6 November 2015
EMA/739152/2015
Compliance and Inspection

Overview of comments on EMA/641479/2014 Draft proposal for an addendum, on transparency, to the “Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014”

Specific comments on text Section 4.5. to Section 5.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes
753-760	12	**Question 13** Proposed change (if any):None
753-760	71	**Question 13** **Comment:** The EGA agrees that this proposal meets the requirements and objectives of the Regulation.

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Line no.	Stakeholder no.	Comment and rationale; proposed changes
753-760	81	**Question 13** **Comment:** Our members agree upon this. Only the final assessment report is interesting.
753-762	10	**Question 13** **Comments:** For the functioning of the Regulation, the MS need to be able to communicate through the portal (and not through email). It can be argued that if drafts and other communications are submitted through the portal, the information has to be stored in the database according to Article 80. Then Article 81(4) will apply to the information, which means that the information should not be made public anyway according to (c) and possibly (b). This is a better justification for secrecy than the one mentioned in the document. Doesn't the existence of the secrecy provision in Article 81(4)(c) show that the intention is that MS should communicate through the portal? It should be clarified if communication between Member States in the 'workspace' outside the Portal will be saved in the same or another database. Further analysis may be needed to clarify if such communication outside the database is confidential or not.
753-762	11	**Question 13** ACRO agrees that the proposal meets the requirements and objectives of the Regulation.
753-762	19	**Question 13** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
753-762	35	**Question 13** EUCOPE agrees that there is no need for submitting the draft assessment report through the portal in the database nor to make it public.
753-762	55	**Question 13** **Comment:** We agree with the proposal that communication between member states in the drafting of assessment

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		reports remain confidential, and that this meets the requirements and objectives if the Regulation.
753-762	57	**Question 13** **Comment:** EuropaBio supports this proposal regarding the protection of confidential communication between Member States in relation to the preparation and drafting of assessment reports.
753-762	60	CCI of Assessment Reports **Comment**: We agree with the proposal in this addendum as stated. **Proposed change (if any):** None
753-762	65	**Question 13** **Comment:** EFPIA agrees with the EMA proposal that the draft AR will not be submitted through the Portal to the Database nor made public.
755-760	14	**Question 13** Referring to Question 13: comment on whether this proposal meets the requirements and objectives of the Regulation: **Comment:** The confidentiality of communication between Member States in relation to the preparation of the assessment report is required to enable the preparation and drafting of assessment reports to be conducted in confidence to ensure that the assessment and hence where applicable the decision making process is not subject to interference. The Regulation does not require the draft assessment reports to be submitted through the portal to the database and therefore they will not be made public. We agree. Nothing to add.
755-760	78	**Comment:** It is supported that draft assessments are not published. Article 81 (4) c) of Regulation 436/2014 applies.
760-762	80	**Question 13** **Comment:** It does meet the spirit of the Regulation.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
761-762	4	**Question 13** EURORDIS agrees with the proposal. Only final conclusions are important to the public (i.e. authorised/not authorised and why). To make draft assessments publicly available could even confuse the public as a trial may finally be authorised even if intermediate assessments mentioned major objections that could then be solved.
761-762	5	**Question 13** **Comment:** The proposal meets the requirements and objectives of the Regulation.
761-762	13	**Question 13** (communication between Member States) This proposal meets the requirements and objectives of the Regulation. There is no value in publishing draft assessment reports.
761-762	28	**Question 13** The proposed protection of confidential communication between Member States in relation to the preparation of the assessment report is adequate and assures that the preparation and drafting of assessment reports and the decision making process will not be subject to interference. And because the definite assessment report will be made public, the draft assessment report is not relevant for the public.
761-762	29	**Question 13** We agree that the proposal meets the requirements and objectives of the Regulation, the draft assessment reports do not have to be made public.
761-762	30	**Question 13** We agree that draft assessment reports should not be published (see also p 15 lines 526-534). However, the final assessment report should faithfully describe possible critical questions emerged during the evaluation process, divergent positions taken at the end of it and the reasons for the minority, whenever the final decision is granted by

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		majority.
761-762	32	**Question 13** Yes
761-762	36	**Question 13** Comment: *The FPM believes that draft assessment reports from the agencies do not have to be made public. We do recommend, however, that the overall outcome of the review is made public.*
761-762	38	**Question 13** **Comment:** We agree with the proposal
761-762	39	**Question 13** **Protecting confidential communication between Member States in relation to the preparation of the assessment report** The proposal includes: "*The confidentiality of communication between Member States in relation to the preparation of the assessment report is required to enable the preparation and drafting of assessment reports to be conducted in confidence to ensure that the assessment and hence where applicable the decision making process is not subject to interference.* The Regulation does not require the draft assessment reports to be submitted through the portal to the database and therefore they will not be made public. " **Outcome (if applicable):** If the product is already in the market then there should not be a problem to publish all the information related with a trial. Openness and publication should be the rule. This should also include the publication of any report by a member state that does not agree with the assessment (minority vote).
761-762	41	**Question 13**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		We concur with this proposal and believe it meets the requirements and objectives of the Regulation.
761-762	46	**Question 13** **Comment:** We agree with this proposal and believe it meets the requirements and objectives of the Regulation.
761-762	48	**Question 13** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014.
761-762	53	**Question 13** we believe this proposal to be appropriate
761-762	54	**Question 13** We feel that these proposals meet the requirements and objectives of the Regulation.
761-762	59	**Question 13** **Comment:** We have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
761-762	62	**Question 13** **Comment:** Agree the proposal meets the requirements and objectives of the regulation.
763-794	14	**Question 14** Referring to Question 14: comment on whether this proposal meets the requirements and objectives of the Regulation: 4.6. Ensuring effective supervision of the conduct of a clinical trial by Member States: 4.6.1. Inspection reports: **Comment:** We agree.

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763-794	17	**Question 14**, Section 4.6 supervision of the conduct of a clinical trial by Member States: **Comments:** The Niedersächsisches Ministerium für Soziales, Gesundheit und Gleichstellung, Germany, acknowledge the need for transparency of regulatory actions to support the public confidence in the clinical trial process and the EU medicines regulatory system while ensuring data privacy and taking into account the legitimate economic interest of sponsors and their service providers. According to articles 79 and 80 and 81 of the European Clinical Trial Regulation 536/2014/EC inspection reports shall be made available to the inspected entity and the sponsor of the relevant clinical trial and shall be submitted through the EU portal and stored in the EU database. According to article 81 Section 4, the information and data of the EU database shall be publicly accessible unless, for all or part of the data and information, confidentiality is justified. The present document (EMA/641479/2014) foresees in section 4.6.1 that GCP inspection reports, which will be stored in the EU database, should be made public once the inspection process is completed and the final inspection report is signed off and issued by the Member State(s) inspectorate. Only personal data of trial subjects and commercially confidential data of the sponsor shall be deleted. Making inspection reports publicly accessible bears the inherent danger of compromising the overall aim of the Regulation to support the public confidence: • The information provided in inspection reports might be misunderstood and misinterpreted by the public who is generally neither familiar with the inspected clinical trials nor with inspection procedures. In addition, medical or trial-specific terms and procedures are likely to further the risk of misinterpretation. • Inspection reports might unsettle trial subjects, who are enrolled in the inspected trial or recruited by the inspected investigator/trial site and alienate potential future trial subjects/patients. Therefore, the publication of inspection reports could have a negative impact on subject/patient recruitment in the EU. Furthermore, the innovation capacity of European medical research might be adversely affected: • To publish inspection reports could have a discouraging effect on potential investigators. They might be concerned

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		about damage to their reputation or their professional career, resulting in a negative impact on the willingness of investigators in the EU to contribute to the conduct of clinical trials. • Article 81 Section 5. of the Regulation states that data contained in the application dossier shall not be publicly accessible before a decision on the clinical trial authorisation has been made. If reports of inspections performed in the context of clinical trial authorisation are publicly available, any application related data in the report would be released to the public well before the final decision on the marketing authorisation. In addition, the publication of GCP inspection reports is likely to compromise the effectiveness of the Member States' supervision of clinical trials as stipulated in Article 81 4. (d) of the Regulation: • Inspection reports are addressed to the inspected entity and the sponsor of the inspected trial in order to remedy deficiencies and to implement corrective and preventive actions. In case of pre-approval inspections, an integrated inspection report is prepared for the competent authority or the European Medicines Agency to support the decision about marketing authorisation. The reports include descriptions of the conduct of the clinical trial at the inspected site as well as explanations and conditions in relation to deficiencies. In many cases they refer to activities of the staff and specifics of the inspected company/facility which makes them sensitive information. Publishing the inspection report as a whole makes it necessary to delete this information in a painstaking and time-consuming process. With a view to making the most effective use of the limited GCP-inspection resources within the EU redacting processes should be limited to a minimum. • According to ICH GCP, section 5.19.3 (d), "To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely request the audit reports…." inspectors should not read the self-inspection reports of the sponsor's quality assurance. The publication of (redacted) inspection reports raises comparable issues, compromising the independence and the value of GCP- inspections. • The requirement to make inspection reports public will give rise to a significant increase in legal action. In case of undesirable inspection findings or results inspected entities will do their utmost to prevent or defer publication. In most Member States, inspection reports are written in *local language*. Therefore, the publication would not be of

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		much use to most of the public unless the report is translated into English. All things considered the overall benefit of the time taken to either translate or publish a report which is unintelligible to most of the people to whom it was intended for remains negligible. The regulation as well as the draft addendum underlines the legitimate economic interests of sponsors, but disregards the legitimate economic interest of contract research organisations and other service suppliers: • As opposed to manufacturers, importers etc., all of whom are subject to regular inspections, only a small proportion of sites involved in clinical trials are subject to GCP inspections. The publication of inspection reports would therefore lead to a distortion of competition amongst contract research organisations and other service suppliers. The Niedersächsisches Ministerium für Soziales, Gesundheit und Gleichstellung, Germany, strongly recommends not to publish inspection reports but to use inspection summaries, based on the already existing attachments to GCP inspection reports: (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/documentlisting_000140.jsp&mid=WC0b01ac05800296c6). These templates specify the deficiencies at the inspected site (e.g. investigator site, sponsor/CRO, and bioequivalence / bioavailability site). They can be adapted to provide all relevant data and information to ensure transparency keeping the aspects above in balance: • All information is in English. • The information is provided in a way that is easily accessible to the public, taking the form of a short overview of the scope, the findings and the outcome of the inspections permitting the preparation of metrics and statistics. • They are means of quick and direct communication/cooperation between Member States and ensure the effective supervision of the conduct of clinical trials (Regulation 526/2014, Article 78(3)). • Time-consuming and legally questionable redaction becomes unnecessary. **Proposed change (if any):** The Niedersächsisches Ministerium für Soziales, Gesundheit und Gleichstellung, Germany,

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		strongly recommends not to publish inspection reports but to use inspection summaries, based on the already existing attachments to GCP inspection reports: (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/documentlisting_000140.jsp&mid=WC0b01ac05800296c6).
763-794	18 34 82	**Question 14**, Section 4.6 Supervision of the Conduct of Clinical Trials **Comment**: The Freie und Hanseestadt Hamburg, Germany, The Regierungspräsidium Darmstadt, Germany, and The Ministry of Health and Social Affairs of the Federal State of Berlin, Germany, acknowledges the need for transparency of regulatory actions to support the public confidence in the clinical trial process and the EU medicines regulatory system while ensuring data privacy and taking into account the legitimate economic interest of sponsors and their service providers. According to articles 79 and 80 and 81 of the European Clinical Trial Regulation 536/2014/EC inspection reports shall be made available to the inspected entity and the sponsor of the relevant clinical trial and shall be submitted through the EU portal and stored in the EU database. According to article 81 Section 4, the information and data of the EU database shall be publicly accessible unless, for all or part of the data and information, confidentiality is justified. The present document (EMA/641479/2014) foresees in section 4.6.1 that GCP inspection reports, which will be stored in the EU database, should be made public once the inspection process is completed and the final inspection report is signed off and issued by the Member State(s) inspectorate. Only personal data of trial subjects and commercially confidential data of the sponsor shall be deleted. Making inspection reports publicly accessible bears the inherent danger of compromising the overall aim of the Regulation to support the public confidence: • The information provided in inspection reports might be misunderstood and misinterpreted by the public who is generally neither familiar with the inspected clinical trials nor with inspection procedures. In addition, medical or trial-specific terms and procedures are likely to further the risk of misinterpretation. • Inspection reports might unsettle trial subjects, who are enrolled in the inspected trial or recruited by the inspected

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		investigator/trial site and alienate potential future trial subjects/patients**.** Therefore, the publication of inspection reports could have a negative impact on subject/patient recruitment in the EU. Furthermore, the innovation capacity of European medical research might be adversely affected: • To publish inspection reports could have a discouraging effect on potential investigators. They will be concerned about damage to their reputation or their professional career, resulting in a negative impact on the willingness of investigators in the EU to contribute to the conduct of clinical trials. • Article 81 Section 5. of the Regulation states that data contained in the application dossier shall not be publicly accessible before a decision on the clinical trial authorisation has been made. If reports of inspections performed in the context of clinical trial authorisation are publicly available, any application related data in the report would be released to the public well before the final decision on the authorisation. In addition, the publication of GCP inspection reports is likely to compromise the effectiveness of the Member States' supervision of clinical trials as stipulated in Article 81 4. (d) of the Regulation: • Inspection reports are addressed to the inspected entity and the sponsor of the inspected trial in order to remedy deficiencies and to implement corrective and preventive actions. In case of pre-approval inspections, an integrated inspection report is prepared for the competent authority or the European Medicines Agency to support the decision about marketing authorisation. The reports include descriptions of the conduct of the clinical trial at the inspected site as well as explanations and conditions in relation to deficiencies. In many cases they refer to activities of the staff and specifics of the inspected company/facility which makes them sensitive information. Publishing the inspection report as a whole makes it necessary to delete this information in a painstaking and time-consuming process. With a view to making the most effective use of the limited GCP-inspection resources within the EU redacting processes should be limited to a minimum. • According to ICH GCP, section 5.19.3 (d), "To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely request the audit reports…." inspectors should not read the self-inspection reports of the sponsor's quality assurance. The publication of (redacted) inspection reports raises

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		comparable issues, compromising the independence and the value of GCP- inspections. • The requirement to make inspection reports public will give rise to a significant increase in legal action. In case of undesirable inspection findings or results inspected entities will do their utmost to prevent or defer publication. In most Member States, inspection reports are written in **local language**. Therefore, the publication would not be of much use to most of the public unless the report is translated into English. All things considered the overall benefit of the time taken to either translate or publish a report which is unintelligible to most of the people to whom it was intended for remains negligible. The regulation as well as the draft addendum underlines the legitimate economic interests of sponsors, but disregards the legitimate economic interest of contract research organisations and other service suppliers: • As opposed to manufacturers, importers etc., all of whom are subject to regular inspections, only a small proportion of sites involved in clinical trials are subject to GCP inspections. The publication of inspection reports would therefore lead to a distortion of competition amongst contract research organisations and other service suppliers. The Freie und Hansestadt Hamburg, Germany, strongly recommends not to publish inspection reports but to use inspection summaries, based on the already existing attachments to GCP inspection reports: (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/documentlisting_000140.jsp&mid=WC0b01ac05800296c6). These templates specify the deficiencies at the inspected site (e.g. investigator site, sponsor/CRO, bioequivalence / bioavailability site). They can be adapted to provide all relevant data and information to ensure transparency keeping the aspects above in balance: • All information is in English. • The information is provided in a way that is easily accessible to the public, taking the form of a short overview of the scope, the findings and the outcome of the inspections permitting the preparation of metrics and statistics. • They are a means of quick and direct communication/cooperation between Member States and ensure the effective

