6 November 2015
EMA/739151/2015
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 received on text Section 4.4.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes
447-725	49	**Comment:** It appears that claiming commercial confidentiality will only be recognised for information which relates to 'the nature of the trial and status of medicinal product being studied'. Such information will belong to organisations who seek to develop and commercialise medicinal products. As a non-commercial organisation (an NHS trust in England), that is not our business. We do act as sponsor for studies including CTIMPs, but it seems that it would be the trial and product that will be looked at, not the commercial/non-commercial status of the sponsor. Thus we feel that it is for commercial organisations to pass comment here and/or the Association of British Pharmaceutical Industry.

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454-459	31	Definition of commercially confidential information From IQWiG's point of view, the suggested definition of commercially confidential information does not consider the general ethical requirements for research in humans and the requirements laid down in the EU Clinical Trial Regulation. To meet the basic ethical requirements of research in humans (e.g. according to the Declaration of Helsinki), methods and results of trials have to be publicly available so that knowledge generation from this research is possible. This requirement defines a public interest that generally overrides economic interests. In addition, publication of the study results is in the public interest because clinical trials aim to improve patient care. In this context, publication of the full information on study methods is also required to enable the assessment of the validity of study results and thus to reliably inform decision making in health care. This position is supported by the EU Clinical Trial Regulation according to which data from a clinical study report should in general 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for granting the marketing authorisation has been completed or the application for marketing authorisation has been withdrawn (Recital 68). In conclusion, the methods and results of in a clinical trial generally cannot be considered commercially confidential. This does not become clear from the definition of commercially confidential information provided in the draft proposal. **Proposed change (if any):** Add the following sentence to the definition: In general study methods and study results cannot be considered commercially confidential information.
454-459	73	Definition of commercial confidentiality **Comment:** The final part of this definition appears to EAHP as very broad and conditional, and could provide large possibilities for information to be withheld that is actually in the public interest to disclose. EAHP suggest EMA consult specifically on this issue. It occurs to EAHP that the definition of what is considered by EMA as 'commercially confidential' is a critical matter to get correct from the beginning of the database's utility. The currently given definition appears to EAHP to offer wide possibilities for keeping information out of the public domain against the public interest. EAHP would like to see a more expansive document from the EMA describing the basis upon which it will make judgments about commercial confidentiality issues. As stated in an earlier part of the consultation document "*The rules need to be applied in a fair*

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		and systematic way, in accordance with the established rules, and not based on repeated human judgement and intervention, which would be impossible to control and create a very large burden on authorities and or sponsors " At least from this consultation document, the procedures for applying commercial confidentiality test do not come across as abundantly clear and EAHP advise some work on explaining to the public precisely how determinations on CCI are/will be made by the Agency can valuably assist public confidence in the trial process.
454-583	15	**Comment:** commercially confidential information (4.4.1) 1. Although we understand the commercial concerns it needs to be understood that clinical trials are invariably performed after patent protection for the products has been obtained in the widest possible sense, a sponsor who has not done this has taken risks on his own account and a guideline should not be designed to cover these risks. This means that the ideas and intellectual property should be protected before a clinical trial is launched to reduce the necessity for secrecy. Therefore public interest of data obtained in clinical trials should not be restricted by IP rights.
454-583	39	***A vague definition of "commercial confidentiality information": clinical trial data are not "trade secrets"*** The EMA proposes to define "commercially confidential information" as: "*any information contained in the data or documents submitted to the database that is not in the public domain or publicly available and where disclosure <u>may</u> undermine the legitimate economic interest of the sponsor*". This definition, which was not the democratically discussed nor accepted during the adoption of the clinical trials Regulation, is more encompassing than that put forward by the European Commission in its proposed directive on trade secrets[1]. Moreover, despite the claim that "*the implementation of the transparency rules of the Clinical Trial Regulation is without prejudice to the application of Regulation (EC) No 1049/2001 and citizens' right to request documents under that Regulation*" (lines 256-257), this definition could influence the way the EMA answers to information requests. The implementation of such a definition would allow clinical trial sponsors to circumvent the publication of scientific data – of public

[1] Trade secrets are defined in Article 2(1) of the proposed directive as: *"information which meets all of the following requirements:*
a) is secret (…);
b) has commercial value because it is secret;
c) has been subject (…) to reasonable steps (…) to keep it secret".

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		interest - on the grounds that their economic interests might *potentially* be undermined. For instance, safety-related clinical data would likely be considered CCI by a clinical trial sponsor and thus withheld. Moreover, the EMA outlines the following as "legitimate economic interest" for the sponsors: • "*because the clinical trial forms part of the development of a medicinal product for commercialisation of that product (i.e. seeking a marketing authorisation or variation)*" (lines 469-470); • "*because the clinical trial is conducted to (…) research on medicines and as such may be part of a process for which research funds have been obtained or may contribute to the obtaining of future research funds*" (lines 471-472). This is unacceptable. The statement that "*specific situations may occur where the* ***overriding public interest would prevail in ad hoc situations*** *over and above the general transparency rules established for the database and documents and data not usually made public may be published or made public at an earlier time point than would be usual*" is not sufficiently reassuring. In fact, no information is provided about the "*decision making process [that] will need to be established in order to invoke use of the overriding public interest in such ad hoc cases*" (line 489), and thus the statement above suggests rather clearly that opacity will be the rule and transparency the exception… ***Whole documents to be withheld: EMA's one size hides all approach*** According to the EMA, to structure "the complex documents" included in the EU database into "*confidential and non-confidential parts would impose a significant burden on sponsors who would have to prepare them for input into the portal in a very different way for the EU compared to elsewhere*". The EMA then goes along to propose the non-disclosure of whole documents, not just sections. It goes as far as claiming that study specific documents – such as the protocol, the subject information sheet, related list of questions to sponsors, response and assessment reports - (line 502) could be considered CCI, as well as product specific documents – such as the investigator brochure, the investigational medicinal product dossier, the related list of questions and the response and assessment reports (line 535). In addition, EMA's **"one size *hides* all approach"** is based on a complicated classification of clinical trial documents into different

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		categories, depending on the "*stage of development*" (phase I trials are considered more "commercially sensitive" than phase IV trials or "low intervention" studies). The rationale behind EMA's approach seems to be that of reducing a subjectively perceived burden on authorities and sponsors rather than improving transparency. **A redefinition and narrowing of the notion of *commercially confidential information* (line 457) is essential to prevent the EMA from relying solely on the self-classification by the sponsor of the information that may undermine the sponsor's economic interest or competitive position** (read right column on page 7). 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 at the same time to prove that non-disclosure would not be detrimental to public health. In light of the objectives pursued in Regulation No 1049/2001 (article 4(2)), CCI can be overturned whenever there is an "*overriding public interest in disclosure*". This needs to be clearly stated in the definition of CCI. In addition, **any exception to disclosure rules should only involve the removal of specific elements of information within a document and never be applied to an entire section or certain types of documents**. As clearly stated in article 4.6 in Regulation No 1049/2001: "*If only parts of the requested document are covered by any of the exceptions, the remaining parts of the document shall be released*." **Outcome (if applicable): *Redefine CCI to become an exception, by adopting transparency as a general rule as follows:*** "***Scientific data that is in the public interest, such as clinical or regulatory data, should not be considered commercially confidential***". **"(…) *CCI can be considered as meaning ~~any~~ information contained in documents submitted to the database that is not in the public domain or publicly available and where disclosure ~~may~~ is duly justified and documented to undermine to an unreasonable degree of prejudice the legitimate economic interest of the clinical trial sponsor, provided there is no overriding public interest that justifies immediate disclosure. The period of time for which commercial confidentiality is required is duly specified*.**

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		Accepted CCI can be blacked out but the document shall be released so that the remaining sections of the documents which do not contain CCI can be publicly accessible." ***Delete the examples presented from line 467 to line 479.***
454-484	69	The EMA definition of commercially confidential information is far too broad and not in line with the intention of legislators when they adopted the Regulation No 536/2014. The EMA definition of what is considered a sponsor legitimate economic interest is so encompassing that it would undermine any meaningful disclosure of information. For example EMA indicates (line 469 -471) that "*information may be commercially confidential because the clinical trial forms part of the development of a medicinal product for commercialization of that product (i.e. seeking a marketing authorisation or variation* " or "*because the clinical trial is conducted to further basic or applied research on medicines and as such may be part of a process for which research funds have been obtained or may contribute to the obtaining of future research funds"* (lines 471 - 473). We consider these interpretations unacceptable.
454-500	35	Article 81(4)(b) of Regulation 536/214 reflects the following order: (1) transparency as the general rule; (2) protection of CCI (exception); (3) omission of the protection of CCI because of an overriding public interest in disclosure (exception of the exception). In that respect, Article 81(4)(b) of the Regulation follows Article 4(2) of Regulation 1049/2001 and the principle of proportionality according to Article 52(1) of the Charter of Fundamental Rights. The order outlined above requires the definition of public interests in disclosure which are capable to override the protection of CCI as a fundamental right. It clearly follows from the relevant legal text that the interest of the public in transparency per se is not capable to override the protection of CCI as a fundamental right because the protection of CCI is the exception which overrides the transparency as the general rule. In respect of a sound balancing and harmonisation of the legitimate objectives involved, it has to be borne in mind that the essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health (Recital 2

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		of Directive 2001/83/EC). In this regard, health and the life of humans rank foremost among the interests protected by the primary law of the EU according to the established case law of the European Court of Justice (e.g. Judgment of the Court of 7 March 1989, Case 215/87, paragraph 17). Since 1965 Community action has always had the dual objective of safeguarding public health by providing Europe with safe and effective medicines, while at the same time creating a business environment that stimulates research, boosts valuable innovation and supports the competitiveness of the industry (see Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions - Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector, COM/2008/0666 final, p. 3). As a result, safeguarding public health and - as a means to safeguard public health - stimulating research, boosting valuable innovation and support of the competitiveness of the industry form the core objectives of the policy of the EU with regard to the pharmaceutical sector. Finally, it has to be borne in mind that the fundamental right to good administration (Article 41 of the Charter) includes the obligation of the European Institutions to respect the legitimate interests of confidentiality and of professional and business secrecy (see Article 41(2b) of the Charter). Against this background, the interest of the public in transparency is not *per se* capable to override the protection of CCI as a fundamental right. Rather, the main public interests that may override the protection of CCI in connection with data included in a clinical study report is public health (see also Judgment of the Court of 6 December 2005, C-453/03, C-11/04, C-12/04 and C-194/04, paragraphs 82-85). The public interest of public health requires the disclosure of such data included in a CSR which have to be known by patients, families, patient groups and all those involved in health care decision making to make sound decisions as to the application of the specific medicinal product. However, this public interest does not require the disclosure of all data included in a clinical study but only such data which shall be published as the “Trial Registration Data Set” defined by the World Health Organisation as the internationally accepted standard of transparency with regard to clinical trials (see WHO, International Standards for Clinical Trial Registries, 2012, P. 3, 4 and 23-30). Thus, the Trial Registration Data Set defined by the World Health Organisation represents a sound balance between transparency and confidentiality
456-459	30	**Comment: Clinical data cannot be considered commercially confidential information.** The definition of commercially confidential information provided in this proposal (any information contained in the data or documents submitted to the database that is not in the public domain or publicly available and where disclosure may undermine the

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		legitimate economic interest of the sponsor) is too vague and too open to misinterpretation. For instance, negative trials data or safety alerts may highly undermine the economic interest of the sponsor but their non-disclosure would be detrimental for public health.
456-466	51	The definition provided for the term “commercially confidential information” is ambiguous. According to the Expert Legal Opinion of Prof. Denninger, all documents and parts of documents must be protected in order to ensure fairness in competition and freedom to choose an occupation, as well as to protect intellectual property (see p. 6, Section 5 and p. 8, Section 7 of translation of Expert Opinion). An unambiguous definition, which is also compatible with EU law, has been provided in German jurisprudence (see p. 10, Section 7 and p. 11, Section 9 of translation of Expert Opinion). Also, the Regulation (EC) NO. 1049/2001 and Regulation (EC) No. 726/2004 take legal precedence over the EMA Policies 0070 and 0043, and the Regulations specifically stipulate the protection of commercial interests (see p. 7, Section 6 of translation of Expert Opinion). Furthermore, the proposed definition would not directly include non-commercial and academic sponsors, as there is no direct economic interest in these cases. Nevertheless, in such cases, an academic interest in confidentiality certainly exists (e.g. in the form of publications). **Proposed change (if any):** All documents and information from sponsors and authorities (experts, agency, working groups) are confidential and not public. Exclusion of “commercial” qualifier in wording.
457-459	29	**Comment:** The proposed definition is very broad so that nearly all information regarding clinical trials could fall under this definition and could be considered CCI. We do not think that this would be meeting the requirements of the Regulation. We propose to narrow this to “data or information where disclosure would undermine the legitimate economic interest of the sponsor”. **Proposed change (if any):** CCI can be considered as meaning any information contained in the data or documents submitted to the database where disclosure would undermine the legitimate economic interest of the sponsor.
457-459	35	EMA defines CCI “as meaning any information contained in the data or documents submitted to the database that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the sponsor.” This definition should be brought in line with Article 39 TRIPS which provides in paragraph 2 that natural and legal persons shall have the possibility of preventing information lawfully within their control from being disclosed to, acquired by, or used by others without their

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		consent in a manner contrary to honest commercial practices so long as such information: (a) is secret in the sense that it is not, as a body or in the precise configuration and assembly of its components, generally known among or readily accessible to persons within the circles that normally deal with the kind of information in question; (b) has commercial value because it is secret; and (c) has been subject to reasonable steps under the circumstances, by the person lawfully in control of the information, to keep it secret. This definition has also been used by the Commission to define the term "trade secret" in the Proposal for a Directive of the European Parliament and of the Council on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure (COM/2013/0813 final).
457-459	80	**Comment:** This is not a good definition of CCI. Instead of a negative, it should be a positive argumentation.
457-466	40	We welcome the definition of commercially confidential information (CCI) set out in 4.4.1.1. In particular, we think it is right that the consideration of what might be commercially confidential is based on the nature of the trial and status of the medicinal product being studied, rather than the nature of the sponsor organisation conducting the trial. Many academic and non-commercial sponsors will have similar commercial considerations to commercial sponsors. For example, Cancer Research UK's Centre for Drug Development (CDD) is the largest specialist sponsor of oncology trials in the UK3. Although the CDD is a non-commercial sponsor, more than 50% of its trial arrangements are with industry partners who may, for example, be providing the drug for the trial free of charge or an intellectual property license to have the study drug made. The assessment and consideration of what might be commercially confidential for such trials should be made in the same way as for commercially sponsored trials.
457-759	7	The EMA draft proposal for an addendum states that "Commercially confidential information can be considered as meaning any information contained in the data or documents submitted to the database that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the sponsor" (l. 457-759, p. 13/28). While it is understood that commercially confidential information can be critical to pharmaceutical companies, CPME insists that all results of clinical trials, whether they are positive, negative or inconclusive, should be made publicly available. The legitimate economic interest of the sponsor should therefore be defined in a restrictive way and should not take precedence over the public legitimate interest to gain knowledge and be informed in a timely manner about prescription and non-prescription medicines that are on the EU market or that are being investigated. In many countries, ethical rules do not allow for physicians to be involved in clinical trials where the outcomes are not transparent/public.
460-466	29	We agree that the consideration of what might be commercially confidential should be based on the nature of the trial and the status

