being in the position to censor information, e.g. on protocol changes from the public release of a CSR the Terms of Use contract allowing trial sponsors to take direct legal action against researchers for possible violation of the Terms of Use which makes researchers vulnerable to protracted legal battles with large companies. The ongoing discussions on commercial confidentiality in the context of the Transatlantic Trade Investment Partnership could also reverse today's move forward. Arguments underlining this position can be viewed on the Website of the All Trials Initiative

Stakeholder no.	General comment
	(http://www.alltrials.net/).
36	EuropaBio welcomes the opportunity to submit on behalf of our members these comments on the draft functional specifications for the EU portal and EU database underpinning the new Clinical Trials Regulation (EU) No 536/2014. The collaborative approach taken to the development of the portal and database is much appreciated.
36	EuropaBio comments on the draft rules are outlined below. We would welcome clarification as to how sponsors would operate the user assignment specifications.
37	The European Contract Research Organisation Federation (EUCROF) welcomes the opportunity to submit these comments and observations on the European Medicines Agency's 'Draft Functional specifications for the EU portal and EU database to be audited' issued for public consultation.
37	Our submission deals with several aspects of the draft functional specifications: 1. Improving user-friendliness 2. Enabling interaction with different players on the user side 3. Implementation of the CTR with regards to publication of Phase 1 registration and results
37	Improving user-friendliness CROs are frequently charged with the task to apply for clinical trial authorisations on behalf of their sponsors and subsequently fulfil the sponsor communication with the MSCs. Consequently, CROs work on a high number of trials simultaneously. It would be very desirable for a CRO, when entering the system (EU Portal), to see a list of trials the CRO is working on and to be able to fast access the trials. This could be reached by assigning unique identification numbers to CROs in a registration process. These numbers would then be used by sponsors when delegating the tasks and assigning access rights. A CRO front-end would make the system user-friendly. A similar entry way would be beneficial for sponsors, seeing the list of trials which are active for them when entering the system. More specific comments to improve user-friendliness are provided in section 2.
37	Enabling interaction with different players on the sponsor side A sponsor can delegate duties and tasks to service providers (CROs) but can also split responsibilities with other parties (co-sponsors). In case a sponsor is located outside the EEA, a legal representative or a contact person is needed. The different types of designees of a sponsor are not addressed in the draft functional specification document. EUCROF thinks that a differentiation is necessary. Situations could arise, that a sponsor has no legal representative as the trial is conducted in one MSC only and that MSC does not require a legal representative, but later on, when another MSC is taken onto the trial, suddenly a legal representative might be needed and access to

Stakeholder no.	General comment
	the EU portal needs to be granted (super user?). The matter of legal representative is not very clear in the EU Clinical Trials Regulation (CTR) itself (Article 74), however unambiguous rules should be defined regarding the use of the EU portal/database. In addition, clear rules are necessary as to which of these parties (sponsor, co-sponsor, legal representative, contact person, CRO) can be a super user. More specific comments to enable interaction with different players are provided in section 2.
37	Implementation of the CTR with regards to publication of Phase 1 registration and results This part of our submission outlines EUCROF's position on specific aspects of the implementation of the CTR for early phase, non-therapeutic, non-paediatric, non-publicly funded clinical trials, performed in healthy volunteers or patients with the target disease. In case of the latter, patients are not expected to gain any health benefit through study participation and therapeutic efficacy is not a primary objective of the study. For simplicity we use the term "Phase 1" to describe these types of studies in this submission. Our submission focuses on the topic of public access to registration information and summary results for Phase 1 studies. We are aware that the publication module of the EU database is still under discussion and whilst mentioned in the draft document, not a matter of consultation on detail. We believe that our input at this time may be useful in drafting the next version of the functional specifications which will more specifically deal with the publication module. We are giving a summary of the issues in this part of the general comment section and make specific proposals on the functional specifications of the publication module in the section allocated to specific comments (please see comments on Table 1, Req.18 & Lines 103-104 & Lines 113-127) Our general comments are structured as follows: We briefly review relevant aims of the CTR and its new transparency requirements affecting Phase 1 studies. We summarise the current regulatory requirements in relation to public accessibility of Phase 1 clinical trials' registration information and summary reports in Europe, the US, as well as requirements of the International Committee of Medical Journal Editors. We consider potential benefits and risks arising for patients, health professionals and the public out of increased public accessibility of Phase 1 information. We propose a simple, transparent process to make Phase 1 trial registration information and summary reports publicly available in stages. We propose that this release proceeds in a pre-determined and pre-authorised fashion at a point when the information becomes relevant for the public, patients and health professionals, in relation to the development of the Investigational Medicinal Product (IMP), IMP/device combination product.

Stakeholder no.	General comment
	The key aims of the CTR are to boost clinical research in Europe, to give patients access to the most innovative clinical research and treatments and to improve existing treatments. It is important to find means of aligning the transparency requirements of the CTR with these important objectives. This submission aims to propose a solution that is beneficial for all stakeholders: study participants, patients, sponsors, regulators and academic and commercial researchers. The implementation of the CTR will introduce **new requirements for Phase 1 studies in Europe**. Phase 1 studies must be registered on a publicly accessible international trials registry platform of the World Health Organization (WHO ICTRP) and published as summary reports and lay summaries within one year from the end of a clinical trial. The CTR permits commercially confidential information to remain confidential, i.e. this type of information does not need to be made publicly accessible and the EU database needs to cater for that in its publication module. In the US, Phase 1 studies are exempt from registration and results submission to a publicly accessible database (except interventional studies of FDA-approved drugs, biologics, or devices, for which results need to be published). Whilst journals following the International Committee of Medical Journal Editors' (ICMJE's) recommendations must register Phase 1 studies using the 20 WHO standard data fields, a number of Clinical Pharmacology journals such as the British and the European Journals of Clinical Pharmacology are not listed as journals following ICMJE recommendations. Following a detailed review of the potential benefits of publicly accessible registration of trials stated by ClinicalTrials.gov, the WHO/International Clinical Trials Registry Platform (ICTRP) and the CTR we found that most are not applicable to Phase 1 non-therapeutic, non-paediatric, non-publicly funded clinical trials. An argument can however be made for release of relevant Phase 1 registration information in pre-determined stages and on a need-to-know basis. With regards to the potential benefits of publicly accessible (lay) summary results of Phase 1 studies, we found that the benefits stated by the above sources will not necessarily affect patients or ongoing clinical research at the time. Benefits will become relevant at various time points during drug or drug/device combination development. This may be earlier or later than one year from the end of a trial. The potential risks of early publication and disclosure of Phase 1 studies' registration information and results may outweigh its benefits for patients, health professionals and the public. During early drug development much of this early phase information is considered commercially confidential. Regulation outside Europe does not require publication of Phase 1 studies, except after FDA approval in the US. Sponsors would therefore likely manage perceived risks by performing Phase 1 studies outside Europe. This would have a detrimental effect for European

Stakeholder no.	General comment
	early and late phase clinical research, which would ultimately translate into disadvantages for patients and the public. Is there a suitable, simple and transparent process for publication of Phase 1 registration information and results, balancing benefits and risks within the remit of the CTR? In accordance with the CTR, Commercially Confidential Information (CCI) does not need to be disclosed: Article 67 […] "Publicly available information contained in the EU database should contribute to protecting public health and fostering the innovation capacity of European medical research, while recognising the legitimate economic interests of sponsors." and Article 81: 4. "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 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;" Non-CCI will be made publicly accessible via a publication module of the EU database which is currently under development and this is the first public consultation on the EU database's functional specifications. The draft functional specifications state in section 5 that "the functional specifications and underlying principles to support the transparency requirements of the CTR will be included as an addition" to the current draft document in sections 4.3 (Table 2) and section 5 and will be subject to further work and a brief public consultation before March 2015. We aim to outline in our specific comments (please see comments on Table 1, Req.18 & Lines 103-104 & Lines 113-127), how in principle CCI can be respected whilst publishing relevant Phase 1 information transparently and in line with the CTR. **We propose making Phase 1 trial registration information and summary reports publicly available in stages**. We propose that this release proceeds in a pre-determined and pre-authorised fashion on a need to know basis, i.e. when the information becomes relevant for the public, patients and health professionals in relation to the development of the Investigational Medicinal Product (IMP), IMP/device combination product. For further information and background on this part of our submission, we include our more detailed position paper. This position paper describes how we assessed the applicability of publication benefits to Phase 1 studies and also describes in more detail the staged publication process and our proposals in dealing with special situations (e.g. study termination on safety grounds, voluntary publication). Comments on Early Phase Clinical Trials: Public Access to the EU Database Repository We hope that EUCROF can be of assistance in the stakeholder working groups leading up to the finalisation of the

Stakeholder no.	General comment
	functional specifications.
38	The document is clear and very exhaustive.
39	We understand that the EuCTR stipulates that all clinical trials, therefore including Phase I, together with their associated information and data, will be registered in this EU database and that this database will be publically accessible. Whilst we welcome moves towards increasing transparency in clinical development of new medicines and recognise the benefits it can have to public health, we have significant concerns about the potential for the EuCTR transparency requirements to detrimentally impact life science and in particular early development research across the EU. Companies undertaking early development trials have to be assured that their intellectual property and commercial strategy will remain confidential; otherwise they will simply choose to undertake this work in other regulatory jurisdictions. It is imperative that the EU maintains a competitive environment to stimulate Phase I clinical trials within the Community and, therefore, a simple and robust mechanism must be implemented to ensure Sponsors are able to readily protect their intellectual property and knowhow during the early stages of development until such a time that it is appropriate to release such Commercially Confidential Information (CCI) into the public domain. There continues to be a great deal of productive discussion in the UK within the early development and Phase I community and we would appreciate an opportunity to share our thoughts and learnings from this debate with the EMA during future consultations. If naming conventions are applied for documents up loaded on to the system it would be beneficial that they are aligned with eCTD naming conventions to facilities lifecycle management.
40	10 Minor clarifications and/or corrections throughout the document are required.
41	EudraCT database and EU Portal/EU database EFPIA has questions around how the current EudraCT database will be integrated, migrated or otherwise linked to the new EU portal. This is also important for clinical trials being initiated while EudraCT is still in place, but continuing and ending after the transition period is finalised. Duplicate data entry should be avoided. In case there are technical considerations on the transition, these should be included in the document or published later on.
41	General comment on transparency requirements Although an addition to the functional specifications regarding the transparency requirements of the regulation is announced in section 5, the table 2 section 4.3 should at a minimum mention that “at least *rules relating to data access, redaction, confidentiality and the management of its evolution to non-confidentiality over time are to be defined.*” We expect the EMA database and portal should be the vehicle for the transparency dispositions of both the

Stakeholder no.	General comment
	Regulation and the EMA transparency policy 0070. Consequently, there is a strong expectation that all transparency related functionalities and notably those around download vs. view-only should be in accordance with the Terms of Use agreements.
41	System flexibility While the focus on the essential elements required for the initial roll-out of the system is Comment acknowledged, it is important to early consider addition of other important functions: For instance, an important extension to the system could include an automatic notification mechanism on newly authorised clinical trials for patients and healthcare following specific subscription. This would allow patients' and healthcare professionals to keep themselves informed on new clinical trials without directly getting involved with sponsors. Such an approach would be consistent with EMA's roadmap for stronger patient orientation.
41	Throughout the document there is discussion around the submission and validation of the documents for the CTAs using the Workspace. EFPIA is proposing that sponsors have the option of using the currently approved standard (eCTD) for submission of the content via EMA Gateway/CESP. Advantages Improve overall quality due to consistent dossier preparation eCTD has already delivered the functionality to meet the needs of good dossier management, this will be of increasing importance with a wider number reviewers trusting the system eCTD would improve the reviewers experience over a Non-eCTD electronic Submission Sponsors can compile and validate dossiers outside of the portal Vendor experience with overlaying security on the eCTD dossier structure Experience available in the use of eCTD for clinical trials in the US including use by smaller sponsors Creation of an additional method for submission of regulatory documents will add cost and complexity for all stakeholders. The FDA today allows for the submission of both investigational submissions and marketing submissions (lifecycle included) via the existing ICH Standard eCTD with additional capabilities in the long term with the next major version 4.0 EFPIA is aware of the need to adequately assess such an approach and is available to assist in this activity.
41	In our understanding the next consultation of this draft document will be focused on functionality and principles only. We fear that leaves a gap regarding the agencies data model and might invite agencies adding other "nice to have" data points in the structured data uploaded to the registry. This would lead to a possible efficiency problem and to avoid that we suggest adding a clarification to the document.

Stakeholder no.	General comment
43	The stakeholder Independent Ethics Committee seems to have been forgotten. Don't the IECs need to have access to the database and to submit their considerations, request additional information and give their authorization?
43	Is the transfer of responsibilities taken into consideration? Responsibilities and roles might change during the conduct of a clinical study. The sponsor may merge with another pharmaceutical company or the entire development programme may be sold to another sponsor. Would this lead to the need of re-entering all study information or can roles be changed and responsibilities transferred in the database/portal? It isn't clear from the draft whether these aspects are taken into account e.g. under points 1.2 and 3.8.
43	Regarding the reporting of events that may change the benefit-risk balance: would this information be needed to be duplicated in the EudraVigilance database and the EU Portal or would those two databases communicate in this respect in order to reduce duplication of information? It would make sense to have all safety related information accessible from one source externally to the EU portal, e.g. within the Safety portal, as outlined in Figure 1. Therefore, it is questionable whether one should utilise the EU portal to access reports of events that may change the benefit-risk balance since such information primarily is within the scope of the Safety portal.
44	Interfaces with MSs CT Systems; it will be helpful to have a functional description of functionalities that will be offered by the EU Portal so that the MSs can anticipate during the development/maintenance of their national solutions.
45	CT dossier content and structure requirements should be designed to facilitate assessment and to allow for automatic publication of the necessary information keeping and showing traceability of changes. Moreover, the system should be "trial & dossier-oriented" and host the information in a structured way. Furthermore should manage the information making use of a relational database models (or other state-of the art database cutting-edge technology) in order to allow sponsors to provide the required information in a meaningful & productive way or even more, they would be able to develop inter-operative APIs to provide such information in an automated way, e.g. from their own Clinical Trial Management System (CTMS). In other words, the use of metadata or plain-text data should prevail over raw documents (e.g. PDF, Word, etc) in order to facilitate project tracking and reporting, as well as final publication of the trial data. The following should be considered additionally for the structure and content of the CT dossier: a. At least, information to be made public showing the CT characteristics, and other information relevant for statistics and structured analysis should be provided as plain text and only once (e.g. WHO basic dataset for ICTRP compatibility). b. For the rest of the dossier data, current duplication of information should be avoided (i.e. IMPD should be limited

Stakeholder no.	General comment
	to Quality part; non-clinical and clinical information should only be in the IB and the protocol should cross refer to such document without reproducing such information; reference safety information and overall risk benefit should be distinct pieces of information or documents). c. Changes in Substantial modifications, at least those related with information to be made public, should only be provided as a summary of changes, including rationale for such substantial modification, together with all the new information. The system should be able to display the previous version of the information affected by the changes ("rollback" feature). d. The IT system should keep traceability of changes approved to a specific information or document per CT.
45	All MS should be able to access with read-only permission to the whole database and trial documentation and related workspaces at any time. However, changes should be only allowed when appropriate ("ongoing" status in the system is set: e.g. during validation, assessment, answer to RMS requests, etc). Ideally, changes should be accompanied by a remark or a relevant descriptive field. Previous versions of documents should also be read-only visible at any time.
45	It is essential that all stakeholders (EC, MSs and sponsors) could be able to gather trial status at a glance, by means of informative score board displaying key performance indexes (KPIs). In addition, CT status should be shown in such way that MS and sponsors see clearly which are the received submissions and pending actions on their side, and also in order to support searches. A proposal is included as an annex that also include the minimum information necessary in the summary status of a certain CT.
45	Trial management and Medicinal product management should be integrated seamlessly (through the above mentioned relational database model), so all MP involved in a given trial are tracked and reported easily and quickly and vice versa, all trials in which a medicinal product have been administered to subject could be shortlisted. This is essential for trial supervision by MS related to quality or safety reasons.
45	The system should be flexible enough to allow corrections of mistakes by sponsors (e.g. application or dossier) or MSs (e.g. assesment report preparation) by menas of relevant features (nullification, previous version roll back, etc) to be defined at a lower level business cases.
45	The system should allow support all real-world situations. Is essential to be able to support all validation, assessment, answer for information, decision issuing and trial publication, etc. But also other business scenarios should be supported, for instance, to ask for additional information at any time (even outside assessment context), and the sponsor to be able to answer it.
45	The system should be able to notificate "de facto" situations, e.g. when certain periods have deemed been lapsed

Stakeholder no.	General comment
	(Reg. arts. 5.5, 6.8, 7.3, 14.6, 14.8, 17.4, 18.6, 20.3, 20.6, 22.3) or when the application has expired (Reg. art. 11). Article 13 should be clarified on how to proceed by the system when sponsor does not answer to RMS at the assessment stage.
45	The system should take into consideration situations in which the owner of the IMPD (quality part) is not the sponsor so the following provisions are made: a. Separate submissions for IMPD-Qpart and rest of the dossier. IMPD-Qpart could be submitted by the MAH/manufacturer and the remaining by the sponsor. b. Questions by RMS related to quality of the medicinal products could be addressed to the MAH/manufacturer only and this one answers to the RMS confidentially. c. Rest of questions by RMS related to other parts of the dossier are addressed to the sponsor as usual and could be answered accordingly.
45	With regards with the Non-authorized Medicinal Product database it is paramount to take into consideration that: a. That the quality of the Non-authorized MP may change (e.g. the pharmaceutical form and/or route of administration) b. The INN may not be available at early stages OF A GIVEN Non-authorized mp. c. All substances/ingredients and Non-authorized MP names may change (i.e they do actually change) during development process So this evolution should be recorded in the Non-authorized MP database (an keep them linked with related trials).
45	Finally, this functional specification is too high level, and it should be accompanied at the time of the audit by detailed business cases defining the specific behaviour of the information system for every process. By other hand overall features as “System performance and scalability” are not defined where a gross metric was expected, e.g. something like “99.5% uptime”.
45	Annex. Summary of CT status at EU level (related to EU CT Number) Together with the EU CT number the system will show the submission number to identify a CT. CT Status: Last status should be displayed. Status temporarily halted, prematurely ended, or urgent safety measures should be displayed when this kind of status apply in at least one MS. In case the CT has been authorised by any MS, even if rejected in others the status should be authorised. The status rejected should apply when the CT was rejected in all MS. In cases where the CT was previously rejected or withdrawn but then the application was re-

Stakeholder no.	General comment
	submitted and the resubmission has been authorised, the status will be authorised. Possible CT Status: Part I Pending (between entry date and reporting date) or Part I application deemed to have lapsed (in case sponsor have not answered validation (V) or assessment (A) request for information. In the last case a link to request for information to be provided) or Withdrawn (the initial CTA has been withdrawn before the reporting date. A link to reasons to be provided) or Part I approved (conclusion of part I AR is CT acceptable or acceptable with conditions. In case of acceptable with conditions, a link to conditions to be provided) or Part I rejected (conclusion of part I AR is CT is rejected. A link to reasons for rejection to be provided) or, Authorised (the decision on both part I and II by at least one MS was CT authorised) or, Authorisation expired (if in all CMS) or, Rejected (all available decisions by MS are CT rejected) or, Recruitment started (at least in one MS date of start of recruitment has been provided) or, Recruitment completed (when date of end of recruitment in all MS has been provided) or CT temporarily halted (a temporary halt has been notified and the restart has not been approved in at least one MS. A link to reasons should be provided) or, CT suspended (the CT has been suspended and a restart has not been authorised in at least one MS. A link to reasons should be provided) or, CT restarted (a restart has been authorised after a temporary halt or suspension) or, CT ended in all MS (once CT has ended in all MS). Prematurely ended (In case the CT has been prematurely ended for reasons affecting the benefit/risk balance in at least one MS. A link to reasons should be provided) or, Results provided. Participating countries names of participating countries to be displayed, with a link to see CT status per MS. List of ongoing part I SM or addition of MS applications. List of notifications received.
45	<u>Summary of CT status per CMS</u> Together with the EU CT number the system will show the submission number to identify a CT.