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		supervision of the conduct of clinical trials (Regulation 526/2014, Article 78(3)). • Time-consuming and legally questionable redaction becomes unnecessary.
763-796	10	**Question 14** **Comments:** We support the proposal with the following remarks. For the application of the document, it should be clarified what "the final inspection report" means. The contents of inspection reports vary between member states. In some cases answers/explanations from the inspected entity are part of the report, in some cases not. As mentioned in the general comments in section 1 above, page 2-3, errors in MS' redaction of inspection reports, might lead to subsequent involuntary publication of either protected personal data or commercially confidential information. Being the data controller of the database, EMA possibly bears the legal responsibility to make sure no such information is made public. The MPA Sweden realises that it is not possible for EMA to manually check submitted documents before they are made public, to make sure they don't contain confidential information and protected personal data. If EMA finds that the risk of publishing secret information cannot be eliminated, the reports should not be made public. We recommend that the Agency's legal responsibilities as data controller regarding the content of the database should be further clarified.
763-796	11	**Question 14** ACRO does not agree that the proposals meet the requirements and objectives of the Regulation. Inspection reports contain detailed information and findings that, taken out of context, would be misleading to the public. We are concerned that only the inspection report would be published and not the inspectee's response, which explains how they plan to correct inspection findings and prevent future occurrences. Additionally, inspection reports sometimes show that, during the limited time available for an inspection, the inspector failed to understand a situation fully. Publication of the inspection report alone would therefore give a biased and potentially (and unnecessarily) damaging view of how the trial was conducted. Often, too, inspection reports may contain detailed information about the trial design that would be considered CCI and while we note the proposal to redact inspection reports, we are concerned

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		that there may be a failure to recognise fully the elements that constitute CCI. We recommend that, rather than publishing the complete (redacted) inspection report, the responsible inspectorate should, after the evaluation of the inspectee's responses is complete, prepare a summary report for publication which gives brief details of the trial and the inspectee, together with the conclusions arising from the inspection. We also recommend that suitable arrangements are put in place for the preparation of similar summaries of inspection reports of third country authorities submitted under Article 53.2. One of the key purposes of inspection is to provide assurance that the data and conclusions generated in a clinical trial can be relied upon for future regulatory decision making, especially at the time of marketing authorisation approval. In order to achieve this aim, the EMA has recognized that individual inspection reports have to be viewed in the overall context of the marketing authorisation application and has established criteria for reviewing the impact of inspection findings on the benefit-risk assessment undertaken during evaluation of the marketing authorisation application (Points to consider on GCP inspection findings and the benefit-risk balance. EMA/868942/2011, 19 September 2012). We consider that this represents a valuable approach to place inspection findings in the overall context of the marketing authorisation application. We therefore recommend that the conclusions of this review of inspection reports is published, together with the proposed summary reports of the inspections on which it is based, at the time of marketing authorisation approval.
763-796	12	**Question 14** **Comment:** EUFEMED is of the view that the publication of inspection reports should have a defined purpose. Only findings that are of relevance to the public should be made publicly available. In case of inspections of early phase clinical research units, national inspection schemes differ widely. Some EU countries have voluntary, non-study-specific inspection schemes (such as the MHRA's Phase 1 accreditation scheme). During these voluntary inspections usually a number of studies will be inspected by the CA in accordance with the relevant schemes' requirements. Full publication of the inspection reports (including minor findings and recommendations) would disclose a large amount of commercially confidential information (such as methods and procedures) that is of no relevance to the public and may be difficult for the public to put into context. On the other hand, this information could be of commercial interest to the units' competitors. This could potentially disadvantage early phase units who voluntarily participate in inspection

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		schemes and/or who are located in countries with more stringent inspection schemes. **Proposed change (if any):** Voluntary inspection schemes should allow for voluntary publication with options to redact all information that should not be disclosed. In regard to for-cause and scheduled mandatory inspections we propose to publish only findings that are of relevance to the public (e.g. critical findings). Furthermore, there should be a clear definition of the time point at which the inspections reports are published. This should never be before the inspected party had an opportunity to respond to findings, which may change their classification. We propose that the EMA establishes an arbitration process for disputed findings. Arbitration should take place prior to publication.
763-796	19	**Question 14** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
763-796	35	**Question 14** EUCOPE supports the proposal that no personal data should appear in the redacted version of the inspection reports. Furthermore, only site information and a brief conclusion should be made public as more extensive release of information without context may be misleading for the public and could undermine confidence in inspections and the regulatory system.
763-796	57	**Question 14** **Comment:** EuropaBio has concerns about these proposals regarding disclosure of inspection reports - only the site information and a brief conclusion should be made public. We believe that full disclosure without context may be misleading for the public and undermine confidence in the inspection and regulatory system. We believe that the process for redaction should involve both the responsible inspectorate and the sponsor.
763-796	70	**Question 14** **Comment:** This comment also applies for Article 53.2 of the CTR (inspection reports of third country authorities).

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		EUCROF does not agree with the unrestricted publication of inspection reports. The publication of inspection reports should have a defined purpose. Only findings that are of relevance to the public should be made publicly available. With regards to the inspection of CROs, there is no unified European system in place to inspect all CROs fairly, equally and in regular intervals using the same methodology and standards. For reasons beyond CROs' influence, one CRO might be inspected and findings would be publicly available, whilst a competitor may not be inspected and therefore no report would be available. CROs are highly competitive service providers. Sponsors will use all publicly available information in their CRO selection process. A CRO for which nothing is published - because it was not inspected - might have an unfair commercial advantage or disadvantage (depending on the circumstances) in attracting business over one which was inspected. Publication of inspection reports within the current inspection systems will inevitably lead to unfair commercial advantages afforded to individual CROs and unintended commercial damages to others. This could have legal implications. Until a standardised and harmonised inspection system and process is available in the EU which includes all CROs, the approach of publishing inspection reports for CROs is considered unfair by EUCROF. In case of inspections of early phase clinical research units, the same applies. National inspection schemes differ widely. Some EU countries conduct regular mandatory GCP/GMP inspections to very strict standards, others do not. During early phase inspections usually a number of studies will be inspected by the CA. Some countries have national voluntary, non-study-specific inspection schemes (such as the MHRA's Phase 1 accreditation scheme) which may be run in conjunction with mandatory inspection schemes. The requirements of the national voluntary schemes exceed those of mandatory schemes and may focus on certain specific areas (e.g. the units' capability to conduct trials of potentially higher risk). Publication of inspection reports could potentially disadvantage early phase units who voluntarily participate in demanding inspection schemes and/or who are located in countries with more stringent inspection schemes. In all cases, full publication of the inspection reports (including minor findings and recommendations) would disclose a large amount of commercially confidential information that is of no relevance to the public. Indeed, it may be difficult for the public to put the information into context. For ongoing trials, the availability of inspection findings to the public

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		(trial participants), who might not have the expertise to judge the findings appropriately, might lead to an overreaction. As a consequence, participants might leave the trial prematurely. This could be to their disadvantage. The information contained in detailed inspection reports will be of high commercial interest to CROs' and early phase clinical research units' competitors. **Proposed change (if any):** (1) National inspection schemes (both voluntary and mandatory) should not be reported via the EU portal. (2) For inspections within the EU framework we propose the following: – The fact that an inspection took place should be made public – Only findings that are of relevance to the public (e.g. established critical safety findings) should be published via the EU portal – Findings should never be published before an inspection has been fully closed out and all findings, responses and outcomes have been agreed – A European arbitration process should be in place in case of disputed findings. Arbitration should always take place prior to publication
763-796	81	**Question 14** **Comment:** Our members agree upon this, especially for inspections performed in the frame of a marketing authorization application.
778-783	51	**Inspection reports** **Comment:** The EMA already publishes Annual reports of the Good Clinical Practice Inspectors Working Group. In these documents, the number and types of findings is described and examples for findings are presented. As only a minority of clinical trials is inspected, it may be difficult for the public to see the inspection results from a broader perspective.

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		There is no possibility for the sponsor to respond to the inspection findings. **Proposed change (if any):** Inspection reports will not be published
778-794	79	4.6.1 **Comment:** • Aufgrund der vorliegenden Transparenzregeln sollen die in das Portal einzustellenden GCP-Inspektionsberichte allen zugänglich gemacht werden. Bestimmte Angaben gem. Art. 81 Abs. 4 der Verordnung (EU) 536/2014 sollen durch das Inspektorat (und offenbar auch unter dessen Verantwortung) geschwärzt werden. U. E. ist fraglich, ob die beabsichtigte Veröffentlichung von Inspektionsberichten –mit oder ohne Schwärzung- den Vorgaben des Bundesdatenschutzgesetzes und des BayVwVfG (Akteneinsicht durch Beteiligte) sowie § 37 BeamtStG (Verschwiegenheitspflicht) entspricht. • Da unklar ist, was ein Betriebs- und Geschäftsgeheimisse ist (und was keines), kann das Schwärzen und Verantwortung darüber nicht vom Inspektorat übernommen werden. Insbesondere die Findings dürften als solche zu werten sein, wonach diese neben den vielen anderen Passagen zu schwärzen wären. Der ursprünglich beabsichtigte Transparenzweck wäre mit größtenteils geschwärzten Berichten gerade eben nicht zu erfüllen. Die Inspektorate dürfen in Bezug auf nicht geschwärzte, aber nach Ansicht der inspizierten Einrichtung schützenswerten Passagen, mit einer Klageflut rechnen. • Behörden und Überwachungsbeamte sind u. U. bei (versehentlicher) Veröffentlichung schützenswerter Daten zudem zivilrechtlicher (Schadenersatz) und strafrechtlicher Verfolgung ausgesetzt. • Weiters ist damit zu rechnen, dass inspizierte Einrichtungen gegen jeden Bericht mit schwerwiegenden oder kritischen Mängeln vorgehen werden, um nicht öffentlich negativ in Erscheinung zu treten. • Insgesamt ist nicht ersichtlich, warum gerade im GCP-Bereich, bei dem nur in geringem prozentualen Anteil Inspektionen von überwachungspflichtigen Einrichtungen erfolgen, eine derartige Transparenz gefordert wird, bei turnusmäßig zu inspizierenden GMP- oder GDP-Betrieben eine gleichartige Transparenz jedoch unterbleibt. Es

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		entsteht zudem ein verzerrtes Bild von Transparenz, da der weitaus größere Anteil der Einrichtungen und Betriebe nicht inspiziert wird bzw. werden kann und daher keine Berichte eingestellt sind. • Die Namen der beteiligten Inspektoren dürfen aus Gründen des Schutzes der Persönlichkeit keinesfalls lesbar sein bzw. veröffentlicht werden. • Nach hiesiger Kenntnis sollen –auch wenn dies in dem Papier nicht abschließend definiert wird- die Berichte in englischer Sprache in das Portal eingestellt werden. Dies bedeutet, dass alle Berichte zu übersetzen sind. Die englische Übersetzung müsste h. E. vollumfänglich die deutsche Fassung, auch in allen sprachlichen Nuancen und vor allem rechtssicher, wiedergeben. Dies kann vom Inspektorat keinesfalls geleistet werden. Sollte diese Forderung umgesetzt werden, kann die Übersetzung nur durch eine autorisierte zentrale Stelle erfolgen, die dann auch die Verantwortung für die rechtsverbindliche Richtigkeit der Übersetzung übernimmt (vgl. hierzu auch Art 23 Abs. 1 BayVwVfG).
778-802	49	**Comment:** Disagree with proposal of making inspection reports public. The reports could be taken out of context, are open to interpretation and can be misleading. This could all be undeservedly damaging to the organisation and could cause anxiety for trial subjects. **Proposed change (if any):** Inspection and Union Control reports are of a confidential nature and should not be made public.
778-843	60	Inspection Reports **Comment**: The text related to Inspection Reports does not distinguish between GCP or GMP inspections. We do however welcome the comment that reports to be made public will be redacted by the inspectorate. Consistent with the non-disclosure of IMPD-Q documents, we suggest that where GMP reports contain proprietary information these should not be released. However as per the existing EudraGMP database, the final conclusion may be made public. We also propose that GCP inspection reports should be made public provided that CCI is redacted **Proposed change (if any):** None

Line no.	Stakeholder no.	Comment and rationale; proposed changes
778-796	55	**Question 14** **Comment:** We agree with points 1, 3 and 4 of the proposal as described in Section 4.6.1; however, we respectfully request further clarification on point 2 as to whether this applies to routine GCP inspection reports.
778-796	65	**Question 14** **Comment:** EFPIA is concerned that the EMA proposed disclosure of inspection reports is too broad. Only site information and a brief conclusion should be disclosed to the public. Information should not be disclosed where this would undermine the confidence in the purpose of inspections, investigations and audits – full disclosure without context may be misleading for the public and undermine confidence in the inspection and regulatory system. In Europe, similarly with other major regulatory agencies, information should be limited such as to the investigator's name, site (city), date and type of inspection without naming the study. In case of sponsor inspection, information should be limited to the date and the type of inspection. Question 14 appears to refer to Member State inspections carried out in context of the of the CTA or MA procedure, According to Article 53, the CTA applicant is also requested to submit through the Portal all inspection reports from third countries. It is assumed that reports from third country authorities are not disclosed, as they would require consent. At present the EMA proposal states that inspection reports shall be redacted by the responsible inspectorate. In line with EFPIA's Major Comment under the heading 'Enable an Efficient System, Balancing Automation with Direct Sponsor Involvement', the process for redaction should involve the sponsor.
779-794	63	Section 4.6.1(4) Inspection Report **Comment:** Redacting/blackening of data is a very sensitive process. It is a balance between what needs to be blackened (e.g. to ensure data privacy and taking into account legitimate economic interests of sponsors and their service providers) and what should be made publicly available to ensure the intended transparency. Clear and detailed rules are needed for blackening in the inspection reports to ensure consistent performance. Experts

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		of the Member States should be involved in the development of such rules. The rules should apply to the EMA/Member States as well as to the sponsors of the clinical trials or the inspected entity, respectively. For Centralized Procedures and in several EU Member States, the comments to the inspection reports from the sponsors of the clinical trials/inspected entities are part of the inspection reports. It is propose that these comments should be submitted to the inspectorates in an un-redacted/un-blackened and a redacted/blackened way by the sponsors/inspected entities. The sponsor/inspected entity should follow the rules for blacking developed by the Member States/EMA. It is proposed that EMA takes over the responsibility for blackening inspection reports generated in the context of Centralized Procedures (Regulation (EC) 726/2004), as EMA coordinates these inspections and has direct contact to the group deciding about publishing of respective clinical trial data.
779-794	71	**Question 14:** **Comment:** The EGA agrees that this approach meets the requirements and objectives of the Regulation; however, additional steps should be incorporated into point 4. The redaction of inspection reports should be reviewed by the applicant/MAH for concurrence on the removal of confidential commercial information prior to being made public. In any case, it should be ensured that CCI is observed in the redaction of inspection reports, especially in the case of Phase I trials, as study-specific details may disclose competitive information.
781	39	**Comment:** Deferral of the publication of inspection reports is not in line with the spirit of the Regulation 536/2014. In fact, recent evidence from the US highlights the importance of having public access to inspection reports in a timely manner.[1] **Proposed change (if any):** Delete deferral of reports and include requirements from prompt publication of inspection reports.