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		of the medicinal product studied rather than the nature of the sponsor conducting the clinical trial. If the sponsor claims that the information should not be made public, the claim would have to be substantiated. The Member States should assess the claim and decide about whether it is reasonable during the initial assessment of part I of the clinical trial.
460-479	31	The draft proposal suggests that the need of non-commercial or academic sponsors to obtain research funding could be a legitimate economic interest allowing to claim that certain information relating to a trial should be considered commercially confidential. The draft proposal further suggests that information may be classified as commercially confidential because this could be required to obtain future research funds or to publish the research in journals. It seems that this would allow publicly funded research to be considered commercially confidential. This seems inappropriate. **Proposed change (if any):** Even if the legislation does not distinguish between different sponsor types, the addendum to the functional specifications should not suggest that publicly funded research could be considered commercially confidential.
460-479 and Q 5 in 895	78	**Comment:** It is strongly supported that the consideration of what might be considered commercially confidential information is based on the nature of the CT and status of the MP being studied without taking into account the nature of the sponsor. **Proposed change (if any):** Therefore, Question 5 in table below line 895 should be deleted.
462-466	65	**Comment:** Please note that the nature of the sponsor organisation conducting the trial may be important for determining what may be commercially confidential.
463-466	37	**Comment:** agree with the approach that the nature of the trial is key rather than the nature of the sponsor organisation conducting the trial in order to crystalize a set-up that is deemed possible to implement and which is also deemed cost-effective for stakeholders
467-468	74	**Comment:** Having a legitimate economic interest in the trial can not be regarded as a basic principle for restricting the otherwise public information. Most sponsors have a legitimate economic interest in the trial but the basic information, including full data contained in study reports, regarding the trial must still be publicly available. See more closely the general comments.
467-471	35	This passage explains the legitimate economic interest of the sponsor seeking a marketing authorisation or variation. To obtain a marketing authorisation or to perform a variation, e. g. related to an adjusted indication according to Part I Module 5.2 Annex 1 of

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		Directive 2001/83/EC the CSR as defined in Article 2(35) of Regulation 536/2014 is the core document to be submitted. To avoid that this core document including its appendices can simply be downloaded from the EU database and then successfully be used by competitors for own marketing authorisation applications, at least those parts redacted by the sponsor to protect CCI and the appendices of the CSR should not be made public. **Proposed change:** After the word (variation) in line 471 the following sentence needs to be added: Because of the relevance of the clinical study report for applications for marketing authorisations or variations at least those parts redacted by the sponsor to protect CCI and the appendices of the clinical study reports shall not be made public.
467-479	29	**Comment:** These should be regarded as possibly legitimating an economic interest, but not generally. Approval should be needed from the Member States in the assessment for part I.
470-475	47	EORTC strongly supports this position that recognises non-commercial sponsors may also have valid reasons to consider clinical trials protocols confidential and defer their release to the general public. Indeed, aside the main research questions, non-commercial clinical trial protocols frequently include correlative research. It may contain some very premature data, for instance on biomarkers and potential clinical correlations which, aside of being potentially patentable, may not be appropriate to be publically released before the research hypothesis is proven or refuted.
471-479	24	**Comment:** EHA welcomes the Agency's appreciation of the importance of academic research where the need to obtain funds for present or future studies and the ability to publish this research constitute a legitimate economic interest.
471-479	40	We welcome the EMA's recognition that sponsors may need to retain some confidentiality of research plans in order to sustain their ability to conduct original research, to maintain funding and publish that research, and to pursue their future research programme. It is important that these concepts are considered to represent legitimate economic interests and we therefore welcome the EMA's proposal that they fulfill the definition of commercial confidentiality for the purpose of the Regulation.
480-484	7	Similarly, the notion of "overriding public interest" (l. 480-484, p. 14/28), through which the confidentiality status of a commercial information can be lifted, should be understood and defined in a broad manner, thus allowing the general public, the research and medical community a wider access to vital information.

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480-484	44	'Overriding public interest can be considered, in this context, as meaning that the general public interest in having information made publically available may outweigh considerations that the same information should remain confidential. The public interest per se is multifactorial, but includes access to information that supports the objectives for transparency set out in chapter 2 part 3 of this document.' **Comment:** Expansion on what constitutes 'overriding public interest' could be beneficial. EGAN believes that the EMA and the pharmaceutical industry should be as transparent and open as practicable.
480-484	51	"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 who, for what reasons and in what process may cite "overriding public interest" (exception to an exception in Regulation (EC) No. 1049/2001).
480-484	65	**Comment:** An overriding public interest should not be considered "the general public interest in having information made publicly available." If that were the case then there would not be a need for an exception because this general interest would exist in every case, meaning that CCI would never be protected. Such a broad reading of the public interest in effect reads the exception out of the rule. Rather, someone seeking disclosure in the case where CCI as defined at lines 457-59 is shown to exist should have to put forth a specific public interest in disclosure applicable to the CCI at issue.
480-487	63	**Comment:** It should be defined which group or body (e.g. reporting MS, CTFG, EMA, KOM) is allowed to decide whether an overriding interest is present. In addition there is a need for guidance documents, on which the decision (presence of an overriding interest or not) has to be taken. The same is applicable for lines 192-193.
480-487	81	**Question 5** **Comment:** Examples should be provided in the addendum document as to what may constitute cases of "overriding public interest".
480-490	24	**Comment:** EHA agrees that a separate decision making process will need to be establish in order to invoke use of the overriding public interest in ad hoc cases. As this decision making process is not included in this consultation, EHA would strongly suggest to consult stakeholders again once such procedure is drafted. Hopefully, at such instance, the Agency is able to allow for a longer consultation period.

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480-490	31	Based on the basic ethical requirements for research in humans and to ensure safe and efficient use of authorised drugs there is a very strong public interest in making available all information on the methods and results of all studies on these drugs. Therefore, the default position should be that for study methods and results there is an overriding public interest requiring publication. Any deviation from this rule requires justification and an independent audit. **Proposed change (if any):** Clarify the overriding public interest in the publication of study methods and results.
480-490	73	Definition of "overriding public interest" **Comment:** The description of how the "overriding public interest" test will be applied in practice appears lacking in the document, which makes it difficult for EAHP to give strong comment on this aspect of the document and intentions for the development of the database. EAHP would welcome EMA giving further clarity on this topic in advance of the database being constructed and operational. This might helpfully include how external stakeholders could prompt use of the test, or question the results of its application.
485-490	40	It is important that the EMA has acknowledged that in, specific situations, overriding public interest would prevail over and above general transparency rules established for the database. As stated in lines 489-490, a decision making process will therefore need to be established outside of the database to invoke the use of overriding public interest. We seek clarification from the EMA over how this decision making process will be drawn up and who will be responsible for invoking the use of overriding public interest.
485-490	65	**Comment:** We suggest that the Database functionality and decision making processes to be applied when invoking the use of "overriding public interest" should allow for consultation with the sponsor prior to disclosure of CCI. Such a consultation will ensure a balanced decision that takes into account any risk of loss of CCI; there should also be an opportunity for appeal of the decision before the information is made available.
485-490	69	EMA indicates that *"specific situations may occur where the overriding public interest would prevail in ad hoc situations over and above the general transparency rules established for the database and documents and data not usually made public may be published or made public at an earlier time point than would be usual"* and that *"a decision making process will need to be established in order to invoke use of the overriding public interest in such ad hoc cases"*. This part of the Addendum is too vague and should be further elaborated and detailed. More generally we think that throughout the document it should be clear that public disclosure is the general rule and that non-

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		disclosure is the exception. Transparency should be the default option. It is up to the sponsors to prove that the disclosure of certain information could damage their economic interests.
488-490	71	**Comment:** Additional clarification pertaining to 'over-riding public interest' is requested. . **Proposed change (if any):** Please clarify the decision making process associated with the notion of 'overriding public interest'
488-490	81	**Question 5** **Comment:** The process should include the following elements: • Upfront information and consultation with the sponsor of planned publication. • Technical option for differentiated approaches, i.e. some information to be made public due to overriding public interest and some other not – to be decided case-by-case as needed. • Appeal option for the sponsor prior to the publication.
491-492	37	**Comment:** agree that the documents and data included in the database can be grouped in the two broad categories mentioned
491-500	30	**Comment:** we disagree on the consideration that "study specific and (active substance/medicinal product) specific documents" contain the same level of commercially confidential information.
491-500	51	All documents included in the approval processes (sponsor and authority) that are uploaded to EU-Portal contain confidential information and data. Subdividing the documents would be a insupportable burden on sponsors. In addition, redactions are dependent on processes of MA. **Proposed change (if any):** All documents and information from sponsors and authorities (experts, agency, working groups) are confidential and not public.
493	15	2. Line 493. Although it is easy for sponsors to declare commercial interest for all their documents, the statement that administrative load would be the reason to do so is not in line with the legal and societal concerns. Additionally, the members of

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		our committee who are involved in this field know that the objections of administrative nature are in fact opportunistic and not realistic.
493-499	71	**Comment:** Additional clarity is required for how both confidential and non-confidential are to be presented e.g. different sections within the same protocol or two versions of the same protocol. To require both a confidential and non-confidential version of a protocol (even if redacted) would impose a non-negligible administrative burden on both the sponsor and regulatory authorities. As an alternative, the system could be constructed such that a sponsor is notified of an information request and the sponsor in turn would provide an appropriate redacted version might be provided. **Proposed change (if any):** Please clarify on the foreseen handling of both confidential and non-confidential information related to protocols.
493-500	29	**Comment:** The proposal, that it would mean too much of an administrative burden to structure the documents in confidential and non-confidential parts would not mean that the documents should not be made public. **Proposed change (if any):** Delete the whole passage.
493-500	31	It should not be possible to withhold information on study methods and study results just because there might be bits of commercially confidential information in a given document.
501	68	**Comment:** Will the documents be made public for all studies with EudraCT numbers, i.e., all back to 2004? And will sponsor be provided adequate time to discern if any confidential commercial information exceptions applies?
501-583	51	Study specific and product specific documents, questions, responses, applications for modifications and assessment reports all contain confidential parts. Redaction of parts or subdivision of documents is impossible and would not ensure transparency for the public (Protection of company secrets, see p. 8-10, Section 7 of translation of Expert Opinion). **Proposed change (if any):** All documents and information from sponsor and authority (experts, agency, working groups) are confidential and not public.

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502	15	3. Line 502. A protocol for a clinical study will go to regulatory bodies and ethical committees who may have to discuss this with experts. It is reasonable not to publish the protocol on the database but this is critically dependent upon the fact that the requirements for the content of summarised elements (line 511) are sufficient. We therefore strongly advise that this content is checked for this as experience has taught us that sponsors tend to limit the information they supply. 4. To consider the subject information sheet as commercially confidential is ludicrous, paradoxical and implausible. Subjects will take this information home and will want to discuss it with their relatives, medical staff and in fact whomever they choose to consult. If a subject would have to sign a secrecy agreement, this would restrain the individual to seek professional advice. This is unrealistic and violating the protection of the subjects. The subject information is therefore public by definition. 5. The Investigators brochure can easily be written to exclude commercially sensitive data (which in the case of a trial are generally production data) and is therefore by definition public with the burden of proof on the sponsor 6. We agree about the commercially sensitive nature of the IMPD. However it is of importance that when the nature of the iMP is published at least coded and abbreviated, information about its mechanism of action is published. Especially for new medicines with an unknown mechanism of action, knowledge about other similar IMP (with a comparable mechanism of action) is very important to assess and determine efficacy and safety. This must be possible to find in the database, rather than coded numbers. 7. We object to the special condition/state of Phase I trials in the publication of data, especially the possibility that (line 734) a sponsor can opt for minimal information to be published. In general the special condition/state for Phase I trials is not logical. This is already outlined in the EU guideline on Clinical Trials (1). In the period after this guideline the traditional Phase I trial has disappeared. This would mean that everyone can call an early phase trial Phase I and escape from the requirement of transparency. 8. The data from an early phase (human pharmacology or therapeutic exploratory studies in the terms of the guideline) have an even more important requirement for transparency than data from later studies. This is exemplified by the serious problems around the FIH trial with TGN 1412. Data about this trial have never or very late been entered in the Eudravigilance and Eudract databases and were not publicly available. If a company would have been trying to investigate a different drug with a similar mechanism they would not have found the side effects in the database.

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		Conclusion 1. Although we generally support the attempts to obtain simplification and transparency in clinical research on EU citizens we find that the Commission has overemphasized commercial concerns. It is possible that these have been introduced in the addendum on transparency by parties that have an overriding commercial interest but if the Commission would follow these suggestions the laudable purpose of this addendum would be misapplied.
502-525	30	**Comment: study specific documents such as the study protocol and the subject information sheet contain very few commercially confidential information if any**. **These documents should be made publicly available as soon as possible, ideally at the time of decision on the trial.** The practice of publishing the study protocols on medical journals is increasing at least among academic sponsors. The publication of the trial protocol as soon as possible - possibly before the trial starts - should be encouraged. Its delayed publication, for instance when the trial results are posted, should be accepted only if fully motivated. No other postponement should be allowed.
502-583	29	**Comment:** It would be sufficient to list the categories and what falls under the categories. It is superfluous to explain what the documents contain and why they **might** contain commercially confidential information. It seems as if EMA wants to trigger special answers to the subsequent questions. We do not agree that the protocol, patient information sheet related question, responses and assessment reports, investigators brochure, IMPD and related question, responses and assessment reports automatically contain substantial commercially confident information. (see comments above) **Proposed change (if any):** Delete all information on the content of the respective documents.
503-515	29	**Comment:** We do not agree that the protocol in general contains extensive confidential information, at least for clinical trials conducted from Phase II onwards. It should therefore not be treated as an entity for the purpose of transparency rules.
503-515 349-350 Appendix 2 CT	31	We disagree that study protocols contain commercially confidential information. Clinical trial methodology as laid down in study protocols is a well-known, publicly discussed scientific methodology. Even indication-specific methods (such as treatment protocols, endpoints or analyses) are generally publicly available. Specifically, clinical trials aiming to support marketing authorisation are performed according to publicly available guidelines by health authorities.

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regulation Annex I D		In general, the methods and results of a clinical trial cannot be considered commercially confidential. To meet the basic ethical requirements of research in humans, methods and results of trials have to be publicly available so that knowledge generation from this research is possible. Time of availability of study protocols A full assessment of study results to support decision making in health care (on the level of an individual patient or on a public health level [e.g. for clinical guideline development or for reimbursement decisions]) requires the availability of detailed information on the planned conduct of the study. Therefore, for this assessment the full study protocol is required. The information provided in the "major study characteristics" according to Draft Appendix 1 is insufficient to understand the study methodology to the extent required for the assessment of study results. Therefore, the full study protocol needs to be available when the summary of study results is published 12 months after the end of the study. Otherwise, the aim of improving transparency by making the study results available as laid down in the EU Clinical Trial Regulation cannot be met. **Proposed change (if any):** The full study protocol (without redactions) is to be made publicly available together with the study results, i.e. 12 months after the trial. Clinical trial methodology cannot be considered commercially confidential information.
503-515	74	**Comment:** Study protocol should as a rule be publicly available after granting of the marketing authorisation. It contains valuable information, e.g. for verification purposes.
510	51	**Comment:** It is absolutely agreed that the trial protocol should be treated as one entity for the purpose of transparency rules. The same should apply for the subject information sheet, related list of questions and the Investigator Brochure.
511-512	29	**Comment:** Does not have any context to the text above or below. **Proposed change (if any):** Delete
516-525 (321)	2	**Comment:** At the time of decision on the trial it is not the plan to make the subject information sheet public. The subject information sheet is the best information to the public about the trial. A potential trial subject is not giving any vow of secrecy when reading the subject information sheet. The subject information sheet hardly contains enough information for a rival company to

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		replicate the trial, even for a phase I study. **Proposed change (if any):** The subject information sheet should be public before the trial begins
516-525	29	**Comment:** We do not agree that the subject information sheet in general contains extensive confidential information, at least for clinical trials conducted from Phase II onwards.
516-525	74	**Comment:** safety information given to trial subjects is important not only from subject's personal point of view but also for general public interest in the conduct of clinical trials and should not, a priori, be considered confidential. **Proposed change (if any):** Subject information sheet should be publicly available unless extraordinary reasons presented by the sponsor give reason to keep them secret
516-525	77	The distinction between study specific and active substance/product specific documents is supported. Although we do find a subject information sheet in general not a document that contains commercial confidential information, we do understand that in specific situations there could be an exception on this. Therefore, we propose to change the text to reflect more that a subject information sheet contains in principle no commercially confidential information, but that there can be an exception on this rule as a result the subject information sheet should not be made public at the time of decision.
517	73	"details of the potential risks and benefits of participation in the trial" **Comment:** EAHP would expect information on the potential risks and benefits of participation in the trial to be made publicly available by default.
526-534	29	**Comment:** We do not agree that the assessment reports contain extensive confidential information. Those should be published at an early time point, i.e. at the time of decision about the clinical trial.
526-534 575-583	72	**Comment:** Regarding the publication after a marketing authorisation has been granted for lists of questions, responses, and assessment reports (except for those related to section Q of the IMPD), much of this information outside of section Q of the IMPD could contain commercially confidential information, for example, on the development or other indications of the IMP. **Proposed change (if any):** Allow sponsors to redact and publish the redacted versions.