Stakeholder no.	General comment
	CT Status: Last status in the MS should be displayed. In cases where the CT was previously rejected or withdrawn but then the application was re-submitted and the resubmission has been authorised, the status will be authorised. Possible CT Status: Initial CTA received [it could also apply to CTA Resubmissions (EU CT Number + submission number) or to an addition of new MS application]. In case of a resubmission there should be easy access to data of previous submission. Status a. to j. could also apply to a SM application. CTA received (RMS to validate, if part I, and/or CMS to send comments to RMS until day 7) CTA validation info request (SP to answer) CTA validation (RMS to validate SP answer) V Deemed to have lapsed (not answer to V request for info) CTA validated (RMS to provide draft AR/CMS to assess part II) CTA assessment coordinated review (CMS to assess draft AR or SP answer) A Deemed to have lapsed (not answer to assessment request for info) CTA assessment consolidation (RMS to end draft or final AR) CTA assessment info request (SP to answer) CTA pending decision (CMS action) Part I/part II application deemed to have lapsed (in case sponsor has not answered validation (V) or assessment (A) request for information. In the last case a link to request for information to be provided) or Withdrawn (the initial CTA has been withdrawn before the reporting date. A link to reasons to be provided) or Part I approved (conclusion of part I AR is CT acceptable or acceptable with conditions. In case of acceptable with conditions, a link to conditions to be provided) or Part I rejected (conclusion of part I AR is CT is rejected. A link to reasons for rejection to be provided) or, Authorised (the decision on both part I and II by MS is CT authorised or authorised with conditions) or, Authorisation expired Rejected (Decision by MS is CT rejected) or, Recruitment started (date of start of recruitment in the MS has been provided) or, Recruitment completed (date of end of recruitment in the MS has been provided) or CT temporarily halted (a temporary halt has been notified and the restart has not been approved in the MS. A link to

Stakeholder no.	General comment
	reasons should be provided) or, CT suspended (the CT has been suspended and a restart has not been authorised in the MS. A link to reasons should be provided) or, CT restarted (a restart has been authorised in the MS after a temporary halt or suspension) or, CT ended in all MS (once CT has ended in all MS). Prematurely ended (In case the CT has been prematurely ended in that MS, for reasons affecting the benefit/risk balance. A link to reasons should be provided) or, Results provided. Participating countries names of participating countries to be displayed, with a link to see CT status per MS. List of ongoing part I SM or addition of MS applications (with possibility to see the status in every one). List of notifications received (with possibility to see the content of every one).
46	AESGP welcomes being consulted on the draft functional specifications for the EU portal and EU database to be audited. Submitting at least partial confidential data on the research and development of medicinal products through a portal and storing that data in a database which will be linked to a public register requires measures to ensure the secure access, the secure transmission of large data packages as well as a secure environment for the data forwarding and storage. The specifications only mention in line 92 a “secure electronic submission system…” and in line 96 a “secure document management system” without further explanation or even recommendation for the audit. This seems not to be sufficient as the audit should also prove the secure upload, handling and storage of confidential data as well as the measures at the agencies side to ensure a trustworthy access to the systems. Therefore, AESGP proposes to add security features to the audit specifications. Furthermore AESGP welcomes the statement in the text (lines 121-127) on the future consultations process for specifications on the publication requirements with the involvement of all stakeholder groups. As this part of the text will need to be completed at the latest by March 2015, AESGP assumes that the “short public consultation” mentioned in line 124 before the extensive endorsement procedures will be long enough to allow internal consultation and discussion with members and also within companies.
47	IPFA welcomes the Draft functional specifications for the European Union portal and European Union database.
47	Comment: Sharing of documents by authorization of users from other member states, for example the patient

Stakeholder no.	General comment
	information letter Proposed change: Will it be possible to share information between Member States?
47	Comment: Database should be able to perform publication of clinical trial data and information Proposed change: Is it possible to link to the ClinicalTrial.gov database for example?

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes
5	21	**Comment:** Consultation instead of endorsement: As of article 82 the FS should be drawn up in cooperation with MS and COM. Therefore the MS should agree on these essential functionalities to be audited. **Proposed change:** 'Confirmation' instead of 'consultation' MS'.
21-34	15	**Comment:** 'ethical soundness…reliability and robustness' take into consideration Consort Statement 25 items for results. This is being backed by WHO. CDISC are developing an XML message which will pick up from the stalled HL7 CTR&R project to present CT registration data in a DEFINE.xml CDISC standard. Other CDISC standards – SDTM – will organise data giving robustness, especially in the advent of CDISC SHARE and ADAM will allow for easy analysis of that SDTM data – many vendor analysis tools are available to do the 'intermediate analysis' as mentioned in Article 37 for intermediate data analysis.
22	34	**Comment:** add end quote **Proposed change:** "the Regulation"
30	15	**Comment:** Line 30 refers to 2001/20/EC having, "….increased the administrative burden, costs and approval process of conducting clinical trials in the EU". Does this imply that the EU Portal and EU Database under 536/2014 would reduce this. If so should a specific requirement, that the system is audited against, be added to table 1? I.e. that the EU Portal and EU Database reduces the administrative burden, costs and approval process. **Proposed change:** add requirement in table 1 that when audited that the system has reduced cost and burden. Auditors need to confirm this requirement of the system.
30-31	1	**Comment:** Why such an increase in cost and to what extent it (the increased cost) may affect the process of CT
36	34	**Comment:** defined in line 22, but again full name in 36. Consider referring to it as the Regulation in line 36, or wait and define it in line 36. **Proposed change:** In accordance with the Regulation, the European Medicines …
42	22	**Comment:** one of the main requirements for the portal is "user friendliness". How can/ will this be verified during the audit? Also, the user friendliness would greatly increase if CROs acting on behalf of the sponsors would have their own access – not only those delegated down from the sponsor. This CRO specific number can be mapped to the relevant trials the CROs are contracted to work on. Thus, CROs would not have to log on and off with various sponsor numbers to perform their responsibilities. This works very well in the Italian model, and considering that "technically advanced" is another

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		requirement for the portal, it should be technically possible (at least it is in Italy for the last 10 years).
44-48	16, 18,	**Comment:** It will be necessary, that any double or even triple data input is avoided. Therefore it must be ensured, that the new database will automatically retrieve data from the EudraCT and EudraVigilance data bases or vice versa. This has to be described in the specifications for the new database and is a prerequisite for the new procedure.
44-48	29	**Comment:** Article 81.2 also refers to the need for the EU portal to be able to link to all other databases under the control of the agency. (at present, but also in the future, e.g. IVD portal)) **Proposed change:** To add at the end of the line 48: "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".
44-48	41	**Comment:** Based on the outline of the migration of data from EudraCT to the EU database shared at the September stakeholder meeting there appears to be a need for a functional requirement that on completion of a trial within EudraCT there is a data migration function to move the data to the EU Database and avoid duplication of entry.
45-46	29	**Comment:** It is not clear if the word controller is used here in the sense of its generic meaning or in the sense of the data protection framework. **Proposed change:** "The Agency shall be considered to be the controller of the EU database, including in the meaning of the applicable data protection framework".
47	39	**Comment:** Database (and validation process) will need to be flexible enough to allow use of both EudraCT and Portal numbers and Portal numbers alone. This assumes that EudraCT database will eventually be superseded by the EU database, when the EU database goes live will the sponsor/applicant be required to obtain a portal number for on-going trials to allow SA/modifications, end of trial notifications etc. to be registered on the EU database and also maintain the information on EudraCT.
47	39	**Comment:** For new submission post implementation of the EU database will sponsor/applicant be required to obtain both a Portal number and an EudraCT number.
47-48	46	**Comment:** The concept as to how the EudraCT database and the new EU database will be maintained by the sponsors after the entry into application of the CT Regulation is not clear. After the 3 years transition period there should be only one database for clinical trials data in Europe. Therefore, the EU database should also contain data from the EudraCT as legacy data. In this case, the last sentence in this paragraph might suggest that sponsors will have to reformat the EudraCT data into a format in accordance with the regulation before it will be integrated into the EU database. **Proposed change:** Either clarify the usage and maintenance of the EudraCT and the data therein once the EU database is up or delete this sentence as the audit will not be able to prove the consistency of data within the database months

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		before the first submission is done according to the regulations requirements.
57	11, 26	**Comment:** According to Article 99 para. 2 VO (EU) 536/2014 the sentence should be completed as follows: **Proposed change:** Six months after the publication of this notice, the Regulation shall apply, but in any event no earlier than 28 May 2016.
58	11, 26	**Comment:** The member states should agree upon the language of communication within the workspace. They should also agree on a language in which all documents have to be submitted for part I. According to Article 26 the member states are free to determine English as language of communication and as language for the application dossier and documents.
59-61	41	**Comment:** It is a bit unclear what the difference is between the first and the second sentence. Line 59-60 says the regulation requires that information passing through the portal is to be stored in the database. Line 60 -61 says that information is in fact stored in the database. So this is saying the EU is complying with its requirement? 59 The Regulation clearly states that all information that is submitted through the EU portal is stored in 60 the EU database (Article 80). Whenever the articles of the Regulation explicitly require that information 61 goes via the portal, then it is stored in the EU database (see table 1).
60	11, 26	**Comment:** The reference to the legal basis should be more precise. **Proposed change:** Article 80 Sentence 3
62	39	**Comment:** The database will need to allow the sponsor/applicant to identify the information/data considered to be confidential In the context of the above comment, how will the applicant or sponsor identify the data that is considered to be confidential and limit the data that will be publically available? Will the applicant be required to provide a redacted version of the data that they wish to be publically available? What will the public see if they request access to data that the sponsor/applicant considers confidential? Will there be standard text justifying the position taken? If the sponsor/applicant identifies information as confidential will there be some sort of confirmation by the authorities regarding the acceptability of this request? What would be the process in case of disagreement? What are the time frames for making data available?
65-67	21	**Comment:** Article 82 is covering the procedure and responsibilities for ensuring functionality prior the regulation comes into force, while article 81 names the functional requirements for the EU database including essential links, searches, and languages. This article should be referred to in totto and not selective parts. **Proposed change:** The functional specifications required by Article 82(1) of the Regulation describe the requirements for the EU portal and the EU database. In order for the EU portal and the EU database to function correctly certain other

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		technical features are essential and these are provided by the workspace.
66-73	41	**Comment:** Clarification is required on the concept of Workspace The regulation does not provide any definition for the concept “Workspace”. Such introduction of new terminology is somewhat confusing if not clearly described. Describing the workspace as being out-of-scope of the regulation but in scope for the specs is likely to lead to loopholes and an incomplete QA audit on the EU portal and EU database. The workspace appears to be a user-interface with some additional functionality required for the functioning of the EU portal. It should therefore be described as part of the EU portal and not separate from it. (see whereas (66; 67; Article80) The workspace is depicted as being also used by 2 other portals (‘Safety portal’ and ‘Other Portal’). If this is the case and it is a new introduction as a consequence of the regulations and the EU portal then it needs to be part of the in-scope specs and audits in its entirety. It cannot be described as out-of-scope of the regulations. **Proposed Change:** Clarify the role and functionality of the EU portal if the workspace is separate from it. If the workspace is new and interlinks all three depicted portals it must be part of the specs in its entirety. To avoid confusion the workspace should be described as part of the EU portal and in-scope of the regulation in order to avoid introduction of terms and IT systems not covered by the spirit and general provisions of the Regulation. OBS: reference to 16(6) in line 70. No such Article section exists in the Regulation?
67-69	20	**Comment:** Paragraph 3 and 4 are contradictory in respect to the CT application form. Paragraph 3 says CT application is prepared in the system while paragraph 4 covers the upload of data like EU CT form. **Proposed change:** Preparation of EU CT form directly in the portal.
67-69, 137 Table 2 3.2	41	**Comment:** Not all sponsors will prepare and compile their documentation in the workspace. The Portal must be able to receive submission files that have been prepared in other systems. **Proposed change** to lines 67-69: “The workspace is required in order to support activities such as the preparation and compilation of the clinical trial application by some sponsors, the drafting…”
67-69 137 Table 2 3.6 4.6	41	**Comment:** The use of XML for upload and download of data is not in itself enough to deliver efficiency and reuse of data. There is an implicit need to apply a data standard for good data quality, effectiveness and efficiency. Can the EMA state its commitment to global standards development as a part of the delivery of the EU database and portal?

Line no.	Stakeholder no.	Comment and rationale; proposed changes
70	21	**Comment:** Review and consolidation will also take place for the requested information; Correction not article 16 but 14. **Proposed change:** 'Articles 6(5) and (8), 14 (6), and 18 (4) and (6)'.
70	42	**Comment:** Please correct the reference. There is no section 6 of Article 16.
71-73	21	**Comment:** Workspace is within the content of the regulation (article 81), while data and information in the workspace are outside the EU portal/database and article 81(1) applies. Further technical features, defined in the text as "workspace" are content of and defined in the regulation. E.g. As of Article 81(2) "The EU database shall establish to enable cooperation between the competent authorities of the MS concerned to the extent that it is necessary for the application of this regulation and to search for specific trials. It shall also facilitate the communication between sponsor and MSc… Article 81(3) supporting the MPD for non-authorised…" This should be reflected in the scope and in addition the MPD should be mentioned in the scope. **Proposed change:** Whilst the workspace is essential to the functioning of 71 the EU portal and EU database (article 81), 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 (article 81(4)).
71	34	**Comment:** remove "of" **Proposed change:** "…essential to track and control these activities."
74 Figure 1	15	**Comment:** Will there be compatibility between the MSs CT systems? Is the data warehouse expected to conform to CDISC standards (submission-ready) or to another standard? I.e. will there be harmonisation of standards across the MSs data?
74 Figure 1	16,41	**Comment:** It seems not clear which functionalities of the workspace are out of scope? Which of them are supposed to be audited? In addition, we think it as a bad approach that EMA has published a revised version of figure 1 without clear notice. Regarding the MS involvement, it should be addressed that National Competent Authorities (NCAs) as well as Ethics Committees (ECs) have access to the Portal/ Database on the MS level. We think this should be clarified in the functional specifications as the involvement of the NCAs and the ECs is foreseen in ICH-GCP (E6) Guidelines. In this context it would also be important that national ECs get access to the EU-Portal/database including the safety database. Also we see it as a misconception of this draft that the interface with MSs CT Systems is not part of the functional specifications or the audit. From the vfa perspective this needs to be addressed to avoid duplicate entries and maintenance, but also to ensure that the processes foreseen by regulation (EU) No 536/2014 (EU-CTR) will be fully operational.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		So the fact that the interface with MSs CT systems is completely out of scope in the revised version of figure one is worrying - this needs to be addressed also in the functional specifications and the audit. If not and national systems will not work properly, the whole EU-CTR might fail to result in a strengthening of Europe as a clinical trials location.
74 Figure 1	16, 41	**Comment:** It is not clear which functionalities of the workspace are out of scope and which of them are supposed to be audited. This should be clarified. In addition, the workspace should be working completely before the audit! Regarding MS, it should be clarified that National Competent Authorities (NCAs) as well as Ethics Committees (ECs) have access to the Portal/ Database. In this context it would also be important that national ECs get access to the safety database. Interface with MSs CT Systems: This is not part of the audit but will need to be addressed to avoid duplicate entry and maintenance. The plan for having the system fully functioning including the additional requirements outlined in Annex I should be described.
74 Figure 1	21	**Comment:** In Figure 1 the in regulation article 81 (3) required medical product dictionary/ EU medical product number and active substance code database are missing. **Proposed change:** Add EV-MPD / EU active substance database to the figure.
74 Figure 1	28	**Comment:** Figure 1 currently suggests that the requirement for registration and assignment lies outside of the scope of article 82 functional specifications and audit. We think this should be inside of the scope and refer to this function being detailed in Table 2, 1.1 and 1.2.
74 Figure 1	29	**Comment:** Figure 1: MAH usually stands for Marketing Authorisation Holder (though this is not specified in the document). The workspace area foresees a space for MAH – however, MAH is not a stakeholder under the CTR (similarly to the CROs), unless in the sense of the Article 37.4, §4 (reporting of the CSR 30 days after MA is granted); however, it is not clear if this separate workspace is foreseen for the needs of Article 37.4, §4 specifically. The link between MAH space and sponsor or its space is not clear. What about results of projects that without prospective intention for registration where conducted by academic sponsors, but at the view of exceptionally positive results are used to support a marketing authorisation (or its extension e.g. rare cancers)? Is MAH space related to the trial or rather to the product? **Proposed change:** To be clarified
74 Figure 1	41	**Comment:** The figure is not self-explanatory as to where the Dossier Builder application would fit. We propose to clarify whether the Dossier Builder is a stand-alone application and whether it is/will be developed by EMA as part of the overall CTR technical solution. Moreover we propose to specify in this document the high-level requirements of the Dossier Builder application.
76	42	**Comment:** Please consider adding a new paragraph that would consolidate all defined terms/abbreviations for the ease of reference.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
77-79, 80, 109	15	**Comment:** The document requires a stronger relationship between the legal requirements listed in section 4 and the functional requirements listed in section 5. There is a column in section 5 designed to ensure this relationship, “Link to the legal requirements presented in Table 1”, however the column is populated very broadly, e.g. Req. 1-17. For this reason it is not immediately clear that all legal requirements are covered and, conversely, that there are no unnecessary functional requirements included. **Proposed change:** Add more detail to the section 5 to define which requirement links to precisely which legal item.
83	39	**Comment:** Sponsors may delegate CT activities: e.g. applicants may be a CRO. Thus, the database and portal should be designed to accommodate this possibility. Text throughout Functional Specification should be amended to reflect that activities currently identified as being undertaken by the sponsor may be undertaken by applicant (i.e. CRO). **Proposed change:** The EU portal and EU database and associated workspace are to provide sponsors/ Clinical Trial applicants (e.g. CROs), applicants to a marketing authorisation, MS, the Commission and the Agency 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.
83-86	10	**Comment:** According to the current wording of the Draft functional specifications it seems that both the EU database and EU portal are intended for Sponsor/MAH only or for primary users (named “super users”). There is no mention of “Sponsor representatives/designee/CROs/third parties” etc. This means that a CRO or other Sponsor’s representatives (e.g. regulatory consultancy companies) are not allowed to directly access the system or register as super users. Considering that most of our clients are based in the US or outside EEA and could be small biotech companies, our CRO will be restricted with respect to accessing the EU portal directly. For us this constraint represents a major point of concern. There, I would propose to the decision making parties to assess a less restrictive access to the system, to all stakeholders, similar to Sponsors or MAHs. **Proposed change:** The EU portal and EU database and associated workspace are to provide sponsors, applicants to a marketing authorisation or their representatives/designees, MS, the Commission and the Agency 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.
83-86	39	**Comment:** The database also provides information to the public. The role of the public is not mentioned in this text.
87	28	**Proposed change:** Change ‘actors’ to ‘factors’.
87	42	**Comment:** ...submission of data and view by the public of information using the EU portal and EU database...
89	1	**Comment:** The reason outlined above might be easily invoked to justify confidentiality and refrain from publishing the