[1] Seife C "Research Misconduct Identified by the US Food and Drug Administration"JAMA Intern Med. Published online February 09, 2015. doi:10.1001/jamainternmed.2014.7774

Line no.	Stakeholder no.	Comment and rationale; proposed changes
788-794 795-796	5	**Question 14** **Comment:** The proposal meets the requirements and objectives of the Regulation in general. Many study specific documents that are in the draft proposal declared not public due to extensive detail of commercially confidential information (study specific documents such as protocol, subject information sheet) are often referred to in the inspection report to describe the findings – both study specific and systematic. Information related to clinical trial subjects (such as data listings, see 4.3.1) which are in the same document considered confidential are as well referred to in inspection reports. Therefore, these findings should also be considered confidential. **Proposed change:** Lines 788-794: The inspection report made public should be redacted, by the responsible inspectorate, in line with the principles set out in accordance with exceptions under Article 81(4) (a) and (b). *The inspection findings and detailed data supporting the findings should not be published to allow the inspectors to report and provide all the relevant details on the study specific findings which may include information on individuals other than the investigator, or commercially confidential information.* The *(redacted)* report should nonetheless identify the relevant clinical trials by their EU number and or protocol number (for third country trials) and the site of the inspection, including where applicable the name of the investigator, and the name of the institution, or for other facilities the name of the facility (e.g. laboratories). Redacted and un-redacted versions should be submitted to the database but only the redacted version made public. No personal data of trial subjects should appear.
795-796	4	**Question 14** EURORDIS agrees with the proposal.
795-796	6	**Questions 14,** Section 4.6 Supervision of the Conduct of Clinical Trials **Comments:** The Land Schleswig-Holstein, Germany, acknowledges the need for transparency of regulatory actions to support the public confidence in the clinical trial process and the EU medicines regulatory system while ensuring data privacy and taking into account the legitimate economic interest of sponsors and their service providers. According to articles 79 and 80 and 81 of the European Clinical Trial Regulation 536/2014/EC inspection reports shall be made available to the inspected entity and the sponsor of the relevant clinical trial and shall be submitted through the

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		EU portal and stored in the EU database. According to article 81 Section 4, the information and data of the EU database shall be publicly accessible unless, for all or part of the data and information, confidentiality is justified. The present document (EMA/641479/2014) foresees in section 4.6.1 that GCP inspection reports, which will be stored in the EU database, should be made public once the inspection process is completed and the final inspection report is signed off and issued by the Member State(s) inspectorate. Only personal data of trial subjects and commercially confidential data of the sponsor shall be deleted. Making inspection reports publicly accessible bears the inherent danger of compromising the overall aim of the Regulation to support the public confidence: • The information provided in inspection reports might be misunderstood and misinterpreted by the public who is generally neither familiar with the inspected clinical trials nor with inspection procedures. In addition, medical or trial-specific terms and procedures are likely to further the risk of misinterpretation. • Inspection reports might unsettle trial subjects, who are enrolled in the inspected trial or recruited by the inspected investigator/trial site and alienate potential future trial subjects/patients**.** Therefore, the publication of inspection reports could have a negative impact on subject/patient recruitment in the EU. Furthermore, the innovation capacity of European medical research might be adversely affected: • To publish inspection reports could have a discouraging effect on potential investigators. They might be concerned about damage to their reputation or their professional career, resulting in a negative impact on the willingness of investigators in the EU to contribute to the conduct of clinical trials. • Article 81 Section 5. of the Regulation states that data contained in the application dossier shall not be publicly accessible before a decision on the clinical trial authorisation has been made. If reports of inspections performed in the context of clinical trial authorisation are publicly available, any application related data in the report would be released to the public well before the final decision on the authorisation. In addition, the publication of GCP inspection reports is likely to compromise the effectiveness of the Member States'

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		supervision of clinical trials as stipulated in Article 81 4. (d) of the Regulation: • Inspection reports are addressed to the inspected entity and the sponsor of the inspected trial in order to remedy deficiencies and to implement corrective and preventive actions. In case of pre-approval inspections, an integrated inspection report is prepared for the competent authority or the European Medicines Agency to support the decision about marketing authorisation. The reports include descriptions of the conduct of the clinical trial at the inspected site as well as explanations and conditions in relation to deficiencies. In many cases they refer to activities of the staff and specifics of the inspected company/facility which makes them sensitive information. Publishing the inspection report as a whole makes it necessary to delete this information in a painstaking and time-consuming process. With a view to making the most effective use of the limited GCP-inspection resources within the EU redacting processes should be limited to a minimum. • According to ICH GCP, section 5.19.3 (d), "To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely request the audit reports…." inspectors should not read the self-inspection reports of the sponsor's quality assurance. The publication of (redacted) inspection reports raises comparable issues, compromising the independence and the value of GCP- inspections. • The requirement to make inspection reports public will give rise to a significant increase in legal action. In case of undesirable inspection findings or results inspected entities will do their utmost to prevent or defer publication. In most Member States, inspection reports are written in local language. Therefore, the publication would not be of much use to most of the public unless the report is translated into English. All things considered the overall benefit of the time taken to either translate or publish a report which is unintelligible to most of the people to whom it was intended for remains negligible. The regulation as well as the draft addendum underlines the legitimate economic interests of sponsors, but disregards the legitimate economic interest of contract research organisations and other service suppliers: • As opposed to manufacturers, importers etc., all of whom are subject to regular inspections, only a small proportion of sites involved in clinical trials are subject to GCP inspections. The publication of inspection reports would

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		therefore lead to a distortion of competition amongst contract research organisations and other service suppliers. **The Land Schleswig-Holstein, Germany, strongly recommends not to publish inspection reports** but to use inspection summaries, based on the already existing attachments to GCP inspection reports: (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/documentlisting_000140.jsp&mid=WC0b01ac05800296c6). These templates specify the deficiencies at the inspected site (e.g. investigator site, sponsor/CRO, bioequivalence / bioavailability site). They can be adapted to provide all relevant data and information to ensure transparency keeping the aspects above in balance: • All information is in English. • The information is provided in a way that is easily accessible to the public, taking the form of a short overview of the scope, the findings and the outcome of the inspections permitting the preparation of metrics and statistics. • They are means of quick and direct communication/cooperation between Member States and ensure the effective supervision of the conduct of clinical trials (Regulation 526/2014, Article 78(3)). • Time-consuming and legally questionable redaction becomes unnecessary.
795-796	13	**Question 14** (inspection reports) Inspection status (eg dated last inspected, number of findings by category) should be published. However, we have concerns about publication of inspection reports of routine audits of clinical trials units. Phase I units in the UK are inspected regularly by the MHRA for compliance with GCP and against the requirements of the MHRA phase I accreditation scheme. Those audits may include review of documents from a random sample of several trials. Is it proposed that those non-trial-specific reports be published? If so, how would that be managed, given that they might include findings from several studies for different sponsors. Also, although inspection reports would be released only when final and redacted, the value to the public could be outweighed by the potential harm to the party inspected, particularly in the case of commercial clinical trials units. If

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		reports are published before the inspected unit has had the opportunity to respond, any findings raised in error have the potential to harm the unit unfairly. Even if the inspection report is not published until the unit has responded to the findings, there is the potential for findings to be misinterpreted by the public (including potential sponsors, volunteers and the press), which could lead to commercial harm. Findings are best dealt with by the regulators, who fully understand the issues and the context, and can work with the unit (and if applicable the sponsor) to resolve them. There should not be the potential for interference in that process by third parties, or for units to be tarnished unfairly. Publication of anonymised summaries of findings of inspections of clinical trials units by the Competent Authorities, and of examples of best practice, would demonstrate supervision of clinical trials and ensure that all units learn from all inspections, without the risk of unfair commercial harm.
795-796	28	**Question 14** The proposed paragraphs ensure an effective supervision of the conduct of a clinical trial by Member States. Secondly, the proposals hold an optimal balance between commercial and public interests. It can be concluded that the proposals meet the requirements and objectives of the Regulation.
795-796	29	**Question 14** The proposals meet the requirements and objectives of the Regulation. There is no need to have more than the redacted final inspection report publicly available.
795-796 801-802 842-843	30	**Questions 14** Proposals seem fine.
795-796	32	**Question 14** Yes
795-796	36	**Question 14**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: *The FPM believes that these proposals meet the requirements and objectives of the Regulation.*
795-796	38	**Question 14** **Comment:** We agree with the proposal
795-796	41	**Question 14** It is recognised that these proposals to make public the inspection reports once the inspection process is completed and signed off has the intention to increase the standards of clinical research undertaken across all Member States, which we fully endorse. However, it is questionable what benefit the release of inspection reports would be to the general public other than to commercially disadvantage the clinical trial unit by virtue of providing such information to its competitors. **Proposed Change:** The inspection status (date last inspected, number of findings by category) should be made public but any detail beyond that needs to be kept confidential and left for discussions between the Inspector, the Clinical Unit and its Sponsors.
795-796	46	**Question 14** **Comment:** That the inspection status of a trial unit (date last inspected, number of findings etc.) should be made public is beyond question, however it is not clear what benefit would be derived by the public having information beyond that. Any such information should be kept confidential between the Inspector, Clinical unit and its Sponsors.
795-796	48	**Question 14** **Comment: No**, this proposal does not meet the requirements and objectives of the Regulation (EU) No 536/2014. The inspections report should only be published a t the time of publication of the clinical trial report, or at earliest at the end of the study. Indeed, there can be corrective measures in place and the publicity of such a report before the end of the trial would bring confusion, unless the site or the sponsor should be debarred.
795-796	51	**Question 14**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: The EMA already publishes Annual reports of the Good Clinical Practice Inspectors Working Group. In these documents, the number and types of findings is described and examples for findings are presented. As only a minority of clinical trials is inspected, it may be difficult for the public to see the inspection results from a broader perspective. There is no possibility for the sponsor to respond to the inspection findings. **Proposed change (if any):** Inspection reports will not be published.
795-796	53	**Question 14** We **do not** support this proposal. We consider the publication of inspection reports to be unnecessary and are not required to fulfil the requirements and objectives of the Regulation. They may contain commercially sensitive data and findings identified in an initial inspection report are often subject to an interactive discussion and clarifications. They would not be very informative to the public and could be subject to considerable misunderstanding which could be a reputational risk to sponsors. This will most likely also slow down clinical research due to very burdensome additional reporting and communication regarding inspection results.
795-796	54	**Question 14** We feel that these proposals meet the requirements and objectives of the Regulation.
795-796	59	**Question 14** **Comment:** We agree with the principal of the results of inspections being made public. Further clarity would be appreciated on the exact details to be made available in the database. **Proposed change (if any):** Further clarity would be appreciated on the exact details to be made available in the database.
795-796	62	**Question 14** **Comment:** The preferred option would be for inspection reports not be made publically available. Agree that only redacted inspection reports should be made publically available after a Marketing Authorisation has

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		been granted.
795-796	67	**Question 14:** Inspection reports should be available by all means and in any occasion as they provide crucial information on the reliability of research developed.
795-796	75	**Question 14** **Comment:** we consider the publication of inspection reports to be excessive in relation to the requirements of the Regulation. These may contain commercially sensitive information and are not easy to interpret by 3rd parties. We do not support this proposal.
795-796	76	**Question 14** **Comment:** we consider the publication of inspection reports to be excessive and may contain commercially sensitive information. We do not support this proposal.
795-796	80	**Question 14** **Comment:** It does meet the spirit of the Regulation.
797-800	55	**Question 15** **Comment:** We agree that the proposal meets the requirements and objectives of the Regulation.
797-802	10	**Question 15** **Comments:** We support the proposal, but want to refer to the comment above regarding consequences of errors in redaction. Also, it is important that it is clear which MS is supposed to redact notices when the initial notice is reported to several MS.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
797-802	11	**Question 15** ACRO agrees that the proposal meets the requirements and objectives of the Regulation.
797-802	12	**Question 15** **Proposed change (if any):**None
797-802	19	**Question 15** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
797-802	35	**Question 15** We agree with the EMA proposal. However, personal information identifying individuals should not be made public.
797-802	57	**Question 15** **Comment:** EuropaBio supports this proposal. However, personal information identifying individuals should not be made public.
797-802	60	Union Control Reports **Comment**: We agree with the proposal in this addendum as stated. **Proposed change (if any):** None
797-802	65	**Question 15** **Comment:** EFPIA agrees with the EMA proposal. The report on Union Control is in the public interest and the Commission will be able to redact CCI and PPD. It should be made public in line with the principles set out in accordance with the exceptions under Article 81 (4). The same approach as for inspection reports (Question 14) could be used when providing public information.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
797-802	70	**Question 15** **Comment:** EUCROF agrees with the EMA proposal
797-802	81	**Question 15** **Comment:** Union control reports have to be redacted by the European Commission. That means this will happen outside the regulations generated in this document. The process of redaction should include the following element: • Upfront information and consultation with the sponsor of planned publication. **Proposed change (if any):** Please add an explaining sentence regarding the process of redaction.
798-800	14	**Question 15** Referring to Question 15: comment on whether this proposal meets the requirements and objectives of the Regulation: 4.6. Ensuring effective supervision of the conduct of a clinical trial by Member States: 4.6.2. Union Control reports: **Comment**: We agree.
798-800	71	**Question 15:** **Comment:** The EGA agrees that this proposal meets the requirements and objectives of the Regulation. The redaction should be reviewed by the applicant/MAH for concurrence on the removal of confidential commercial information prior to being made public. **Proposed change (if any):** Please refer to the involvement of the applicant/MAH in this process.
798-800	79	**4.6.2** **Comment:**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		• Art. 79 Abs 2 der VO (EU) 536/2014 legt fest, dass die Kommission die Kontrollberichte „über das EU-Portal übermittelt“. Es ist jedoch nicht festgelegt, dass die Berichte über das Portal allgemein veröffentlicht werden. • Die Schwärzung der Berichte soll durch die Kommission vorgenommen werden. Hier ist unklar, nach welcher Maßgabe die Schwärzung erfolgt, da „Betriebs- und Geschäftsgeheimnisse“ und schützenswerte Daten einer Behörde nicht definiert sind. Da datenschutzrechtliche Bestimmungen in der EU vollkommen unterschiedlich gehandhabt werden, ist damit zu rechnen, dass der Schutzstandard nicht dem hiesigen Standard entspricht. • Sollten die Unionskontrollen nur in stichprobenartigem Umfang erfolgen, ergibt sich kein transparentes Gesamtbild, sondern es werden über das EU-Portal ggf. einzelne Behörden „zur Schau gestellt“.
801-802	4	**Question 15** No opinion.
801-802	5	**Question 15** **Comment:** The proposal meets the requirements and objectives of the Regulation.
801-802	13	**Question 15** (immediate publication of Union control reports) The proposal meets the requirements and objectives of the Regulation.
801-802	28	**Question 15** The proposal meets the requirements and objectives of the Regulation in ensuring effective supervision by the Commission. It is highly desirable that the final report of a Union Control will be made public in order to develop a deeper and/or better understanding of the Regulation.
801-802	29	**Question 15** We agree with the proposal.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
801-802 795-796 842-843	30	**Questions 15** Proposals seem fine.
801-802	32	**Question 15** Meets requirements
801-802	36	**Question 15** **Comment:** *n/a*
801-802	38	**Question 15** **Comment:** We agree with this proposal unless the redaction renders the document meaningless.
801-802	41	**Question 15** We concur with this proposal and believe it meets the requirements and objectives of the Regulation.
801-802	46	**Question 15** **Comment:** We agree with this proposal and believe it meets the requirements and objectives of the Regulation.
801-802	48	**Question 15** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014.
801-802	51	**Question 15** **Comment:** Principles of redaction of personal data or commercially confidential information to be carried out by the Commission are not explained in detail. **Proposed change (if any):** proposal should be removed