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526-534 and 575-583	78	**Comment:** Taking into account that the protocol normally contains product specific information it should be difficult to differentiate questions study specific and product specific except with respect to quality of the product and GMP issues. **Proposed change (if any):** Quality of the product (including GMP requirements) assessment report should be separated from the rest of part I assessment.
535-574	30	**Comment:** product specific documents could contain commercially confidential information. We agree that the quality section of the Investigational Medicinal Products Dossier (IMPD) should remain confidential. On the other hand, the Agency should promote the disclosure of the safety and efficacy sections of the IMPD at the time of posting of trial results (i.e., 12 months after the trial completion). These documents contain information relevant to increase the knowledge about the risk benefit profile of a given drug and thus may be essential to understand the real value of a new drug. We recognise that in some exceptional situations their disclosure may be deferred to the end of the marketing authorisation procedure.
536-552	29	**Comment:** One of the key objectives of the Regulation is to increase the knowledge about the clinical trials conducted and to foster innovation. Therefore it would be important that the Investigator Brochure is – with some exceptions – published at an early time point, i.e. at the time of the decision about the clinical trial.
553-574	29	**Comment:** One of the key objectives of the Regulation is to increase the knowledge about the clinical trials conducted and to foster innovation. Therefore it would be important that the safety and efficacy section of the IMPD is – with some exceptions – published at an early time point, i.e. at the time of the decision about the clinical trial. We agree that the Quality section of the IMPD should not be public at all.
553-574	74	**Comment:** IMPD can not as such be considered commercially confidential. We agree that the quality section of IMPD can contain commercially confidential information but the safety and efficacy section of the IMPD contain valuable information that should be publicly available. **Proposed change (if any):** Safety and efficacy sections of the IMPD should be public information.
571-574	37	**Comment:** agree that the IMPD-Q section, list of questions, responses from the authorities and the IMPD-Q related part of the

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636-640		assessment report shall remain confidential indefinitely due to the sensitive nature of the information contained therein
575-583	29	**Comment:** We do not agree that the assessment reports contain extensive confidential information. Those should be published at an early time point, i.e. at the time of decision about the clinical trial.
584	33	**Proposed change (if any):** 1.2
584-605	16	**Comment**: Taking into account the objective of **maximum transparency** for clinical research and to avoid unnecessary duplications of clinical trials, we decide to have the information of clinical trials the most accessible and public of all the options given in the draft document. Therefore, we choose option 1.1 “once a marketing authorisation has been issued, by al least one Member State, for the active substance contained in the medicinal product”. **Proposed change (if any):** None
584-605	31	**Question 6**: 4.4.2. How should the status of marketing authorisation of the medicinal product be applied in the context of Article 81(4)(b) of the Regulation? The availability of comprehensive study information (methods and results) is required at the latest when a drug becomes available on the market. At that point in time the drug can be used both within the approved indication (label) or off-label. Therefore, IQWiG supports proposal 1.1 defining marketing authorisation status by the authorisation of the active substance in at least one Member state. Proposals 1.2 and 1.3 would mean that study information on use in indications that are not yet licensed would not be available, although the drug may already be used in these indications in clinical practice. Another problem with proposals 1.2 and 1.3 is that a clear definition of “indication” in this context is difficult.
584-605	73	**Comment:** EAHP supports proposal 1.2. the assesessment is more linked to the active ingredient and the dosing used in the indication, less to the formulation which could cause unintended consequences for adaptive licensing.
584-609	11	**Question 6** We consider that proposal 1.3 is the only option that meets the requirements and objectives of the Regulation. This is the only

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		option that recognises fully the requirement of Article 81.4(b) that protection of CCI will take into account the status of the marketing authorisation for the product, unless there is an overriding public interest in disclosure. The marketing authorisation applies to a specific medicinal product that is characterised in terms of the active substance, indication, formulation and route(s) of administration. Only information associated with the specific approved indication and formulation of the product should be published at the time of the product's marketing authorisation. Information related to line extensions and/or new indications will be included in additional marketing authorisation applications and therefore should be made public when the relevant additional marketing authorisation is issued.
584-609	12	**Question 6** **Comment:** We support Proposal 1.3: Commercially confidential information should be considered taking into account, in particular, the status of the marketing authorisation using the following concept: "Once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation/route of administration under study." Justification: • A significant number of clinical trials conducted by EU Clinical Pharmacology Units investigate new indications, formulations and/or route of administrations of medicines that have a marketing authorisation in at least one Member State for the active substance contained in the IMP. These studies are considered Phase 1 (non-therapeutic) clinical trials. • Sponsors do not wish to disclose information on new indications and/or formulations early, as this may disclose programme strategy and affect patent protection. • If a marketing authorisation has been issued, by at least one Member State for the active substance contained in that product, a wealth of information is available to the public for the active substance concerned. • For non-therapeutic trials it would be difficult to justify an overriding public interest requiring publication of study specific and product specific documents prior to marketing authorisation for the studied indication, formulation and/or route of

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		administration. • If early disclosure would be required in the EU, it is likely that these trials will be conducted outside the EU. This would not only result in the EU losing clinical research to other regions, it would also result in the public having less access to trial information or data than if the study would be conducted in the EU. Proposed change (if any): N/A
584-609	19	**Question 6** **Comment:** Option 1.3 best meets the meet the requirement and objectives of the Regulation (EU) No 536/2014, as the formulation. Route of administration under study could be one aspect of commercially sensitive information.
584-609	35	The concept and the proposals in this passage do not take into account that for certain application types, e.g. well-established use, traditional herbal and homeopathic medicinal products - the clinical trial report (sometimes without appendices) is the core document to obtain authorisations (e. g. with improved indications), especially due to the fact that for those products regulatory data protection is often not available and thus competitors could use the data for their own applications. To avoid that competitors successfully use copies of downloadable reports for their regulatory applications at least the appendices of the study reports should not be made public. **Proposed change:** Add after line 605: *In any event before and after a marketing authorisation has been issued the appendices of the clinical study report shall not be made public. Due to the specific importance of the clinical study report for marketing authorisation (e. g. with adjusted indications for well-established use, traditional herbal and homeopathic medicinal products) clinical study reports related to such products should generally be considered CCI.*
584-609	35	**Question 6** **EMA Proposal 1.3 is the most appropriate to be selected for inclusion in the final rules.** Article 81(4)(b) of the Regulation does not refer to the definition of undisclosed information to be protected as intellectual property applicable according to Article 7 and 17(2) of the Charter in the light of Article 39 TRIPS. According to this definition the status of a marketing authorisation is irrelevant for the status of data included in a clinical study report as CCI.

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		Furthermore, the statement in Recital 68 of Regulation 538/2014 that, for the purposes of this Regulation, "in general" the 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, does not sufficiently reflect the definition of undisclosed information to be protected as intellectual property according to Article 7 and 17(2) of the Charter in the light of Article 39 TRIPS. Recital 68 does not sufficiently distinguish between the question of the status of CCI and the question of the existence of an overriding public interest to disclose the CCI. Notwithstanding the above, Proposal 1.3. best meets the requirements and objectives of the Regulation. According to No 4 of the Guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms (EMA/CPMP/EWP/280/96 Corr1, p. 7) if a new chemical entity is developed first as a modified release formulation, the submitted dossier should contain the appropriate pharmaceutical and chemical data, necessary preclinical studies and a complete clinical data package as for any full application. This is even truer for locally applied or locally acting products (see EMEA, Note for Guidance on the Clinical Requirements for Locally Applied, Locally Acting Products Containing Known Constituents, CPMP/EWP/239/95 final). In addition, "formulation" should be amended to "each pharmaceutical form."
584-609	57	**Question 6** **Comment:** EuropaBio believes that proposal 1.3, 'once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation/route of administration under study', is the most appropriate proposal that would adequately protect commercially confidential information. If either proposals 1.1 or 1.2 were to be adopted, the triggers for timing of publication described in lines 709-721 may not provide adequate protection of commercially confidential information on new and future indications and pharmaceutical forms included in the study or product specific documents. This could compromise the protection of future intellectual property rights, proprietary information and legitimate economic interests of sponsors. In addition we would suggest replacing "formulation" at line 601 by "pharmaceutical form".
584-609	60	Application of the status of the MA **Comment**: We believe Option 1.3 best meets the objectives of the regulation. We wish to suggest that that specific dose

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		information could also be a component of this definition. In the lifecyle management of drug development as more information is gained on the safety and efficacy of a product, Sponsors may explore new indications but also additional doses or dose regimens. Given the additional investments that Sponsors must undertake in such activities, the definition should be expanded to increase specificity of Option 1.3 to also address dose/dose regimens. **Proposed change (if any):** We recommend a revision to option 1.3 to read as follows: "1.3. once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation/route of administration **and dose/dose regimen** under study."
584-609	65	**Question 6** **Comment:** Please refer to EFPIA's Major Comments under the heading of "Determining Marketing Authorisation Status". As explained in detail under our 'Major Comments', EFPIA believes that proposal 1.3 (i.e., "once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation/route of administration under study") is the optimal choice.[2] **Proposed change:** The disclosed information should likewise be specific to the actual 'dosage strength' within the marketing authorisation.
584-609	68	**Comment:** There is preference for proposal 1.3, as confidentiality of alternative formulations might be covered. We would like to have clarification of what is meant by "formulation/route of administration" in suggestion 1.3. What is a different formulation in the scope of the document? Would this also apply for new fixed dose combinations with no reference product? If bioequivalence studies are considered as well, all options will always be fulfilled, as there is always the approval of the reference product. This would mean the marketing authorization status is considered as "with a marketing authorization". This will disclose confidential information on the pipeline of a generic company to direct competitors much too early in generic

[2] However, if EMA were to adopt a proposal other than 1.3 for the definition of marketing authorisation, then there would need to be additional protections in place for CCI for indications, formulations or strengths still in development. In this case, the triggers for timing of publication related to Question 10 (lines 709-721) may not provide adequate protection of CCI on new/future pharmaceutical forms or indications included in the study or product specific documents."

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		development. **Proposed change (if any):** Add bioequivalence studies to point 2 next to the bio-similars.
584-609	70	**Question 6** **Comment:** EUCROF believes that proposal 1.3 meets best the requirements and objectives of the Regulation. Commercially confidential information should be considered taking into account, in particular, the status of the marketing authorisation using the following concept: "Once a marketing authorisation has been issued, by at least one Member State, for a medicinal product **using that active substance** and **for the indication** and **formulation / route of administration under study**." Rationale: EU Clinical Pharmacology Units are frequently involved in clinical trials investigating new formulations and/or routes of administrations of medicines and/or trials in new indications of active substances with marketing authorisations in at least one MS. These trials usually have no therapeutic/prophylactic intent (Phase 1). At an early stage of formulation/route of administration or new indication development, sponsors can – for commercial reasons – not disclose information to the public as this would disclose programme strategy and affect patent protection. In our view there is no plausible overriding public interest in disclosing information publicly for these studies prior to the timelines stipulated in option 1.3. a) If a marketing authorisation has been issued for the active substance, a significant amount of information on the active substance is available in the public domain. b) There is no risk of duplication of research (any different, new formulation, route of administration or indication will require new, specific trials). c) If a trial is negative (e.g. unfavourable pharmacokinetics and/or tolerability of a new formulation or route of administration), then this is of importance to the manufacturer who may wish to test a different formulation or route of administration, but not to

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		the public. d) For studies without therapeutic/prophylactic intent, there is no overriding need of the public to know that these studies are ongoing. Once studies reach the stage of therapeutic intent, there may be potential benefit, but not before. Public disclosure would first and foremost serve the manufacturers' competitors. If early disclosure of information would be required in the EU, it is certain that many of these trials would be conducted outside the EU. **Proposed change (if any):** We wonder why dosage changes are not mentioned in this context. Should this scenario be included in the definition: "Once a marketing authorisation has been issued, by at least one Member State, for a medicinal product **using that active substance** and **for the indication** and **formulation/dose/route of administration under study"**
584-703	7	The above comments apply similarly to clinical trials on products that have already obtained a marketing authorisation and to those for which no marketing authorisation has yet been delivered (sections 4.4.2 and 4.4.3.6). Not all clinical trials will lead to a marketing authorisation. The data of these trials should however still be made public. Indeed, the legitimate interest of the public to access information on eg. sister molecules or generic drugs should not be considered lower than for the investigation on originator drugs. The same disclosure policy should apply to these clinical trials.
586-605	27	**Comment:** we suggest proposal 1.3. Rationale: in this way, the information will be made public without affecting the commercially confidential information during the earlier phases of drug's development.
586-605	69	BEUC supports the less restrictive option 1.1 "once a marketing authorization has been issued, by at least one Member State, for the active substance contained in that medicinal product". Information from all trials on a given product should be made public, including those for non-approved indications.
586-609	55	**Question 6** **Comment:** In our opinion, proposal 1.3 best meets the requirements and objectives of the regulation, by balancing the fostering of innovation and increasing transparency. This proposal will encourage significant innovation during the life cycle of the active substance, such as improved efficacy, improved safety and treatment compliance, to the benefit of patients, whilst still enabling the

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		legitimate requirements of the Clinical Trial Regulation to be met. We disagree with proposal 1.1, which could seriously impact on further innovation once a first marketing authorisation with an active substance had been achieved, including impacting significant benefits from investment in clinical research into extension of indications and populations. We disagree with proposal 1.2, which could stifle innovation in the development of dose forms for existing or new routes of administration and safer and more effective dose forms. In our opinion proposal 1.3 should be clarified to apply once a marketing authoriation has been issued, by at least one Member State for a medicinal product using that active substance and for the indication and for the formulation, **and** for the route of administration under study. This will clarify that significant innovation through clinical research into novel formulations, by an existing route of administration is equally to be encouraged. **Proposed change:** Line 600: Change 1.3 to read "once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation and route of administration under study."
589-605	71	**Question 6** **Comment:** Proposal 1.3 best meets the requirements and objectives of the Regulation. This proposal is the most conservative and preferred approach as any other option could give commercial advantage to other competitors. Proposal 1.1. would imply that the study results of any new formulation of an active substance or any generic formulation would immediately be made public, independently of the marketing authorization status of this product, thus preventing the possibility to protect early stages of development and commercially confidential information completely. Proposal 1.2 is similar in that study results of new formulations would also be published immediately, without protection of commercial information.
589-609	10	**Question 6** **Comment:** In this version of the document, it is a bit unclear what will be made public, since there are words missing in the text before the different proposals (which begin "once a marketing").