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 1		data.
89 Table 1	13	**Comment:** Any changes made should be immediately advised and updated in the portal so that a complete change history can be available at any time. **Proposed change:** Just tell "Update any changes to the clinical trials".
89 Table 1	15	**Comment:** 'Sponsor – request of a unique EU Trial number…' **Proposed change:** Perhaps use ISO 3166 codes to prefix country code to a unique number. Utilise and work with WHO who have UTR numbers already in wide use moving towards a global standard.
89 Table 1	15	**Comment:** 'Record and submission of medicinal products….substances' **Proposed change:** Standards will put data in upstream such as substance identity information.
89 Table 1 42 137 Table 2	15	**Comment:** Section 4, table 1 forms the bedrock on which section 5 is built. It would benefit section 5 to include all regulatory requirements in table 1, not just the activities, so that section 5 can make better use of table 1. For example line '42' of the document confirms that Article 80 states that, "The portal shall be technically advanced and user-friendly….". If this is a specific legal requirement then this should be included in table 1. This would in turn improve section 5 as this could be referenced in the last column, e.g. specify 'user-friendly' as the legal requirement behind 3.11 in table 2. Legal requirements listed under 4.2, 'Systems Overview', could also be moved up into table 1 for the same reason. **Proposed change:** Perhaps add a rating scale on the importance of each of the items. Move all legal requirements into table 1, so they will gain a 'Req.' number that can be referenced in table 2.
89 Table 1	20	**Comment:** For each trial conducted one trial identification number should be assigned to ensure that global studies that are registered in multiple international registers can be unambiguously identified. This number will also be mentioned in any peer review journal publication for clear identification. It should not be required to request a region specific EU number for a CT if it has already another unique trial identifier. **Proposed change:** "Request a unique EU trial number to identify each CT, if another clinical trial identification number (such as NCT#) has not yet been assigned." Question: In case of a re-submission, will the clinical trial number be the number of the previous clinical trial application although (Article 13 states that the application shall be deemed to be a new application for authorisation of another clinical trial)?
89 Table 1	20	**Comment:** For CTs involving new substances it should only be required to request an active substance number from the medical products dictionary. Not all CTs conducted are leading to marketed products. Medicinal product numbers should only be assigned during the MA process and after the substance has received the marketing authorisation as a

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		specific medicinal product. If the CT is with a marketed product, this number can be looked up in the medical product dictionary and linked. **Proposed change:** Delete “request for MP number” or replace by “request for provisional MP number”.
89 Table 1	20	**Comment:** Only final CT results should be submitted. Intermediary results will be submitted as part of the regulatory application (E.g. follow-up assessment, PASS, PAES or variation procedure). In addition, according to Article 37 (4, 8) “…the sponsor shall submit to the EU database a summary of the results of the clinical trial…” **Proposed change:** Please add “Submission summary CT results” to Req. 7. Please delete “intermediary data analysis (when applicable)” listed in Table 1, Stakeholder: Sponsor, because according to Article 37 (4, 8) sponsor shall submit a summary of CT results within one year from the end of a clinical trial or within one year of the intermediate data analysis date (if intermediate data analysis is required prior to the end of the clinical trial, and the respective results of the clinical trial are available).
89 Table 1	20	**Comment:** The submission of CSRs needs to be co-ordinated with the EMA 70 policy CSR submission/publication mechanism. It must be clarified which system is used to display the redacted CSRs in only one place.
89 Table 1	20	**Comment:** According to Article 5 (1) “The sponsor shall propose one of the Member States concerned as reporting Member State.” **Proposed change:** Please add to Requirement 3 and Annex 2 the missing sponsor’s requirement.
89 Table 1	22	**Comment:** Table 1 Stakeholder column; Abbreviations need explaining, for instance "MSC" is not explained – assumption is “Member State Concerned”. **Proposed change:** MSC (Member State Concerned Stakeholder column; Section on Applicant needs completing. Currently "Applicants (marketing authorisation)" is the stakeholder the marketing authorisation holder? **Proposed change:** "Applicants (marketing authorisation holder).
89 Table 1	24	**Comment:** In Table 1 (EU clinical trial portal and EU database activities and requirements), when discussing public accessibility it is noted that some data shall not be made publically available due to regulation (EC) No 45/2001. In interpreting this requirement of the regulation, we must consider the proportionality of the results. When considering if affected by rare conditions should be included in the database or excluded due to the risk of re-identification, we should balance the risks associated with re-identification with the disbenefits arising from excluding their data. In many cases the rare disease patient community would rather support further work on their condition. Perhaps more than those affected by more common conditions, rare disease patients rely on the collection and sharing of data across national boundaries in order to establish a useful evidence base. When rare disease patients agree to

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		participate in a clinical trial, their consent includes recognition that the rarity of their condition puts them at increased risk of being identified from the clinical trial data. For those patients who participate, they have already understood this risk and have decided that the benefits of the trial for themselves as individuals, as well as for others affected by their condition, outweighs this risk. The regulations that govern which data are made publicly available on the EMA database and portal should mirror the consent patients give when agreeing to participate in the clinical trial itself. This would avoid setting a damaging precedent for this and future databases that risks precluding the involvement of rare disease patients.
89 Table 1	24	**Comment:** Table 1 also states that commercially confidential information shall not be publically accessible. EGAN believes that the EMA and the pharmaceutical industry should be as transparent and open as practicable. Greater detail is necessary regarding what type of information would constitute as commercially sensitive and would need to be publicly withheld.
89 Table 1	26	**Comment:** Is not necessary for Sponsor to send DSURs and annual reports? Cannot see in the list below.
89, Table 1	26	**Comment:** Substantial modifications. Guarantee of traceability.
89 Table 1	26	**Comment:** Monitoring reports: The submission of Inspection reports will include monitoring reports?
89 Table 1	28	**Comment:** Table 1 should include the requirement for sponsors to upload a summary of results, to include a lay summary, as recognized in Annex 2.
89 Table 1	32	**Comment and suggestion:** Preferably the same term that is used in the legal text for Regulation 536/2014 should be used. As an example, Table 1, page 8/28, first row under column Requirement – 'determination' should be replaced with 'selection'. (Same comment for Table 2 below, page 20/28, fifth column Details for item 3.4 first bullet.) **Proposed change:** see above
89 Table 1	37	**Comment:** One sponsor requirement is to assign users of the EU portal and database who will access the system on behalf of the sponsor. The following parties need to be differentiated per trial (if applicable) and corresponding tasks and access rights need to be defined: Co-sponsors (Article 72) Legal Representative (Article 74) Contact person (Article 74)

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Individuals, companies, institutions or organisation to whom tasks are delegated (later called “contract research organisations (CROs)” (Article 71) Marketing Authorisation Holder (MAH) Even if a legal representative or a contact person of the sponsor are assigned to be the addressee for all communications with the sponsor provided for in the CTR (as Article 74 states), the sponsor still has to be the top level entity on the sponsor site. **Proposed change:** Requirements: The sponsor to assign users and allocate tasks. Legal Basis (Art): Article 71, 72, 74
89 Table 1 103-104 113-127	37	**Comment:** We propose making Phase 1 trial registration information and summary reports publicly available in stages. We propose that this release proceeds in a pre-determined and pre-authorised fashion on a need to know basis, i.e. when the information becomes relevant for the public, patients and health professionals in relation to the development of the Investigational Medicinal Product (IMP), IMP/device combination product. (A) We suggest that, based on the fields in the current EudraCT database, a limited amount of non-commercially confidential registration information is made publicly accessible via the EU database after clinical trial authorisation and prior to study commencement (subheadings only): [A Trial Identification] A1 Member State (Country in which the submission is made) A2 EudraCT number A3 IMP name only, no study title A4 Sponsor’s protocol number A5 Additional international study identifiers, if available A6 Re-submission Y/N A7 Part of Paediatric Investigation Plan Y/N A8 EMA decision number of PIP [B Identification of the sponsor] B1 Sponsor details B3 Commercial/non-commercial B5 Contact point designated by the sponsor for further information on the trial [C Applicant Identification] C1 Request for the Competent Authority

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		C2 Request for the Ethics Committee [E General information on the trial] E7.1 Trial Phase (to confirm “applicability”, i.e. Phase 1 and feasibility study) [F Population of trial subjects] F1 Age range (to confirm “applicability”, i.e. non-paediatric study). (B) The clinical study protocol should clearly define all further publication milestones: access to further registration information summary results and lay summary General rules for publication, (e.g. if a study has been terminated on safety grounds) Publication milestones should be described as nominal times in relation development phases, rather than actual dates. As a result, all publication timelines will be authorised as part of the protocol when a trial receives Clinical Trial Authorisation. (C) For any changes to the authorised publication process and timelines, a Substantial Modification would need to be submitted and authorised prior to implementation. It would be the responsibility of the sponsor and investigator to comply with the commitments made, in the same way as they must comply with other parts of the clinical trial and its authorisation(s). As this process is in line with normal practice of protocol writing and change management, the additional administrative effort would be manageable for all parties concerned, including Member States and its regulators. Such a firm commitment to staged release of relevant Phase 1 information to the public will provide all stakeholders with information at the right time and assure the public of the presence and reliability of the EU database and its systems to monitor clinical trials. **Proposed change:** We propose to insert appropriate wording to that effect into the next version of the draft functional specifications.
89 Table 1	37	**Comment:** Article 80 provides that the “EU portal shall be technically advanced and user-friendly so as to avoid unnecessary work”. This is essential for making the clinical trial authorisation process more attractive than in other countries. User-friendly front-ends (see General Comments) should be available. The access to all parts of the portal should be granted without requirement for the successful training (as it is currently required for EudraVigilance and XEVMPD, for example). The United Kingdom IRAS system has shown that this is possible. A comprehensive handbook should be available for users. EudraVigilance, where a handbook is only available when you attend an official training, is not an example to be followed.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change: Requirements: The Agency to ensure that the EU portal is user friendly. Legal Basis (Art): Article 80
89 Table 1	41	**Comment:** There is no reference to the ability to request an appeal. NOTE: Functional requirement 3.8 in Table 2 does refer to the need for a MSC to overturn a decision based on an appeal.
89 Table 1	41	**Comment:** EU clinical trial portal and EU database activities and requirements: The following requirement, under the responsibility of the Sponsor, is missing: submit a summary of the results of the clinical trial (legal basis, Article 37). The table covers the submission of “CT results intermediary data analysis” and “Submission Clinical Study Report” but seems to be missing the summary of results.
89 Table 1	42	**Comment:** Unless the language selected by the MS will not be pre-defined as a default, please consider adding a new requirement that would allow for the language selection pursuant to Article 26.
89 Table 1	42	**Comment:** Please consider adding Art 14 (7), MSC, Article 14(8).
89 Table 1	42	**Comment:** Please consider adding Article 84, The Agency, Article 81 (1).
89 Table 1 Req. 1	39	**Comment:** Req. 1: For on-going trials Sponsor/applicant will be required to link the EU trial number to the EudraCT number This assumes that once the portal is live activities for on-going trials will be maintained in both the EudraCT database and the EU database and those new trials will only be the EU database. Is this the case? The stakeholder for Requirements 1 to 8 is identified as the Sponsor but one or more of these activities may be delegated to a CRO or other organisation. How will the system accommodate this?:
89 Table 1 Req. 1/2	41	**Comment:** Include the step of the sponsor´s proposal of the Reporting member state as part of the submission on the initial CT application.
89 Table 1 Req. 1-8	41	**Comment:** Description of the role of the sponsor: Sponsor to submit an initial CT application, substantial modification or an additional MS in a CT/Conduct of the trial, supervision by the sponsor. **Proposed change:** To submit an initial CT application, substantial modification or request an additional MS in a CT/Conduct of the trial, supervision by the sponsor.
89 Table 1	21	**Comment:** Submission of a restart 38(2) missing. **Proposed change:** Add 38(2)

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Req. 3		
89 Table 1 Req. 3 Reg. 7-8	29	**Comment:** Requirements 3, 7-8 (sponsor role): it shall be more transparent that submissions as per these requirements may also take place after the end of the trial. **Proposed change:** Text of requirements 3.7-8 shall include "… including after the end of the trial".
89 Table 1 Req. 3	42	**Comment:** Please add Article 38(2) because it deals with the substantial modification, and consider adding Article 11.
89 Table 1 Req.4	8	**Comment:** "Reporting" MS instead of Reference Member State. **Proposed change:** Reporting Member State.
89 Table 1 Req. 4 Req. 12	21	**Comment:** Missing RFI on corrective measure if applicable. **Proposed change:** Add Art 77(2).
89 Table 1 Req. 5	16	**Comment:** The text is not very clear regarding inspection reports. It should be made clear that this information is confidential and can only be shared among the MS, not to other sponsors. In addition, it should be made clear that these reports will not be published in the public access domain.
89 Table 1 Req. 5	41	**Comment:** The wording is different from the Regulation which implies that only inspection reports pertinent to the Clinical Trial need to be uploaded - this appears to expand the scope.
89 Table 1 Req. 6	1	**Comment:** It should be clearly defined what might constitute AN UNEXPECTED EVENT.
89 Table 1 Req. 6	36	**Comment:** End of Trial in the EU should be automatically populated with the End of Trial date in the last EU Member State.
89 Table 1 Req. 6	41	**Comment:** Start of clinical trial - Article 36(1).