Line no.	Stakeholder no.	Comment and rationale; proposed changes
801-802	53	**Question 15** Unable to respond as terminology unclear in this context
801-802	54	**Question 15** We feel that these proposals meet the requirements and objectives of the Regulation.
801-802	59	**Question 15** **Comment:** We have no concerns about the proposal this question relates to Proposed change (if any): Not applicable
801-802	62	**Question 15** **Comment:** Unable to comment because we are not familiar with Union Control reports.
801-802	80	**Question 15** **Comment:** It does meet the spirit of the Regulation.
803	51	**Comment:** Serious breaches should not be published unless they lead to a corrective measure by a Member State. It may lead to a unilateral view of the proceedings, as the corrective and preventive actions following a serious breach do not fall within the scope of the Clinical Trial Regulation **Proposed change (if any):** Only serious breaches leading to a corrective measure by a Member State should be published.
803-841	71	**Question 16:** **Comment:** The EGA agrees that this proposal meets the requirements and objectives of the Regulation.
803-841	79	**4.6.3**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: • Sofern GCP-Verletzungen an mehrere EU-MS gemeldet werden, soll ein Mitgliedstaat federführend den Vorgang bearbeiten (…they may decide on one Member State taking the lead in evaluating the case…). Es ist unklar, nach welchem Verfahren der federführende Mitgliedstaat ermittelt wird. • Der Begriff „schwerwiegender Verstoß“ i. S. v. Art 52 Abs. 2 der VO (EU) 536/2014 („Im Sinne dieses Artikels bezeichnet ein "schwerwiegender Verstoß" einen Verstoß durch den die Sicherheit und die Rechte eines Prüfungsteilnehmers oder die Zuverlässigkeit und Belastbarkeit der im Rahmen der klinischen Prüfung gewonnenen Daten wahrscheinlich erheblich beeinträchtigt werden“) ist dehnbar und in verschiedene Richtungen hin auslegbar, so dass betroffene Firmen/ Einrichtungen mit allen rechtlichen Mitteln dagegen vorgehen werden, um nicht öffentlich negativ in Erscheinung zu treten. In der Folge ist mit langwierigen ressourcenzehrenden Verwaltungs- und Gerichtsverfahren zu rechnen. • Zur Veröffentlichung der Verletzung von GCP-Regularien ist ebenfalls fraglich, ob dies den Vorgaben des Bundesdatenschutzgesetzes und des BayVwVfG (Akteneinsicht durch Beteiligte) sowie § 37 BeamtStG (Verschwiegenheitspflicht) entspricht.
803-843	10	**Question 16** **Comments:** We support the proposals with the same remark as above regarding consequences of possible errors in MS’ and sponsors’ redaction of either protected personal data or commercially confidential information in notices and summaries.
803-843	11	**Question 16** ACRO agrees for the most part that the proposals meet the requirements and objectives of the Regulation, but have reservations about the proposed timing of publication of information on serious breaches and corrective measures. We are concerned that the draft addendum section on serious breaches and corrective measures does not refer to Article 81.4(d) of the Regulation, which allows for information not to be published should doing so compromise the ability to ensure effective supervision of the conduct of a clinical trial by Member States. Additionally, there are cases (e.g.,

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		fraud) where a serious breach could lead to criminal charges and legal action undertaken outside of medicines law and regulation. Such legal action could be compromised by premature publication of the serious breach (even if it is in accordance with arrangements implemented under Regulation 536/2014) and we strongly recommend that this should be recognized in the addendum.
803-843	12	**Question 16** **Proposed change (if any):**None
803-843	19	**Question 16** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
803-843	35	**Question 16** EUCOPE agrees that serious breaches should be disclosed only after investigations have been completed and conclusions have been reached.
803-843	49	**Question 16** **Comment:** Agree in principal, but we have concerns over consistent reporting- how would this be achieved and monitored? Option 1.6 is preferable, allowing a more comprehensive report to be published from the sponsor, whilst protecting individuals. The regulator's notice would need to be limited.
803-843	55	**Question 16** **Comment:** We agree with the proposal as described in Section 4.6.3 as it meets the regulation's objectives for data transparency and the protection of the patient's well-being. However we would like to emphasize the need for an executive summary to be published (rather than the full breach report) to avoid any commercially sensitive information being made public.
803-843	57	**Question 16**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: EuropaBio supports these proposals. We believe that serious breaches should be disclosed only after they have been fully investigated and the conclusion has been reached.
803-843	60	Serious Breaches **Comment**: We agree with the proposal in this addendum as stated. **Proposed change (if any):** None
803-843	65	**Question 16** **Comment:** During the process, disclosure of serious breaches may jeopardize countries' ability to act per the article 81(4) (d). For this reason, it is important that serious breaches are not disclosed until after they have been investigated and the conclusion has been reached. Under point 1.6, it should also refer to exception 81(4)(d). In terms of information made public once the action plan has been set up and the breach has been solved, this information should be limited to the site and study concerned, a factual description of the serious breach and corrective actions. Industry should be afforded the opportunity to comment on the format and content of the template that will be implemented EU-wide for the reporting of serious breaches, to ensure consistency with current practice.
803-843	70	**Question 16** **Comment:** EUCROF agrees with the EMA proposal, however with the limitations made under Question 14 for inspection reports.
803-843	81	**Question 16** **Comment:** Agreed and consistent with 4.6.1.
804-841	14	**Question 16** Referring to Question 16 comment on whether this proposal meets the requirements and objectives of the Regulation:

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		4.6. Ensuring effective supervision of the conduct of a clinical trial by Member States: 4.6.3. Serious breaches and corrective measures: **Comment:** In general, we agree. But it should not left at the discretion of the sponsor what information to include. That should be decided by inspectors and Member States.
804-841	29	**Comment:** It is not clear to us, which data will be made public and what needs to be in the notice to substantiate that a serious breach has occurred. A standardised approach and hard criteria are needed, so that every MS is judging serious breaches on the same agreed principles.
823-841	63	**Question 16** **Comment:** Point 1.5 refers to corrective measures by MS concerned unrelated to a serious breach. Therefore reference to conditions 1.6 which mainly refer to serious breaches is not correct. In general, no summary of sponsor might be provided for corrective measure which is an action by MSc. Anyway publication should be in line with article 81 (4) a and b. Point 1.6 is not applicable for corrective measure, see above. **Proposed change (if any):** Point 1.5 (line 825-826) delete reference “in line with conditions set out in 1.6”; add “ in line with article 81(4)”. Point 1.6 (line 832) delete “and/or corrective measures”
826	54	**Comment:** Further action may be required, for example some supervision to ensure continuing compliance. This would not be regulatory action such as an inspection or suspension of a trial etc, but would be supportive measures to ensure that the sponsor has taken appropriate action. This type of action should also be mentioned here. The vast majority of the UK serious breaches are handled this way. **Proposed change (if any):** If the Member State decides to administer additional supervision to ensure continuing

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		compliance then the notice detailing the serious breach and action should be included in the database, and published once the supervisory period is completed and the serious breach has been closed.
832-833	21	**Question 16** **Comment:** Disagree. The notice of serious breach made public by MS should use all relevant information including that obtained during the investigation of the serious breach. **Proposed change:** Delete "The notice of serious breaches and/or corrective measures made public by the Member State should use the summary provided by the sponsor". This would only lead to disagreements about how the breach is reported in public.
842-843	4	**Question 16** EURORDIS agrees with the proposal.
842-843	5	**Question 16** **Comment:** The proposal meets the requirements and objectives of the Regulation.
842-843	13	**Question 16** (serious breaches) The publication of serious breaches would be counterproductive, as it could discourage commercial research in the EU. In the UK, serious breaches are dealt with by the MHRA, sponsor and clinical unit. Clinical trial units are contractually obliged to notify the sponsor immediately of any serious breach, and the sponsor notifies the MHRA. An agreed corrective and preventative action (CAPA) plan is implemented before the breach is closed out. Often serious breaches are quite simple in nature, caused either by process failure or human error, and are readily rectified by an appropriate CAPA plan. We are not aware of a serious breach that has caused actual harm to a trial participant or irredeemable harm to the integrity of a trial. However, if made public, the very fact that a unit has had a serious breach could put the clinical unit at an immediate commercial disadvantage. Without all the facts and an understanding of the context and technical details, a serious

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		breach could easily be misinterpreted by sponsors, potential participants and the press. • Sponsors, particularly those outside the EU, who are unfamiliar with the process, are likely to blacklist units with any serious breach, rather than read and assess all the details before making a decision about a unit's suitability. • Given the stigma associated with serious breaches, volunteers or patients may decide against participating in a study at a unit that has had any serious breach. • A breach could be misreported in the local and national press, which would have a negative impact on the unit and on clinical research overall. Therefore, the publication of serious breaches has the potential to cause real commercial harm. Serious breaches are best left to individual Member States to deal with accordingly. The status of any unit/site is monitored and controlled by the CA Inspectorate – a unit/site would not be allowed to do clinical research if the CA Inspectorate deemed it unsuitable to do so. In the event of an important serious breach, if the CA suspended all activities at a unit, the unit would be obliged to inform all interested parties (all sponsors of ongoing trials). We are also concerned about the potential for inconsistency in the interpretation of serious breaches among Member States. How will consistent approaches be guaranteed to ensure that all sponsors and units in all Member States are treated fairly? It would be unfair if a serious breach in one Member State were not considered a serious breach by another Member State. A further concern of clinical research units is that the sponsor would control the information that is published. The sponsor may not fairly represent the investigator, unit (or another contractor). Even if a unit or contractor is at fault, that party should have the opportunity to present its case. There is the also the potential for individuals working for the sponsor to try to shift blame onto units or other parties. Publication of anonymised summaries of serious breaches by the Competent Authorities would demonstrate supervision of clinical trials, and ensure that all units learn from them, without the risk of unfair commercial harm.
842-843	28	**Question 16**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		The proposal meets the requirements and objectives of the Regulation in ensuring respect for the rights, safety, and wellbeing of subjects. Information about serious breaches can also be relevant for trial subjects of other clinical trials that are not related to the same sponsor. Therefore information about serious breaches should be made public.
842-843	29	**Question 16** In general, we agree with the proposals. We agree that information on serious breaches should not be made public until those have been investigated in more detail and the breach is confirmed. Still more detailed information / definition is needed on what a serious breach means, e. g. to reach a harmonised approach of the different MS when substantiating whether a serious breach has occurred. It is very important that all MS have the same approach and evaluate a notice of a potential serious breach in the same way. The criteria for a serious breach need to be standardised. Confirmed fraud (e. g. manipulation of data base) should be published with the according details. We would find it helpful if it would be made more clear which data will be published and what information will be included in a redacted version. What would have to be included in a description / notice of a serious breach?
842-843 795-796 801-802	30	**Questions 16** Proposals seem fine.
842-843	32	**Question 16** Yes
842-843	36	**Question 16** **Comment:** *The FPM believes that these proposals meet the requirements and objectives of the Regulation.*
842-843	38	**Question 16** **Comment:** We agree with the proposal

Line no.	Stakeholder no.	Comment and rationale; proposed changes
842-843	41	**Question 16** As with the release of inspection reports we recognised that the ultimate purpose of making public details of any serious breaches is to increase the standards of clinical research within the EU, which we support entirely. However, we believe that the publication of serious breaches on the EU database would be a counterproductive step and could seriously discourage commercial research in the EU. This is for a number of reasons 1. There is potential for differences in interpretation of the Serious Breach guidelines among Member States, which may result in confusion between Sponsors and CROs and potentially disadvantage CROs if the Serious Breaches guidelines are more strongly adhered to in one territory versus another. This leads to an important question of how will consistency in approaches taken be guaranteed by the agency to ensure that all Sponsors and clinical units are treated fairly across the Member States. 2. In addition there is risk that as the Sponsor is in control of the information which is ultimately published and the Principal Investigator and contracted clinical unit may not be fairly represented by the Sponsor. 3. Often serious breaches can be quite simple in nature caused either by process failure or human error and are readily rectified by appropriate CAPA plan. However, the general public and patients may not be familiar with clinical research and the terms used and therefore there is potential for over-reaction to a serious breach due to misinterpretation, which in turn may ultimately lead to a decline in the willingness of patients and volunteers to participate in clinical trials. Serious breaches may also be misreported in the local and national press which would also have a negative impact on clinical research overall. Therefore the publication of serious breaches has the potential to cause real commercial harm and is best left to individual Member States, who fully understand the issues and the context, to deal with them accordingly. Ultimately the status of any clinical unit/site is very much under the control of the CA Inspectorate and a clinical unit/site would not be allowed to undertake any research if the CA Inspectorate deemed that it was unsuitable to do so. Also CROs are contractually obliged to notify the Sponsor immediately of any serious breach and subject to severity of action the CA Inspectorate decides to take (e.g. suspension of activities) may have to notify all of the Sponsors it is working with at

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		the time. **Proposed Change:** As the Serious Breach reporting is extended across the EU, every CA should be encouraged to share their experiences and learnings from this process, which then could be made public but in an anonymised report.
842-843	46	**Question 16** **Comment:** The publication of serious breaches has the potential to be misleading, divisive and commercially damaging to individual units conducting clinical trials and is best left to the CA of individual Member States to resolve. A serious breach could be the result of e.g. a single human error but, if reported on the EU database, could deter both Sponsors and volunteers from using that unit. More widely than an individual unit, it could have a deleterious effect on commercial clinical trials in the EU as a whole.
842-843	48	**Question 16** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014.
842-843	51	**Question 16** Serious breaches are not always caused culpably. There is a danger of prejudgment and misperception by the public. This would seriously undermine the reputation of clinical research, which would not serve the objective of the Regulation to strengthen clinical research in Europe. Future sponsors would lose faith in European clinical research practice and would conduct their clinical trials outside the European Union.
842-843	53	**Question 16** We have significant reservations regarding the publication of serious breach information and consider that the proposal DOES NOT meet the requirements and objectives of the Regulation as stated in Article 77 but is excessive public release of trial conduct information which could be inappropriately detrimental. Whilst it is understood that the proposal has the intention of supporting transparency in the conduct of the trial, Article 77 refers to circumstances where the trial is no longer meeting the requirement of the Regulation and major action is