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		Proposed change: Clarify the wording before the proposals (lines 592-593) by describing what will happen (what information will be made public) once a marketing authorisation has been issued. Proposal 1.1. should not be used, since it could lead to publication of information that the sponsor would like to protect to be able to use it at a later stage of development. Proposal 1.2. is probably the best alternative since it protects development to a reasonable extent and encourages efforts for early access to medicines. Proposal 1.3. seems to be unnecessary strict. At this point of time, the main product development is finished.
594-595	30	**Comment:** salts, esters, isomers of the active substance may be included providing that they have the same biological effects may be considered. **Proposed change (if any):** "once a marketing authorisation has been issued, by at least one Member State, for the active substance ***(and its salts, esters, isomers, if having the same biological effects)*** contained in that medicinal product,
594-602	81	**Question 6** **Comment:** Only option 1.3 is suitable to protect CCI of the originator. **Proposed change:** Please delete Options 1.1 and 1.2.
600-602	37	(concept of marketing authorisation) **Comment:** agree with the 3rd option, i.e. no. 1.3 The down side of the approach is that it leaves much administrative work on Member States and/or EMA since indications etc. may differ from Member State to Member State. A codification process will therefore be needed.
603-605	10	**Comment:** Section 2 seems to be unnecessary and might even cause confusion. Is it not understood that medicinal products containing active substances which are bio-similars are other products than the originator products? **Proposed change:** Remove section 2.

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603-605	78	**Comment:** Active substances are not bio-similars, only the medicinal product containing it. **Proposed change (if any):** paragraph in lines 603-605 should be modified to " .... medicinal products containing active substances of biological origin should be considered new active substances with respect to the originator product until biosimilar character is granted with the marketing authorisation".
606	51	**(Question 6)** **Comment:** In case that a marketing authorization has been issued for an active substance for a particular indication and route of administration, all information contained in documents for trials investigating other indications and routes of administrations with this active substance should still be regarded as commercially confidential (according to proposal 1.3). The indications may differ substantially for the same active substance administered via the same route (e.g. finasteride for benign prostate hyperplasia or hair loss) or dependent on the route of administration (e.g. tacrolimus administered systemically for prevention of graft rejection vs. topical treatment of atopic dermatitis). Thus, considering all information for an active substance as not commercially confidential once approved will discourage clinical development in other indications.
606-609	4	**Question 6** EURORDIS would prefer option 1.2 : *once a marketing authorisation has been issued, by at least one Member State, for a 597 medicinal product using that active substance and for the indication under study* This is because some active substances in the public domain may be tested for several possible indications (drug repurposing). When a first authorisation is granted, it is important to protect the information on other trials, for other indications; else the developer of the medicine may lose its competitive advantage. The same reasoning could apply to Paediatric Use Marketing Authorisations: here only the data can be protected, and the developer taking the risk of conducting trials for a new indication should be able to preserve confidentiality for other trials with the same substance for other paediatric indications.
606-609	5	**Question 6** Comment: The proposal 1.3 best meets the requirements of the Regulation 536/2014. Commercially confidential information is not

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		adequately protected by proposals 1.1 and 1.2.
606-609	9	**Question 6** **Comment:** We support proposal 1.1. Information from all trials on a drug – including trials for non-approved indications – should be made public. Such uses are extremely common in routine clinical practice. It is therefore senseless and dangerous for trials on such uses to be exempted from robust reporting requirements.
606-609	13	**Question 6** (marketing authorisation) Option 1.3 best meets the requirements and objectives of the Regulation. Products, not active substances, are licensed, and licenses apply only to approved indications. So option 1.3 is the only one that aligns public disclosure with the scope of the product license. Options 1 and 2 give no protection to the commercially confidential information of sponsors wishing to develop new formulations or routes of delivery, or to investigate their medicines in new indications. In the context of transparency, marketing authorisation status must apply to product, indication and formulation, or there will be no commercial drive to develop new formulations and investigate new indications in the EU. Sponsors are likely to move those R&D activities to more favourable regulatory environments (eg USA).
606-609	21	**Question 6** **Comment:** Option 1.1. is preferred. Having early info will help patients apply for subsequent trials.
606-609	23	**Question 6:** I think proposal 1.2 applies as far as I am concerned. 1.1. Is too vague and does not define the indication. 1.3 also dictates the formulation/ route of administration. However provided the PK/PD of the drug is known, I do not think different route of administration from the one of the original marketing authorization should preclude authorization/ access to the drug
606-609	28	**Question 6** Proposal 1.3 follows the usual definition of the concept of marketing authorization. The definition in the proposals 1.1 and 1.2 can

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		compromise the confidentiality of information in the case of academic investigator initiated research to a new indication and or formulation/route of administration. And as stated in rules 462-466 “The legislation does not distinguish between different types of sponsor organisation (e.g. commercial, non-commercial or academic). The consideration of what might be commercially confidential is therefore based on the nature of the trial and status of the medicinal product being studied, rather than the nature of the sponsor organisation conducting the trial.” Therefore proposal 1.3 best meets the requirements and objectives of the Regulation.
606-609	29	**Question 6** We are of the opinion that **proposal 1.1** (once a marketing authorisation has been issued, by at least one Member State, for the active substance contained in that medicinal product) should be chosen to apply the status “marketing authorisation” as it best meets the requirements and objectives of the Regulation. Otherwise - e. g. in paediatric research, in a lot of oncology research - important information could not be used for the further development of treatments, even if the MAH of the active substance is not interested in developing e.g. a paediatric indication.
606-609	30	**Question 6** the proposal 1.1 (“once a marketing authorisation has been issued, by at least one Member State, for the active substance contained in that medicinal product”) as amended according to the previous comment best meets the requirements of the Regulation. The other two proposals are more difficult to implement and will dramatically restrict the number of trials that will be fully disclosed.
606-609	32	**Question 6** 1.1. : No 1.2. : No 1.3. : Yes If an additional process is not implemented to guarantee the confidentiality of study specific documents then in 1.3 this will be more or less covered

Line no.	Stakeholder no.	Comment and rationale; proposed changes
606-609	36	**Question 6** **Comment:** *The FPM believes that proposal 1.2 best meets the requirements and objectives of the Regulation. It is appropriate that marketing authorisation status is taken into account when considering what product/trial information is made public. There needs to be reasonable commercial confidentiality around drugs being explored in new indications. However, in the case of phase IV/lifecycle management (LCM) trials with new routes of administration or formulations, the requirement for commercially-confidential information (CCI) is less so.*
606-609	38	**Question 6** **Comment:** Our preference is for proposal 1.2. We consider that 1.1 is too wide as there may be a number of indications for a particular active substance. We also consider that 1.3 is too restrictive.
606-609	39	**Question 6** **4.4.2. How should the status of marketing authorisation of the medicinal product be applied in the context of article 81(4)(b) of the Regulation?** Article 81(4)b of the Clinical trials Regulation states "*The EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the following grounds: protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product, unless there is an overriding public interest in disclosure*". *"Taking into account the status of the marketing authorisation for the medicinal product*" means to us "*once a marketing authorisation has been issued, by at least one Member State, for the active substance contained in that medicinal product*" (proposal 1.1. of the consultation document). This is in fact the notion borne in mind by the EU Parliament and the Council when defining a "*low intervention trial*" and **there is no reason to interpret it differently**. Proposal 1.1. is the most inclusive proposal since it regards the active substance, not the specific medicinal product, nor the particular indication.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Access to information about other clinical trials concerning the same active substance (even if in different medicinal products) might be relevant to the public, sponsors, healthcare professionals and patients. In addition, proposals 1.2. and 1.3. could be used to delay the entry into the market of generics and of biosimilars. **Outcome (if applicable):** Choose option 1.1.
606-609	40	**Question 6** We support proposal 1.3: that the concept of marketing authorisation (MA) should be applied once a MA has been issued, by at least one member state (MS), for a medicinal product using that active substance and for the indication and formulation/route of administration under study. This proposal would ensure that a product with MA being tested outside of its indication will have any new confidentially commercial information protected, supporting the development and broaden of use of existing treatments. We are not supportive of proposal 1.1 as we believe it has the potential to discourage the further investigation of products already marketed, in a new indication. Under this scenario we understand that future study and product related documents relating to investigation of the product, in a new indication, would be published at the time a decision on the trial is made or possibly deferred until publication of summary results if justified. This may discourage sponsors from considering an early licensing approach in small indications of unmet medical need, preferring instead to wait until an MA in a larger indication can be achieved in order to protect the study and product specific information. We have similar concerns that proposal 1.2 has the potential to discourage the development of novel and/or innovative formulations for agents already marketed due to the requirement to publish study and product related documentation at the time a decision on the trial is made or possibly deferred until publication of summary results.
606-609	41	**Question 6** Proposal 1.3 is the most appropriate option described. This is the only option that synchronises the scope of commercially confidential information to be made public with the scope of the MA license to be granted. It provides a productive environment for a Sponsor to undertake further research and development on further disease indications, and/or new formulations and/or drug

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		delivery routes for the active substance. Conversely, Proposals 1.1 and 1.2 would prevent a Sponsor from protecting their commercially confidential information on new formulations, drug delivery routes, and/or new disease indications. Ultimately, these proposals (1.1 and 1.2) would drive Sponsors to undertake such research and development activities outside of the EU in more favourable regulatory territories (e.g. the USA).
606-609	46	**Question 6** **Comment: Proposal 1.3** is the only proposal which not only meets the requirements and objectives of the Regulation but safeguards the competitiveness of the clinical trials industry in Europe. This proposal allows synchronization of the scope of Confidential Information to be divulged with the scope of the MAA license to be granted. It provides an attractive environment for a Sponsor to continue their R&D which may result in new formulations, disease indications and/or drug delivery routes for the active substance. Proposals 1.1 and 1.2 would preclude protection of a Sponsor's Confidential Information resulting from R&D as described above and would strongly suggest that this activity would be better undertaken in a commercially safer environment for clinical research i.e. outside Europe.
606-609	48	**Question 6** **Comment: Proposal 1.3** best meets the requirements and objectives of the Regulation. Indeed, indication extensions, Active Substance and route of administration as any other development may be of significant commercial interest to the sponsor. Keeping the details of studies in this respect as commercially confidential information is critical to stimulate innovation.
606-609	51	**Question 6** **Comment:** Referencing the date of the granting of the marketing authorisation as a means of determining whether or not clinical data is commercially confidential information is not convincing. The status of this information does not change when a marketing authorisation is granted. The marketing authorisation does not provide any protection mechanism for protecting the information from misuse by competitors in or outside the EU. Beyond the fact that the selection of the date of the marketing authorization appears to be arbitrary, Regulation (EC) No. 1049/2001, Article 4 clearly states that EU institutions must refuse access to documents disclosure would undermine the protection of commercial interests (see Expert Legal Opinion, Prof. Denninger). By

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		defining the date of the marketing authorisation as the time point from which onward the documents may be published without continuing to protect commercial interests, the proposals 1.1., 1.2. and 1.3 do NOT meet the requirements and objectives of the Regulation. **Comment:** In case that a marketing authorization has been issued for an active substance for a particular indication and route of administration, all information contained in documents for trials investigating other indications and routes of administrations with this active substance should still be regarded as commercially confidential (according to proposal 1.3). The indications may differ substantially for the same active substance administered via the same route (e.g. finasteride for benign prostate hyperplasia or hair loss) or dependent on the route of administration (e.g. tacrolimus admistered systemically for prevention of graft rejection vs. topical treatment of atopic dermatitis). Thus, considering all information for an active substance as not commercially confidential once approved will discourage clinical development in other indications.
606-609	53	**Question 6** we support the proposal not to differentiate between non-commercial and commercial sponsors in the definition of trials with commercially sensitive data. This is of particular relevance in trials which are collaborations between academia and industry partners and avoid discrimination against these important collaborative efforts. The definition of the time period for which data remains commercially sensitive must be precisely defined. The concept of overriding public interest is open to interpretation and the body who make this decision will need very clear guidelines to follow and would need to be very exceptional cases. In terms of the preferred proposal for inclusion in the final rules; we would prefer option 1.1:' once a marketing authorisation has been issued, by at least one Member State, for the active substance contained in that medicinal product'. Both options 1.2 and 1.3 carry of risk of minor alterations in use of substance being used as a reason to revert back to being highly commercially sensitive. This would not be in the public interest and could result in unnecessary duplicate trials being undertaken. Once an active product has MA, subsequent studies looking at different application of that active substance should NOT carry the same level of commercial sensitivity.
606-609	54	**Question 6**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Regarding Section 4.4.2, we agree that the status of the Marketing Authorisation should be taken into account in deciding which information/documents in the EU database shall be publicly available. Regarding which proposals for how the status of marketing authorisation of the medicinal product should be applied in the context of Article 81(4)(b), **we think proposal 1.3 best meets the requirements and objectives of the Regulation**. This would be once a Marketing Authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation/route of administration under study. This is because different products regarding indications, route and formulation can exist under one Marketing Authorisation and whilst they have the same Marketing Authorisation, they still have commercially confidential information that would be substantially different to other products contained under the same Marketing Authorisation. Under the other proposals, information relating to these different products could be released prematurely (i.e. before the grant of a Marketing Authorisation. The release of this information could potentially harm commercial interests.
606-609	59	**Question 6** **Comment:** We believe option 1.3 best meets the requirements and objectives of the regulation. The regulation supports innovation within the EU. By following the rules outlined in options 1.1 or 1.2 commercially sensitive information may be released on products or new versions/formulations of products still under development. This may discourage Sponsors from developing such products within the EU. **Proposed change (if any):** Not applicable
606-609	61	**Question 6** **Comment:** LEO Pharma is of the opinion that option 1.3 is in need of clarification. Under the assumption that the proposal must be read as “once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication, route of administration and formulation under study”, LEO Pharma is in favour of option 1.3. In a clinical development, for instance for topical products, it is not uncommon that several studies with same route of administration and different formulations are done. Since the publication will largely be automated based on rules, the precise meaning of "/" will be important.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		It is considered that application of the status of the MA is central for all transparency aspects of the Regulation. LEO Pharma is of the opinion that there is a substantial risk of jeopardising critical commercial confidential information with the two other proposals. The risk is related to disclosure of product-specific, rather than study-specific information.
606-609	62	**Question 6** **Comment:** Disagree with option 1.1 because this will provide information to the wider public after one Member State has provided approval and it covers the whole active substance. What if the active substance was being used in a new innovative medicinal product before appropriate commercial protection was in place? Disagree with option 1.2 because approval from one Member State does not signify general European approval for a product and substantial work may still be required to get the product approved in Europe. Option 1.3 would be the preferred option because this protects commercial interest on a medicinal product that may be developed for different routes of administration and different indications.
606-609	63	**Question 6** **Comment:** 1.1. Time point too early with regard to ongoing development in different indications, routes, formulations … 1.2. Might be too early too, depending on formulation and/or on route different opportunities for development e.g. s.c. development of new class in diabetes followed by development of oral, or IM and SR formulation, lead once daily. Both are improvement of treatment. 1.3. Agreed. This proposal supports development in EU. 2. Biosimilars – agreed. **Proposed change (if any):** Proposal 1.3. Agreed.
606-609	67	**Question 6:** Preferably: 1.3. once a marketing authorisation has been issued, by at least one Member State, for a medicinal product using that active substance and for the indication and formulation/route of administration under study.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
606-609	72	**Question 6** Proposal 1.3 would be preferred as it narrows down the information that may overlap with continued development of an IMP. If this proposal is chosen, then exceptions should be made for commercially confidential information for the same medicinal product that has a different indication or formulation and would be information that is not considered already publically available. For example, the IB should not be made public after marketing authorisation is granted if it contains such information; as development can change rapidly it may be difficult to determine if a company is still in development for a product for another indication.
606-609	75	**Question 6** **Comment:** we consider Option 1.3 acceptable. Although rare for our trials to include an unlicensed product it is more likely that a produce with a marketing authorisation is used for another indication and formulation / route. In order to apply commercial confidentiality protection to our trials Option 1.3 would be required to be adopted.
606-609	77	**Question 6** **Comment:** We are in favour of proposal 1.3 because in the other two proposals(1.1 and 1.2) new developments with active substance /medicinal product is not taking into account. We consider another formulation/route of administration to be a new development of the substance/product for which the rules for commercial confidential information should apply.
606-609	80	**Question 6** **Comment:** 4.4.2.1.3. is the best characterisation of a modern marketing authorisation.
610-634	35	The proposal largely refers to the status of the marketing authorisation when applying the concepts of CCI (as does Recital 68 of Regulation 536/2014 – cf. lines 221-236, it should be noted that a Recital is not a legally binding provision and its contents is not reflected in the Articles of the Regulation). This assumption, however, is not based upon primary EU law. According to the case law of the European Court of Justice the protection of intellectual property rights has to be interpreted in view of general principles relating to and international obligations. In this respect we refer to the comments on TRIPS as set out in our General Comments above. As a result, the definition of undisclosed information to be protected as intellectual property within the meaning of Article 39 TRIPS is applicable to the protection of business secrets as a fundamental right according to Article 7 of the Charter and applicable to the protection of intellectual property rights as a fundamental right according to Article 17(2) of the