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change: Start of clinical trial in each MSC First visit of the first subject – Article 36(2) **Proposed change:** First visit of the first subject in each MSC End of the recruitment – Article 36(3) **Proposed change:** End of recruitment for each MSC Re-start of recruitment – Article 36(3) **Proposed change:** Re-start of recruitment for each MSC.
89 Table 1 Req. 7	8	**Comment:** There is a need to add also the submission of summary of results within 1-year after the end of the trial.
89 Table 1 Req. 7	39	**Comment:** Req. 7: Submission of CT results - System should allow submission of the standard summary and the laypersons summary. Depending on the timing of the results submission system will need flexibility for CT results to be provided by Sponsor/applicant (i.e. CRO) / MA applicant or other organisation.
89 Table 1 Req. 7	41	**Comment:** Submission of CT results, CSRs and intermediary data analysis. It has to be made clear that business rules are needed so that interim analysis results are not made public until after the completion of the trial and authorisation of a product for marketing, as this could prevent the use of the trial for regulatory use. This approach is consistent with the provisions for submission and publication of CSRs only after authorisation for marketing in Article 37(4), with Article 81 4(b) of the Regulation and as Comment acknowledged under policy 070. In addition, for any publication the particular status of Phase I studies needs to be taken into consideration, as Comment acknowledged under Point 5 in COM Guideline 2012/ C 302/03.
89 Table 1 Req. 8	8	**Comment:** Please mention the sponsor as stakeholder for this requirement N°8.
89 Table 1	10	**Comment:** Any changes made should be immediately advised and updated in the portal so that a complete change history can be available at any time.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Req. 8		**Proposed change:** Just tell “Update any changes to the clinical trials”.
89 Table 1 Req. 8	41	**Comment:** Can safety information for a given drug be submitted at a “program level” in a single step (e.g. a change in IB for all protocols that involve that same medication)? A system that would allow reporting safety information of a drug that affects several protocols in a single step would simplify the process significantly for all parties involved.
89 Table 1 Req.9	5	**Comment:** This requirement is assigned to “Applicants (marketing authorisation)” in the first column. However, the referenced article 37(4) of EU Regulation 536/2014 assigns this responsibility to the sponsor. Please clarify.
89 Table 1 Req. 9	21	**Comment:** All sponsors need to submit summary of results Article 37(4) Paragraph 1; In addition the MAH need to submit the CT report. **Proposed change:** Add to Req. 9 submission of summary of results
89 Table 1 Req. 9	31	**Comment:** The document refers to the requirement of stakeholders who are submitting the study for a marketing authorisation to submit a Clinical Study Report. There does not appear to be any reference the requirements for trials not undertaken for marketing authorisation to upload a summary of the results (as specified in Annex 4 of the Clinical Trial Regulation) which includes a lay summary for all trials. **Proposed changes:** Functionality to upload a summary of the results (as specified in Annex 4 of the Clinical Trial Regulation) which includes a lay summary for all trials needs to be provided and the distinction needs to be made from the end of trial report submitted for marketing authorisation.
89 Table 1 Req. 9	39	**Comment:** Req. 9: Depending on the timing of the study report submission system will need flexibility for CSR to be provided by Sponsor/applicant/CRO/ MA applicant or other organisation.
89 Table 1 Req. 10	16	**Comment:** The table is only addressing the concerned Member State (cMS/MSC) so it seems as if the reporting MS is missing here, or do the same requirements apply to the reporting Member State (rMS) as well as to the cMS? If yes, it must be made clear here.
89 Table 1 Req. 10-16	16	**Comment:** General comment on inclusion of Ethics Committees: Regarding the member states level, it should be clarified that National Competent Authorities (NCAs) as well as Ethics Committees (ECs) have access to the Portal/ Database. Ethic Committee members should be added as new category of stakeholders. Indeed Recital 18 mentions the cMS responsibility in organizing the EC assessment but in many instances EC opinion is mentioned as a prerequisite (art 4 ; art 8.4 ; art 14.10 ; 19.2 ; 20.7 ; 23.4 ; 44.3). The situation where an EC refuses to grant approval shall be part of the functional specifications. It is indeed to be understood from table 2 that the different functional specifications concern both the NCAs and the ECs (as per column

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		header 4). We propose to clarify earlier in the document, e.g. in table 1 under MSC that the respective roles refer to both NCAs and ECs. Having the EC directly accessing the applications is the key to ensure smooth functioning at the MS level. But also we think this should be clarified as the involvement of the NCAs and the ECs is foreseen in ICH-GCP (E6) Guidelines – and to be in line with ICH-GCP must be respected also in this draft for the functional specifications.
89 Table 1 Req. 10-16	41	**Comment:** General comment on inclusion of Ethics Committees Regarding MS, it should be clarified that National Competent Authorities (NCAs) as well as Ethics Committees (ECs) should have the opportunity to have access to the Portal/ Database. Ethic Committee members should be added as a new category of stakeholders. Indeed Recital 18 mentions the MSC responsibility in organizing the EC assessment but in many instances EC opinion is mentioned as a prerequisite (art 4 ; art 8.4 ; art 14.10 ; 19.2 ; 20.7 ; 23.4 ; 44.3). The situation where an EC refuses to grant approval shall be part of the functional specifications. EFPIA proposes to clarify earlier in the document, e.g. in table 1 under MSC that the respective roles refer to both NCAs and ECs. Having the EC directly accessing the applications is the key to ensure smooth functioning at the MS level.
89 Table 1 Req. 11/13	16	**Comment:** Seems as if the preliminary AR that is prepared by the rMS and forwarded to the cMS after day 26 is missing here. This should be mentioned as separate action (see Article 6 (5) of the CTR).
89 Table 1 Req. 11/13	41	**Comment:** The preliminary AR that is prepared by the rMS and forwarded to the MSC after day 26 is missing. This should be mentioned as a separate action (see Article 6 (5) of the CTR).
89 Table 1 Req. 12	21	**Comment:** Initial application missing article 41 (modification of AE recording and reporting) Also missing article 36, 37, 38, 42, 43, 44, 53, 54, 55, 77 (with no restrictions)“ **Proposed change:** add article 41, 36, 37, 38, 42, 43, 44, 53, 54, 55, 77
89 Table 1 Req. 12 Req. 14	21	**Comment:** RFI could also happen for surveillance of a CT during gits life cycle and for safety reporting. These covered articles are moved to workspace (3.4 communication between MS and sponsor) which can only be accepted if this part of the workspace is within audit, while workspace is with regulation and outside public (article 81). **Proposed change:** see below
89 Table 1	22	**Comment:** Validation should be addressed uniformly across all member states, instead of letting the member states address validation individually. The establishment of validation procedures for the portal will streamline and guarantee

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Req. 12		data quality and integrity.
89 Table 1 Req. 14	21	**Comment:** Art 77(2) is RFI not a notification **Proposed change:** delete here and add to Req. 4 and 12
89 Table 1 Req. 14	40	**Comment:** Missing Legal Basis: Article 18.4b (for Part I), Article 20.5 (for Part II) **Proposed change:** To add this legal basis to document (and to Req. 14)
89 Table 1 Req. 14	41	**Comment:** Req. 14 needs to include the requirement for a detailed justification to be recorded "Where a Member State concerned disagrees with the conclusion on the basis of the second subparagraph, it shall communicate its disagreement, together with a detailed justification, through the EU portal, to the Commission, to all Member States, and to the sponsor."
89 Table 1 Req. 15	22	**Comment:** There should be a consolidated plan and project for planning, conducting and reporting of Member States Inspections. Since this an EU Portal, an EU inspection efforts with MS input seems reasonable with results publicly available if allowable by regulation.
89 Table 1 Req. 18	15	**Comment:** Once something is made public it cannot be redacted. Does the document need to define how the confidentiality decisions will be made to ensure details are made public in a timely manner? Please also reference Policy 70: European Medicines Agency policy on publication of clinical data for medicinal products for human use.
89 Table 1 Req. 18	35	**Comment:** The portal should give a statement describing the procedures adopted for ensuring data protection/confidentiality/privacy including duration of storage of personal data for the user of the EU portal and the EU database. This sentence gives much room for interpretation and the official path and the entitled personnel to justify an overriding public interest in disclosure should be announced. Commercially information on interventional trials with medicinal products with marketing authorisation shall be publicly accessible.
89 Table 1 Req. 18	35	**Comment:** This sentence gives much room for interpretation and the official path and the entitled personnel to justify an overriding public interest in disclosure should be announced. Commercially information on interventional trials with medicinal products with marketing authorisation shall be publicly accessible.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
89 Table 1 Req. 18	36	**Comment:** Protection of personal data and commercially confidential information should be achieved by flagging the document as confidential without the need for redaction of parts of documents submitted in the initial clinical trial application or substantial modification.
89 Req. 19	29	**Comment:** The Agency shall be the controller in the sense of data protection framework (and the database will contain the personal information on clinical trial sponsors, applicants and other contact details of individuals (not patients) **Proposed change:** Text of requirements 19 shall include “Compliance with applicable data protection framework”.
90-95 134 Table 2 1.1	31	**Comment:** User access management refers to the system enabling MS and the Sponsor to create and log on with their own credentials, administer their own group, assign roles, enable electronic signatures etc. and user registration and authentication. As discussed at the stakeholders meetings, academic sponsors usually consist of very few individuals and most sponsor activity is delegated to a third party (e.g. clinical trials unit or clinical research organisation). **Proposed changes:** It is therefore imperative that, 1) more than one person at the sponsor’s level has high level permissions to create and manage the user groups; 2) all activity for a trial can be easily delegated to a third party. The delegation of numerous individual tasks would be extremely laborious and time consuming and many academic sponsors will not have the man power to undertake this role. Hence it should be possible for a sponsor to delegate all tasks easily and simultaneously while maintaining read-write access themselves. This is unless it is envisaged that the “super user” resides in an organisation other than the sponsor’s office in which case I would be concerned if there was no verification system in place to check that that third party has been given approval to create the trial in the database on behalf of the sponsor.
91-108	16	**Comment:** For the user groups please note that as a large number of users can be established by a sponsor or by an MS, it must be easily possible to include as many users as needed with clear “working packages”. Also this section raised questions on how this should work on the national levels. The review of the national part could, for example, be coordinated by the national NCA, while the lead and all participating ECs are included in the User Group. The national ECs are not defined as a separate stakeholder and must therefore be integrated over the MS. But this needs to be addressed also in the functional specifications – if not and national systems will not work properly, the whole EU-CTR might fail to result in a strengthening of Europe as a clinical trials location. In this context it would also be important that the national ECs - if they are allowed as part of the User Group of the MS, also get access to the pharmacovigilance database to view the SUSARs directly for the trial they are working on/assessing on the national level.
92	9	**Comment:** ACRO agrees that secure electronic submission for the stakeholders is an essential prerequisite. Other than account controls, the consultation document includes little information on security measures that will be applied to the

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		network. **Proposed change:** Include greater detail on planned security measures.
92	39	**Comment:** The public are defined as a stakeholder in Table 1 – This line implies that they will be submitting information. Clarification required that the public will not be making electronic submission to the system.
93	37	**Comment:** Besides enabling MS and sponsors to create and log on with their credentials, other stakeholders should also be addressed in this sentence (EC, Agency, MAH). **Proposed change:** User access management system to enable MS, EC, the Agency, sponsors and MAHs to create and log on with their credentials (username and password), administer their own user group, assign roles, enable electronic signatures etc.
93-94	22	**Comment:** CROs acting on behalf of the sponsors should have their own access – not only those delegated down from the sponsor. This CRO specific number can be mapped to the relevant trials the CROs are contracted to work on. Thus, CROs would not have to log on and off with various sponsor numbers to perform their responsibilities. **Proposed change:** …to enable MS, sponsors and CROs to create … Electronic Signatures – is this the legally binding equivalent signature. If these are then the electronic signatures requirements should be specified cf Annex 11 clause 14 requirements. **Proposed change:** Specify the Electronic Signature requirements and functional specifications.
93-95	29	**Comment:** Sponsors may delegate tasks to other users, text of the like 93 do not express this. Similarly it does not take into account the co-sponsorship. **Proposed change:** User access management system to enable MS and sponsors to create and log on with their credentials (username and password), administer their own user group, assign roles, enable electronic signatures etc.; it shall enable sponsors to delegate any of their tasks and responsibilities to other users, including from different organizations and shall take into account co-sponsorship arrangements allowing each co-sponsor to fulfil its role and responsibilities".
93-95	39	**Comment:** Clarification required on whether the public will be required to register to access the database? Line 1.1 in table 2 state that the system will limit access and rights to authorised users. . If public have to be an authorised user (and even if they don't) will companies be able to obtain a list of who is accessing the database. Would a member of the public have to state any company affiliations? **Proposed change:** User access management to allow members of the public to log on to the system.
93-95	39	**Comment:** System required flexibility to allow applicant (in cases where the sponsor is not the applicant) to create and log on etc.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change: User access management system to enable MS and sponsors/applicants to create and log on with their credentials (username and password), administer their own user group, assign roles, enable electronic signatures etc.
93-95	41	**Comment:** User access management system suggests that MS and sponsors are the only groups to be able to log on with their credentials. Sponsors might have delegates (e.g. CROs) who would equally need access rights to the system. **Proposed change:** User access management system to enable MS and sponsors and their delegates to create and log on with their credential.
94	20	**Comment:** For security reasons a three factor login with the adoption of, e.g. token, should be considered.
96-97	15	**Comment:** 3rd bullet refers to '… retrieval, maintenance and disposal of records…'. How will the version controlling work?
96-97	22	**Comment:** The phrase "disposal of records" should also include applicable metadata. Also, during the stakeholder meeting on 30 September 2014 it was stated that all records will be kept for an unlimited time, and this is also documented in section 4.2 on page 25 of the document. This seems contradictory to this statement on page 10 about disposal of records. Please clarify. Therefore data & documents will not be disposed of, but there should be a mechanism for "quarantining" or archiving superseded information.
97	39	**Comment:** Disposal of records of clinical trial information is identified as one of the requirements of the system. Please clarify what documents would be disposed of and why?
98-102	32	**Comment:** The fourth bullet point on timelines could be expanded. Add: 'Regulation 1182/1971 will be taken into account when calculating timelines' (see comments above and addendum below).
101	21	**Comment:** Shorten timeline – can only be performed with direct link to alert MSC. **Proposed change:** "… to shorten time line and alert MSC…"
103	15	**Comment:** The document does not discuss submission standards. Should the document and system audit, confirm that the information captured by the EU Portal and EU Database is sufficiently standardised so that the public and developers can make sense of it.
103-104	20	**Comment:** Need to ensure data privacy protection and protection of IP. **Proposed change:** Download functionalities based on adherence to data privacy and confidentiality principles as outlined in Regulation 536/2014.
103-108	22	**Comment:** When data are kept for an unlimited time, how is accessibility of these data guaranteed, considering

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		potential software changes and potential changes in the functionality of the portal? This should also be part of the audit specifications.
106	20	**Comment:** It is unclear which "current" functionalities are referred to. As the system is very different from today's EudraCT and EU registry, we understand that a new system is being developed. If it is meant to highlight the fact that the system must be sufficiently flexible to allow evolving according to scientific and business needs, this must be clearly stated.
113-114	16, 18	**Comment:** In lines 113 / 114 it is mentioned, that the database will be publicly available – that means for any interested person or institution. Nevertheless the authorization procedure has to be clarified i.e. conc. confidential data. The same is true for the so-called authorised user.
114	22	**Comment:** Confidentially of the data as outlined in the above table is important. The functional specifications must give the sponsors the assurances that their confidential documents and data are protected, and still protect person identifiable information of subjects in those trials. This goes hand in hand with establishing data quality and integrity principles.
115-127	41	**Comment:** It is good to set deadline for different project milestones. The importance of the provisions is well understood as per Regulation 536/2014. Given the experiences with the discussion on transparency provisions under the new Policy 070, however EFPIA is of the opinion that it is of greater importance to have ensured sufficient stakeholder input into transparency provisions as opposed to a "short public consultation". Moreover, the deadline March 2015 is inconsistent with the overall deadline for specifications indicated on page 1. **Proposed change:** Remove time frame in line 127. "This process will need to be completed at the latest by March 2015".
117	32	**Comment:** The sentence "…EU Portal and EU Database to be audited" should be clarified. Add: 'according to Article 82.1 of the Regulation 536/2014'.
122-127	21	**Comment:** We agree that the development of the additional text should be handled in same way as this document. That means that the text is set up by the agency in collaboration with the MS and the Commission. The time for public consultation should be long enough to allow involved parties an adequate approval. **Proposed change:** This additional text and additions to Table 2 will become integral parts of the Functional Specifications and will not change the existing text in this document. This additional text and table section will be set up and agreed via the same bodies as the current Functional Specification document, that is to say to set up review and agreement within the Expert group in collaboration with the Member States and the European Commission, an adequate short public consultation, then consultation of the European Commission and the Member States on the final document

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		and endorsement of the EMA Management Board followed by sign-off by the EMA Executive Director and publication. This process will need to be completed at the latest by March 2015.
124	36	**Comment:** Although it is important for the IT project to progress at the appropriate pace, it is important that all stakeholder views are heard and considered. We suggest removing the wording “short” before public consultation.
125	20	**Comment:** We understand that the transparency requirements will be added to the functional specification at a later date. We would like to highlight that the requirements should be developed in consistency with the newly established EMA Policy 70 to avoid any confusion or inconsistency. Experience from the EMA stakeholder consultations should be taken into account to ensure a balanced and fair system that supports the objectives of the regulation.
127	36	**Comment:** We suggest deleting this statement: “This process will need to be completed at the latest by March 2015“. It is of importance to have the ‘right’ and considered functional specifications to support the transparency requirements.
128-130	22	**Comment:** Auditing system performance, scalability and security is important; all three of these attributes must be fully vetted during the development of the portals and the design of the architecture to guarantee effectiveness. With the numerous reports of companies being “hacked”, the commission must guarantee the best security precautions are being built into the system and not added on at a later date.
129	41	**Comment:** Security is a key requirement and must be described with respect to all specifications in the document as a system requirement, for instance, under paragraph 4.2 **Proposed change:** Add the following text: The specifications should be sufficiently detailed especially regarding access control and security as these forms the basis for the audit qualifying the system for implementation.
129-130	41	The system should ensure there are checks on valid users after set periods of time (by all parties) to prevent that users that are no longer assigned to a given protocol have access privileges.
134 Table 2	1	**Comment:** Just like in the rest of the document, the role of patients’ organization is not listed. Consultation takes place between many stakeholders, except patients’ organizations (unless of course we are listed under public consultation).
134 Table 2	10	**Comment:** As per the Draft functional specifications the security controls features only the “super user” (i.e. Sponsors) will have the primary access to the database and the right to appoint other users in order to assign them work packages. Could a CRO/regulatory consultant company based in EEA, as one of the stakeholders, receive “super user” rights on behalf of the Sponsor? **Proposed change:** Enable the identification of a super user for each trial at the sponsor/its representative level and for each MS.
134	10	**Comment:** In order to become a registered user (i.e super user) does one need to be certified through a specific

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2		training process (similar to accessing EV) or the EU portal and EU CT database will be sufficiently user friendly (similar to EudraCT CTA form) to allow any stakeholder representative to use it without specific certification?
134 Table 2	21	**Comment:** In Column header it is distinguished between MS/EC. As of regulation integration of EC/NCA is up to MS. Access will be provided via user roles granted by super users. Same is true for sponsor/applicant. Access will be provided via user roles granted by super user **Proposed change:** harmonise
134 Table 2	25	**Comment:** Specifications regarding serious breaches should be considered. There should also be a built-in possibility for whistle blowers to report concerns. This is not a formal procedure for trained users and should be a simple procedure. It is unclear whether it is ensured that delegations from sponsors to CROs are visible for member states, for instance if a CRO is reporting serious breaches, SUSARs etc. on behalf of a sponsor.
134 Table 2	37	**Comment:** Sponsor / Applicant should be supplemented by "MAH" The MAH would submit documents/data as well (2.2). MS / EC should be supplemented by "The Agency" The Agency is defined as a user as well (see 1.2, for example).
134 Table 2 1.1	5	**Comment:** Please clarify what is meant with "…a super user for each trial at the sponsor level…": Will there be one sponsor super user per trial (i.e., there may be several independent sponsor super users, each responsible for a certain set of trials) or will there be one sponsor super user per sponsor, as indicated by "sponsor level"? Please consider clarifying the wording. **Proposed change:** Enable the identification of a super user for each trial on the sponsor's side and for each MS.
134 Table 2 1.1	5	**Comment:** It should be possible to change the sponsor super user for a trial. Please add this requirement.
134 Table 2 1.1	8	**Comment:** authorised users only – Who will be the authorised users precisely? Will there be a limited number of authorised users per sponsor / MS? This needs to be clarified. User and super user roles to be clarified & provided
134 Table 2 1.1 1.2	9	**Comment:** Point 1.1: "The users of the EU portal will have access to workspace functionalities according to their user's role(s)" This section states that the Users of the EU Portal will have access to Workspace functionalities according to their User's role, so the system will display the appropriate data. It will be important for CROs to have full visibility on project