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		initiated by the Member State, for example; suspension of a trial or revocation of the clinical trial authorisation (Article 77 1a-b). Whilst this type of intervention may arise as an action following the reporting a serious breach, in many cases, simple measures are put in place to avoid recurrence of the breach and there is no substantial change imposed on the trial status by the member state. The investigation and reporting of a potential serious breach is an important part of the role of the sponsor and is intrinsic to the sponsor's quality management and audit processes. Whilst it is proposed that the published report would be a summary with personal data and commercially sensitive data redacted, the nature of a serious breach is often complex and needs to be seen in a more detailed context of the report. Point 1.1.1. in particular is excessive and exceeds the Regulation's requirement. Currently sponsors will err on the side of caution and report a potential serious breach, while a more detailed investigation is on-going. In the subsequent investigation it can become apparent that the event does not meet the criteria of a serious breach or in the opinion of the competent authority, no serious breach has occurred. There is no value in publishing this exchange of information and does have the potential to lead to mis-understanding or mis-interpretation when released in the public domain. To meet the requirement and objectives of the Regulation, it is suggested that a summary of a serious breach and the measure should be published ONLY IF the actions described in Article 77 1a-c occur: i.e. the member state revokes the authorisation of a trial, suspends a trial or requires the sponsor to modify any aspect of the trial. All these points would be clear and in the public interest.
842-843	54	**Question 16** We feel that these proposals meet what is outlined in the Regulation but does not encompass all actions that Member States may take. For example, further action may mean supervision to ensure continuing compliance. This would not be considered corrective measures as per Article 77 in Regulation (EU) No 536/2014, but would be considered as supportive measures to ensure that the sponsor has taken appropriate action. We would generally take these measures before deeming it necessary to take corrective measures as outlined in the Regulation. We feel that this type of (less extreme) action should also be mentioned here as this would still relate to action taken to address a serious breach.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		The vast majority of the UK serious breaches are handled this way (proposed text to insert detailed in table below).
842-843	59	**Question 16** **Comment:** We have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
842-843	62	**Question 16** **Comment:** Agree the proposal meets the requirements and objectives of the regulation.
842-843	75 76	**Question 16** **Comment:** we consider the publication of serious breaches to be excessive and may contain commercially sensitive information. We have serious concerns regarding the impact on sponsor resources and the potential for sensationalisation within the media and potential harm to organisational and individual reputation.
842-843	80	**Question 16** **Comment:** It does meet the spirit of the Regulation.
844-857	11	**Question 17** ACRO agrees for the most part that the proposals meet the requirements and objectives of the Regulation, but have reservations about the proposed timing of publication of information on reporting of unexpected events and urgent safety amendments. In such cases, it is very likely that the unexpected event or urgent safety amendment will ultimately result in an application for substantial modification of the clinical trial authorisation. We therefore recommend that details of the unexpected event or urgent safety modification (redacted to protect CCI) are published at the same time as information on the resulting substantial modification.
844-858	10	**Question 17** **Comments:** We support the proposals with same remark as above regarding consequences of possible errors in

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		sponsors' redaction of personal data.
844-858	12	**Question 17** **Comment:** In early phase clinical trials (e.g. First-in-Human trials), it is not unusual that the benefit-risk balance of a trial changes during the conduct of a trial. This is due to the exploratory nature of these trials. The design of trials (i.e. study protocol), and in particular the use of adaptive trial design, accommodate this by requiring continuous evaluation of evolving data and consecutive adaptation of studies to minimise risk. In many cases, non-substantial modifications of the trial can thereby avoid changes of the benefit-risk balance. For some early phase trials the benefit-risk balance may change in such way that a substantial modification of the trial becomes necessary to manage the risk. This would require MS approval before the study can proceed further. Such a substantial modification may be non-urgent or an urgent safety measure/substantial modification. Study Participants will always be updated of any changes in benefit-risk balance as this is a GCP requirement and forms part of all subject information sheets. Publication at the time of reporting could hinder Competent Authorities, sponsors and investigators in investigating and dealing with these events using established and safe mechanisms. It could also hinder continued conduct of a trial (following the necessary authorisations). The requirement for early publication could become a barrier to reporting unexpected events or introducing urgent safety measures. As a result unexpected events may be under-reported and necessary safety measures may not be taken to avoid publication. This would have a negative impact on participant safety. Moreover, there will be no benefit to the public, as all necessary information will be routinely made available to (prospective) study participants. **Proposed change (if any):** It is our firm opinion that in case of Phase 1/non-therapeutic studies, information on non-serious unexpected events (in compliance with Article 53) and urgent safety measures should not be made public at the time they are reported. Established mechanisms of reporting and modifications of trial design and conduct should be used to deal with these issues in early phase research.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
844-858	19	**Question 17** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
844-858	35	**Question 17** Unexpected events should not be disclosed during the assessment process. If this leads to an Urgent Safety Measure (USM), while it may be of public interest to be disclosed, it should be redacted in a way that does not reveal CCI.
844-858	49	**Question 17** **Comment:** Agree.
844-858	57	**Question 17** **Comment:** EuropaBio supports the proposals of making information about unexpected events and urgent safety measures public. We believe that unexpected events should not be disclosed during the assessment process. In the event this leads to an urgent safety measure, the report made public should be redacted to protect personal data and commercially confidential information.
844-858	60	Unexpected Events **Comment:** We agree with the proposal in this addendum as stated. **Proposed change (if any):** None
844-858	65	**Question 17** **Comment:** An unexpected event should not be disclosed during the assessment process. In some instances, it could be seen as part of the normal procedure of CTA modification to be implemented after approval. The EU Database/Portal should have a path allowing linking of serious breaches, Urgent Safety Measure (USM) and unexpected events (e.g. an unexpected event leading to a USM).

Line no.	Stakeholder no.	Comment and rationale; proposed changes
844-858	70	**Question 17** **Comment:** We request that a distinction be made between Phase I/II trials and later phase studies with regard to risk management and the publication of *"unexpected events which affect the benefit-risk balance of the clinical trial, but are not suspected unexpected serious adverse reactions […]"* and *"urgent safety measures […] where an unexpected event is likely to seriously affect the benefit-risk balance […]"* (Art 53.1 and 54 CTR). Early phase trials are well contained, with small numbers of participants and investigators; in the case of Phase I trials, there is usually just one investigator. Due to the exploratory nature of these trials, continuous and contemporaneous risk evaluation is an essential process, in particular during First-time-in-Human and consecutive Phase I trials. It is common during exploratory studies that unexpected events occur which may (seriously) affect the benefit-risk balance of a trial. If an unexpected event occurs, changes to the benefit-risk balance can sometimes be avoided by using innovative trial designs, such as adaptive trial design. Adaptive trial design manages risk through modification of trial conduct by way of non-substantial amendment (modification). If the benefit-risk balance of a trial cannot be maintained by non-substantial amendment (modification) then a study can - under current regulation - not proceed further until a substantial amendment (modification) to the trial protocol and subject information sheet/Informed Consent has been approved by the CA and Ethics Committee. In situations where urgent safety measures are required to protect the safety trial participants who are enrolled in an ongoing trial, these measures can be taken prior to approval of a substantial amendment (modification). Nevertheless, other than those urgent safety measures, the trial cannot proceed further until a substantial amendment (modification) has been approved by the CA and Ethics Committee. This tried and tested process ensures that all parties (CA, Ethics Committee, trial participants, sponsor and investigator) involved in early phase studies are fully aware of any changes in benefit-risk balance and agree with the risk management prior to proceeding further. We do not believe that publication of unexpected events and/or urgent safety measures at the time of reporting would add benefit to the established process for Phase I and II studies. On the contrary, the requirements may bring about

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		under-reporting and failure to undertake necessary safety measures. It may hinder the investigation of the events. Publication may have an unwarranted, negative impact on participant recruitment and study conduct. **Proposed change (if any)**: In case of Phase I and II studies, information on unexpected events which may (seriously) affect the benefit-risk balance of a trial should not be made public at the time they are reported. The authorised application of (non-) substantial modifications of the trial and the use of urgent safety measures, where necessary, are established and successful mechanism to deal with these events.
844-858	81	**Question 17** **Comment:** Regarding the reports of unexpected events it has to be stated that 15 days from the date the sponsor became aware of this event is mostly a point in time when the case investigation is not yet completed. The adequate time for publication is "once assessed" as given in Appendix 4, page 62. **Proposed change (if any):** Please change the wording in Lines 846-847 to "should be made public at the time the unexpected event is once assessed".
846-856	14	**Question 17** Referring to Question 17: comment on whether this proposal meets the requirements and objectives of the Regulation: 4.7. Reporting of unexpected events in accordance with Article 53 and urgent safety measures in accordance with Article 54: **Comment:** We agree.
846-856	71	**Question 17** **Comment:** It is recommended that unexpected events not be reported if investigations are still on-going (lines 846 – 848), but is otherwise in alignment with the regulation.
846-858	55	**Question 17** **Comment:** We agree with the proposal as described in Section 4.7 as it meets the regulation's objectives for data

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		transparency and the protection of the patient's well-being. However we would like to emphasize the need for data privacy in relation to how any patient details associated with an unexpected event or urgent safety measure are made public.
851-856	69	Sponsors should not be allowed to redact the report of unexpected events made public in accordance with Article 53 and urgent safety measures in accordance with Article 54.
857-858	4	**Question 17** EURORDIS agrees with the proposal.
857-858	5	**Question 17** **Comment:** The publication timing rules presented in section 4.4.3 should also be applied to the documents related to unexpected events and urgent safety measures.
857-858	9	**Question 17** **Comment:** Trial sponsors should not be principally responsible for redacting information about unexpected events. Where redactions are necessary to protect personal or commercially confidential information, they should be justified and those justifications should be independently audited.
857-858	13	**Question 17** (unexpected events) Provided that, as described, reports can be redacted (for reasons of commercial or personal confidentiality) by the sponsor before publication, this meets the requirements and objectives of the Regulation.
857-858	28	**Question 17** The proposal meets the requirements and objectives of the Regulation in ensuring respect for the rights, safety, and wellbeing of subjects. Information about unexpected events (as defined by Article 53) can also be relevant for trial subjects of other clinical trials that are not related to the same sponsor. Therefore information about these unexpected

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		events should be made public.
857-858	29	**Question 17** We agree with the proposal. Unexpected events and urgent safety measures should be published at the time of reporting; this meets the requirements and objectives of the Regulation.
857-858	30	**Question 17** The proposal on reporting of unexpected events and urgent safety measures is acceptable.
857-858	32	**Question 17** Yes
857-858	36	**Question 17** **Comment:** *The FPM believes that these proposals meet the requirements and objectives of the Regulation.*
857-858	38	**Question 17** **Comment:** We agree with the proposal
857-858	39	**Question 17** **Reporting of unexpected events in accordance with Article 53 and 844 urgent safety measures in accordance with Article 54** We do not agree that the reports of unexpected events made public are to be "*redacted, by the sponsor, (…).*" (line 851) **Modify text as follows:** "The report made public in accordance with Articles 53 and 54 ~~***should***~~ ***can*** be redacted, by the ~~***sponsor***~~ ***regulatory authorities***, in line with the principles set out in accordance with exceptions under Article 81(4)(a) [protection of personal data] ~~***and (b)***~~. The report should nonetheless identify the relevant clinical trials by

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		their EU number and or protocol number (for third country trials). Redacted and unredacted versions should be submitted to the database but only the redacted version made public. No ***identifiable*** ~~***personal***~~ data of trial subjects should be included."
857-858	41	**Question 17** We concur with these proposals and believe they meet the requirements and objectives of the Regulation.
857-858	46	**Question 17** **Comment:** We agree that these proposals meet the requirements and objectives of the Regulation.
857-858	48	**Question 17** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014. In case of unexpected events which should affect the benefit/risk balance of the study, interactions between the sponsor and the authorities would be made public by Dear Healthcare Provider Letters and appropriate measures.
857-858	51	**Question 17** **Comment:** The current reporting practice for SUSARs effectively ensures the dissemination of information on unexpected events to the affected professional circles, thereby ensuring the safety of other trial subjects. A publication of such events that goes beyond the current practice would not provide any value-add in respect to patient safety. The proposed redaction is inadequately defined. Therefore, it is not possible to say if this proposal meets the requirements and objectives of the Regulation. **Proposed change (if any):** Removal of the proposal, no publication
857-858	53	**Question 17** Whilst we agree that publishing of reported unexpected events and safety measures as defined in article 53 and 54 is of public interest, there is potential for mis-interpretation of such data when in the public domain. It is crucial that this

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		also includes the measures taken and there needs to be sufficient time for the full investigation unexpected events by the sponsor and the measures to be implemented before such information is made public. This full investigation by sponsor is likely to extend beyond the required initial reporting time-frame via the EU portal (15 days). Ensuring a time-interval between the initial reporting of unexpected events and safety measures and making publically available will also enable time for information to be provided to participants before there is a public release of information.
857-858	54	**Question 17** We feel that these proposals meet the requirements and objectives of the Regulation.
857-858	59	**Question 17** **Comment:** We have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
857-858	62	**Question 17** **Comment:** Disagree with the proposal. This database should not be used to report unexpected adverse events. Separate Pharmacovigilance Agreements should already be in place for reporting unexpected adverse events.
857-858	63	**Question 17** **Comment:** 1. Unexpected event changing benefit risk: In case a report is triggering a corrective measure by MSc or an inspection (the later might also be possible): This report first needs to be assessed, maybe leads to RFI and finally to corrective measures – this can't be at time of reporting. Please modify 4.7.(1.) …"…at the time it is reported assessed, unless…section 4.6.3…." 2. What's meant by redacting as of 81(4) (b): Meaning if CT itself is not published yet the report isn't go public? **Proposed change (if any):** Clarification needed. 4.7. (1.) Please modify …"…at the time it is reported assessed,

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		unless…section 4.6.3….”
857-858	73	**Question 17** EAHP supports the proposals made
857-858	75 76	**Question 17** **Comment:** we recommend that the portal includes a period of time where the information will not be in the public domain in order that communication regarding an urgent safety measure, where appropriate, be made to patients on the trial via appropriate routes i.e. not via the media.
857-858	77	**Question 17** **Comment:** Reports of unexpected events (art 53) and urgent safety measure (art 54) can also be seen as a study specific or product specific document and the rules should be accordingly. To make this public at the time of reporting is too early. The cMS will assess this information and will come with a conclusion (no action, corrective measure, other?). So the moment of this conclusion might be better.
857-858	80	**Question 17** **Comment:** They do meet the spirit of the Regulation.
859-860	78	**Comment:** The principles set in lines 156 to 158 and 293-297 should apply with respect to the publication of the clinical study report (i.e. automatic publication without human intervention and the report should be available to the public freely viewable, searchable and downloadable from the portal without entering into any further agreement or intervening restrictions being required). Therefore, the content of the information to be published from the CSR should be clear.
859-870	31	**Question 18**: Please comment on whether these proposals meet the requirements and objectives of the Regulation. From IQWiG’s point of view the proposals do not meet the requirements and objectives of the Regulation.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		According to the Regulation (Recital 68), data included in a clinical study report should not be considered commercially confidential once a marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed or the application for marketing authorisation has been withdrawn. Therefore, the full clinical study reports without redaction of information on study methods and study results should be published. Redaction of information because it is considered commercially confidential information should not be possible. Any separate guidance on the content and publication of clinical study reports needs to meet these requirements of the Regulation, even if prepared outside the functional specifications for the EU portal and EU database. For this question the current discussion between EMA and the European Ombudsman on the redaction of clinical study reports by AbbVie is of particular concern. The examples of commercially confidential information supported by EMA do not seem sufficiently justified. For example, the fact that results from a secondary endpoint do not alter the overall benefit/risk assessment based on a primary endpoint in regulatory decision making does not mean that there is no public interest in these data. These data can be required for decision making in other contexts, e.g. for individual treatment decisions, clinical guidelines or decisions on reimbursement and pricing.
859-870	71	**Question 18:** **Comment:** The EGA agrees that these proposals meet the requirements and objectives of the Regulation. **Proposed change (if any):** The Policy 070 should at least be referenced in the functional specifications to clarify the standards to be applied in redacting clinical study reports
859-872	10	**Question 18** **Comments:** We question the reasons stated for not specifying how the contents of the reports should be handled within the structure of the database. The reports can contain commercially confidential information and the system has to be able to cope with the information, once it arrives. There is also reason to apply stricter rules for the automated process of making information public, than the rules that