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Charter. According to the definition of Article 39 TRIPS the grant of a marketing authorisation, the completion of the procedure for granting the marketing authorisation, or the withdrawal of the application for marketing authorisation are no criteria which would lead to a change of the data included in a CSR status of undisclosed information (or trade secrets or CCI). In particular, such data are still secret and still have commercial value because they are secret and still are kept secret after marketing authorisation.
610-640	24	**Comment:** EHA agrees that the IMPD-Q section should remain CCI indefinitely, post marketing authorization.
610-642	11	**Question 7** We support the proposal that, regardless of marketing authorisation status, the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered as commercially confidential and not made public for any trial at any time, as this deals with the manufacturing and related pharmaceutical development information which continues to be CCI, indefinitely, post-marketing authorisation.
610-642	12	**Question 7** **Comment:** We strongly support the EMA's proposal that the IMPD-Q section and the related list of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time for the reasons stated in lines 638 to 640 in the draft proposal. **Proposed change (if any):** N/A
610-642	19	**Question 7** **Comment:** Agree that the IMPD-Q section should remain confidential since this information will continue to contain commercially confidential information for an indeterminate period of time and the information related to manufacture and related pharmaceutical development is unlikely to be of public interest.
610-642	26	**Comment:** We agree that "regardless of marketing authorisation status the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time, as this deals with the manufacturing and related pharmaceutical development information which continues to be CCI, indefinitely, post marketing authorisation." Since the Investigational Medicinal Product Dossier (IMPD) includes manufacturing and related pharmaceutical development information, we agree that this continues to be commercially confidential

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		information that should not be made public at any time. **Proposed change (if any):** NONE
610-642	35	**Question 7** EUCOPE agrees that without doubt IMPD-Q section on IMP Quality and related lists of questions, responses and assessment report sections are commercially confidential and will not be made public for any trial at any time. However, in addition, EUCOPE believes that similar arguments against the release of these documents, at any time, should equally apply to the Investigator Brochure ("IB"). In particular: 1. IBs are not connected to any specific clinical trial, do not give a lot of details about any given trial, are not included in marketing authorisation applications, and are not used by EMA as part of their evaluation of MAAs. 2. IBs are not tied to a single MAA; they are often connected to a number of MAAs over a period of years. It can well happen that the first MAA (the fastest indication to market) is not the most important. The CCI that warrants for not disclosing an IB before the first MAA, should also apply to follow-up MAAs. 3. As pointed out in paragraph 4.4.1.2 b), IBs contain extensive details of a commercially confidential nature, they have to be updated on a yearly basis and therefore are very difficult to redact (more so than a CSR or any submission document). 4. International regulations require industry to maintain a single IB including all indications and forms of a compound so long as the efficacy and safety profiles are related, even though these different forms would be approved and marketed as separate products. For example, an IB for a product already on the market will as well keep information for a new route of administration which is still in Phase I and years away from filing an MAA. All of the latter information would have to be considered CCI, and the two are not easily separated. 5. The purpose of transparency as set in the objectives of the Regulation 536/2014 will be achieved via the dispositions that will allow all the clinical trials that are encompassed in a given compound IB to be accessed through the portal and the database. The context in which these trials are presented in an IB is of a commercially confidential nature for as long as the compound will be in development.

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		We therefore believe that **paragraph 4 of section 4.4.3 (lines 636-640) should also mention the IB as follows:** "*Regardless of marketing authorisation status, the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time, as this deals with the manufacturing and related pharmaceutical development information which continues to be CCI, indefinitely, post marketing authorisation. Likewise, the Investigator Brochure, given its product specific nature, the fact it presents a detailed and permanently updated development summary for the compound is therefore extensively filled with up-to date CCI and should not be made public for any trial, at any time.*"
610-642	65	**Question 7** EFPIA fully agrees with the EMA's proposal and reasoning that the IMPD-Q section on IMP Quality and related lists of questions, responses and assessment report sections should be considered commercially confidential and not be made public for any trial at any time. However, in addition, EFPIA believes the same arguments against the release of these documents, at any time, should equally apply to the IB. In particular: 1. IBs are not connected to any specific clinical trial, do not give a lot of details about any given trial, are not included in Marketing Authorisation Applications (MAAs), and are not used by EMA as part of their evaluation of MAAs. 2. IBs are not tied to a single MAA; they are often connected to a number of MAAs over a period of years. It can well happen that the first MAA (i.e., the fastest indication to market) is not the most important. The CCI that warrants for not disclosing an IB before the first MAA, should also apply to follow-up MAAs. 3. As pointed out in § 4.4.1.2 b), IBs contain extensive details of a commercially confidential nature, they have to be updated on a yearly basis and therefore are very difficult to redact. 4. International regulations require Industry to maintain a single IB including all indications and forms of a compound so long as the efficacy and safety profiles are related, even though these different forms would be approved and marketed as separate products. For example, an IB for a product already on the market will as well keep information for a new route of administration which is still in Phase I and years away from filing an MAA. All of the latter information would have to be considered CCI, and

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		the two are not easily separated. 5. The purpose of transparency as set in the objectives of the Regulation (EU) 536/2014 will be achieved via the dispositions that will allow all the main characteristics of clinical trials and a summary of their results that are encompassed in a given compound IB to be accessed through the Portal and Database. **Proposed change:** We therefore believe that the § 4 of section 4.4.3 (lines 636-640) should also mention the Investigator Brochure as follows: "*Regardless of marketing authorisation status, the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time, as this deals with the manufacturing and related pharmaceutical development information which continues to be CCI, indefinitely, post marketing authorisation*". *Likewise, the Investigator Brochure, given its product specific nature, the fact it presents a detailed and permanently updated development summary for the compound is therefore extensively filled with up-to date CCI and should not be made public for any trial, at any time.*
610-642	70	**Question 7** **Comment:** EUCROF agrees that the IMPD-Q section should be considered as CCI and therefore should never be made public. **Proposed change (if any):** N/A
610-642	81	**Question 7** **Comment:** As commercial sponsor our members absolutely support this proposal regarding the IMPD-Q section. It is of vital importance that the Drug Substance Part and the Drug Product Part remain confidential to protect our expert know-how about the CMC topics against competitors inside and outside of the EU.
615-617	29	In general, it seems to be sensible to apply a graduaded approach.
615-634	14	**Question 6** Referring to Question 6: 4.4.3. When should information that may be considered commercially confidential, be made public taking into account the marketing authorisation status of the medicinal product and unless there is an overriding public interest? (Please

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		provide a brief rationale for your choice of proposal and explain briefly disagreement with the other proposals.) **Comment:** Our choice is 1.2. [2. Currently there is no structured codification of the indications and formulations that would allow these to be determined automatically. The sponsor would have to indicate the marketing authorisation status of the medicinal product, in response to questions in the clinical trial application form. As part of the assessment of the dossier the Member States would have to assess this status and decide whether or not the clinical trial is using the IMP within or outside the labelled indications/formulations/routes of administration or established therapeutic guidance (for lowintervention trials). The decision of the Member States should be final. This also relates to the determination of the lowintervention trial status of some trials so both aspects could be considered together.], because thereby the decision is left of Member States and it is arbitrary. We disagree with the others two options because the first might be cumbersome and not be met (the extent of information made public progressively could not be submitted) and the third option could subtract transparency and the public information of this early investigation will be lost.
617	39	**Comment:** "In applying the concepts of protecting commercially confidential information, in particular taking account of the marketing authorisation status of a product, and of overriding public interest, a graduated approach could be taken to the release of information on clinical trials. Thus, the extent of information made public could progressively increase during the development period to the marketing authorisation of a medicine from first in human Phase I trials to post-authorisation Phase IV and low-intervention trials. " **Proposed change (if any):** This general consideration needs clarification, only if the EMA would refuse option 1. What does the EMA consider a graduated approach? Patients and healthcare professionals are interested in consulting information on ongoing clinical trials regardless of the trial Phase.
618-620	71	**Comment:** The decision criteria to render information public are not spelt out. It is also unclear whether a mechanism is foreseen for Marketing Authorisation holders to be notified prior to the information is made public. **Proposed change (if any):** Please clarify
620	22	**Comment:** "low-intervention trial" remains undefined **Proposed change (if any):** please consider adding footnote 6 of page 18 already here

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621-629 293-303	55	**Comment:** The document under consultation (lines 293-303) sets out that rules for the database need to be established and will operate in an automatic way. This is necessary for the volume of applications. The rules need to be applied in a fair and systematic way, in accordance with established rules and not based on repeated intervention. In the context of decisions on the marketing authorisation status of products, the document under consultation states that the sponsor will indicate this on the form (622-624). As part of the assessment of the dossier the Member States would assess this status and decide whether or not the IMP is being used according to label. It further states that the decision of the Member states should be final. The process for deciding the marketing authorisation status of a product subject to clinical trial is therefore not yet clear. The Sponsor would be best placed to judge the marketing authorisation status of the product.
624-626	5	**Comment:** For assessment of the marketing authorisations status according to proposal 1.3 above, the data should be easily available to the Member States. This should cover all marketing authorisations regardless of the approval procedure (centralised/national).
627	71	**Comment:** Considering that the actual approval of a given clinical trial is still at the national level, please clarify what will be the process for ensuring alignment amongst all the Member States. . **Proposed change (if any):** Please provide details for the process for such decision-making.
630-635	29	**Comment:** It is not clear, why this paragraph is included in the general considerations. What is the proposal? Clinical trials like this are especially important and the information should be available as soon as possible. 630- 634: what is the proposal??? / For what reason is this mentioned here? Information on clinical trials carried out on non-authorised medicines in the early phases of development prior to marketing authorisation , which are never later used in a marketing authorisation e. g. as the developments of the medicines is discontinued is very important for the future clinical research. It would be very important to know, which scientific questions /Hypothesis did not work out, when tested, to avoid duplication of efforts and unnecessary involvement of subjects in clinical trials. **Proposed change (if any):** Delete

Line no.	Stakeholder no.	Comment and rationale; proposed changes
630-640	47	EORTC agrees with the statement 3 that some trials may end-up in contributing to the basic research rather than to the development of medicines as such.
634	80	Comment: "…, but rather as basic research." This formulation is misleading: Trials not reaching marketing authorisation are therefore not automatically basic research.
635-640	51	**Comment:** We fully agree that it is absolutely crucial to consider the IMPD-Q section as commercially confidential, irrespective of the marketing authorisation status of the IMP.
635-642	10	**Question 7** **Comment:** We support the proposal regarding the IMPD-Q section, for the reasons stated in the document.
635-642	60	Confidentiality of IMPD-Q **Comment:** We agree that the IMPD-Quality section (IMPD-Q) is CCI and should never be made available to the public due to the proprietary nature of the content. **Proposed change (if any):** None
635-642	73	**Question 7** **Comment:** The same "public by default" position should apply to IMPD-Q sections. Deferrals may be allowable but, as with others, must be justified and open to audit.
636-640	14	**Question 7** **Comment:** support or disagreement with this proposal regarding the IMPD-Q section ("section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time"), We agree because the information contained in IMPD-Q section must be a continuous process related with the development and the manufacturing during all lifetime of a drug.
636-640	71	**Question 7**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: The EGA is in agreement with the following approach: "4. Regardless of marketing authorization status the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time, as this deals with the manufacturing and related pharmaceutical development information which continues to be CCI, indefinitely, post-marketing authorization." The information in this section is in most cases also patent relevant and should be regarded as confidential information and should be protected at all times.
636-642	55	**Question 7** **Comment:** We agree with the proposal that the IMPD-Q section and related questions, responses and assessment report sections should not be made public for any trial at any time. Public disclosure of this Commercially Confidential Information could compromise the legitimate economic interest of the sponsor.
636-642	57	**Question 7** **Comment:** EuropaBio supports the proposal that the IMPD-Q section on IMP quality and related lists of questions, responses and assessment report sections should be considered commercially confidential and not be made public for any trial at any time. We are in agreement with the rationale provided by the Agency.
641-642	4	**Question 7** EURORDIS agrees with the proposal. Manufacturing information is key for the MAH to minimise manufacturing costs while maintaining a high quality production. Any such information could be captured by generic manufacturers, even years after the data are released if they are. The generic manufacturers would have an unfair and asymmetrical advantage over the originator company.
641-642	5	**Question 7** **Comment:** We fully agree with the proposal regarding the IMPD-Q section.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
641-642	9	**Question 7** **Comment:** The default should be transparency. IMPD-Q sections should be made public and any request to withhold that information should be justified and those requests should be regularly audited.
641-642	13	**Question 7** (IMPD-Q section) For IMPs in clinical development, the IMPD-Q section contains highly commercially confidential information that could unfairly advantage competitors. Furthermore, information in the IMPD-Q section could unfairly benefit manufacturers of generic products *after* licensing of the medicine. There is no information in the IMPD-Q section that would be of value to prescribing physicians or patients. In accordance with Article 81(4) of the Regulation, we support the proposal that the IMPD-Q section should not be made public at any time, to protect commercially confidential information.
641-642	28	**Question 7** No comment.
641-642	29	**Question 7** We agree that the IMPD-Q section can be regarded as confidential throughout the lifetime of the product.
641-642	30	**Question 7** as stated above, the proposal of keeping confidential the quality section of the IMPD is considered acceptable as this information pertains to the product development process that should be protected as any intellectual property. **This protection cannot apply to any clinical data.**
641-642	32	**Question 7** Yes, the IMPD-Q section could be kept confidential

Line no.	Stakeholder no.	Comment and rationale; proposed changes
641-642	33	**Question 7** Completely in line with the EMA statement that the IMPD-Q section is should be considered strictly confidential and not be made publicly available
641-642	36	**Question 7** **Comment:** *The FPM supports the proposal regarding the IMPD-Q section.*
641-642	38	**Question 7** **Comment:** We would agree UNLESS particular problems in the manufacture of the active substance have been identified as potential patient safety issues.
641-642	39	**Question 7** We do not agree to *indefinitely* withhold important scientific information as it would hamper science. Research is largely based on knowledge transfer. The IMPD-Q section constitutes regulatory data that needs to be made publicly available particularly when relevant from a patient and public health perspective (impurities, stability). Regulatory data protection safeguards the interests of innovator companies by preventing generic and biosimilar companies from using this data for 10 years. In specific circumstances, such as a new manufacturing process or new analytical methods for example, it could be accepted that the information would only be made available after a defined period of time, but that should be decided on a case-by-case basis. It is not acceptable to withhold other IMPD sections (efficacy and safety) or trial-specific documents.
641-642	40	**Question 7** We support that the IMPD-Q section on Investigational Medicinal Product (IMP) quality and the related lists of questions, response and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		time. As outlined in the text in this section the IMPD-Q section provides full and detailed manufacturing and quality information for the IMP, which may also often include other proprietary formulation and manufacturing information. We therefore agree that this section should remain confidential indefinitely. We also agree that any related lists of questions, responses and assessment reports should remain confidential for the reasons outlined above.
641-642	41	**Question 7** We concur with the agency that the IMPD-Q section on IMP quality and the related list of questions, responses and assessment report sections should be considered as commercially confidential and not be made public for any trial at any time. The reason for this is that this information would provide invaluable insight to a competitor or generic manufacturer or company based in a territory where patent law is less stringent. This would adversely affect the attractiveness of EU as a territory in which to conduct clinical research.
641-642	46	**Question 7** **Comment:** We absolutely agree with the proposal regarding the IMPD-Q section. The release of this information would serve only to provide valuable insight to a competitor.
641-642	48	**Question 7** **Comment: Yes**, we agree that regardless of marketing authorisation status the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time, as this deals with the manufacturing and related pharmaceutical development information which continues to be CCI, indefinitely, post marketing authorisation.
641-642	51	**Question 7** **Comment:** Regardless of marketing authorisation status the IMPD-Q section on IMP quality and all the other sections safety (IMPD-S) and efficacy (IMPD-E) of the IMPD should be considered to be commercially confidential and not be made public for any trial at

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		any time. Furthermore, the term “extensive non-clinical and clinical trial data” used in line 564 is not explained. Therefore, there is no reason for publication of safety and efficacy section of the IMPD.
641-642	53	**Question 7** it is entirely appropriate to consider information relating to the IMPD-Q section to be commercially sensitive
641-642	54	**Question 7** We support the proposal for the IMPD-Q section. This is in line with our thinking and how we apply commercially confidential information in that all information relating to the quality of an active substance or product is generally considered as commercially confidential and should be treated as such regardless of Marketing Authorisation status.
641-642	59	**Question 7** **Comment:** We have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
641-642	61	**Question 7** **Comment:** LEO Pharma agrees that, regardless of the MA status, the IMPD-Q section on IMP quality and the related lists of questions, responses and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time. Disclosure of this data can jeopardise the developer’s investments and future research.
641-642	62	**Question 7** **Comment:** Agree with the proposal not to make details relating to the IMPD-Q section publically available.
641-642	63	**Question 7** IMPD-Q never public **Comment:** Agreed.