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		activities when they are responsible for the conduct of full-service scope. Point 1.2 “Enable all super users to administer and manage their group of users and assign roles/work packages to users” The roles/work packages permitted by the system should be sufficiently precise that they do not impact the principle of Article 71 of Regulation 536/2014 that a sponsor may delegate any or all of its tasks. Assignment of CRO super users would enable improved administration of CRO users who are delegated responsibilities by Sponsor Users. ACRO recommends that such an option is possible if CROs are expected to be able to extract information from the reports within the system. The super-user is permitted to assign back-ups for different tasks. After this, it is important that the assigned registered user is immediately able to perform assigned tasks, without incurring any delay e.g. for processing/activation. Any such delay could be a challenge in an emergency e.g. where an assigned user and any previously assigned back-up are both unavailable. No allowance is made for appointing more than one super-user per trial. An additional super-user will allow for a given super-user to act as back-up on a particular trial. The guidance allows for a given individual to act as super-user per trial. **Proposed change:** Tasks should not be grouped together so that the sponsor is limited to delegating only groups of tasks/work packages relative to the portal/database and is unable to select specific individual tasks that will be delegated to a third party. The length of time permitted for the super-user to assign a task to a registered user should be minimised. The possibility of appointing more than one super-user should also be considered. Super-user status at the sponsor level would be beneficial giving single point access to all trials for a given sponsor. Similarly, super-user status at the CRO level would be beneficial giving single point access to all trials assigned to a given CRO. This should allow, within a single search, identification of all trials associated with that sponsor/CRO (see also line 137, 3.10).
134 Table 2 1.1	14	**Comment:** The login for MS users according to their roles has to consider the competent federal state authorities which are responsible for the supervision of clinical trials. In addition to that also the federal agencies (BfArM and PEI), which are responsible for the approval of clinical trials and for the marketing authorization, have to be taken into account regarding login.
134 Table 2	15	**Comment:** The concept of the 'super user' implies two distinct responsibilities which may conflict. Firstly, they are the accountable individual (senior staff) within the applicable organisation and secondly they are an administrator assigning

Line no.	Stakeholder no.	Comment and rationale; proposed changes
1.1 1.2		user roles and updating address details etc. within the system (less senior task). It may work better if the super user has an approval role, rather than a doing role, in the system, e.g. approve user role assignments and street address changes, rather than make the changes directly. **Proposed change:** clarify the expectation of the super user. If the super user is accountable then this should be a local system owner who would then not be a local system admin. Perhaps introduce a role of local system owner?
134 Table 2 1.1	16	In Table 2, section 1.1 the super user is mentioned. This position has to be clearly defined in more details in advance for all levels (EU, national authorities, sponsor, etc.), otherwise it will not be possible to maintain important timelines (Ethical review board etc.). As a clear definition is missing, it will be hard to fully foresee the possible outcomes. Also it must be clear that multiple super users might be needed at MS-level and at sponsor level (e.g. in case of absence). This is not clearly addressed in this section. In the last paragraph the text is mentioning to “allow single logging for MS users”. This should also be possible for sponsors.
134 Table 2 1.1	18	**Comment:** A super user is mentioned. This position has to be defined in advance for all levels (EU, national authorities, sponsor, etc.), otherwise it will not be possible to maintain important timelines (Ethical review board etc.).
134 Table 2 1.1	20	**Comment:** Allow sponsors single logging to ensure access to workspace and Medicinal Product dictionary when preparing their applications. Automatic log-out of the use after 15 min of inactivity should be implemented.
134 Table 2 1.1	21	**Comment:** The MS shall have access to all CTs in CT IT system (portal, database, workspace...) not only to the ones they are concerned with MSC. This is essential for assessing new CTA as well as surveillance of CTs including cooperation in assessing safety reporting. Please add. At least read and download (part I and all surveillance tasks) by super user and super user can assign rights according to user roles. **Proposed change:** Enable the identification of a super user for each trial at the sponsor level and for each MS. While MS have access to all CT in the system independent if they are concerned with or not.
134 Table 2 1.1	21	**Comment:** There is more than one EVdatabase **Proposed change:** EudraVigilance databases
134 Table 2 1.1	22	**Comment:** This Detail needs to also included security: “Enable the identification of a super user for each trial at the sponsor level and for each MS.” What type of additional privileges does the super users and MS need vs. a normal user. There should be clear definitions what is granted to whom and why.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Also, include CRO level super users and users. For reason of back-up and continuity of use for all involved parties it might be better to have 2 or more super users trained and registered. Please include withdrawal of permissions for users (& super users) and who will determine this and according to what rules and what notifications to all parties concerned? **Proposed change:** Add "withdrawal" of permissions to specification.
134 Table 2 1.1	22	**Comment:** "Issue single logging for MS". What does this mean?
134 Table 2 1.1	23	**Comment:** 1.1 User registration and authentication : Add a control to check that users are allowed to access to the EU portal before giving them login, password and role. This verification should be made for example by the super user.
134 Table 2 1.1	26	**Comment:** "Allow single logging for MS users" (General functional specification of the draft EMA document) could be problematic. A single logging for MS users might bring some difficulties on accessing the portal. Different stakeholders, namely Competent Authority and Ethics Committees, from the same Member State, should have different logging. This would avoid any misunderstandings or mistakes. The future cooperation between Competent Authority and Ethics Committees involved in clinical trial assessment is somehow unclear, at least for some member states. **Proposed change (if any):** Different logging for stakeholders from the same Member State (i.e. Competent Authority and Ethics Committees)
134 Table 2 1.1	28	**Comment:** We would like the EMA to define 'super user'. Within this definition we would like clarity over how the super user is assigned, especially in the instance of co-sponsorship, and the responsibilities of a super user.
134 Table 2 1.1	28	**Proposed change:** Change 'enable the trial number' to 'enable the unique EU trial number'.
134 Table 2 1.1	29	**Comment:** "The system will limit access and rights to authorised users only." It is essential to clarify the term of "authorized" to avoid that the process of authorization becomes a new barrier to research. **Proposed change:** "The system will limit access and rights to authorised users only. The authorisation process shall be easy and user friendly aiming to minimise administrative burden".

Line no.	Stakeholder no.	Comment and rationale; proposed changes
134 Table 2 1.1	29	**Comment:** "Enable the identification of a super user for each trial at the sponsor level and for each MS" The existence of different types of sponsors shall be taken into account: organization versus individual. For sponsors-persons (physical person), user and super user are the same. For sponsors – organizations it shall also be taken into account that in some of EU countries an academic organization does not need to be incorporated nor to be a moral person (Nordic countries e.g. Denmark). The process of super user identification for these organizations shall take into account the fact that they are not a moral person. Suggestion – given the heterogeneity of legal frameworks in EU, instead of a request of documentation, can each sponsor be "confirmed" by the MS of its registered office? For example, AFMPS would confirm EORTC is having the appropriate status to be the sponsor of non-commercial clinical trials (so that when we run a clinical trial in Poland, Polish authorities will not seek any additional confirmation / identification). Such a system can be put in place for sponsors – organisations (whether moral person or not), not for sponsors – persons (taking the responsibility as single individual). Co-sponsorship needs to be taken into account. **Proposed change:** "Enable the identification of a super user for each trial at the sponsor level and for each MS. The super user identification process shall be easy and user friendly aiming to minimise administrative burden; there may be cases where the user is also a super user; super user identification shall take into account co-sponsorship arrangements allowing each co-sponsor to fulfil its role and responsibilities"
134 Table 2 1.1	31	**Comment:** We are unclear on the definition of a 'super user' in the context of this document. It is also unclear how a super-user would be defined in the context of co-sponsorship as described in the Clinical Trial Regulation.
134 Table 2 1.1	31	**Comment and proposed changes:** Last row text states "Enable the Trial Number to be …." Please clarify - does this mean EU CT number sometimes referred to as EU trial number (e.g. page 26, No 4.5)? If so, terminology needs to be consistent.
134 Table 2 1.1	32	**Comment:** In the column Details: "Enable the identification of a super user…". Replace a super-user with 'one or more super-users'.
134 Table 2 1.1 1.2	34	**Comment:** It appears that sponsor super users are only at a clinical trial level rather than an organizational level. A user role / permissions setup similar to that which is provided on ClinicalTrials.gov PRS would be preferred for greater control at a Sponsor organizational level rather than at a single person level, albeit a "super user" level.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
134 Table 2 1.1	36	**Comment:** Can we assign more than one super user per trial? Can the sponsor super user see information of all super users and trial information under their remit? What about an administrative role for all trials conducted under a sponsor?
134 Table 2 1.1	37	**Comment:** The role of the “super user” should be defined. Who is entitled to be a super user? Is the essence of the super user that it is the only entity allowed to enable / disable other users or does it have other functions in addition to a non-super user?
134 Table 2 1.1	37	**Comment:** The sponsor should be able to replace the super user and any other user (without getting approval from the affected [super] user), because super users and users might suddenly disappear (change jobs, are replaced by the sponsor because of malperformance or die). **Proposed change:** Add in “Details”: Enable replacement of the super users and any other user.
134 Table 2 1.1	37	**Comment:** When a sponsor ceases to exist or merged with or is absorbed by another sponsor, and the assets for the clinical trials are transferred to another sponsor, then the new sponsor must be able to get access to the trial data of the former sponsor. The new sponsor must be able to replace the former super user with a new one. This replacement must be protected against entities which make false claims of being the new sponsor. **Proposed change:** Add to “Details”: Enable replacement of a sponsor by a new owner of the assets of a former sponsor. Enable a new sponsor to confirm or terminate assignment of a sponsor’s legal representative and/or contact person and/or CRO. Enable the sponsor’s legal representative to confirm or terminate legal representation in case of a sponsor change (the former legal representative might not be willing to represent the new sponsor).
134, Table 2 1.1	37	**Comment:** When the sponsor is located outside the EEA, at which level should the “super user” be defined: At the level of the sponsor or at the level of its legal representative? This links back to the need of more clarity regarding the super user (see also General Comments).
134 Table 2 1.1 1.3 2.1 2.2-2.4 2.6	39	**Comment:** 1.1: Specification should allow the sponsor to be amended 1.1: Specifications should allow the sponsor super user to be amended 1.3 Will the auditing indicate if the record was accessed by a member of the public? 2.1: Specification should allow sponsor or delegate(i.e. pv provider) to submit information 2.2 Validation rules are referenced. Have the validation rules been defined? Do they relate to the content or the format of the documentation? 2.3/2.4 Are the reasons for deletion/withdrawal visible to the public? 2.6 The portal interface should be designed so that the sponsor/applicant can make a single choice at the start of ‘log –

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		in' regarding the language used that log-in.
134 Table 2 1.1	41	**Comment:** User registration and authentication: A single sponsor super user linked to individual studies is not sufficient. Transparent user management by a sponsor requires an administrator at the sponsor level that would oversee all users for that sponsor and their roles for all clinical trials conducted by that sponsor. EFPIA proposes that the requirements allow for the assignment of multiple sponsor super user roles for each individual trial. Additionally, sponsors should be given a single login to ensure access to workspace and Medicinal Product dictionary when preparing their applications. More specifics on the concept of sponsor "Super User" role in Section 1.2 of Table 2 would be helpful.
134 Table 2 1.1	41	**Comment:** User Registration and authentication In Table 2, section 1.1 a super user is mentioned. This position has to be clearly defined in advance for all levels (EU, national authorities, sponsor, etc.), otherwise it will not be possible to maintain important timelines (ethics committees etc.). As this clear definition is missing, it will be hard to fully foresee the possible outcomes. Also it must be clear that multiple super users might be needed at MS-level and at sponsor level (e.g. in case of absence). This is not clearly addressed in this section. In the last paragraph the text states "allow single logging for MS users". This should also be possible for sponsors.
134 Table 2 1.1	41	**Comment:** User registration and authentication: If registration is expanded to public users, it should be required for them to sign up to get an access to the public domain and when they want to download clinical trial information. Information access and download should be subject to specific terms of use..
134 Table 2 1.1	44	**Comment:** User registration and authentication; the management of users can be a burden for Member States if there will be a super user for each trial at the Member State Level. Will MSs be responsible of managing Ethics Committee?
134 Table 2 1.2	5	**Comment:** Please clarify: The updates to the sponsor information by the sponsor super user for a trial will apply to all trials by this sponsor. If so, please add a requirement that the system will generate automated information to all super users of this sponsor when such changes are implemented.
134 Table 2 1.2	8	**Comment:** Enable all super users to administer and manage their group of users. – There is a need to clarify and give guidance on this aspect, i.e. any limited number of users per sponsor?

Line no.	Stakeholder no.	Comment and rationale; proposed changes
134 Table 2 1.2	14	**Comment:** The systems have to be able to filter the data according to federal state to ensure each federal state authority receives only the affected data (and not data of whole Germany).
134 Table 2 1.2	16	**Comment:** If the concept of the super user – user system should work, it must be clear that this might not be a single person. So the text should talk here about user or user groups. In addition, in the first line in batch 3 of the text the word “group” must be corrected to “group(s)” as this could be more than one group. What needs to be done in case the sponsor/or the super user changes during the conduct of the trial? It should be possible to have more than one super user per trial per sponsor/ MS.
134, Table 2 1.2	21	**Comment:** What is meant by MS requirements? ‘EMA to assign and administer super users for the regulatory network, according to the member state requirements, and the Commission.’ **Proposed change:** clarify
134, Table 2 1.2	21	**Comment:** The MS shall have access to all CTs in CT IT system (portal, database, workspace…) not only to the ones they administer. **Proposed change:** Enable MS super users to administer and manage their group of users and assign roles/work packages to users either per trial or per group of trials including all trials they administer if necessary. The assignment may be done by assigning several roles/work packages to a user. MS super users have access to all CTs.
134 Table 2 1.2	21	**Comment:** Reassigning a task should be possible. Add if not covered. **Proposed change:** Assigned tasks can be reassigned by super users.
134 Table 2 1.2	22	**Comment:** Include CRO level super users and users. **Proposed change:** “… enable to sponsor super user to update … and the CRO access rights …”
134 Table 2 1.2	28	**Comment:** Academic sponsors’ offices usually consist of very few individuals and most sponsor activity is delegated to a third party, for example, clinical trials units. It is therefore imperative that: more than one person at the sponsors level has high level permissions to create and manage the user groups that all activity for a trial can be easily delegated to a third party. The delegation of numerous individual tasks would be extremely laborious and time consuming and many academic sponsors will not have the man power to undertake this role.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		We would like the EMA to confirm that this will be possible under function 1.2.
134 Table 2 1.2	29	**Comment:** "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 of trials including all trials they administer if necessary." More clarity is needed to possible roles & work packages. It is understood that their number cannot be unlimited, but system shall be flexible enough to enable different types of collaborations (e.g. multi-sponsorship academic trials). **Proposed change:** ""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 of trials including all trials they administer if necessary. The system shall be flexible and take into account co-sponsorship arrangements allowing each co-sponsor to fulfil its role and responsibilities".
134 Table 2 1.2	36	**Comment:** Super users should be able to reassign roles and packages and also reassign super users in the event they leave the company and other persons are assigned their duties. It should also be possible to assign multiple users to the same role/work package. **Proposed change:** 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 of trials including all trials they administer if necessary. The assignment may be done by assigning several roles/work packages to a user and/or several users to a role/work package.
134 Table 2 1.2	37	**Comment:** Because the sponsor's legal representative shall be responsible for ensuring compliance with the sponsor's obligations, the legal representative has to have full access to the information to which the super user at the sponsor level has access, in case the super user and the legal representative can be different parties (to be clarified). **Proposed change:** Add to "Details": Grant the sponsor's legal representative full access to the information to which the super user at the sponsor level has access (in case legal representative and super user can be different).
134 Table 2 1.2	37	**Comment:** The roles of the sponsor and its legal representative are not fully interchangeable when it comes to more than one clinical trial. It should be clarified that a sponsor can assign one legal representative per trial and that the legal representatives can be different. For one trial, the legal representative of the sponsor "shall be the addressee for all communications with the sponsor provided for in the CTR. Any communication to that legal representative shall be deemed to be a communication to the sponsor", as article 74 says. **Proposed change:** Add to "Details": Allow sponsor to assign different legal representatives for each trial. Limit access of legal representative to the data set for a clinical trial and to those trials for which the legal representative represents the sponsor. Again, it must be clarified whether the legal representative is allowed to define a super user for each trial he is