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		regard publication after manual assessment, as in the mentioned policy.
859-872	11	**Question 18** ACRO does not agree that the proposals as written meet the requirements and objectives of the Regulation. With regard to submission of the clinical study report (CSR) for publication, there are discrepancies between the appendices required by the text of the draft addendum, by Appendix 7 of the draft addendum, and by EMA Policy 0070 on publication of clinical data for medicinal products for human use (EMA/240810/2013, 2 October 2014). We recommend that the requirements for publication of CSRs under the Regulation are aligned with EMA Policy 0070. We also recommend that, for clinical trials authorised under the Regulation, there should be inter-operability between the database and the publication system established under Policy 0070 so that a sponsor need submit an individual CSR for publication on one occasion only.
859-872	12	**Question 18** **Proposed change (if any):** None
859-872	19	**Question 18** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
859-872	35	**Question 18** According to this passage the general rule shall be that CSR including all appendices except those listing individual patient data shall be made public within 30 days after the marketing authorisation has been granted. The preparation of the content of the reports prior to being loaded shall be addressed by a separate report taking account of CCI considerations and their redaction. CSR as defined in Article 2(35) of Regulation 536/2014 are the core Module 5 documents in applications for marketing authorisations. Making these documents fully publically available would make it very easy for competitors to download these core documents and then use them for own regulatory submissions. Because of this particular importance of CSR

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		at least their appendices should generally not be made public. **Proposed change:** This passage needs to be rephrased as follows: *Clinical study reports including all appendices except those listing individual patient data, will be submitted to the database by the marketing-authorisation applicant/holder within 30 days after the day the marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed or the applicant has withdrawn the application. The appendices to clinical study reports will not be made public. The preparation of the content of the reports including necessary principles of redaction of CCI prior to being loaded into the system should be part of separate guidance to be developed by the appropriate EU expert group. However, no changes to the content/structure should be made without collaboration at an international level, e.g. through ICH. As regards the principles for redaction of CCI in the clinical study report, the specific nature of the product (e. g. well-established-use, traditional herbal or homeopathic medicinal product) and the related particular importance of the clinical study report for regulatory submissions should be taken into account.*
859-872	35	**Question 18** It is important that the content of the reports (including relevant appendices) and redaction of CCI is aligned with Policy 0070 to avoid unnecessary bureaucracy.
859-872	49	**Question 18** **Comment:** This is not applicable to us as we would not be the MA applicant or holder.
859-872	55	**Question 18** **Comment:** The proposals for clinical study reports to be submitted to the database and made public within 30 days of marketing authorisation grant, procedure completing or withdrawal meet the requirements and objectives of the Regulation. We understand that this applies to reports for clinical trials that were subject to the new approval process (May 2016 earliest start) and it will not be applied retrospectively.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
859-872	57	**Question 18** **Comment:** EuropaBio supports the proposals of submitting clinical study reports to the database to be made public in accordance with the EU Clinical Trial Regulation. It is of importance that the content of the reports (including relevant appendices) and redaction of commercially confidential information is aligned with the EMA's Policy 70 to provide consistency and avoid unnecessary bureaucracy. Any consideration of changes to the structure/content of the reports, including relevant appendices, as per the 'Note for guidance on structure and content of clinical study reports (CPMP/ICH/137/95)' and 'Note for guidance on the inclusion of appendices to clinical study reports in marketing authorisation applications (CPMP/EWP/2998/03)', should be made via international collaboration, e.g. through ICH.
859-872	60	**Comment**: We agree with the proposal in this addendum as stated, in so far as Policy 70 has been adopted by the agency. **Proposed change (if any):** None
859-872	65	**Comment:** Please refer to EFPIA's Major Comments under the heading of "Alignment of EMA's Policies and Processes". The policy for the management of CSRs submitted to the EU Database should be consistent with EMA's approach in its Policy 70 and the interaction between the two processes should be clarified. The draft Addendum appears to give confusing messages on what needs to be submitted as part of a CSR once the product has received an MA. Line #861 states, "Clinical study reports including all appendices [emphasis added] except those listing individual patient data, will be submitted to the database", Appendix 7 of the draft addendum provides a list of the CSR appendices to be submitted, EMA's Policy 70 requires a different set of appendices to be submitted; consistency is needed. EFPIA proposes that the requirement to submit CSRs to the EU database should be aligned with Policy 70. Thus, the CSRs (and their appendices) that EMA has determined will be released under Policy 70 should be the same CSRs (and appendices) that are to be submitted to the EU database. As there will be duplication of submitting CSRs to the EMA, over time, EFPIA strongly recommends that a process be implemented to streamline and make consistent the CSRs submitted as part of the MAA process, considering the EMA

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		should avoid unnecessary duplication between EMA systems as per Art 81 (2) '...and hyperlinks shall be provided to link together related data and documents held on the EU database and other databases managed by the Agency. If applicable, the redaction principles (CCI) laid down in the EMA Policy 70 for certain parts of Module 2 and 5, should also be relevant to parts of IMPD Efficacy and safety section (e.g., certain innovative methods, bioassays, immunogenicity assays).
859-872	70	**Question 18** **Comment:** EUCROF agrees with the EMA proposal
859-872	81	**Question 18** **Comment:** Requirements regarding redacted CSRs should be the same than per EMA policy 70.
861-870	14	**Question 18** comment on whether this proposal meets the requirements and objectives of the Regulation: 4.8. Clinical study reports submitted by the marketing- authorisation applicant/holder: **Comment:** We agree.
861-870	65	**Question 18** **Comment:** It is unclear if there are intentions to update CSR guidance in the near-term. If so, EFPIA supports the concept of developing guidance outlining the information, data and documentation that may contain CCI, prior to them being loaded into the system. If this is the intention, given that the content and format for CSRs is covered by ICH guidance, any adjustment would be accomplished through international agreement. EFPIA would welcome the opportunity to work with the EMA in progressing this idea.
866	39	**Comment:** Clarify what is meant by EU expert group, who is in that group and how members are selected.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): clarification of who will sit in that group, how will member recruitment take place, what will be the timeline for development of raw data sharing guidelines.
871-872	4	**Question 18** EURORDIS agrees with the proposal.
871-872	5	**Question 18** **Comment:** The proposal meets the requirements and objectives of the Regulation.
871-872	13	**Question 18** (clinical study reports) Publication after completion of the marketing authorisation process strikes an appropriate balance between the needs of prescribing physicians, patients, and the public and those of sponsors investing in development of new medicines.
871-872	28	**Question 18** The clinical study reports that were part of the marketing authorisation application dossier should be available at the day when the marketing authorisation has been granted. Therefore a time line of 30 days is reasonable.
871-872	29	**Question 18** We agree that the proposal meets the requirements and objectives of the regulation.
871-872	30	**Question 18** The Agency should request that the clinical study reports contain de-personalised individual patients data in a re-usable format (datasets). In principle, clinical study reports should also include the trial data that have been analysed and any raw data (source data) that are of importance to the interpretation of the trial results. Meta-data necessary for understanding the trial data and make them usable for reanalysis or inclusion in meta-analysis should also be included. The benefits of data sharing is widely recognised: it increases the value of data collected during clinical trials, respecting the trial participants, allows the generation of new research hypotheses, promotes effective data synthesis in

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		meta-analyses, allows for reanalysis of data, and avoids unnecessary duplication of research. As stated above, access to depersonalised datasets for research purpose should be possible and the development of the new European portal for clinical trials should facilitate this process. We encourage the EMA to align this policy and the one on access and publication of clinical data towards the highest transparency standards possible.
871-872	32	**Question 18** Yes
871-872	36	**Question 18** **Comment:** *The FPM believes that these proposals meet the requirements and objectives of the Regulation.*
871-872	38	**Question 18** **Comment:** We agree with the proposal
871-872	39	**Question 18** ***Clinical study reports submitted by the marketing-authorisation applicant/holder*** Listings of de-identified individual patient data should be made available to allow independent reanalysis of data.
871-872	41	**Question 18** We concur with these proposals and believe they meet the requirements and objectives of the Regulation.
871-872	46	**Question 18** **Comment:** We agree that these proposals meet the requirements and objectives of the Regulation.
871-872	48	**Question 18**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: No, this proposal does not fully meet the requirements and objectives of the Regulation (EU) No 536/2014. **We agree** that Clinical study reports including all appendices except those listing individual patient data, will be submitted to the database by the marketing-authorisation applicant/holder and made public within 30 days after the day the marketing authorization has been granted, i.e. the procedure for granting the marketing authorisation has been completed. **However, we do not agree** that it should be made public when a negative opinion has been granted since the Applicant may call for a re-examination procedure. Publication should only occur until completion of all procedures, including ending of the withdrawal part of it. Recommendation should be made to delay the publication until after the procedure has been completed.
871-872	51	**Question 18** **Comment:** Questions concerning the structure and content of clinical reports should not be subject to or reference the EMAPolicy 0700. This policy has no legal basis, as has been noted by the Agency itself (see also the attached Expert Legal Opinion of Prof. Denninger). **Proposed change (if any):** Content and structure of clinical reports should be guided by the CONSORT Criteria. **Comment:** The right/permission to manual override to convert protected documents to public documents or to remediate errors is not restricted to an institution and is possible without consultation of the MAH, who is responsible for structure and design of documents (public and non-public section). The term „Overriding public interest“ is ambiguous. The European Court has determined that the principle of legal certainty requires that a rule or regulation must be clear and precise (see p. 9, section 7 of translation of Expert Opinion). The Policy does not make clear which persons, for what reasons and in what process may cite “overriding public interest” (exception to an exception in Regulation (EC) No. 1049/2001). **Proposed change (if any):** Only (…) has the permission to manual override. Overriding errors caused by data processing errors or where publication of information was contrary to the rules requires consultation with the MAH or sponsor.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
871-872	53	**Question 18** no comment as it relates to the processes around applying for MA
871-872	54	**Question 18** We feel that these proposals meet the requirements and objectives of the Regulation.
871-872	59	**Question 18** **Comment:** We have no concerns about the proposal this question relates to within the limits of the information provided. Further concerns may become apparent once additional details are released **Proposed change (if any):** Not applicable
871-872	62	**Question 18** **Comment:** Disagree that the appendices of a Clinical Study Report should be made publically available. The main results of the study will already be included in the text of the Clinical Study Report. The appendices will not add any additional value. Furthermore, there is a concern with including the appendices that the study results may be taken out of context. In addition, there is concern that the appendices may contain individual patient data that has not be correctly redacted.
871-872	67	**Question 18:** We ask for direct accessibility together with a very easy access.
871-872	80	**Question 18** **Comment:** The proposal 4.8.1. does not meet the requirements and objectives put into the Regulation. Absolutely de-identified individual patient data, i.e. raw data, have to be presented as well in order to allow independent study re-

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		analyses. In order to guarantee that re-analyses are performed at the same level of scrutiny as sponsor-conducted analyses, adequate measures have to be taken by the then responsible EMA, e.g. the control of a scientifically valid statistical analysis plan of the requester of a re-analysis. To permit maximum transparency on the one side, and to inhibit its misuse on the other side actually represents a major concern of ESMO with the new CTR and its implementation by the EMA.
873-892	40	We are broadly supportive of the proposed addendum to the functional specifications. We agree with the EMAs approach to ensure the publication of clinical trial information occurs by an automated process based on predefined rules to be agreed through this consultation. We are also supportive of the manual override option, but would welcome clarification from the EMA over who would be responsible for this manual override and the decision making process for initiating this. Although we understand that the additional questions to be included in the application form will need to be adjusted based on the final outcome of this consultation, we do not consider that question 5 or 6 would be necessary in any instance. The suggestion by the EMA to include these is at odds with its proposal set out in 4.4.1.1, which considers the nature of the sponsor organisation to be immaterial when considering what might be commercially confidential.
873-898	49	**Comment:** It is difficult to comment on this without knowing what the consultation response will be.
873-898	51	**Question 19** **Comment:** See cumulative previous comments. Referring to the comments on confidential data in the application dossiers, substantial modification dossiers and other documents: these documents excluded from public access. **Proposed change (if any):** Exclusion of appendices 2,3 and 4 from public access
873-898	57	**Question 19** **Comment:** EuropaBio is supportive of the proposed addendum, subject to clarification of certain elements.
873-898	81	**Question 19**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: Our members agree upon this. It is essential to have still the possibility of a manual intervention to avoid or retract immediately illegal publication of information. With regard to the IMPD the text should be made more precise. With regard to the additional questions the text should be more precise. **Proposed change:** Please change the statement on the IMPD as follows: "The IMPD should be structured to enable each section (Q, S, E) to be identified unambigiously, to be separate and have different application rules applied to each." Please supplement Point 8 with examples for additional questions.
873-899	10	**Question 19** **Comments:** We support the proposals. As mentioned in the document, the questions in application form have to be adjusted based on the final outcome of the consultation. For instance might question 1 need to be removed since it will not be necessary and besides that, probably difficult for sponsors to answer. Question 5 -6 should be removed, since 4.3 has been changed compared to earlier draft text of this document. Note that non-commercial, academic sponsors also have legitimate economic interests, e.g. regarding a new indication for an already marketed product.
873-899	19	**Question 19** **Comment:** The proposed addendum to the functional specification meets requirement and objectives of the Regulation (EU) No 536/2014.
876-898	71	**Question 19** **Comment:** The EGA agrees that these proposals meet the requirements and objectives of the Regulation.
876-899	55	**Question 19** **Comment:** In general the proposed addendum appears to meet the requirements. With respect to item number 4 in

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		the text to be added to Table 2 section 4.3 previously published i.e. “4. Do the formulation(s)/route(s) of administration appear in any marketing authorisation already granted in the EU for that active substance” – This should be amended to allow criteria of formulation and route of administration to be considered separately and independently. This will clarify that significant innovation through clinical research into novel formulations is independent of route of administration. **Proposed change:** Delete: 4. Do the formulation(s)/route(s) of administration appear in any marketing authorisation already granted in the EU for that active substance? Replace with: 4. Do the formulation(s) appear in any marketing authorisation already granted in the EU for that active substance? 5. Do the route(s) of administration appear in any marketing authorisation already granted in the EU for that active substance? Renumber following sections accordingly.
887-898	60	Proposal for Addendum **Comment**: We agree that the addendum is generally clear but requires some refinement based on comments received on this draft proposal. However, we wish to query question #8 on pg. 27 which is proposed as an item for inclusion in the functional specification. This reads, “Additional question as required”. This is overly broad and warrants either removal or the provision of additional details to ensure Sponsors can be compliant with the required information that will be requested. We find the colour coding of appendices describing the data and documents to be very helpful. We recommend that the Agency provide additional details on the manual over ride scenario as it is still unclear under which scenarios CCI would be made public at an earlier time point in the interest of the public. **Proposed change (if any):** Please provide additional specificity or examples with respect to question #8 on pg. 27 to

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		ensure sponsors can be compliant with the request. Please provide additional details on the manual over ride scenario as it is still unclear under which scenarios CCI would be made public at an earlier time point in the interest of the public.
890-892	29	**Proposed change (if any):** Should read "Any type of document/data that fall under the grounds for exception described in Article 81 (4) of the Regulation and detailed in the above mentioned section will not be made…
894-895	27	**Table 2** **Comment:** according to us, only if proposal four (lines 682-702) is chosen, the question n. 1 should be included.
894-898	11	**Question 19** ACRO does not agree that the proposed Table 2 Section 4.3 to be added to the functional specification document as an addendum meets the requirements and objectives of the Regulation. Specifically, it does not address which functionalities will be audited, and we question the need to include some (but not all) of the questions in the application form that will provide data points on which to base certain of the publication rules. We also note that the draft addendum states that the "system should identify all data and documents in the EU database regarding their public or non-public status and any timeframe/event to trigger that publication, and include the necessary rules to ensure their availability at the required time." We recommend that all of the details of this arrangement are published so that they are clearly available to users of the portal and database.
894-898	12	**Question 19** **Comment:** We agree with the concept of text being added to Table 2, Section 4.3 as an addendum, the content of which will depend on the outcome of the final consultation. We also agree with the concept of the application form containing a set of questions which will then trigger select pathways of publication. We note that the proposal states that protocol synopsis and protocol should be separate and have different publication rules applied to each. Although the draft proposal currently does not seem to use this facility in any of its proposals, we believe that this separation would facilitate the implementation of e.g. Proposal 4 (Table 1) which proposes an