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641-642	72	**Question 7** The proposal regarding the IMPD-Q section we agree with what has been proposed as this section and associated questions, responses, and assessment report sections always contain commercially confidential information that continues indefinitely.
641-642	76	**Question 7** **Comment:** we consider this proposal appropriate.
641-642	77	**Question 7** **Comment:** No comment, support rational given in lines 636-640
641-642	80	**Question 7** **Comment**: ESMO completely agrees. Such data seem to be less important for clinicians, but may be indispensable to be protected commercially for companies.
643-651	24	**Comment:** Giving sponsors the option to defer publication for Phase IV and low-intervention trials will adversely affect the proposal's stated objective to increase public trust and should be omitted. **Proposed change (if any):** Delete lines 648-651
643-651	31	**Question 8**: Please comment and give a brief rationale for your support or disagreement with this proposal regarding clinical trials on products with a marketing authorisation. From IQWiG's point of view it is important that for trials on products with a marketing authorisation, the "major characteristics of the trial" according to Appendix 1 are available at decision on the trial and that the full study protocol and the summary of study results according to Appendix 5 and 6 (without redactions of study methods and results), as well as a clinical study report according to Appendix 7 (without redactions of study methods and results), are available 12 months after the end of the trial. IQWiG disagrees that study methods or results of a trial on a product with a marketing authorisation could be considered commercially confidential (see above). From the text of the guidance it seems that it would be the sponsors' decision whether any information would be commercially

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		confidential. Any decisions on commercial confidentiality would need to be justified and independently audited.
643-651	37	(Phase IV trials and low-intervention trials) **Comment:** agree to the suggested approach
643-651 652-654	47	EORTC supports statement 5. Indeed, low-intervention trials may contain CCI. Indeed, aside the main research questions, non-commercial clinical trial protocols frequently include correlative research. It may contain some very premature data, for instance on biomarkers and potential clinical correlations which, aside of being potentially patentable, may not be appropriate to be publically released before the research hypothesis is proven or refuted.
643-651	71	**Question 8:** **Comment:** The EGA is in agreement with this approach as it opens the option to apply for a deferral until results are uploaded. This question actually pertains to products 'with' a marketing authorization. There is a typographical error in the question. **Proposed change (if any):** Please clarify how a sponsor should indicate that it wishes to opt for deferral and whether a rationale for the request will have to be given. Please edit the sentence highlighting this applies to products which are authorised. (with a marketing authorisation)
643-651	73	**Question 8** Phase 4 trials should not have a deferral option as the product is on the market.
643-654	10	**Question 8** **Comment:** We support the proposals. However, there is a risk that many (all?) sponsors will use the option to defer the publication, resulting in more secrecy than is actually needed. But this might be a risk worth taking, since it is important in general to encourage trials within the EU and therefore to use a principle of cautiousness in case of doubt if the information should be made public or not.

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643-654	11	**Question 8** We support the proposal to allow the sponsor to defer publication of information on a clinical trial on a product with a marketing authorisation until the time that the summary of trial results is loaded into the database and made public. While information on the product will be in the public domain following approval of the marketing authorisation, the specific design of an individual post-authorisation trial may include elements of CCI that must be protected.
643-654	12	**Question 8** **Comment:** We agree with the proposal that there should be an option to defer publication of study and product specific documents for trials of products with a marketing authorisation until the time that summary of trial results are published. This is due to the fact that there would be no perceivable public benefit of publishing these documents until summary results also become available. On the other hand the sponsor may have justified economic interests in protection commercially confidential information until that time. **Proposed change (if any):**N/A
643-654	19	**Question 8** **Comment:** This approach is supported as it appropriately balances public interest with the interests of sponsor organisations.
643-654	26	**Comment:** We concur with Proposal 3 – a differential treatment based on clinical trial stage that would treat data release more conservatively in the earlier stages of development but less conservatively for those trials that have progressed through Phase 3. This would most balance the public's interest in the data pertaining to a compound that has advanced into pivotal trials with the appropriate protection of commercially confidential information important to sponsors that may be considering the next development steps for a product without marketing authorisation. Further, this more conservative approach protects the public from any assumptions of accuracy in small data sets on products that have not yet been shown to be safe or effective (or unsafe or ineffective), and then from relying on analyses that are potentially significantly flawed. **Proposed change (if any):** NONE
643-654	35	**Question 8** We agree with the EMA proposal that sponsors are given the option to defer publication for Phase IV trials as these may contain

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		exploratory endpoints, i.e. CCI.
643-654	55	**Question 8** Please comment and give a brief rationale for your support or disagreement with this proposal regarding clinical trials on products [~~without~~] **with** a marketing authorisation **Comment:** For products with a marketing authorisation, we agree with the proposal to provide the sponsor with the option of deferring publication of study specific and product specific documentation until 12 months after the end of the trial, when summary of trial results is loaded into the database and made public. Such a deferral is desirable to take account of the fact that clinical trials on products with a marketing authorisation, whether or not currently marketed, support legitimate commercial interest of sponsors which should be balanced against legitimate public disclosure. In the context of Over the Counter medicines, there is strong competition between companies to the public advantage, and therefore we respectfully suggest that the full deferral of information, as is applied being applied to Phase I volunteer studies should be applied to products with marketing authorisation.
643-654	57	**Question 8** **Comment:** EuropaBio supports the proposal that sponsors will be given the option to defer publication of Phase IV trial documentation until the time that the summary of trial results is made public in order to protect commercially confidential information. We recommend that the deferral is automatic and clinical trials with authorised products are treated similarly to Phase I-III trials to simplify the process, with an option for the sponsor to allow disclosure of study and product specific information at an earlier time point.
643-654	60	**Question 8** Timing of CCI release for products with a MA **Comment:** We agree with the proposal that study and product specific information could be made public for clinical trials on a

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		product with a MA, with a 12-month option for deferral at the time of result posting. This agreement is based on the understanding that this is for so-called low intervention trials. Studies with products with a MA that are not considered 'low intervention' would not be within scope of this definition (e.g. new indications). Given the fact that much information would already be available in the public space for products with MA, posting study and product specific information would be aligned with the increased transparency objective of this Regulation. Although caution should be exercised in terms of multiple components being available to the public that present overlapping information, as also reflected in the subsequent comment. We wish to point out an error in Question 8 which states, "…products without a marketing authorisation". Please correct to read, "…product **with** a marketing authorisation" **Proposed change (if any):** None
643-654	65	**Question 8** **Comment:** EFPIA agrees with the EMA information on Phase IV trials may contain CCI (e.g., exploratory endpoints). Therefore EFPIA advocates that clinical trials with authorised products be treated by default the same as Phase I-III trials rather than to systematically disclose study-specific information (e.g., full protocol) at the time of decision on a CTA. Also, of note, some Phase IV trials (low-intervention or "real-world" trials) run for a long time and interim reports may be prepared before the actual end of the trial. In this case, disclosure of trial information should be deferred until the time that the summary of final trial results is made public. There is a need to clarify in the Addendum the principles on which this deferral will be granted (i.e., based on a request by the sponsor, acceptable justification).
643-654	70	**Question 8** **Comment:** This question should probably read "[…] *with* a marketing authorisation" EUCROF agrees with the proposal to offer the possibility to defer the publication of study specific and product specific information until the time that the summary of results is loaded into the database and made public, as there might be intellectual property in trial documents which relates to new approaches in relation to endpoints and/or procedures. There would be no credible public

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		benefit of publishing these documents until summary results also become available. **Proposed change (if any):** N/A
643-654	81	**Question 8** **Comment:** Our members agree upon this. The deferral option for phase IV trials is justified in order to protect CCI.
648-651	29	**Comment:** It should be stated, that the decision on a deferral is by the Member States. **Proposed change (if any):** Add a sentence on who decides about a deferral.
652	72	**Question 8** Please refer to Question 6 **"Question 6** Proposal 1.3 would be preferred as it narrows down the information that may overlap with continued development of an IMP. If this proposal is chosen, then exceptions should be made for commercially confidential information for the same medicinal product that has a different indication or formulation and would be information that is not considered already publically available. For example, the IB should not be made public after marketing authorisation is granted if it contains such information; as development can change rapidly it may be difficult to determine if a company is still in development for a product for another indication."
652-654	5	**Question 8** **Comment:** We agree that there should be a possibility to defer the publication time for clinical trials on products with marketing authorisation.
652-654	9	**Question 8** **Comment:** There should not be an option to defer publication of registration information of a Phase IV trial on a product with marketing authorisation. Details about these trials can provide information about the risks and benefits of treatments currently being prescribed and taken by patients. Patent laws will protect any potential commercially confidential information about these

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		trials.
652-654	13	**Question 8** (proposal concerning phase IV/low-interventional trials of IMPs with a marketing authorisation) This proposal meets the requirements and objectives of the Regulation. *Note that this question is incorrectly worded in the draft consultation document – as it follows the description of clinical trials of IMPs with a MA, we have assumed that it refers to those trials.*
652-654	21	**Comment:** The study and product specific information should be made public at the time of decision on the trial. Since MA has been granted, there is no need for option to defer this publication of basic trial information. As mentioned before: Having early info will help patients apply for subsequent trials.
652-654	28	**Question 8** The proposal offers adequate protection of non-commercial and academic interests.
652-654	29	**Question 8** We agree with the proposal that the information will be made public at the time of the decision of the clinical trial for clinical trials on products with a marketing authorisation. Any deferrals should be substantiated and agreed by the Member States. In general the respective documents would not contain economically important information but information on hypothesis of alternative treatment options, comparison of treatment options etc. which would be of interest for other researchers too. **Proposed change (if any):** It should be added that Member States decide on a deferral.
652-654	30	**Question 8** given that the definition of marketing authorisation status is defined according to the proposal 1.1 at page 17, the proposed timelines for the publication of study and product documents are acceptable
652-654	32	**Question 8** Proposal 1: No

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		Proposal 2: No Proposal 3: Yes Proposal 4: No
652-654	33	**Question 8** In line with EMA statement
652-654	36	**Question 8** **Comment:** *The FPM supports this proposal. However, we believe that it should be made explicit that a request to defer publication of trial material is an exception that needs to be justified rather than just a simple box to tick.*
652-654	38	**Question 8** **Comment:** We have answered this on the basis that there is an error in the question and it should read "Please comment and give a brief rationale for your support of disagreement with this proposal regarding clinical trials on products WITH a marketing authorisation." We disagree with this proposal on the basis that the deferment of publication could lead to duplication of research.
652-654	39	**Question 8** If clinical trial sponsors in Phase IV and low-intervention trials are given the possibility to defer the publication of documents until 12 months after the end of the trial, they will most likely do so. Yet, there is no public health rationale in accepting such a deferral, since information about these types of trials is of value to healthcare professionals (the product has already been approved). It often concerns research being done outside the indication for which the drug has been approved (off-label use). We would therefore urge the EMA not to introduce any deferral, as timely access to this information is key to protect patients from avoidable harm. **Outcome (if applicable):** Do not include any deferrals for *Phase IV and low-intervention trials.* In addition, Phase IV trials and low-intervention trials in the same category, as their aims and their potential harms are very

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		different.
652-654	40	**Question 8** As outlined in response to question 6, we think that the concept of MA should be applied once a MA has been issued, by at least one MS, for a medicinal product using that active substance and for the indication and formulation/route of administration under study. Using this concept of a MA, we do not think that confidentiality could be justified on the grounds of protecting CCI for trials conducted solely on products with a MA and would therefore disagree with the proposal outlined in paragraph 5 (lines 648-651). We believe that the study and product specific documents from phase IV and low-intervention trials should be made public at the time of the decision on that trial. In such case, sponsors should not have the right to defer the publication of study specific and product specific documents. We are concerned that the current text of the addendum does not outline when study and product specific information from a trial with two or more IMPs, and where one or more IMP does not have a MA, should be made publically available. A significant number of early phase trials sponsored through the CRUK's CDD or coordinated through the charity's Combinations Alliance initiative (see case study below) involve the investigation of a novel IMP given in combination with another novel IMP, chemotherapy (IMPs with a MA often used within their licensed indication) and or radiotherapy. For the purpose of implementing the transparency provisions of the Regulation, we consider that such trials should be treated as clinical trials on products without a MA and should not be required to make study and product specific documents publically available at the time of the decision on that trial (see response to Question 10 for further information). CR-UK Combinations Alliance Case Study Established in 2010, the Combinations Alliance is a joint initiative between CRUK's Centre for Drug Development, the ECMC network and industry. It plays a significant role in the fight against cancer by increasing the number of early phase clinical trials investigating novel drugs in combination with other novel drugs, chemotherapy and or radiotherapy among people in the UK with cancer. The Combinations Alliance initiative is built on partnerships with pharmaceutical companies, to gain access to their portfolio of investigational oncology agents which can then be investigated in academic sponsored (NHS Trust or University) trials in combination with other agents, many of which may already be licensed and standard of care for patients. The Alliance is unique and is proving to be an attractive model for industry and the ECMC network. It provides companies with an