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		responsible for or whether only the sponsor can do this. Allow the same entity to be assigned as the legal representative for different sponsors.
134 Table 2 1.2	46	**Comment:** The process for the transfer of super user accounts should be described (in case the super user changes). This transferring process should be fast and without administrative burden as companies cannot afford to lose time during a submission with tight timelines.
134 Table 2 1.3 2.3 2.4 3.13 4.1	15	**Comment:** Regarding the audit trail (1.3), what is retained in the audit trail following deletions covered in 2.3, 2.4, 4.1 and 3.13. Is this information kept? This may mean that the audit database becomes very large very quickly. **Proposed change:** Include in the document how the audit trail is impacted and accessed once these types of deletions occur.
134 Table 2 1.3	21	**Comment:** Experiences display that safety reports, serious breaches as well as information on inspections are reported after end of CT as well as reporting of CT. To ensure completeness of audit records this should be taken up. **Proposed change:** The requirement to create Clinical Trial audit records is to record the activities that were performed during the lifecycle of a CT from application to end of reporting and unlimited thereafter.
134 Table 2 1.3	22	**Comment:** Which clinical trial audit records are referred to? Is this the audit certificate(s) as included in the clinical study report? Or the date of each individual audit and/or audit report? Please clarify.
134 Table 2 1.3	25	**Comment:** The defined period from application to end of reporting is not sufficient. There could be serious breaches discovered later or pre-inspection activities, which need to be included.
134 Table 2 1.3	28	**Comment:** It is crucial that all changes made in the EU database are logged and we welcome the audit function. However, we are unclear whether recording 'activities that were performed during the lifecycle of a CT', encompasses all changes made by users to information in the EU database. We are aware that function 3.8 specifies that such changes will be tracked, but does not specify that they will be recorded. We recommend that the EMA revises that text on the detail of function 1.3 to make it clear that all changes made in the database, by any user, will be logged.
134 Table 2 1.3	32	**Comment:** "…during the lifecycle of a CT from application to end of reporting…" Add: 'in order for users to be able to follow the events'.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
134 Table 2 1.3	41	**Comment:** Audit record: We propose to specify which type of activities are audit tracked in the system and allow the sponsor to have access to the tracking capabilities for activities which were performed in the workspace.
134 Table 2 1.4	15	**Comment:** Regarding system performance and scalability, and the reference at line 30 to, "technically advanced", will the system be hosted in the cloud, e.g. Amazon AWS or similar architecture, where the system can be readily scaled as the system grows? **Proposed change:** Consider hosting within cloud based server services, e.g. Amazon AWS or similar, to be 'technically advanced' and for improved scalability as the system grows.
134 Table 2 1.4	16	**Comment:** When will the detailed requirements be available? Is a public consultation foreseen for the detailed requirements? How can the stakeholders provide input to the detailed requirements?
134 Table 2 1.4	45	**Comment:** Gross estimated "System performance and scalability" not defined. Nevertheless we propose to define a "System performance and reliability". **Proposed change:** System performance and reliability equal of above 99.5% uptime (a maximum of 44 hours downtime per year). Scheduled maintenaince works should be performed overnight or over the weekend whenever possible.
134 Table 2 1.5	37	**Comment:** Article 80 provides that the "EU portal shall be technically advanced and user-friendly so as to avoid unnecessary work". **Proposed change:** A new item should be added with the following entries: Functional specification: User-friendliness Sponsor/Applicant: Y MS/EC: Y Details: The access to all parts of the portal should be granted without requirement for successful official training. A comprehensive handbook should be available for the public. There should be a technical helpdesk for all users. Questions from users and answers from the helpdesk concerning technical features should be made publicly available. The independent auditors deciding on the user friendliness of the EU portal/database should involve individuals representing different stakeholders (large pharma companies, pharma companies which are SMEs, academia, CROs).
136 Table 2 2.x	21	**Comment:** Search in portal should be possible for users, like in workspace (3.10) **Proposed change:** Please add search in portal

Line no.	Stakeholder no.	Comment and rationale; proposed changes
136 Table 2 2.1 2.3	9	**Comment:** Point 2.1: "Sponsor to be able to submit information related to a new IMP and 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 of substance code can be granted." Some Sponsors will request that CROs conduct the uploading of new IMP information to the EU Portal. Therefore, such an option should be incorporated into the functionality of the system. **Comment:** Point 2.3: "Allow MS super user to request the deletion/withdrawal of an application/notification & provide a reason (e.g. duplicate). Allow such request to put the assessment on hold if applicable." Regulation 536/2014 does not include provision for an assessment to be put on hold. In the cited example of duplicate applications/notifications, is it foreseen that one or both assessments would be put on hold? What timelines would apply if such a hold were implemented? Additionally, to ensure traceability, accountability and an appropriate audit trail, there should be no deletions from the system. All alterations should be attributable and the reason for change recorded. **Proposed change:** Greater clarification is needed on the procedures for placing an assessment on hold, the circumstances in which this would be applied, how such a situation would be resolved and the timelines for resolution. Additionally, the reference to deletion of an application/notification should be removed, and the system should ensure that all alterations are attributable and the reason for change recorded.
136 Table 2 2.1	15	**Comment:** What information would be needed relative to a new IMP being obtained? Can an example be given?
136 Table 2 2.1	16	**Comment:** Could an EU MP number not be linked to multiple clinical trials because there are multiple trials running with the same IMP and thus multiple CT numbers could apply for one EU MP number, correct? If so please make this aspect clearer in the wording of this section.
136 Table 2 2.1	20	**Comment:** Explain what happens to provisional MP numbers for IMPs that do not receive a marketing authorisation.
136 Table 2 2.1	21	**Comment:** A new IMP is not per se a new substance; it might only be new formulation. Replace and by or/and. **Proposed change:** Sponsor to be able to submit information related to a new IMP or/and a new substance through the EU Portal and obtain
136	21	**Comment:** EU database must be structured in a way to allow for search functions concerning MP numbers and

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 2.1		substance codes to identify prior applications. **Proposed change:** Should be addressed in 'User Requirements´.
136 Table 2 2.1	21	**Comment:** Who is responsible for validating this entry to EV MPD? Who can perform corrections if needed? **Proposed change:** Needs to be clarified.
136 Table 2 2.1	21	**Comment:** Annex 2 isn't complete. **Proposed change:** An overview of all most the information submitted through the portal is provided in annex 2.
136 Table 2 2.1	28	**Comment:** The EMA should consider reviewing the Medicinal Products Directory with a view to making changes that will ensure data held in this directory are of a consistent and high standard. The directory would also benefit from the inclusion of Summary of Product Characteristics data. The EMA should clarify the process and timings for assigning provisional and final EU Medicinal Product (MP) numbers.
136 Table 2 2.1	40	**Comment:** It should be better to have active substance number (unique identification) before submission of the Clinical Trial Application.
136 Table 2 2.1	41	**Comment:** Support the recording and submission to the Medicinal Product Dictionary…: It should be made clearer that the intent is that an EU MP number is to permit linking between multiple clinical trials running with the same IMP.
136 Table 2 2.1	46	**Comment:** It is understood that there will be a direct linkage between the EU MP number and an EU CT number. In the second paragraph of the "Details" for FR 2.1 it is written that the request for an EU MP number should be linked to a specific EU CT number. Normally if a sponsor plans to conduct the first study with a new substance, he will first apply for an EU MP number for product in development (4th para in the same field) and then apply for an EU CT number. **Proposed change:** Rephrase the sentence to: "The request for an EU CT number should be linked to a specific EU MP number either in the medicinal product dictionary for an already authorised product or to a provisional EU MP number for a product in development."
136, Table 2, 2.2	13	**Comment:** "validation rules" are not specified **Proposed change:** to explain how validation is ensured, add rationale and explanation for rules
136	14	**Comment:** A general system of ´automatic notifications´, see general comment above, would allow the federal state

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 2.2		authority to receive notifications and information according to requirements 5, 6, 8, 15, 16 in a timely manner.
136 Table 2 2.2	21	**Comment:** In case of serious breaches an rMS need to be selected which is not mandatory the one of initial CT assessment. This needs to be taken care of. This holds true for safety reporting (ASR or/and SUSAR) too. **Proposed change:** Implementation of selection of rMS for serious breaches (and safety reporting) independent of rMS selection for initial CT will be given.
136 Table 2 2.2	22	**Comment:** Validation Rules need to be documented here since this is going to control the submission of documents and data. Please add them to the document/ audit specifications.
136 Table 2 2.2	40	**Comment:** Only the reporting Member State (RMS) may request additional info, but during TC was taken in account possibility of automatic generation of queries from other MS in case of failure of RMS.
136 Table 2 2.3	16	**Comment:** The wording is focussing on the cMC, is this also relevant for the reporting member state? If yes, this must be specified in the text.
136 Table 2 2.3 137 Table 2, 3.13	20	**Comment:** It is noted that system administrators can alter or delete records. It is not clear what the safeguards are to prevent fraudulent activities by system administrators. Sponsor/MS should be notified by the EU portal automatically about incoming correspondence – it should be avoided that Sponsor/MS needs to check every day for incoming information.
136 Table 2 2.3	21	**Comment:** RFI or actions are required. **Proposed change:** MSC to put request for information or action to the sponsors and for the sponsor to communicate back to the MSC in relation to these requests.
136 Table 2 2.3	21	**Comment:** In addition to the exchange requested information between the MS, MS shall communicate measures, which will be taken (article 77) or reasons for withdrawal of an application (article 12). These two “communication terms” should be added. **Proposed change:** MSC to put request of information, reasons or measures to the sponsors and for the sponsor to communicate back to the MSC in relation to these requests.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
136 Table 2 2.3	21	**Comment:** Should correction only be possible by sponsor? MSC should also be able to correct. **Proposed change:** add MS able to correct their responsible information.
136 Table 2 2.3	21	**Comment:** Not clear what's meant by: Allow such request to put the assessment on hold if applicable. **Proposed change:** clarify
136 Table 2 2.3	28	**Comment:** We would like reassurance from the EMA that Member State super users will not be able to request to delete an application or notification. **Proposed change:** 'Deletion/withdrawal' in line 1 of paragraph 4 should be changed to 'withdrawal'.
136 Table 2 2.3	37	**Comment:** It should be clarified whether the sponsor is able to submit additional information without a request from the RMS during the assessment period of part I. It could be that some additional information becomes available during the period of 45/76 days which was not requested by the RMS but which the sponsor wants to submit (and has not submitted initially).
136 Table 2 2.3	40	**Comment:** instead of "Req. 3 to 4" should be "Req. 6".
136 Table 2 2.3	42	**Comment:** Please consider modifying to read Req. 4 through Req. 14.
136 Table 2 2.4	11, 26	**Comment:** Correction of wording according to Article 12 S. 1 VO (EU) 536/2014 **Proposed change:** the reporting date
136 Table 2 2.4	29	**Comment:** Distinction shall be made between a permanent withdrawal and a withdrawal for later re-submission. In case of withdrawal for later re-submission trial shall keep its EU portal number (and EUdraCT number) and the workspace shall keep the dossier for further correction / completion (to avoid the need to upload all documents again) and this up to 2 years after withdrawal date. **Proposed change:** "Allow the sponsor to withdraw an application at any time until the reporting time and to submit reason for withdrawal and the eventual intention to re-submit the dossier to same or different MSs within a maximum of 2 years after withdrawal"
136	42	**Comment:** Please add Req. 6

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 2.4		
136 Table 2 2.5	21	**Comment:** The functionality should distinguish between system related and trial related GCP inspection. Data or information submission should be possible for clinical trials as well as participating sites of stake holders (clinical site, sponsor, CRO…). **Proposed change:** Please add this functionality for system related GCP information.
136 Table 2 2.5	25	**Comment:** The portal should support/facilitate registration of systems inspections at both sponsor and CRO sites.
136 Table 2 2.5	36	**Comment:** Clarification is requested as to whether the sponsor would be alerted about the planned inspection dates via the portal.
136 Table 2 2.5	42	**Comment:** Please add Req. 16
136 Table 2 2.5	46	**Comment:** We assume that this information about planned inspections will not replace the official announcement by the Regulatory/Supervisory Authority for the sponsor company. In addition, this should not be publicly available information.
136 Table 2 2.6	28	**Comment:** We would like clarity on the distinction between 'portal interface' and 'strict user interface'.
136 Table 2 2.6	32	**Comment:** "…have the capacity to incorporate multiple languages whereas the strict user interface…" Please clarify what is meant by the "capacity to incorporate multiple languages" vs. "the interface".
136 Table 2 2.6	36	**Comment:** What is the default language, and is there an option for the user to set a default language?
136 Table 2 2.6	42	**Comment:** If the fifth comment above regarding language selection is accepted and a new Req. is added such new Req. should be reflected herein.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
136 Table 2 2.7	44	**Comment:** Dependencies on others systems; please indicate if it concerns only the systems at EMA or not.
136 Table 2 2.7	16	**Comment:** Should EudraVigilance be added here as well? Enabling the transition of CT safety data, e.g. SUSARs to be transmitted from EudraVigilance to the EU Portal/ Database? This would be important to avoid unnecessary work and additional burden for double entry. At least it should be clear that all data from EudraVigilance can be transferred and all data fields are compliant.
136 Table 2 2.7 137 Table 2 3.12	21	**Comment:** For clarity some essential links need to be listed less high level. **Proposed change:** This feature applies to user access management tools and master data (e.g. substances, products, organizations, referential, pharmacovigilance other master data` source) to be made available in the portal, like …..
136 Table 2 2.7	22	**Comment:** How will these data interdependencies be audited if e.g., the safety part of the portal is not part of the audit? Please explain.
136 Table 2 2.7	28	**Proposed change:** The text refers to 'EUTCT'. We think this is meant to read 'EudraCT'
136 Table 2 2.7	36	**Comment:** Clarification is requested as to which "other systems" will be available for selection in the portal.
136 Table 2 2.7	41	**Comment:** Dependencies on other systems: Under the functional specification "dependencies on other systems" it is stated: "To avoid duplication of entry, the portal will allow for data stored in other 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, organizations, referential, other master data` source) to be made available in the portal." EFPIA proposes to include a clarification as to whether this specification applies to information stored in the EudraCT and EudraVigilance databases.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		The transition of CT safety data from EudraVigilance to the EU Portal/ Database should be enabled to avoid unnecessary work and additional burden for double entry. At least both systems are supposed to have the MP identifiers mapped in order to be able to recall safety data from the EU Portal/ Database.
137 Table 2 3	22	**Comment:** Having a dashboard is great tool to navigate the system. However, using the phrase “a friendly presentation” is a difficult requirement to build, trace and test. **Proposed change:** Suggest to revised to “Have a dashboard that meets the users requirements for navigation, creation, maintenance and reporting …”
137 Table 2 3.1	9	**Comment:** Point 3.1: “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 and edit.” In order to effectively fulfill their responsibilities as “Delegates,” CROs should have similar access to a Workspace as Sponsor Users.
137 Table 2 3.1	21	**Comment:** Integration of pharmacovigilance database is needed for MS for proper surveillance of a CT. Same holds true for information on serious breaches. Tracking should be possible, and alerts on new information/document should be sent to the dashboard. The user friendly link should be within audit the other should be taken up for workspace. In general all alerts on dashboard. **Proposed change:** Add Dashboard will also display alerts and is linked to pharmacovigilance database as well as serious breaches.
137 Table 2 3.1	25	**Comment:** In order to minimize the resources spend in MS for monitoring the status of the procedure, we would like to propose that it should be very easy to detect the status of a procedure visually and whether a task is pending for RMS or CMS’s. Targeted alerts could be useful if targeted to the MS which have an uncompleted task. Different solutions could be envisaged i.e. colour change, illustration of process flow etc. As examples it is important that the status change for a CMS case once the assessment report is available, once CMS has responded to a task (comments to assessment report, comment to consolidated report, comments to response from sponsor etc.). The same is applicable for the role as RMS.
137 Table 2 3.1	28	**Comment:** Could the EMA clarify whether the portal will allow users a complete overview of all trials that they have been given access to review?
137 Table 2 3.1	28	**Proposed change:** At the end of the 5th paragraph we think that ‘substantial submission’ should read ‘substantial amendment’.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
137 Table 2 3.1	29	**Comment:** The dashboard shall also provide a visual help to track new information / communication being available; users shall also be able to "sign". **Proposed change:** "… and according to the user's roles enable read, write, edit or sign".
137 Table 2 3.1	36	**Comment:** The dashboard should present a list of all the user's CTs for ease of navigation to the desired CT.
137 Table 2 3.1	36	**Comment:** Workflow analysis and searches require repeatable and consistent processes to track workflow gateways and performance requirements. **Proposed change:** We suggest adding Allow for workflow information data to be configured by the assigned sponsor user.
137 Table 2 3.1	40	**Comment:** To add …and search (to user`s roles] **Proposed change:** 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 and edit and search.
137 Table 2 3.1	41	**Comment:** Dashboard: A visible procedure clock - noting deadlines (hours not just days considering the multinational nature of clinical trials and use of CET) – would be helpful for all stakeholders.
137 Table 2 3.2	5, 11, 12, 26	**Comment:** Typo: The EU CT number format should be: yyyy-xxxxxx-zz (one "y" missing in the draft).
137 Table 2 3.2	6	**Comment:** 3.2. Preparation of documents/data: "Allow sponsors to prepare application dossier using a dossier builder including the upload feature for documents formats including PDF and commonly available documents formats and documents consisting structured data (…)." **Proposed change:** "Allow sponsors to upload electronic dossiers according to eCTD specification or to prepare application dossier using a dossier builder including the upload feature for documents formats including PDF and commonly available documents formats and documents consisting structured data (…)."
137 Table 2 3.2	8	**Comment:** why not using the same number for EU CT number & Eudract number ? would be simpler than having slightly different numbers between the two. **Proposed change:** Eudract number to be used to access portal.
137	9	**Comment:** Point 3.2: "Allow sponsors to prepare application dossier using a dossier builder including the upload feature

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 3.2		for documents formats" The ability to prepare the application dossier within the workspace will be beneficial for many sponsors. However, this should not be a mandatory feature of the system as many sponsors building clinical trial application dossiers for submission internationally will develop these dossiers, and their individual components, outside the workspace. In addition, ACRO recommends that – in order to promote successful validation of submission dossiers – that the application builder includes information relating to the requirements for provision of local language documentation or other specific elements that are required within Part II of the dossier for certain MS. **Proposed change:** It should be clarified whether documents will be able to be uploaded in multiple sessions (logging out of the system in between) or if they must all be uploaded in a single session. The system should be sufficiently flexible so that a sponsor may choose whether to prepare the application dossier within the workspace or to simply upload the final application dossier to the portal.
137 Table 2 3.2	11, 26	**Comment:** It is not acceptable that documents are accepted in (all) commonly available formats. It has to be assured that these formats can be read at least throughout the time the sponsor has to archive the Trial Master File (20 years after the end of trial). E. g., although there are still import filters for old MS Word documents they do not necessarily show them as they have been originally. It should also be clarified that documents containing text must be uploaded in a searchable format. **Proposed change:** [..]for documents formats including PDF and other commonly available document formats, if this format is documented as open source and readability can be assumed for at least 20 years after the end of trial, and documents consisting of structured data (e.g. XML for the EU CT form). Documents containing text must be uploaded in a searchable format.
137, Table 2, 3.2	20	**Comment:** Paragraph 3 and 4 are contradictory in respect to the CT application form. Paragraph 3 says CT application is prepared in the system while paragraph 4 covers the upload of data like EU CT form. **Proposed change:** Preparation of EU CT form directly in the portal.
137, Table 2, 3.2	21	**Comment:** Further details concerning the preparation/ format of MS documents (assessment report, consolidated assessment report, decision and information for the public) are necessary. **Proposed change:** Should be addressed in 'User Requirements´.
137, Table 2, 3.2	21	**Comment:** To clarify that exchange with sponsor is often needed to assess certain information. **Proposed change:** Allow MS to prepare their validation, assessment (e.g. assessment report, request of information) and decision tasks.
137	25	**Comment:** It is unclear whether it will be possible to use the functionalities for communication within a member state,