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		earlier publication of study specific documents than Proposals 2 and 3. If, for studies with therapeutic intent, publication at the time when first summary results are posted would be limited to the protocol synopsis (and the full protocol be published at MA or 9 years after first summary results are posted), we believe this would serve all parties very well. **Proposed change (if any):** We propose to update the definition of study specific documents in section 4.4.1.2a and Table 1 accordingly, distinguishing between protocol synopsis and protocol publication pathways as outlined above.
894-898	70	**Question 19** **Comment:** We agree with relevant text being added to Table 2, Section 4.3 as an addendum, depending on the outcome of the final consultation. We also agree with the principle that the application form will contain a set of questions which will then trigger select pathways of publication. **Proposed change (if any):** TBC
895	14	**Question 19** comment on whether the proposed addendum to the functional specifications meets the requirements and objectives of the Regulation: **Comment:** If not important the distinction between commercial sponsors, academics, and so on, why in the addendum do the distinction between commercial and non-commercial sponsors?.
895	29	**Comment:** Items 5+6: It is irrelevant for the application of the transparency rules whether the clinical trial is carried out for commercial purposes. The only trigger for a possible exception is that commercially confident information needs to be protected. Commercial purpose and commercially confident information cannot be equated. Item 6: The question is strange as it seems the sponsor (if the sponsor has to answer the questions) can decide at which time point the information should be published.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Who will be answering the questions / items at the end of the addendum? If the sponsor is answering those, the Member States have to assess whether the answers are correct.
895	39	**Comment:** The publication of clinical trial documents and/or information will be an automatic process, with “No manual intervention”. It is mentioned that a “manual override” will be made available to enable publication in exceptional circumstances" but transparency will be an exception rather than the overall rule. **Proposed change (if any):** Transparency must be the rule, not the exception, therefore manual intervention will take place when a company invokes that the information is commercially confidential. Companies must be required to provide detailed information that shows that the release of information that they claim to be commercially confidential would truly harm their interests and that non-disclosure would not be detrimental to public health.
895	47	Commercial purpose is not defined in the regulation. National legislations may refer to non-commercial trials which are defined somehow differently within the EU (e.g. Belgian law definition is not the same as Italian, some other countries may not give any definition). **Proposed change (if any):** EORTC would recommend clarifying what is meant by item 5 (e.g. does it includes post-marketing surveillance trials conducted by the pharmaceutical industry?) or modifying item 5 to: “is this trial a non-commercial trial?” EORTC would recommend considering a generic question at the end: “Is there any other aspect that would justify that all or some information is to be considered as commercially confidential?”; this question will specifically be important for non-commercial sponsors to be able to justify either aspects of correlative research or potential implications for their grant applications as recognised justified earlier in the document.
895	61	**Comment:** Point 4 reads: “Do the formulation(s)/route(s) of administration appear in any marketing authorisation already granted in the EU for that active substance?” Since the publication will largely be automated based on rules, the precise meaning of "/" will be important and this needs to be clarified – see also our comments to Question 6.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
895	63	Table 2 section 4.3 **Comment:** Manual override is agreed. Nevertheless clarification is needed which body will decide exemptions and who is responsible for override. **Proposed change (if any):** Please clarify.
895	63	Table 2 section 4.3 **Comment:** Example questions 5/6 on non/commercial purpose is no criteria for publication. **Proposed change (if any):** Delete example question 5 and 6.
895	65	**Table 2, Section 4.3** **Comment:** Please refer to EFPIA's Major Comments under the headings of "Enable an Efficient System, Balancing Automation with Direct Sponsor Involvement" and "User-friendly and Harmonised with International Standards". Also, the draft Addendum states that a manual override may be used to remediate errors where information has been published contrary to the established rules, or where data processing errors have occurred. The inefficiencies associated with remediating errors could be reduced if the system provided a means of enabling sponsors to preview a public representation of the data and documents that would be published in the future. According to the functional specifications document, the public interface will allow queries and download functionalities. Similar to the EMA Policy 70 on proactive disclosure of Module 2 and 5, EFPIA recommends that a watermark is applied (at least to IMDP section E+S)? "The protocol synopsis and protocol should be separate and have different publication rules applied to each. " It is assumed that "protocol synopsis" is referring to the protocol summary to be made public by default after CTA decision. As stated in our comments to Lines 322-324, information for the synopsis should come from the relevant fields of the CTA form.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Within this table and throughout the document, EMA uses several terms for a product such as “therapeutic” and a combination term “therapeutic/prophylactic”. Since vaccines are not (generally) considered therapeutic, the combination term could be used throughout the document or it could be defined/footnoted at the beginning of the Addendum.
895	65	**Table 2, Section 4.3** **Comment:** In terms of technical standards, the draft Addendum states that the “system should identify all data and documents in the EU database regarding their public or non-public status and any timeframe/event to trigger that publication, and include the necessary rules to ensure their availability at the required time.” To improve predictability and clarity for the sponsor, EFPIA recommends that the Database schema be published, documenting the unambiguous business rules applied to disclosure of individual fields and documents with the associated timing for release. In addition, EFPIA is concerned that there is no auditable requirement to ensure the system is adequately secured. EFPIA, therefore also recommends that as a part of the evidence provided to the auditors of the CT Portal/Database, the EMA should provide results of independent penetration testing of the system.
896-898	4	**Question 19** EURORDIS agrees with the proposal.
896-898	13	**Question 19** (addendum to functional specifications) The IMPD is referred to as containing 3 sections: Q (quality), S (safety) and E (efficacy). That is not in line with the terminology used in the Regulation, which describes the 3 sections as: ‘Quality data’; ‘Non-clinical pharmacology and toxicology data’ (non-clinical data); and ‘Data from previous clinical trials and human experience’ (clinical data). The terminology in the Regulation is more appropriate – for example, results from phase I trials in healthy volunteers should be presented in the clinical data section, but would not fit logically into an ‘efficacy’ section. Note that, for all of our early phase studies, the IMPD contains only quality data: non-clinical and clinical data are described in the IB and cross-referred by the IMPD. So, our applications would contain only an IMPD quality section and

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		an IB. Apart from the need to clarify the IMPD sections, the addendum otherwise meets the requirements and objectives of the Regulation.
896-898	28	**Question 19** No comment.
896-898	29	**Question 19** The proposed addendum will have to be adjusted according to the outcome of the consultation. Therefore, at this time it cannot be said whether it meets the requirements and objectives of the Regulation. The current wording of the proposed addendum (line 876-895, including table 2, section 4.3) to the functional specifications does not meet the requirements and objectives of the Regulation as it does currently not reflect (and cannot at this stage reflect) the result of the consultation. In our view question 3 and question 4 of the addendum should be deleted. Question 5 and 6 would have to be rephrased as for the application of exemptions it is not relevant whether the trial is conducted for commercial purposes, it is only relevant whether – on the grounds of the Regulation and the detailed exemptions- the information meets the criterion of "CCI". Question 6 as currently worded is not meeting the requirements of the Regulation.
896-898	32	**Question 19** Yes
896-898	35	**Question 19** EUCOPE supports the proposed addendum subject to revision in accordance with our comments provided in this response.
896-898	36	**Question 19**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: *The FPM believes that these proposals meet the requirements and objectives of the Regulation.*
896-898	38	**Question 19** **Comment:** We agree with the proposal
896-898	41	**Question 19** We assume that the comment made previously about extending the deferral for Phase I clinical trial results from 12 to at least 24 months, if accepted, will be reflected in the appendices.
896-898	46	**Question 19** **Comment:** It is assumed here that change requested to extend the deferral period from 12 months to a minimum of 24 months, if accepted, will be reflected in the Appendices. It is further assumed the Confidential Information as may be revealed through e.g. the EU Product Code, CAS number, target indication, trial specific information, in insurance certification and by other routes in the Appendices will be protected by the most suitable means as discussed above.
896-898	48	**Question 19** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014. However, clarification is needed with respect to item 3, i.e. the definition of an active substance in case of biological product.
896-898	53	**Question 19** see answers to qu 8-10
896-898	54	**Question 19** We feel that the proposed addendum to the functional specifications meets the requirements and objectives of the

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Regulation.
896-898	59	**Question 19** **Comment:** It is not clear at this time why the commercial nature of the study should impact upon the information to be released. The regulation does not distinguish between commercial and non-commercial studies so this should not impact upon the release of information. **Proposed change (if any):** Removal of questions relating to the commercial nature of the study.
896-898	62	**Question 19** **Comment:** No comments on this section.
896-898	67	**Question 19:** We support the proposed addendum to the functional specifications.
896-898	76	**Question 19** **Comment:** we consider a simplified approach with a single approach for timing of release of study related documents linked to the timing of final study report for all trials to be preferable. This approach will protect commercial and academic research interests whilst ensuring that trial information is ultimately in the public domain for all trials.
896-898	80	**Question 19** **Comment:** Yes, it is in line therewith.
Appendices	10	The name of appendices 2 and 3 should define that it is the final version of the documents at the time of the decision taken by the Member States concerned.
Appendix I	47	EORTC in general agree with the appendix I when applied to drug only trials. However, trials with registered drugs that would fall under several EU regulations (clinical trials & IVD and/or devices etc…) may need to be treated slightly

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		differently as CCI justification may not be related to the status of the drug, but to another aspect (e.g. IVD status). **Proposed change (if any):** EORTC would advise to keep some flexibility to enable system to adjust for the above cases. EORTC suggest sponsors are recommended to group (as far as possible) non-drug aspects that may justify some information would be considered as CCI aside, so that the rest of information can be made public.
Appendix 1	78	**Comment:** The content of the appendix should be reconsidered in order to include all necessary data in the structured CT data set (e.g. CTA scope -part I, part I and II, part II-, Ethics Committee involved per MS, proposed reporting MS, rational/justification of the CT, statistic plan,…), avoid unnecessary information (e.g. IMP/AMP list needs only to include the product name chosen from the MP Dictionary and all linked information will be downloaded from that dictionary. Non authorised MP will be described by the EU MP number or by a name included in the EU MP number request, treatment per CT arm should be better described, etc… The structured CT dataset should include all CT characteristics to be published, including EU CTA form, protocol summary, information to be populated in the assessment report, and CT characteristics to be included automatically in the summary trial results and in the summary trial results for lay people. WHO ICTRP label correspondence is not always correct.
Appendix 1 A.5.3	11	The WHO Universal Trial Reference Number (WHO UTN) is required by Annex 1(B.6) of the Regulation but is not required by Article 25.6, which simply requires that a trial should be registered in a public register which is a primary or partner registry of, or a data provider to, the WHO International Clinical Trials Registry Platform. The ClinicalTrials.gov number is also required by Annex 1(B.6) but not by Article 25.6. ClinicalTrials.gov is not a data provider to the WHO registry, so there would need to be an additional request for the WHO UTN, if this were to be mandatory. The additional administrative burden that this could create has been raised by several sponsors. We therefore recommend that the request for the EU Clinical Trial Number should trigger the automatic creation of both the WHO UTN and the EU CTN.
Appendix 1 A.8 EMA decision number of Paediatric Investigation Plan	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial The PIP decision number reveals commercially sensitive information (eg chemical name of the active substance, pharmaceutical form, route, and the target indication(s)).

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): The option of deferral of publication must be included for phase I trials.
Appendix 1 A.8	41	The decision number reveals commercially sensitive information (e.g. chemical name of the active substance, pharmaceutical form, route, and the target indication(s)), so the option of deferral of publication must be included.
Appendix 1, C.1.4.3 C.1.4.3.1 C.1.4.3.3 C.1.4.3.4	11	The draft proposal states that the application address will not be in the public domain at any time. However, the components of this will be published -- i.e. street address, post code and country. **Proposed change:** The text should be revised to state that C.1.4.3.1,3,4 will not be published.
Appendix 1 D.3.2 EU product code	13	**Comment:** Proposed public disclosure: • Options 1–4: decision on trial • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial If the EU product code reveals the *pharmaceutical form* or chemical name of the IMP, it should be deferred. **Proposed change (if any):** If the EU product code reveals the *pharmaceutical form* or chemical name of the IMP, it should be deferred for options 2–4 and phase I trials (as is currently shown for options 2–4 for D.3.4 pharmaceutical form).
Appendix 1 D.3.2	41	If the EU product code reveals the pharmaceutical form, it should be deferred for options 1–4 and Phase I (as is currently shown for options 2–4 for D.3.4 pharmaceutical form).
Appendix 1 D.3.4 Pharmaceutical form	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.4	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.7 Routes of administration	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.7	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.9.1 CAS number	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. The CAS number reveals the chemical structure of the IMP, which is commercially sensitive. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.9.1	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial. The CAS number reveals the chemical structure of the IMP, which is commercially sensitive.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Appendix 1 D.3.9.3 Other descriptive name	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.9.3	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.9.4 EU substance code	13	**Comment:** Proposed public disclosure: • Options 1–4: decision on trial • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial If the substance code reveals the chemical name of the active substance, it should be deferred in options 2–4, and for phase I trials, until after MA/10 years after the end of the trial. **Proposed change (if any):** If the substance code reveals the chemical name of the active substance, it should be deferred in options 2–4, and for phase I trials, until after MA/10 years after the end of the trial.
Appendix 1 D.3.10	51	**Comment:** Strength of IMP is confidential information. **Proposed change (if any):** change to amber
Appendix 1 D.3.11.1 Active substance of chemical origin	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.1	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.2 Active substance of biological/biotechnological origin (other than ATIMP)	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.2	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3 ATIMP	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Appendix 1 D.3.11.3.1 Somatic cell medicinal product	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.1	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.2 Gene therapy medical product	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.2	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.3 Tissue engineered product	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.3	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.4 Combination ATIMP (ie involving medical device)	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.4	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.5 CAT has issued a classification for this product	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.5	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.5.1	13	**Comment:** Proposed public disclosure:

Line no.	Stakeholder no.	Comment and rationale; proposed changes
CAT classification and reference number		• Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial There seems to be a mistake, as options 2–4 allow deferral for phase I studies until after MA/10 years after the end of the trial. There can be no justification for publishing details of phase I trials before those of later phase trials, since phase I trials are more commercially sensitive. **Proposed change (if any):** Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.3.5.1	41	Options 2–4 allow deferral for Phase I studies until after MA/10 years after the end of the trial. Phase I trials should also be deferred until after MA/10 years after the end of the trial.
Appendix 1 D.3.11.4	51	**Comment:** Exclusion of both categories of medical products is not reproducible. **Proposed change (if any):** change to amber
Appendix 1 D.3.11.4	65	**Comment:** For explorative combinations (including biomarkers), encompassing phase I and phase IIa, patents may not be in place and information should be considered CCI. The disclosure should be delayed until a confirmatory trial is available or later.
Appendix 1 D.3.11.5	51	**Comment:** Exclusion of both categories of medical products is not reproducible. **Proposed change (if any):** change to amber
Appendix 1, E.1.1 and subheadings	10	Why should the medical condition being investigated not be published at the time of the approval for Phase I and Phase II trials? This information is anyhow understood from the title of the trial and other public fields and the information is of public interest, e.g. for participating in in Phase II trial carried out in patients?
Appendix 1 E.1.1 Medical conditions being investigated	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial The target indication is usually entered on the application form, even if the trial is in healthy volunteers. The target indication is commercially sensitive, so the option of deferral of publication must be included.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): The option of deferral of publication must be included for phase I trials.
Appendix 1 E.1.1	41	The target indication is commercially sensitive, so the option of deferral of publication must be included.
Appendix 1 E.1.1	63	**Comment:** Will medical condition in Phase I be public by decision on trial (as in proposal 1 to 4) or could it be matter of deferral? **Proposed change (if any):** Clarification needed.
Appendix 1 E.1.1.1 Medical condition in easily understood language	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial The target indication is usually entered on the application form, even if the trial is in healthy volunteers. The target indication is commercially sensitive, so the option of deferral of publication must be included. **Proposed change (if any):** The option of deferral of publication must be included for phase I trials.
Appendix 1 E.1.1.2 Therapeutic area	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial The target indication is usually entered on the application form, even if the trial is in healthy volunteers. The target indication is commercially sensitive, so the option of deferral of publication must be included. **Proposed change (if any):** The option of deferral of publication must be included for phase I trials.
Appendix 1 E.1.1.2	41	The target indication is commercially sensitive, so the option of deferral of publication must be included.
Appendix 1, E.1.2 and subheadings	10	Why should the MedDRA classification not be published at the time of the approval for Phase I and Phase II trials? Se comment above.
Appendix 1 E.1.2 MedDRA code,	13	**Comment:** Proposed public disclosure:

Line no.	Stakeholder no.	Comment and rationale; proposed changes
version, level, term, and SOC		• Phase I healthy volunteers: decision on trial The target indication is usually entered on the application form, even if the trial is in healthy volunteers. The target indication is commercially sensitive, so the option of deferral of publication must be included. **Proposed change (if any):** The option of deferral of publication must be included for phase I trials.
Appendix 1 E.1.2	41	The target indication is commercially sensitive, so the option of deferral of publication must be included.
Appendix 1 E.1.2	63	**Comment:** Will medical condition in Phase I be public by decision on trial (as in proposal 1 to 4) or could it be matter of deferral? **Proposed change (if any):** Clarification needed.
Appendix 1 E.6.6-E.6.12	51	**Comment:** Data on efficacy of IMP is confidential information **Proposed change (if any):** change to amber
Appendix 1 E.6.10	65	**Comment:** Pharmacogenetics are explorative (potentially retrospectively) modelling and pattern recognition. The decision disclosure should be delayed until a confirmatory trial is available or later.
Appendix 1, E.8.6.2	10	What is the rational for the category 'Trial being conducted completely outside of the EEA'. Does such a trial have any relevant decisions in the Clinical Trial Regulation?
Appendix 1 E.8.6.2	65	**Comment:** Trial being conducted completely outside of the EEA: if the trial is conducted completely outside the EEA, there is no EU decision on the trial as no application has been made.
Appendix 1, F.3.3.6.1	10	The group 'incapable of giving consent' should be divided further into 'minors' and 'incapacitated subjects', with the latter divided further into a subgroup 'subjects in emergency situations'.
Appendix 1, H.4.1. N	10	Ethics committee opinion (per Member State) should be changed to 'Part II' decision (since Ethics Committees and competent authorities may be involved both in Part I and Part II assessments, as decided in each Member State)

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Appendix 1, H.4.1. N	10	Decision on the trial per Member State should also systematically list the 'opt-out' possibilities mentioned in Art 8.
Appendix 1, page 47, H.4.1 N	11	A field is proposed for the ethics committee opinion (per Member State). This is not a requirement of the Regulation, which requires a single approval covering both regulatory and ethical aspects of the clinical trial by each Member State. We recommend that this field is deleted as it is already covered by the Conclusion on Part I of the assessment and the Decision on the trial (per Member State), which are required by the Regulation.
Appendix 1, N	11	While the regulation requires a positive EC opinion on a trial, there is no requirement for this to be included in the database. **Proposed change:** Delete text to reflect the regulation.
Appendix 1 N Conclusion on part I of the assessment	13	**Comment:** Proposed public disclosure: • Options 1–4: decision on trial • Phase I healthy volunteers: decision on trial Trial-specific conditions of approval may reveal commercially sensitive information, particularly if they concern the IMPD-Q section. **Proposed change (if any):** Ideally, defer publication of any conditions of approval until after MA/10 years after trial. If that is not possible, allow the option to defer publication of any conditions of approval of phase I trials until 12 months after the trial. Allow redaction if the conditions concern the IMPD-Q section.
Appendix 1 N Ethics committee opinion (per member state)	13	**Comment:** Proposed public disclosure: • Options 1–4: decision on trial • Phase I healthy volunteers: decision on trial Trial-specific conditions of approval may reveal commercially sensitive information, particularly if they concern the IMPD-Q section.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): Ideally, defer publication of any conditions of approval until after MA/10 years after trial. If that is not possible, allow the option to defer publication of any conditions of approval of phase I trials until 12 months after the trial. Allow redaction if the conditions concern the IMPD-Q section.
Appendix 1 N Decision on the trial (per member state)	13	**Comment:** Proposed public disclosure: • Options 1–4: decision on trial • Phase I healthy volunteers: decision on trial Trial-specific conditions of approval may reveal commercially sensitive information, particularly if they concern the IMPD-Q section. **Proposed change (if any):** Ideally, defer publication of any conditions of approval until after MA/10 years after trial. If that is not possible, allow the option to defer publication of any conditions of approval of phase I trials until 12 months after the trial. Allow redaction if the conditions concern the IMPD-Q section.
Appendix 1 N	41	Any trial-specific conditions of approval should not be published as they may reveal commercially sensitive information. Please defer conditions of approval until 12 months after the trial.
Appendix 1 N	65	**Comment:** Ethics committee opinion (per Member State) is listed in the information to be disclosed. This is not relevant for the functioning of the CTR given that we expect the AR for Part I, AR for Part II and Decision per Member State. **Proposed change:** Replace 'Ethics Committee Opinion' with 'Conclusion on Part II of the assessment'. Also, regarding the AR for Part I, in order to protect commercial interests of the sponsor/MAH, public information should be limited to the outcome i.e., 'the conduct of the clinical trial is acceptable', 'is acceptable under conditions' or 'is not acceptable'.
Appendix 1 P47 "Ethics opinion per MS"	63	**Comment:** It should be clarified, which opinion (on part I /on part II) is meant.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Appendix 2	35	As per comments on line 636-640, the line regarding the Investigator Brochure on page 51 (E) should be turned to red, with no text.
Appendix 2	78	**Comment:** Duplication of information should be avoided in the CT dossier (e.g. CT structured dataset instead of EU application form, cover letter and protocol summary; IMPD without information already in the Investigator's Brochure)
Appendix 2 Annex 1	41	Requires clarification. Does it mean that publication will be guided by the information in the letter – i.e. if information in the letter corresponds to information in Appendix 1 that will not be published until after MA/10 years after trial, the publication of the letter will be delayed until that time? The letter may contain commercially sensitive information – currently, a link to any EMA decision on a paediatric investigation plan should be included, which is commercially sensitive (see A8 above), and special features of the trial (e.g. first in man study) should be highlighted). So, for Phase I trials, publication should be no earlier than at least 24 months after the end of the trial.
Appendix 2 Annex A Cover letter	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: In line with information in initial CTA and application dossier (IMPD-Q not public) This is unclear. Does it mean that publication will be guided by the information contained in the letter – ie if information in the letter corresponds to information in Appendix 1 that will not be published until after MA/10 years after trial, the publication of the letter will be delayed until that time? The letter may contain commercially sensitive information – eg a link to any EMA decision on a paediatric implementation plan (which is commercially sensitive - see A8 above), and special features of the trial (eg first in man study). **Proposed change (if any):** For phase I trials, publication should be no earlier than 12 months after the end of the trial, or in line with options 1–4, whichever is later.
Appendix 2 Annex C EU application form	13	**Comment:** Proposed public disclosure:

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		• Options 1–4: decision on trial • Phase I healthy volunteers: decision on trial or deferral to 12 months after the trial Should this not cross-refer to Appendix 1, as some fields will not be published until after MA/10 years after the trial? **Proposed change (if any):** Please clarify that Appendix 1 will determine publication of individual fields.
Appendix 2 Annex C	41	Should this not cross-refer to Appendix 1, as some fields will not be published until after MA/10 years after the trial.
Appendix 2 E	65	As per comments to line 636-640, the row regarding IB should be turned to red, indicating that it will not be made public due to CCI.
Appendix 2 Annex I Paediatric investigation plan	13	**Comment:** Proposed public disclosure: • Options 1–4 and phase I healthy volunteers: decision on trial The plan reveals commercially sensitive information (eg chemical name of the active substance, pharmaceutical form, route and the target indication(s)), so the option of deferral of publication must be included. NB phase I trials may be done throughout the drug development lifecycle. **Proposed change (if any):** The option of deferral of publication must be included for phase I trials.
Appendix 2 Annex I	41	The plan reveals commercially sensitive information (e.g. chemical name of the active substance, pharmaceutical form, route and the target indication(s)), so the option of deferral of publication must be included.
Appendix 2 Annex K Recruitment arrangements	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial Recruitment arrangements could reveal whether special populations are being studied, eg special arrangements must be made to recruit healthy Japanese participants for bridging studies. Details of those arrangements would reveal the objective of the trial. Option of deferral of publication must be included.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): The option of deferral of publication must be included for phase I trials.
Appendix 2 Annex K	41	Recruitment arrangements could reveal whether special populations are being studied, e.g. special arrangements must be made to recruit healthy Japanese participants for bridging studies. Details of those arrangements would reveal the objective of the trial. Option of deferral of publication must be included.
Appendix 2 Annex O Proof of insurance cover or indemnification	13	**Comment:** Proposed public disclosure: • Phase I healthy volunteers: decision on trial Insurance certificates are often trial-specific and include the full title of the trial. Option of deferral of publication (or redaction) must be included. **Proposed change (if any):** The option of deferral of publication (or redaction) must be included for phase I trials.
Appendix 2 Annex O	41	Insurance certificates are often trial-specific and include the full title of the trial. Option of deferral of publication (or redaction) must be included.
Appendix 2 Page 53	65	**Comment:** Reference is made to the "EMA SAWP public information", which refers to EMA advice only. In some cases meeting minutes from third country HA advice might be part of a CTA dossier. It is assumed that this data will not be made public.
Appendix 3	13	**Comment:** Proposed public disclosure: • All options state: in line with information in the initial CTA and application dossier. This is unclear. However, for phase I healthy volunteers, the draft proposal makes it clear that there will be an option such that no information on substantial modifications will be published until 12 months after the end of the trial. We support that deferral option. Also, presumably, for option and phase IV/low intervention trials, 'decision on trial' should read 'decision on modification'.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change (if any): Please clarify, and ensure that the publication of modifications is in line with the proposal to defer publication of information in phase I trials. Also, for all other trials, information on modifications should be published after the decision on the modification, rather than the trial.
Appendix 3	41	All options state: in line with information in the initial CTA and application dossier. This is unclear. However, for Phase I, the draft proposal makes it clear that there will be an option such that no information on substantial modifications will be published until 12 months after the end of the trial. We concur with the inclusion of a deferral option. Also for Option One and Phase IV/low intervention trials, 'decision on trial' should read 'decision on modification'.
Appendix 4 Serious breaches, corrective measures, unexpected events which affect risk/benefit and inspection reports	13	**Comment:** See general comments above. Publication of inspection reports and serious breaches has potential to cause commercial harm.
Appendix 4	41	For serious breaches, corrective measures, unexpected events which affect risk/benefit and inspection reports, see comments on draft proposal (Lines 842-843).
Appendix 4 P 59	63	**Comment:** Content of assessment report part 2 differs from part 1, will not be section Q S E. **Proposed change (if any):** Delete Q, E, S section in part 2 assessment report.
Appendix 4 Serious breaches p 61	63	**Comment:** It is proposed that in case an official hearing of an involved party is deemed necessary, this should be performed before the serious breach and its investigations are closed, and before the serious breach documentation is published. EMA should seek legal advice whether and how it can be prevented that judicial actions against publishing of serious

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		breach information impede the intended transparency.
Appendix 4 Inspection Report p 62	63	**Comment:** According to the appendix, the inspection report should be published after the report is issued, unless there is a judicial procedure or MAA ongoing. There will be clinical trials for which the publication of trial application documents' will be restricted e.g. as described in lines 467-479. It is proposed to implement a system, which allows an exchange of information related to the application, assessment, and inspections and ensures that those specific trials undergo an extra examination to which extent they can be published. EMA should seek legal advice whether and how it can be prevented that judicial actions against inspection reports impede the intended transparency.
Appendices 5 & 6 Summary of results & lay summary	13	**Comment:** Publication of phase I results 12 months after the end of the trial could harm sponsors. It may not allow sponsors to progress development of their IMP sufficiently to reduce the impact of disclosure on commercial competitiveness. Also, 12 months after the end of a trial gives insufficient time to analyse and review the results of a trial and make a patent application, given the need to keep secret all data within the first year after filing the application. **Proposed change (if any):** Defer publication of phase I results until at least 2 years after the end of the trial and ideally not until the first results from therapeutic trials are available. Consult with the pharma industry and other stakeholders over a suitable deferral period.
Appendices 5 & 6	41	As described above publication of Phase I results 12 months after the end of the trial could harm Sponsors. It may not allow Sponsors to progress development of their IMP sufficiently to reduce the impact of disclosure on commercial competitiveness. Also, 12 months after the end of a trial gives insufficient time to analyse and review the results of a trial and finalise a patent application, given the need to keep confidential all data within the first year after filing the application.
Appendix 5 and 6	78	**Comment:** There is common information on both reports, sponsor should only provide information once.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
Appendix 5 F ADDITIONAL INFORMATION	31	**Comment:** There should be an additional field for inclusion of information on study publications Proposed change (if any): Insertion of an additional field
Appendix 7	41	No comments.
Appendix 7	65	**Comment:** All sections and appendices of the CSR are marked as "Green", indicating that they will be made public. Only those appendices required under EMA's Policy 70 should be submitted to the database (see also response to Q18). In support of this position, it should be noted that the following sections and appendices of the CSR will contain personal information that must not be disclosed to the public: 6 Investigator & Study Admin Structures; 16.1.3 List of IEC / IRBs; 16.1.4 List of investigators 16.1.5: Signatures In addition, it should be noted that full transcripts of publications in appendices 16.1.11 and 16.1.12 are subject to copyright, and so should not be made public through the Database.
General comment on search functionalities	31	Although the search functionalities of the public user interface are not part of the functional specifications to be audited as set out in Article 82, we would like to include some general comments on them. **Comment:** The public user interface should include up-to-date search functionalities (as in ClinicalTrials.gov). **Proposed change (if any):** It should be possible to: • truncate search terms,

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		• implement a search in all or single search fields, • enable a search with synonyms (including the display of relevant synonyms), • enable the use of brackets to structure the search, • use Boolean operators, • save searches, • combine different search lines, • save or copy the search history. **Comment:** The public user interface should enable different download options (as in ClinicalTrials.gov). **Proposed change (if any):** It should be possible to export and download: • single hits or all hits retrieved by a search query • different download options (e.g. study summaries, selected fields or all fields) • different download formats (e.g. XML, plain text, tab-separated values, comma-separated values)