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		opportunity to explore the potential of their drugs in patient populations and in combinations they may not otherwise explore. In time, this could provide key evidence that could substantially expand the number of patients who may benefit from the novel agents. Patients also benefit through the Alliance as they get access to treatments that may not otherwise be available in a clinical trial in the UK.
652-654	41	**Question 8** We concur with the proposal regarding clinical trials with a marketing authorisation in principle but suggest that the option to defer the publication of results is increased from 12 to **at least** 24 months after the end of the trial on the basis of providing the Sponsor with sufficient time to gain patent protection for any line extensions, where required. Any amendment to a patent application made on the basis of the results of such clinical trial(s) would be invalidated if the results were published within one year of the patent application so any release of results after only 12 months would undermine a Sponsor's patent process. This would lead to Sponsors placing their clinical trials outside of EU. **Proposed change:** The deferral period should be set **at least 24 months**.
652-654	46	**Question 8** **Comment:** Whilst we agree, in principle, with the proposal regarding clinical trials with a marketing authorisation we do not agree with the proposed length of the deferral period before publication. A period of 12 months after the end of a trial is not sufficient to allow a Sponsor to gain patent protection for any line extensions. Any amendment to a patent application made on the basis of the results of such a trial would be invalidated if the results were published within one year of the patent application. This would threaten a Sponsor's ability to obtain proprietary protection and would lead them to seek to do their trials in a more favourable regulatory environment i.e. outside Europe. **Proposed Changes:** The deferral period should be set at a minimum of 24 months.
652-654	48	**Question 8** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014. It is acknowledge that in some circumstances deferral of publication will be necessary since study documents related to a phase IV study with the objective of positioning the product in the therapeutic armamentarium should be considered as commercially confidential as it may

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		contain, for example, novel ways of assessing efficacy or safety of the product.
652-654 704-708 722-725	51	**Question 8+9** The same publication rules should apply for Phase IV studies as are applicable for Phase I, II and III studies. The application documents submitted for authorised medicinal products still contain confidential commercial information, especially when the studies concern indication extensions or new routes of administration. Therefore, please see the comments on other questions and the Expert Legal Opinion of Prof. Denninger. Publication practices after the new Regulation becomes applicable should generally adhere to the current legal rules. As already discussed in the general comments, the current national and EU rules already ensure adequate transparency, in a way that meets the requirements and objectives of the Regulation. Publication practices as proposed in proposals I to IV infringe on the constitutionally protected rights of sponsor or document owner who is submitting the documents to the database. This infringement constitutes an infringement on the freedom to choose an occupation (Article 15 Charter of Fundamental Rights of the European Union). Furthermore, the proposals are contrary to the principle of fair competition and infringe upon the right to conduct a business (Article 16 Charter of Fundamental Rights of the European Union). Overall, this is a violation of objective law. In addition, the right to property and the freedom to choose an occupation / engage in work are infringed upon, which are “acknowledged as general principles of Community Law (No. 78), [… and] were elevated to the status of European fundamental rights”. Furthermore, the data to be submitted according to proposals I through IV constitute independent assets - a circumstance that only becomes obvious when the competitive advantage of the applicant is realized in the desired marketing authorisation. Publication practices in accordance with proposals I through IV or publication of confidential information from clinical trials that an applicant has gathered and analysed at substantial cost in time and monetary resources would violate the principle of freedom of competition and the principle of an open market economy with free competition. The essence of the abovementioned rights and freedoms would be undermined by the proposed publication rules, and would disregard the principles of proportionality with the principles of meeting objective of general interest, of appropriateness and necessity and the need to protect the rights of others (see also the attached Expert Legal Opinion of Prof. Denninger). Finally, the primacy of the confidentiality of the data is codified in Regulation (EC) No. 726/2004 (Article 57) referencing Article 11 of Directive 2001/20/EC.
652-654	53	**Question 8** the question states: **Please comment and give a brief rationale for your support or disagreement with this proposal**

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		regarding clinical trials on products without a marketing authorisation; however the section of text referred to pertains to low intervention trials and trials using products **WITH** marketing authorisation.
652-654	54	**Question 8** We support the proposal regarding clinical trials on products with a marketing authorisation. We agree that trials without the intention of supporting a marketing authorisation application should be more transparent (no commercial confidentiality reasons). However if there are reasons such as commercial intent, then we agree that these can be deferred only until the summary of trial results are published (12 months after end of trial at the latest).
652-654	59	**Question 8** **Comment:** Assuming the question relates to products with a marketing authorisation we have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
652-654	61	**Question 8** **Comment:** LEO Pharma is providing this answer under the assumption that the actual question reads “Please comment and give a brief rationale for your support or disagreement with this proposal regarding clinical trials on products ***with*** a marketing authorisation”. LEO Pharma is in favour of offering sponsors the option to defer a publication of study-specific and project-specific documents until the summary results are loaded into the database. In general, project-specific documents may contain significant confidential information and for such information the status of the MA (as specified in Proposal 1.3 - Question 6) shall be taken into account.
652-654	62	**Question 8** **Comment:** Agree with the proposal. However, this will only be helpful if option 1.3 is adopted (refer to Q6).
652-654	63	**Question 8**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Deferral Phase IV or LIT **Comment:** In case sponsor opts for a deferral he should reason/justify CCI not only tick. Deferral might be matter of decision. **Proposed change (if any):** Please add ". The sponsor should indicate and justify.... "
652-654	67	**Question 8:** Phase IV (post marketing surveillance) is the most important for Primary Care: it is about real life use. Here the most important is to make it accessible for guideline developers and drug bulletins, most journals are not interested in this research but to make the trade of between benefit and risk in real practice this information is very important and often lacking (or only available for EMA/FDA) We ask for direct accessibility together with a very easy access (searching in the EMA websites is not always simple)
652-654	74	**Question 8** **Comment:** check the timelines
652-654	75	**Question 8** **Comment:** for our current trials portfolio in the majority of cases we would wish to defer publication of study specific and product specific documentation on the grounds of protection of commercially confidential information. We are concerned that the current approach is complex and may lead to misunderstanding and misinterpretation.
652-654	76	**Question 8** **Comment:** we consider a simplified approach with a single approach for timing of release of commercially sensitive information for all trials to be preferable. Having a separate approach for low interventional/phase IV trials will result in those trials being subject to the greatest levels of up front scrutiny, the benefit of which is unclear. The proposal could compromise academic/pharma company collaborations (i.e. where a company is providing funding/drug FOC to an academic sponsor) if the sponsor is required to make public information that is commercially sensitive to the company.
652-654	77	**Question 8** **Comment:** How about trials with authorised products but used in the trial for another indication? Who decide that deferral is

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		acceptable. Is there a commercial confidential issue for low-intervention trials?
652-654	80	**Question 8** **Comment:** To In clinical trials on medicinal products without MA, the deferment of publication seems acceptable. Especially, as we will face times when MA will be given not exclusively for phase III clinical trials, but already at earlier study phases, proposal four (6.4.) of Table 1 fits best the actual situation. In addition, proposal four encompasses also e.g. phase 0 trials, being non-therapeutic by definition.
652-703	4	Question on products without a marketing authorisation EURORDIS agrees with proposal Four. **Proposal One**: the information presented in 4.2, including investigators sites, satisfies the needs of most patients, potential participants or trial participants, carers etc. Study specific documents and product specific documents are not needed at the time of decision on trial. **Proposal Two**: Would apply to all types of trials, and in case the delay should be 9 years after first summary results are posted, EURORDIS considers this delay being too long. A 9-year delay would prevent another sponsor/company to conduct clinical trials e.g. for a different indication, or would deprive it of important information when designing its own studies. **Proposal Three**: some sponsors are sometimes unclear regarding the phase of the trial. Some trials are presented as phase II/III, or strictly II, or strictly III but the frontiers are not completely defined. In order to delay the publication of some data, some may be tempted to simply requalify a phase II/III trial into a phase II just to avoid having to publish everything when first summary results are posted. **Proposal Four**: for the above mentioned reasons, Eurordis would prefer this option as it seems to protect the interests of sponsors for non- therapeutic trials, while informing the interested parties, i.e. the public, on therapeutic trials as soon as a first summary of results are posted.
652-703	69	BEUC supports the “Proposal One”. The study specific and product specific documents should be made public at the time of the decision on the trial.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposal two, three and four are not in line with the Regulation (EU) No 536/2014 and therefore they should not be considered. Phase IV clinical trials provide vital information on the safety of medicines currently used by many patients. There should not be an option to defer the publication of information about clinical trials on medicinal products with marketing authorization.
654	29	It should read “with a marketing authorisation”.
654	54	**Comment:** The sentence ‘without a marketing authorisation.’ This is incorrect and should read ‘with a marketing authorisation.’ **Proposed change (if any):** with a marketing authorisation.
655-702	16	**Comment:** Taking into account the objective of **maximum transparency** for clinical research and to avoid unnecessary duplications of clinical trials, we decide to have the information of clinical trials the most accessible and public of all the options given in the draft document. Therefore, we choose proposal 4 “Study specific documents – Non therapeutic trials (time of MA or 9 years after first summary results posted and Therapeutic trials (time when first summary results are posted). Product specific documents – Time of MA or 9 years after first summary results posted”
655-702	37	(Phase I, II and III) **Comment:** agree with proposal no. 2 We take the view that proposal no. 2 is the most straightforward option to apply while it also provides for a balanced approach between disclosure of information and the protection of information deemed to be commercially confidential. Proposal no. 1 we deem insufficient as it does not provide for a balance between transparency towards the public and the legitimate need to protect commercially confidential data (for a certain period of time) Proposal no. 3 we deem very complex to implement in practice. From a general perspective, the rationale holds true in some cases, but there may very well be situations where the opposite is true. Proposal no. 4 we deem close to impossible to implement as the term “therapeutic intent” is not well defined and therefore detailed guidance would need to be developed for sponsors and assessors.
655-703	14	**Question 8**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Referring to Question 8: support or disagreement with four proposals regarding clinical trials on products without a marketing authorisation (the so called Phase I, II and III trials), **Comment:** We agree with the proposal two (6.2. Proposal Two: The study specific and product specific documents (with the exception of the IMPD-Q section, which would not be made public at any stage) should only be made public after the earlier of the conditions set out in paragraph 6.5 below are met: 6.5. **Triggers for timing of publication** (in relation to proposals two, three or four above regarding clinical trials on products without a marketing authorisation): 6.5.1. The granting, refusal, or the withdrawal of the marketing authorisation application has triggered the loading into the EU database (and therefore publication) by the marketing authorisation applicant of the clinical study report for the same trial. 6.5.2. Nine years have elapsed from the date on which the first summary of results of the trial should have been published and therefore at least 10 years after the end of the trial, taking into account that for some trials an extension of the time limit for publication of the summary of results can be justified (for scientific reasons) in accordance with Article 37(4) of the Regulation). The period of 10 years have been chosen to give a reasonable period after the trial has been completed, before publication, 10 years corresponding, by analogy, though not actually linked to, the data protection period provided for in the EU.) because from my point of view the study specific and product specific documents (with the exception of the IMPD-Q section), must be made publics at sometime but protecting commercially confidential information.
655-703	14	**Question 9** Referring to Question 9: comment on proposals one, two, three or four regarding clinical trials on products with a marketing authorisation indicating which proposal best meets the requirements and objectives of the Regulation (Please provide a brief rationale for your choice of proposal and explain briefly disagreement with the other proposals.) **Comment:** We agree with the proposal two and I disagree with proposal one (see rationale for these opinion in previous comment). I disagree with proposals three and four due to these proposals are cumbersome and for this purpose is not important distinction between stages/phases I, II and III and between with/without prophylactic and therapeutic intentions and additionally not only are important prophylactic and therapeutic intentions (also others such as diagnostic and safety intentions).
655-703	24	**Comment:** EHA favours Proposal Three. This proposal allows for differentiating between phases to balance commercial confidentiality with the public interest. EHA supports the notion that the wider availability and increased use of products in Phase III

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		trials constitute an overriding public interest.
655-703	31	**Question 9**: Please comment on proposals one, two, three or four regarding clinical trials on products without a marketing authorisation indicating which proposal best meets the requirements and objectives of the Regulation. Please provide a brief rationale for your choice of proposal and explain briefly disagreement with the other proposals. The regulation foresees publication of summary study results 12 months after the end of the trial. This publication is independent of the marketing authorisation status. These results can only be interpreted appropriately if the full study protocol is available. The methodological information available in the "major characteristics of the trial" is insufficient for study assessment. Therefore, the full study protocol should be published together with the study results. Otherwise, the aims of the publication of study results as laid down in the regulation cannot be met. IQWiG therefore does not support the delay of publication of study protocols as outlined in proposal 2, 3 and 4.
655-703	68	**Comment:** On the attempt to distinguish between Phase I, II, III and IV trials it is suggested that the degree of commercial confidentiality changes during the development as more information becomes available on the product. One reason the EMA might feel it is legitimate to delay the disclosure of phase 1 trials is to give time to the MAH to apply for patents to protect its products. It should be stressed that secondary patents (strength / dosage regimen) are usually filed later on during the development and that early disclosure of phase II / III trials might undermine the validity of these secondary patents.
655-708	10	**Question 9** **Comment:** Proposal one should not be used since it does not take the status of the marketing authorisation into account properly. Too much information is made public too early. We don't recommend proposal 2, since it does not distinguish between the phases of the trial. Proposal 3 is the best alternative for the reasons stated in the document. Proposal 4 is probably too difficult for sponsors to apply. **Proposed change:** Use proposal 3. It should be clarified how trials combining several phases in one trial application will be regarded. Moreover, the sponsor's proposed

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		category for a trial need to be confirmed by the Member States in their decisions, recognizing the importance of correct phase allocation in proposal 3. Update table 1 once the final proposal (1-4) has been chosen, and add the information in section 4.4.2 (proposal 1.1, 1.2 or 1.3, whichever is finally chosen).
655-708	11	**Question 9** We consider that Proposal Two best meets the requirements and objectives of the Regulation. Proposal One would result in publication of more detailed information on the clinical trial at a much earlier stage than required in any other regulatory jurisdiction – we anticipate that this will be of significant concern to sponsors with regard to publication of CCI and would significantly damage the attractiveness of the EU for clinical research. We consider that Proposals Three and Four would be too complicated to administer and subject to error. We see Proposal Three as problematic because judgement as to which phase a clinical trial falls under may be subjective and open to interpretation, and an adaptive clinical trial may span more than one phase. Similarly, in relation to Proposal Four, we consider that the distinction between a therapeutic and a non-therapeutic trial can be open to interpretation.
655-708	12	**Question 9** **Comment:** We support Proposal 4: • the distinction between non-therapeutic/therapeutic trials • and the staging of publication accordingly Justification: • The public will be able to access relevant information for all types of trials via the summary reports at predetermined time points • Protocols in particular contain information (as outlined in the draft proposal's section 4.4.1.2), that is likely to be considered commercially confidential beyond the time of summary report publication • For non-therapeutic trials it would be difficult to justify an overriding public interest requiring publication of study specific documents at the time of the summary report being posted

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		• For therapeutic trials on the other hand there may be conceivable benefits of public access to the specified study specific documents at the time of the first summary report being posted (e.g. development of best methods and trial designs) • This proposal is best aligned with our view that information should be published when it becomes relevant to the public (including patients), health professionals and researchers). • It is also best aligned with our definition of Phase 1 trials (i.e. trials in healthy volunteers and patients without therapeutic or prophylactic intent). **Proposed change (if any):**N/A
655-708	19	**Question 9** **Comment:** Proposal four best meets the requirements and objectives of the regulation since trials with a therapeutic intent are likely to be of more interest to the public than those of non-therapeutic intent; the differential approach protects the commercial interests of sponsors of non-therapeutic trials and therapeutic trials that have yet to have summary results posted.
655-708	26	We concur with Proposal Two: "The Study specific and product specific documents (with the exception of the IMPD-Q section, which would not be made public at any stage) should only be made public after the earlier of the conditions set out in paragraph 6.5 below are met." This would most appropriately balance protections for commercial confidentiality with the public's interest in the data. **Proposed change (if any):** Choose Proposal Two.
655-708	55	**Question 9** Q9 Please comment on proposals one, two, three or four regarding clinical trials on products [~~with~~] **without** a marketing authorisation indicating which proposal best meets the requirements and objectives of the Regulation. Please provide a brief rationale for your choice of proposal and explain briefly disagreement with the other proposals. **Comment:** For products without a marketing authorisation, we consider that proposal two best meets the requirements and objectives of the Regulation. This provides reasonable warranted delay for protection of CCI linked to either the date of outcome of marketing authorisation or