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 3.2 3.3		e.g. between NCP and an ethics body. It would be beneficial if this was possible. For this reason we would like a clarification on whether system functionalities to support coordination between involved bodies. i.e. the NCA and the ethics committees are envisaged, and if so, which processes are supported.
137 Table 2 3.2	26	**Comment:** Portal number and EudraCT number can mislead when searching a number of CT.
134, Table 2, 3.2	28	**Comment:** We would like greater clarity over how the EU-CT numbers will assigned and how sequential submissions will be numbered. It would be useful for this section to list the acceptable document formats.
137 Table 2 3.2	29	**Comment:** Please confirm the understanding is correct that EU portal number will with time completely supersede the EUdraCT number. **Proposed change:** To add: “After the end of transition period no new EudraCT numbers will be issued”.
137 Table 2, 3.2	34	**Comment:** Possible typo: The EU CT number format should be: yyyy- rather than yyy-?
137 Table 2 3.2 3.7 4.3 4.7	39	**Comment:** 3.2 see comment earlier on EudraCT number vs portal number and dual use. 3.7 Implication is that the completeness of study documentation may be judged by the number of documents present in the submission. This may need to be flexible as in some cases additional documentation may be included to address specific issues. 4.3 How will the language issue be addressed? 4.7 Does this mean that all publically available documents need to be provided in all union official languages?
137 Table 2 3.2	40	**Comment:** To add one „y“ to EU CT number format. **Proposed change:** The EU CT number format should be: yyyy-xxxxxx-zz.
137 Table 2 3.2	41	**Comment:** Will it be possible in the system to link a certain CT number to other clinical trials conducted with the same IMP? Or to link the current CT to previous CT numbers/ submission packages? This should be made clear here.
137 Table 2	41	**Comment:** Preparation of documents/ data: Will it be possible in the system to link a certain CT number to other clinical trials conducted with the same IMP? Or to

Line no.	Stakeholder no.	Comment and rationale; proposed changes
3.2		link the current CT to previous CT numbers/ submission packages? This should be made clear here.
137 Table 2 3.2	41	**Comment:** Preparation of documents/ data: The current text states: “The EU CT number format should be: yyy-xxxxxx-zz.” It should read ”The EU CT number format to yyyy-xxxxxx-zz”
137 Table 2 3.2 3.6	41	**Comment:** Preparation of documents/ data / Upload/ Download: The Sponsor should have the option to prepare the Application Form directly in the system or to be able to upload it from an external system.
137 Table 2 3.2	41	**Comment:** Proposed additional requirement related to the secure transfer and data formats to be added: Provide for secure electronic submission to avoid unauthorised access including non-repudiation of message dispositions in accordance with ICH M2 recommendations. (http://www.ich.org/products/electronic-standards.html)
137 Table 2 3.2	46	**Comment:** There is a typo in the second paragraph, the EU CT number format misses a ”y”, four “y” are needed for the year. **Proposed change:** Add 1 “y”
137 Table 2 3.2	46	**Comment:** In our opinion it should be also mentioned here that for the initial application the sponsor has the right to propose the reporting Member State. This proposal should not only be “hidden” in the cover letter but also be visible at first glance by ticking a box.
137 Table 2 3.3	8	**Comment:** Only mention of communication flow between member states; would need to identify communication flow and collaboration between individual Member state and the Ethics committee(s) of the MS – will they get user rights also for assessment?
137 Table 2 3.3	21	**Comment:** Collaboration between MS is needed throughout the lifetime of a CT for proper surveillance of the CT including assessment of safety reporting (article 44). Wording should reflect this. Validation phase is missing **Proposed change:** ...and the features are to enable: Validation, (b) reporting Member State.... These features revolve around the assessment (initial or during life cycle e.g. SM, inclusion further MSC or safety relevant information) and supervision would lead to:
137 Table 2 3.3	40	**Comment:** grammar **Proposed change:** 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.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
137 Table 2 3.3	44	**Comment:** Collaboration between MSs in the context of assessment and supervision of clinical trials; is all the communication between MSs will be recorded in the system during the assessment and consolidation phase? Will it be in a form of XML message?
137 Table 2 3.4	9	**Comment:** Point 3.4: "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". Article 81 of Regulation 536/2014 states that "The EU database shall contain the data and information submitted in accordance with this Regulation." Therefore, there should be no "informal requests" for data and information that are not specified in the Regulation. **Proposed change:** Delete the reference to informal requests.
137 Table 2 3.4	21	**Comment:** Communication between MS and sponsor is not only be triggered by information or notification submitted by sponsor, therefore also an ad hoc workflow is needed to be set up by MSC. Request of information and/or action is needed e.g. regarding corrective measures (article 77), serious breaches (aricle 52). **Proposed change:** Please add this possibility. MS are able to initiate an ad hoc workflow related to surveillance of one or multiple CTs or an IMP/AMP. MS able to request an action and/or request of further information anytime in lifetime of a CT including serious breaches.
137 Table 2 3.4	32	**Comment:** Preferably the same term that is used in the legal text for Regulation 536/2014 should be used. Replace 'Determination' with 'Selection'.
137 Table 2 3.4	36	**Comment:** We suggest including serious breaches within the scope of this functional specification. **Proposed change:** Allow MSC 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.
137 Table 2 3.4	40	**Comment:** Req.6 provides legislative background for notifications made by sponsor not for request of additional information in relation to the notifications by Member State concerned (MSC). Request for additional information if validation is not identified in the Regulation for Articles 11 and 14 refers to Req. 13.
137 Table 2 3.4	46	**Comment:** Beyond the frame of article 11 and 14, could the sponsor address informal requests to the MSC if necessary using the EU portal. Is that foreseeable?
137	21	**Comment:** AR templates should generate data out of metadata to avoid duplication. To cover all possible CT types

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 3.5		some flexibility is needed. In addition development and proposal of AR template's content lies within responsibility of CTFG. **Proposed change:** To be considered.
137, Table 2 3.5	36	**Comment:** What further report functionalities are available to MS? Can the AR be downloaded and in multiple formats?
137 Table 2 3.5	46	**Comment:** Any assessment report will be written in the member states by two different organisations involved. Authorities and ethics-committees. To assist an incremental approach for the AR to be written partly in parallel according to their responsibilities and combined at the end, please involve member states and perhaps also ethics-committees for the development of such a template. This will grant more efficient support of the decision process under heavy time constraints. Such a template should be developed in co-operation with the MSs and the ethic committees without temporal constraints. We acknowledge the importance of such a template to support automated processes and harmonized approaches in submission and readability across member states; however we wonder whether such a template should really be part of the audit specifications. **Proposed change:** Change text to: "Functionalities to support the production and exchange of EU- wide harmonized structured Assessment Reports by the availability of a commonly accepted template (to be joint developed with the MS and finalised before June 2016)."
137 Table 2 3.6	21	**Comment:** Up-/download of bulk should be possible (at least for MS). In addition up/download to/from portal should be easily possible. Please clarify in text. **Proposed change:** Allow users to upload or download data as bulk, Up-/download to portal is given.
137 Table 2 3.6	29	**Comment:** This requirement shall not be understood as giving public the possibility to download documents freely in an uncontrolled way.
137 Table 2 3.6	36	**Comment:** Clarification is sought on the different document formats being considered. What does similar technology mean? The portal should allow users to upload folder and folder structures rather than individual documents, with the ability to upload multiple files at once.
137 Table 2	41	**Comment:** There is no specification regarding the rights of the Sponsor and its delegates/other stakeholders regarding documents and information as well as with respect to deletion of documents prior to submission.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
3.6		**Proposed change:** Add a Specification: Prior to submission all data and information contained in documents in the workspace / EU portal remain the sole property of the user entering that data. The user may delete any such information without record in the EU portal or EU database. Only after submission through the EU portal, will any documents be regarded as being part of the EU portal and EU database. This means also that the workspace needs to be adequately protected and that until submission the User has full rights to delete and modify.
137 Table 2 3.7	9	**Comment:** Point 3.7: "Typical validation of application "and "Users to be able to validate their application package at any time". We believe that these items refer to validation checks on the clinical trial application dossier and other submissions to be filed through the portal. However, the terms "application" and "application package" have different meanings in the IT community. For clarity, therefore, we recommend that slightly different wording is used. In certain cases it may not be possible or applicable to prepare and provide all documentation that may normally be required to fulfill the electronic validation requirements. To support this type of situation it would be beneficial to permit certain aspects to be omitted and justification to be provided, for assessment at the time of the validation by the MS. **Proposed change:** Use the term "submission dossier" instead of "application" or "application package".
137 Table 2 3.7	23	**Comment:** 3.7 Technical Validation of application before submission of documents/data Complete the specifications with : Allow users to save the modifications before validation and submission.
137 Table 2 3.7	29	**Comment:** There shall be a possibility for the sponsor to annotate validation errors (in case there is a valid explanation) **Proposed change:** "Users to be able to validate their application package at any time during the course of the dossier preparation, to annotate errors as applicable and receive feedback on the validation errors "
137 Table 2 3.7	37	**Comment:** Experience with clinical trial application forms in EudraCT has shown that the validation function alerts for failures where no failures exist. Therefore, the validation function itself must be fully validated. In addition, the EU portal shall allow for submissions of applications even if the validation checks signals issues. The issues would then be addressed in the frame of the validation performed by the RMS. **Proposed change:** Add to "Details": Enable submissions of applications even if the validation checks signal issues.
137 Table 2 3.7	37	**Comment:** To keep the tight timelines, even "normal" users (non-super users) must have the possibility to submit applications, without release by super users, when the super users have granted the respective user rights to the "normal" users. Clinicaltrials.gov should not be taken as example in this respect as it allows this submission of data without the release of a superior user (the "administrator") only if the user himself has administrator rights. **Proposed change:** Add to "Details": Enable non-super users to submit applications without release by super users, in

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		case the super users have granted the respective user rights.
137 Table 2 3.7	41	**Comment:** EFPIA proposes the addition of a requirement that validation criteria can be made independent of the EU database and published in order that they can be incorporated into third party systems.
137 Table 2 3.7	41	**Comment:** Technical validation…: We propose that validation criteria are made publically available with appropriate version control.
137 Table 2 3.7	44	**Comment:** Technical validation of application before submission of documents/data; it will be necessary to define all validation rules with Status Pass/Fail/Warning.
137 Table 2 3.8	5	**Comment:** Regarding the system-generated information on coming deadlines: Please add a requirement that the user should be able to customize the advance notice time of such notification prior to the actual dead line.
137 Table 2 3.8	5	**Comment:** Regarding reassignment/redirection of tasks during foreseen absences: Please consider adding a requirement for management of unforeseen absences, e.g. a tool that allows other pre-defined users at the sponsor's to reassign/ redirect tasks to themselves (after submission of relevant accreditation) when the original user/super-user becomes unavailable.
137 Table 2 3.8	8	**Comment:** Will the alerts serve as reminders/warnings to MS/Sponsor prior to the end of the review period? Will alert be in the portal or alerts by email to users? **Proposed change:** we would recommend the alerts are also addressed by email to users.
137 Table 2 3.8	9	**Comment:** Point 3.8: "MS user (super user) to have the administrative right to delete or update MS information submitted and to enter a reason." To ensure traceability, accountability and an appropriate audit trail, there should be no deletions from the system. All alterations should be attributable and the reason for change recorded. **Proposed change:** Delete the words "delete or" from this sentence, and the system should ensure that all alterations are attributable and the reason for change recorded.
137 Table 2 3.8	9	**Comment:** Point 3.8: "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 between 23rd December to 7th January (for multinational CT only) and the reference time zone adopted for the system (the CET)." For single country applications, it appears that MS and Sponsors would be expected to work to standard timelines over

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		the Christmas and New Year time periods (notwithstanding national holidays within that period). It would be helpful for the absence of any such clock-stop to be confirmed for all single-country studies in all EU MS to clarify this situation, as some MS may prefer to apply such a clock-stop under such circumstances. Moreover, the methodology for calculating timelines should be outlined, given the different public holidays in each MS.
137 Table 2 3.8	9	**Comment:** The text proposes that alerts be sent when a new pending task has arrived or a deadline is coming. **Proposed change:** It should be clarified whether it will be possible for the sponsor to receive an alert advising that the MS has completed a task even where there is no follow up task required of the sponsor and no new deadline coming e.g. MS completing assessment of the relevant submission (Part I, Part II, substantial modification, etc.), decision, outcome of inspections.
137 Table 2 3.8	9	**Comment:** The guidance states that the system should be able to track activities and inform users that a new pending task has arrived or a deadline is coming. **Proposed change:** It should be possible for the system to display a confirmation of submission of any item in order that this can be printed, if required. The confirmation screen should identify the trial and the documents submitted (including the associated version numbers).
137 Table 2 3.8	11, 26	**Comment:** Although the member states and the stakeholders (so far) informally agreed on a clock stop between 23rd December to 7th January, this agreement may be considered to be neither in accordance to the VO (EU) 536/2014, nor covered by the regulation EWG/EURATOM 1182/71. If a member state fails to notify the sponsor of its decision within the relevant period the assessment report shall be deemed to be the decision of the Member State concerned on the application for authorization of the clinical trial (cf. Article 8 para 6 VO (EU) 536/2014). Even if the EU portal would not notify the sponsor about this “tacit approval”, legally speaking the trial would have received authorization form the concerned member state. We refer also to Article 8 para. 8, Article 6 para. 8 5 VO (EU) 536/2014. The member states have to assure that decisions are made within the legal timeframe. If the last day of the timeframe falls on a holiday, the decision has to be notified the next working day. In our opinion the informal agreement cannot overrule the actual text of the regulation. Implementation of such a rule would obviously result in legal uncertainty.
137 Table 2 3.8	15	**Comment:** With specific reference to table 2, item 3.8, there is a risk that the EU Portal and EU Database will gather a lot of unneeded information, all audit trailed, during the course of a CT. This could add considerably to the administrative burden and costs. Information submitted later in the process is more likely to be complete, but then it may not be timely for assessment. The balance between timing and completeness should be carefully specified, so that as much as possible workings are done outside the system and only finished work is submitted. **Proposed change:** Add a requirement, to table 1, that the system be audited against this specifically, that only

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		required data is requested by the EU Portal and EU Database.
137 Table 2 3.8	16	**Comment:** The super user must have an overview on all tasks directed to certain users and should have access to the different tasks in order to be able to redirect tasks to other users (in case the respective user is absent for a longer time).
137 Table 2 3.8 4.1	16	**Comment:** According to table 2 section 3.8 it will be possible to delete or update information / data. This has to be documented in the system. The same applies for section 4.1 (altered / deleted records). It remains unclear if this is part of the mentioned “audit record”.
137 Table 2 3.8	18	**Comment:** It will be possible to delete or update information / data. This process and the details have to be documented in the system. The same applies for section 4.1 (altered / deleted records).
137 Table 2 3.8	21	**Comment:** With regard to the timeline discussion, the agreed calendar solution should be added here. It is unclear who is adopting a MSC calendar solution? Needs to be clarified. **Proposed change:** Calendar solution part I and decision: Till RMS selection the timeline of the slowest MSC will apply; after notification of a RMS the calendar of the RMS apply; after reporting date or last day part II the calendar of MSC applies.
137 Table 2 3.8	21	**Comment:** Shorten has an impact on other MSC, therefore an alert is needed. **Proposed change:** MS user (super user) to be able to extend or shorten the deadlines within limits set by the Regulation. In case of the first an alert is send to the other MSC.
137 Table 2 3.8	21	**Proposed change:** Alerts with direct link to the task (e.g. additional request for information, serious breaches, safety relevant information).
137 Table 2 3.8	21	**Proposed change:** Please add Initiating a new ad hoc workflow and its control should be possible by MS.
137 Table 2 3.8	23	**Comment:** 3.8 Workflow Control **Proposed change:** User or super user also be able to reassign/redirect tasks if they cannot handle them (people on leave for instance).
137 Table 2	28	**Comment:** We welcome the provision for users to be informed of a new pending task or deadline. We recommend that this notification is administered by email and that the EMA amends 3.1 to specify this.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
3.8		
137 Table 2 3.8	29	**Comment:** There shall be a tool that would enable users to annotate tasks (so in case of need to take over by another user, there will be more information available on the status of dossier: example of note “review asked to xy user, awaiting confirmation by dd/dd/yy” or “to be cross-checked with the new version of the protocol” etc.. **Proposed change:** To add: “The system shall allow annotating tasks”.
137 Table 2 3.8	32	**Comment:** “…-1182/1971 of the Council of 3 June 1971”. Add: ‘For initial validation processes before a reporting member state have been selected and for all national processes, the calendar of all Member States concerned will be applied’.
137 Table 2 3.8	32	**Comment:** “MS user (super user) to have the administrative right to delete…”. Same comment for page 25/28, fifth column for item 4.1 last bullet: Replace delete with ‘inactivate’ or a similar word e.g. ‘nullify’. No information should be deleted.
137 Table 2 3.8	36	**Comment:** Super users should be able to remove users and reassign/redirect roles and packages if staff are absent or are on leave.
137 Table 2 3.8	41	**Comment:** Workflow control: 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. The system should allow alerts to be sent via E-mail. **Comment:** Will these alerts be sent via e-mail? **Comment:** Sponsor super users should be able to access all tasks to ensure business continuity. Thus, the super users should be able to reassign/redirect tasks if necessary (e.g. when people are on leave).
137 Table 2 3.8	41	**Comment:** Workflow control: The clock stop informally agreed between 23rd December to 7th January is raising concerns, certainly for Multinational CT involving ex-EEA countries, where specific activities may need to be performed in the system and could not afford a 2 weeks delay. **Proposed change:** Timelines should be calculated as calendar days and no clock stop in the system should be allowed for Xmas holidays or only 24th- 26th Dec plus 31st Dec and 1st Jan, for a total of 5 calendar days.
137 Table 2 3.8	41	**Comment:** Workflow control/ Document store and database: According to table 2 section 3.8 it will be possible to delete or update information / data. This has to be documented in the system. The same applies for section 4.1 (altered / deleted records).

Line no.	Stakeholder no.	Comment and rationale; proposed changes
4.1		
137 Table 2 3.8	46	**Comment:** As the clock stop between 23rd December to 7th January is agreed on also by stakeholders, AESGP assumes this clock stop is also valid for processes and timelines where the sponsors are required to react. E.g. additional request for information by MSCs. **Proposed change:** Rewrite the 4th bullet point: Alerts with direct link to the task (e.g. additional request for information) considering the requirements of Regulation (EEC, Euratom) No 1182/71 of the Council of 3 June 1971 and the informally agreed clock stop between 23rd December to 7th January.
137 Table 2 3.8	46	**Comment:** Is the alert function also applicable for informal requests (cf our related comment on 3.4)?
137 Table 2 3.9	8	**Comment:** Will there be standard reports prepared upfront to ease the process review/status by users? **Proposed change:** to set up standard reports
137 Table 2 3.9	9	**Comment:** “Possibility to create reports for the users to monitor the processes governed by the workflow” A CRO may be responsible for various (and different) tasks delegated by different sponsors across multiple clinical trials. There should be functionality to allow a CRO to obtain consolidated reports across all of the portal/database activities delegated to it for these multiple trials. That is, to enable CROs to fulfill their responsibilities on behalf of Sponsor Users, and provide information to Competent Authorities upon request, CROs should be able to query all studies upon which the CRO is acting as a delegate. Additionally, it should also be possible for a sponsor to obtain consolidated reports across all of the portal/database activities for their clinical trials. **Proposed change:** Include sponsor/CRO access to consolidated reports identified by sponsor and by CRO as appropriate.
137 Table 2 3.9	21	**Comment:** Up/download from workspace needed for MS. **Proposed change:** Add section that MS can up/download from workspace, including bulk.
137 Table 2 3.9	41	**Comment:** Reporting features: In addition to users creating reports super users should be able to run aggregate reports.
137 Table 2	9	**Comment:** “The system should allow the users to search and filter specific topics based on basic search criteria” The basic search criteria should include CRO name and sponsor name.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
3.10		**Proposed change:** Search criteria should include CRO name and sponsor name.
137 Table 2 3.10	9	**Comment:** 3.10: "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." - To enable CROs to fulfill their responsibilities on behalf of Sponsor Users, and provide information to Competent Authorities upon request, CROs should be able to query all studies on the basis of metadata applied to the information within the EU Portal.
137 Table 2 3.10	14	**Comment:** The system should allow the users to search and filter not only based on Member State but also based on affected federal state. Data concerned Sponsors and investigators scaled to affected federal state.
137 Table 2 3.10	21	**Comment:** Search functionality should cover also linked databases, like search from dashboard in EU portal and database as well as EudraVigilance databases including MPD and workspace. Searches with regard to inspection purposes are need, like for clinical trial site, CRO, other contractors of sponsor. **Proposed change:** Specify link with other databases. And add User friendly link via dashboard e.g. for PV databases, MPD. Searches include inspector specific requirements like clinical trial site, CRO, other contractors of sponsor.
137 Table 2 3.10	28	**Comment:** Although we appreciate that the search criteria listed is not exhaustive, we would like to emphasise the importance of the facility to search by Sponsor.
137 Table 2 3.10	31	**Comment and proposed changes:** Referring to the search functionalities to be built into the database; whilst appreciating that this is not a full list of search criteria, it is essential that the facility to search by Sponsor is included.
137 Table 2 3.10	36	**Comment:** The user interface should be adjusted to meet super user and user preferences. **Proposed change:** We suggest adding. Allow the configuration of the user interface to promote ease of use and local user requirements.
137 Table 2 3.10	40	**Comment:** Authorised access should be defined – MSC, European Commission and subject, who submitted it (not allow for other Sponsors to view e.g. SUSAR or ASRs of other Sponsors).
137 Table 2 3.10	41	**Comment:** Search functionalities: EFPIA proposes to that the use of controlled vocabulary to facilitate / support search functionalities is encouraged.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
137 Table 2 3.11	20	**Comment:** More clarity is needed on areas where data availability will be enabled to avoid duplication with other systems.
137 Table 2 3.11	23	**Comment:** 3.11 Training and help for users Add the possibility to access to hotline.
137 Table 2 3.11	26	**Comment:** More emphasis needs to be given to training and defined guidelines on using the system so that as much as possible all users are using the systems in the same way. This will be important to maintain the quality of the data and also for reporting features and future business intelligence uses. Such reports will be meaningless if the quality of the data (in terms of accuracy, completeness, validity etc.) can be assured.
137 Table 2 3.11	28	**Comment:** We welcome the inclusion of this function to provide training and help for users. Currently, the draft specification details that this will include online help and tooltips. As part of this provision, we would like the EMA to provide an online training version of the database to facilitate the training of all staff that have access to this system. We would also like the EMA to consider additional support. Online help provided for other EMA-managed, IT systems, for example the EuroVigilance Database Management System, can be slow and unhelpful. A telephone helpline would ensure that users of the EU portal and database are more fully supported and would also help the EMA to be aware of any emerging issues with the system, as flagged by users, so that these can be quickly addressed.
137 Table 2 3.11	31	**Comment:** We are supportive of the proposed training and help for users. **Proposed changes:** The provision of a training version of the database would be a great advantage, facilitating the training of all staff that will have to access this system.
137 Table 2 3.11	36	**Comment:** What does the online help entail? Interactive chat or an online support ticketing system would be helpful to address queries/problems.
137 Table 2 3.11	41	Training and help for users: EFPIA proposes to include access to on-line (web) training modules.
137 Table 2 3.11 4.8	45	**Comment:** It would be desiderable to have a training environment (similar to Eudravigilance's one) to be used during training courses or by users on their own. **Proposed change:** Add: "A training environment will be provided".

Line no.	Stakeholder no.	Comment and rationale; proposed changes
137 Table 2 3.13 4.1	9	**Comment:** Points 3.13 and 4.1: “Records may be altered or deleted by system administrators” To ensure traceability, accountability and an appropriate audit trail, there should be no deletions from the system. All alterations should be attributable and the reason for change recorded. **Proposed change:** Delete the words “or deleted” from this sentence, and the system should ensure that all alterations are attributable and the reason for change recorded.
137 Table 2 3.13 4.1	15	**Comment:** Regarding 4.1 and 3.13, how is the process controlled when system administrators alter or delete data. **Proposed change:** Identify the controlled process followed by system administrators when they alter or delete data.
137, Table 2 3.13 4.1	15	**Comment:** How does the Workflow data store in 3.13 differ from the EU Database data store in 4.1? Should be only one data store. **Proposed change:** should 3.13 remove the bulleted text and refer to section 4.1?
137 Table 2 3.13	21	**Comment:** Same comment as 2.7:
137 Table 2 3.13 4.1	21	**Comment:** Prior records be altered or deleted by system administrators the owners of information need to give permission. **Proposed change:** Records may be altered or deleted by system administrators after agreement of information’s owner.
137 Table 2 3.13	21	**Comment:** How long is the retention period unlimited assumed. **Proposed change:** Clarify in text.
137 Table 2 3.13 4.1	28	**Comment:** We would welcome greater detail as to how the workspace and EU database will enable the storage and retrieval of documents and data. We are particularly concerned by the specification of a function to allow records may be altered or deleted by the system administrators. We recommend that this function is removed from the text. We would like the EMA to clarify that application dossiers will be retained for reference purposes and accessible to sponsors and authorised users in the case that an application has lapsed, been withdrawn, or been refused authorisation. This would greatly assist the sponsor if they wish to resubmit an application.
137,	29	**Comment:** Who are system administrators? If this is the agency, no deletion or change shall be permitted without

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Table 2 3.13 4.1		informing sponsors and having their agreement, unless sponsor does not exist anymore and no other sponsor has taken over.
137 Table 2 3.13 4.1	31	**Comment:** Within the workspace functionality there is functionality specified that allows records to be altered or deleted by the system administrators. This is a concern and we would welcome information on EMA's rationale for this specification.
137 Table 2 3.13	41	**Comment:** Workspace database: The specifications should clarify how the applicants will be informed of modifications/deletions made by system administrators.
137 Table 2 3.13	44	**Comment:** Dependencies on other systems; please indicate if it concerns only the systems at EMA or not.
137 Table 2 4.1	22	**Comment:** "Records may be altered or deleted by system administrators." Why would administrators be able to deleted data created by other users, e.g. sponsors? How is it defined what can be deleted by whom? Will audit trials capture these events and the previous records? If not, why?
137 Table 2 4.1 4.2	22	**Comment:** EU Database must have a robust Business Continuity Plan which includes backup and recovery procedures built in from the beginning and tested annually. This should be included in the audit specifications.
137 Table 2 4.1	25	**Comment:** We find there is a need for optional bulk download of records for archiving according to MS national laws.
137 Table 2 4.1	44	**Comment:** Document store and database; would it be possible for MSs to make customs query to retrieve documents from the database?
137 Table 2 4.1	46	**Comment:** "The clinical trial data and information is to be made publicly available through a publication module according to detailed rules to be defined." In any case we expect that the IMPD will not be made publicly available. How is it guaranteed (technical solution) that the IMPD will not be made publicly available?

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		It has to be borne in mind that highly confidential intellectual property especially regarding the manufacturing, the technological approaches and certain data in the development of an innovative medicinal product in the IMPD are of crucial value for the sponsor company. Without any reliable protection of this value innovation might be impeded significantly. The negative consequence might be that clinical trials would increasingly be conducted in third countries in order to safeguard the innovation and the intellectual property. This would contradict the main objective of the new Regulation.
137 Table 2 4.2	5	**Proposed change:** Retention period to be unlimited and readability of data to be ensured for the entire retention period.
137 Table 2 4.2	41	**Comment:** Document and data retention: Does “unlimited” mean configurable or forever?
137 Table 2 4.3	15	**Comment:** Take into account Consort statement as above.
137 Table 2 4.3	16	**Comment:** Automated rules for publication: Will there be a separate public consultation for these rules? Or will this topic be discussed in another EMA subgroup? Stakeholders should have the possibility to comment on the automated rules.
137 Table 2 4.3	22	**Comment:** As Inspection Reports will be stored in the EU database then it is presumed that the public will have access to these. It’s not clear if these will be redacted/un-redacted reports or will the publication module exclude these records from view and search?
137 Table 2 4.3	23	**Comment:** 4.3 Publication of CT data and information Specify if the rules of clinical trial data publication limit access to this data when the restriction of confidentiality applies.):
137 Table 2 4.3	36	**Comment:** The rules need to take into consideration the marketing authorisation status of the product (including indication, pharmaceutical form and/or route of administration) as this will be important to determine what is commercially confidential and protect such information contained in the clinical trial submission package. **Proposed change:** The rules are to be automated and implemented through the publication module taking into consideration the workflow of the trial and the marketing authorisation status of the medicinal product, indication, pharmaceutical form and/or route of administration of that product used in the clinical trial.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
137 4.4 4.5	15	**Comment:** Table 2 top of page states “3-workspace”. The heading should be "4 - EU DATABASE" **Proposed change:** 4 - EU DATABASE
137 Table 2 4.4.	21	**Comment:** Search functionality for MSC needs to be specified, since they should be able to get information of interest. See also comment to 3.10 **Proposed change:** Specify search functionality.
137 Table 2 4.4	22	**Comment:** The assumption is that the rules defined in the publication module will also be applicable to the Search Functionality, i.e. metadata search is prevented for excluded records.
137 Table 2 4.4	29	**Comment:** No public user (which can be anyone, including investigators participating in trials) shall be able to download any document without appropriate terms of use. In general public access is mentioned as being subject to a separate consultation. Example 1: clinical trials investigator downloads the wrong version of the protocol (old one) instead of working with the document provided by the sponsor and treats patient accordingly. Sponsor shall be able to trace this fact… Example 2: a different sponsor downloads the full protocol and repeats the trial (by copy-pasting the protocol) in a different part of EU without a proper acknowledgement or the reference to the author of the original (plagiarism)… This shall be traceable. **Proposed change:** To be deleted and transferred into the future document on specifications of public access or to be modified: 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 associated with appropriate terms of use in case of download, enabling traceability and transparency of download”.
137 Table 2 4.4	36	**Comment:** The search functionality should allow querying in multiple languages.
137 Table 2 4.6	15	**Comment:** Also consider ADAM data sets for analysis – the CT regulation mentions the aiding of research and research will be better facilitated by use of such standards.
137 Table 2	26	**Comment:** The download option should be restricted to pdf or a similarly protected format so that the content cannot be altered.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
4.6		**Proposed change:** Restriction of the download.
137 Table 2 4.6	29	**Comment:** Idem as above **Proposed change:** To be deleted and transferred into the future document on specifications of public access or to be modified: The public user interface to enable the download of document and data as XML and other document format (e.g. pdf, word, excel etc.). Download modalities shall be associated with appropriate terms of use in case of download, enabling traceability and transparency of download".
137 Table 2 4.6	41	**Comment:** Download option: What is the anticipated scope: single study information or tabulated multi-study information? This needs to align with Policy 0070.
137 Table 2 4.6	41	**Comment:** Download option: The introduction of the appropriate watermarks/stamping to ensure non-commercial use (as per Policy 0070) needs to be considered.
137 Table 2 4.6	46	**Comment:** The download of documents by the public should be restricted to non-changeable PDF documents.
137 Table 2 4.7	44	**Comment:** Public interface; the public interface will support all Union official languages. Will the content be translated in all Union official languages? If yes, who will the responsible for the translation? Member States or Sponsor?
137 Table 2 4.9	40	**Comment:** Also Req. 19 should be added **Proposed change:** Req. 1 to 17 and Req. 19
138 Annex 1	21	**Comment:** Integration of safety surveillance (e.g. ASR, SUSAR, other safety relevant information/notification) is essential for surveillance of a CT during its life time. This should be taken up. **Proposed change:** 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.
138 Annex 1	21	**Comment:** Essential is the link of portal /database to EudraVigilance for surveillance of a CT too. This should be taken up. **Proposed change:** Add the link of portal /database to EudraVigilance for surveillance.
138	21	**Comment:** Integration of pharmacovigilance database is needed for MS for proper surveillance of a CT. Tracking should

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Annex 1		be possible, and alerts on new information/document should be sending to the dashboard. The user friendly link should be within audit the other should be taken up for workspace. **Proposed change:** Add Similar functionality as given for the CT application or SM process should apply for safety surveillance/assessment including tracking, alerts via dashboard.
138 Annex 1	25	**Comment:** Postponing this functionality will necessitate parallel systems in the EU. We would like to encourage an integration already in version 1 as the needed functionalities i.e. creating af record and initiate a workflow is already available in the system from the beginning.
138 Annex 1 2	31	**Comment:** The text refers to a reduction in administrative burden for NCAs, which in itself implies that there will still be parallel systems where study sponsors will still have to deal with several different NCAs and the EU portal system. There are positive examples that NCAs try to harmonize their procedures, for example: http://www.pei.de/EN/information/license-applicants/clinical-trial-authorisation/electronic-submission-applications/electronic-submission-applications-node.html **Proposed changes:** The EU portal should replace the systems which are now in use by NCAs or will be implemented until the EU portal and the EU databases have achieved full functionality. An example is the “Electronic submission of applications for the authorisation of clinical trials for investigational medicinal products” of the Paul-Ehrlich-Institute in Germany. It should not be necessary for sponsors to use and to meet the requirements of more than one electronic submission system. Also, the requirements of different NCAs should be discussed in public. Ideally, there should be no different national requirements for submissions. In addition: In order to simplify submissions in the EC and the US the EC-portal should - as far as possible and useful - resemble or be compatible with the FDA Electronic Submissions Gateway.
138 Annex 1 2	32	**Comment:** Automated two-way…”. Add: “…including the capability for Member States Concerned to download a complete case or all cases related to a specific trial”.
138 Annex 1 3	15	**Comment:** ‘3.’ Again ADAM will facilitate the reporting with the right vendor tools.
138 Annex 1 3	15	**Comment:** 3rd bullet refers to ‘Additional reporting capabilities…’ . So, will user B be able to view User A’s activity, when producing the report? Is there transparency around this? Or will security settings prevent this?

Line no.	Stakeholder no.	Comment and rationale; proposed changes
138 Annex 1 3	21	**Comment:** Statistical information per IMP would be useful for MS. **Proposed change:** Statistic functionality per IMP needs to be implemented.
138 Annex 1 3	31	**Comment:** The section seems to imply that the reporting capabilities will only be available to the Member States. **Proposed changes:** The reporting functionality should also be made available to the Sponsors.
138 Annex 1 4	11, 26	**Comment:** The legal basis for delegation or change (?) of the rMS needs clarification. The regulation itself does not foresee a change of the rMS.
138, Annex 1 5	15	**Comment:** '5. 'SDTM safety can be tracked.
138, Annex 2	16	**Comment:** The workaround with the ECs on the part of the MS is not shown in this graphic description. This functionality - i.e., review and input by ECs - must be shown here (specific wording to be added in the relevant sections). How should MS exchange and comment on the preliminary assessment report? EU Portal needs to support also the submission of the preliminary assessment report by the rMS to the cMS. In addition, providing comments to the preliminary assessment reports is required as well and needs to be supported by the Portal. This is not clear for the current figure.
138, Annex 2	21	**Comment:** The figure is not complete – missing e.g.: Sponsor: - Submit submission... SM, addition of MSC - Submission to MPD, active substance code - Submit notification: restart of recruitment, urgent safety measures - Submission of CT result, and intermediate results MSC: - Surveillance of a CT, communication of request of action or further information. **Proposed change:** add see above.
138, Annex 2	21	**Comment:** Sponsor submissions lack Urgent Safety Measures (article 54) and the Lay Summary is also not specifically mentioned.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change: Sponsor submissions to include "Urgent Safety Measures". Sponsor "submissions of clinical study report summary including lay summary".
138, Annex 2	29	**Comment:** Annex 2 is inconsistent with the text: are missing re-submission, urgent safety measure notification on the side of the sponsor and communication on decisions to suspend, halt or stop CT and reaction on urgent safety measures on the side of MS. **Proposed change:** Annex 2 to be updated to be fully consistent with the rest of the document.
138 Annex 2	41	**Comment:** Submission through the EU Portal to the EU Database: EFPIA believes that the following elements are missing from the figure: the exchange and comment on the preliminary assessment report; the EU Portal needs to support the submission of the preliminary assessment report by the rMS to the MSC. In addition, providing comments to the preliminary assessment reports is required and needs to be supported by the Portal. Acknowledgement and Technical Validation.