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		reasonable passage of time if the clinical study was not used to support a marketing authorisation. Proposal two is a simpler and more transparent approach than proposals three and four. Proposal one is considered not acceptable, as this does not take due account of the legitimate protection of CCI.
655-708	57	**Question 9** **Comment:** Comment: EuropaBio supports **Proposal Two**: "The study specific and product specific documents (with the exception of the IMPD-Q section, which would not be made public at any stage) should only be made public after the earlier of the conditions set out in paragraph 6.5 below are met." This corresponds to the time of marketing authorisation or 9 years from the date of publication of the first summary of results of the trial. Proposal two is preferred among the 4 proposals being considered and should be included in the final rules.
655-708	65	**Question 9** **Comment:** EMA proposes four options for clinical trials on products without an MA. Please refer to EFPIA's Major Comments under the heading of "Approach to Clinical Trials on Products without a Marketing Authorisation" for our full rationale as to why Proposal 2 under 6.2 is the optimal approach.
655-708	70	**Question 9** **Comment:** EUCROF favours **Proposal 3**, because it is most in line with our view that information should be made public at the point of plausible overriding public interest in that information. We do support the distinction between trials without and with therapeutic/prophylactic intent, and would for that reason have liked to give our support to Proposal 4 (which uses that same distinction). However, we cannot support the automatic release of the study protocol and subject information sheet for therapeutic studies (including early Phase II studies) into the public domain at the time when first summary results are posted. Study protocols and subject information sheets are characterised by the detailed description of methods, techniques and advanced designs. This information is likely to be considered commercially confidential well beyond the time of summary report publication for Phase II trials. As a result we support **Proposal 3** which in our understanding can be applied in conjunction with our proposed definition of Phase I

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trials as follows:

Document	Publication via EU Portal
All documents	Voluntary publication by the sponsor should be permitted
Study specific documents - **Protocol synopsis**- *"as set out in the clinical trial application form – being in effect a structured synopsis of the clinical trial protocol"* (draft proposal lines 322 - 323)	Phase I trials (without therapeutic/prophylactic intent) - Time of first summary results being posted
	Phase II and III trials (with therapeutic/prophylactic intent) – At the time of decision on the trial
Study specific documents - **Subject information sheet**	Phase I and II trials - Time of MA or 9 years after first summary results posted
	Phase III trials - Time of first summary results being posted
	Note: For Phase II and III trials (with therapeutic / prophylactic intent) – Patients and other interested parties can approach sponsor and/or investigator to obtain a subject information sheet at the time of decision on

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		<table><tr><td></td><td>a trial. Contact details and study synopsis are available via EU portal at that time.</td></tr><tr><td>Study specific documents - **Protocol**</td><td>Phase I and II trials - Time of MA or 9 years after first summary results posted</td></tr><tr><td></td><td>Phase III - Time of first summary results being posted</td></tr><tr><td>Product specific documents – **IMPD S** and **E** sections and **investigator brochure**</td><td>Time of MA or 9 years after first summary results posted</td></tr></table> We believe that, if applied as tabled above, the public will be able to access relevant information for all types of trials at suitable, predetermined time points via the EU portal. Any supplementary information can, if required, be requested by patients, carers, health professionals etc. using the normal pathways of obtaining confidential information. In the case of obtaining a subject information sheet, this can be done by a simple call to the investigator, which does not require any effort over and above what patients would normally do. At the same time, there will be a barrier for competitors to access confidential information. We therefore believe that this proposal achieves a suitable balance between publication of relevant information and legitimate commercial interests of sponsors and researchers involved in a trial that is being published.
655-708	73	**Question 9** EAHP supports Option 3, recognising that for medicines without authorisation publication of protocols before marketing authorisation could be detrimental for commercial sponsors and unhelpful to the European research environment.
655-708	81	**Question 9** **Comment:** Proposal 6.2 is most appropriate.

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		Rationale: a) Appropriate balance between public interest and the sponsor's need to protect CCI. b) Among Proposals 6.2., 6.3, and 6.4, the Proposal 6.2 is the least complex. Setting clear milestones it is less burdensome in respect of operations and easier to understand for all stakeholders. c) Proposal 6.1 would leave the sponsor's CCI unduly unprotected.
655-725	35	**Question 9&10** We agree with EMA Proposal Two. In addition, as proposed by EMA, consideration should be given to extending the duration for publication in relation to trials for specific products, e.g. ATMPs as Member States have additional time to review these applications which in effect prolongs the duration for development.
655-725	60	***Timing of CCI release for products with a MA*** **Comment:** With regard to clinical trials on medicinal products without marketing authorisation (MA), we recommend the inclusion of Option #2 in the final rules because the proposed timing is the most clearly defined; i.e. at time of MA or 9 years after first results posted. A phased approach may diminish efficiency by introducing complexity, increasing Sponsor burden by having to adhere to different deadlines and be potentially subject to differences in interpretation between sponsors. Option #2 provides a clear and concise approach and leaves no room for alternate interpretation. With regard to product specific documents, it is unclear the value added with the release of the IB as well as the IMPD-S and IMPD-E sections once the MA is granted and as such, is not believed to serve the objectives of the regulation. Considering the content of these documents will be reflected in the items covered by EMA Policy 70, release of multiple documents containing overlapping scientific content but that are written at different times by different individuals will be confusing to the general public. Furthermore, if the release of the IB is retained in the finalized version of this addendum, we believe some options should be available that take into account if development is continuing for the product addressed by the IB. Therefore the release deadline of these product specific documents should be extended where justifiable i.e. where they contain information pertinent to continuing

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		clinical studies that would not otherwise be eligible for rendering public. Finally, clarification is requested as to whether the IB proposed in table 1 (p. 20) is the IB that was originally used to support the approval of the specific trial, or the IB that is current at the time the disclosure becomes effective. We propose that the documents submitted as the basis of approval of the study be disclosed. This will provide patients and researchers with the evidence/information the Agency reviewed for its approval decision, which echoes our previous comments in lines 411-414, stressing the overarching objective of transparency both at the Sponsor and Agency levels. **Proposed change (if any):** We suggest changes in line with the comments expressed above; i.e. Proposal Two for Product Specific Documents "Time of MA or 9 years after first summary results posted. **Sponsor may opt to defer to the time that first results from final studies are posted, where documents are supporting ongoing development**".
655-730	27	**Comment:** according to us, individual each study-specific documents should not be made public since the clinical study report, which will be loaded into the EU database, will include them. Some details (population, indication and inclusion/exclusion criteria) could be made public at the time of the decision on the trial. In addition, product specific documents could be made public at the time of the decision on the trial in order to share the most updated information regarding the efficacy/safety of IMP.
656-658	71	**Comment:** It is not clear whether there will be an option to request deferral for products without a marketing authorization. It is recommended that such an option be available and included. **Proposed change (if any):** Please include an option for deferral for products without an MA.
659	29	**Comment:** It is stated that only one of the proposals will be selected for inclusion in the final rules. What, if a proposal five would be the best choice. Is this not regarded as a possibility?
660-662	29	In general we feel that this proposal best meets the purpose of the Regulation. We would only make an exception for non-therapeutic trials (Phase I): for Phase I trials the information should only be published at the time the summary of results has to be submitted to the database. This should be added. For the IMPD-Q section we agree that this information does not have to be made public.

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660-696	78	**Comment:** It should be ensured that relevant CT data (i.e. structured CT dataset) are sequentially published for all CT. Provided that after the end of the clinical trial and not later than the date when the summary trial results the proposed structured clinical trial data set, the subject information sheet the safety reference information and all other relevant information for safety as included in our proposal are published, certain delay in publication of documents subject to a waiver could be acceptable. Categorization "with or without therapeutic or prophylactic intent" does not provide any relevant information with respect to categorization of trials in phase I to IV, considering as an special group phase I CT in healthy volunteers and therefore is not supported. **Proposed change (if any):** In case "with or without therapeutic or prophylactic intent" is maintained, "diagnostic" should be added before intent.
660-703	71	**Question 9** **Comment:** Proposal Two is the preferred approach, as it reflects the degree of commercially confidential information which needs to be protected by MAHs during different development stages. In this respect, it is of low importance if the trial is non-therapeutic or therapeutic. Option 1: When exploring indications, there is a considerable amount of confidential information provided thereby requiring a tremendous redaction effort prior to publishing. This option would additionally give an advantage to competitors who may be developing the same molecule. Option 3: This option would be acceptable, but Phase III trials still can contain confidential commercial information. The proposal would need to be more restrictive with regard to the information being made public. Option 4: Additional clarity is requested regarding this proposal. **Proposed change (if any):** An option to request deferral should be included in proposal 2.
663-665	29	We do not agree with this proposal and do not think this meets the objectives of the Regulation. It is far too late from a scientific point of view to make the protocol and all other information available at the time of granting, refusal or withdrawal of the MAA or nine years after the first summary of results is published (this would be from 10 years and longer after the decision about the trial).

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		In most cases the information would be of no scientific value for the scientific community any longer. There is no justification for this proposal in the Regulation and this would not lead to more transparency compared to the current situation.
666-681	29	We do not agree with this proposal and again we do not think this meets the objectives of the Regulation. We would not put Phase I and II together as this is different points in the development and different sensibility of data. With regards to the time of publication for Phase I and II see comment for proposal two. For Phase III trials we find it too late if the information is published at the time of posting the summary of results which could be several years after the decision on the clinical trial. We also see no difference between study and product specific information, except for the quality section of the IMPD.
682-702	29	To take a differential approach, which differentiates between non-therapeutic and therapeutic clinical trials is appreciated, but again the time points are not serving the purpose and objectives of the Regulation. For non-therapeutic trials the information should be publicly available at the time the summary of results is posted. For all other clinical trials the information should be posted at the time of decision on the clinical trial.
693	68	**footnote 7 and 8** **Comment:** In generic development we do not prove effectiveness only bioequivalence. However it may be substance specific that we cannot do a study in healthy volunteers. We need to go into patients that suffer from this disease. Can such a study also fall under this category: without “therapeutic intent”/”prophylactic intent”?
693-696	30	Disclosure on trials without therapeutic or prophylactic intent is equally relevant for increasing the knowledge (and transparency) around medicinal product safety.
703	66	**Comment:** The best option seems to be the time of decision on the trial. Early phase trials could have a delay of one year before publication. Additional delays made the database unuseful
704	72	**Question 9** Proposal 3 would be the preferred choice for products without a marketing approval. Proposal 1, 2, and 3 do not account for the differences in development and impact on commercially confidential information. Proposal 4 takes into account the status of the

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		medicinal product, but proposal 3 seems to be a more appropriate measure. Proof of concept (Phase 1 and 2 trials contain information about results and future trials (for example possible indication of efficacy) that may give companies an unfair competitive advantage if study specific or product specific documents are made public. This has the potential to adversely impact a sponsor's legitimate economic interest in the trial or medicinal product. Consequently, only phase 3 studies should have information beyond the minimal required information under the regulation and EudraCT made publicly available.
704-708 (643-651)	4	Question on products with a marketing authorisation EURORDIS agrees with the proposal.
704-708	5	**Question 9** **Comment:** The proposal Three best meets the requirements and objectives of the Regulation 536/2014. Proposals One and Two do not protect commercially confidential information adequately. Proposal Four would protect commercially confidential information to some extent, but cannot be supported because it would create additional work (providing and assessment of rationales whether a study has a therapeutic/prophylactic intent or not) without providing any advantages compared to proposal Three.
704-708	9	**Question 9** **Comment:** We support Proposal One. Study and product specific documents should be made public at the time of the decision on the trial. The default should be to make information public. Deferrals in making that information public should be justified but each of the other proposals would result in information being withheld without justification.
704-708	13	**Question 9** (proposals 1–4 for publication of study-specific and product-specific documents relating to trials of IMPs without a marketing authorisation) Proposal 2 best meets the requirements and objectives of the Regulation. It allows sponsors to protect their confidential information throughout the drug development process, as they can in other regulatory environments, eg USA. Proposal 2 would maintain the EU's competitiveness in commercial clinical research, and ensure that the EU's patients continue to benefit from clinical trials. Proposal 1 gives sponsors no protection for the commercially confidential information in which they will have invested heavily

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		(including the identity of the IMP, pre-clinical data and clinical data). It would seriously harm commercial research in the EU. Proposals 3 and 4 describe similar approaches to transparency, with greater protection of study-specific documents from early stage/non-therapeutic trials than later stage/therapeutic trials. Compared with Proposal 2, either of these options would disadvantage Europe (and its patients) as a location for later stage commercial clinical trials. Premature disclosure of study-specific documents would not benefit patients or prescribing physicians. *Note that this question is incorrectly worded in the draft consultation document – as it follows the description of clinical trials of IMPs <u>without</u> a MA, we have assumed that it refers to those trials.*
704-708	21	**Question 9** **Comment:** Proposal One; At the current pace of research, info ten years after end of trial loses major part of value for further analysis (e.g. meta-analysis). Second best would be proposal four, since it is at least taking in account that the possibility of gaining market access based on phase II results also diminishes the differences between different stages of clinical development. Time points defined under 6.5 have to be adjusted (see comment in question 10).
704-708	23	**Question 9:** I think proposal three best applies as allows a graded approach based on the stage of development of the medicinal product, but without too complex impositions on sponsors (as for example in proposal four).
704-708	28	**Question 9** After considering the given proposals preference is given to Proposal Four: Proposal One does NOT offer adequate protection of commercial, non-commercial or academic interests. Proposal Two offers adequate protection of commercial interests taking into account the marketing authorisation status, but does NOT take into account relevant public and/or scientific interests. Proposal Three offers a balance between adequate protection of commercial interests and public interests. It is not uncommon that

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		results of phase III studies on unregistered medicinal products (not holding marketing authorization) are being presented on scientific and medical events, meetings and symposia. Therefore, to a certain degree, this information can be considered public information. To create an equal playing field between those involved in the public (scientific) discussions, the (scientific) public should have access to the same information as the researchers who presented the results at scientific events. Proposal Four has the same advantage as proposal Three, but makes a better distinction between the different kinds of trials that are being conducted in real life. Not all sponsors follow the same nomenclature for classifying clinical trials (e.g. phase I, II, III and IV), therefore a distinction based on therapeutic intent better fits reality.
704-708	29	**Question 9** In general, the publication of the information in the application dossier should be at a point of time where the publication is still relevant for the scientific community, as is foreseen by the regulation (at the time of decision on the clinical trial). Most of the proposals make the exemptions to a general rule and can therefore not be supported. Therefore, in our **view proposal one** best meets the requirements and objectives of the Regulation. But we would suggest including a differential approach with regard to non-therapeutic and therapeutic and prophylactic trials. For non-therapeutic trials, the time point for publication of other than the minimal information (see 4.2) the data (study specific and product specific) in the database is postponed to the time the summary of results is included in the database. So we basically suggest a proposal five. With regard to Proposal Two, Three and Four, we do not find that the time points suggested for publication of data/ documents meet the requirements and objectives of the Regulation. With regard to Proposal Three we additionally do not find it useful to differentiate between Phase I/II and Phase III.
704-708	30	**Question 9** regarding those clinical trials on products with a marketing authorisation (as defined according to the proposal 1.1 at page 17), the proposal one best meets the requirements and objectives of the Regulation. The postponement foreseen by the proposals number two, three, and four described in the section “Triggers for timing of publication” at page 21 cannot be considered acceptable, especially for study related documents and (safety and efficacy) clinical

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		data. Moreover, the introduction of a gradual increase of transparency from early to late stage of the development (proposal three and four) seems to be poorly applicable in the context of mixed design (i.e., phase I/II) and adaptive designs, which are currently very common.
704-708	32	**Question 9** Proposal 4
704-708	33	**Question 9** Proposal three meets the requirements best as it keeps clinical trial data confidential for phase I and phase II and II till MA
704-708	36	**Question 9** **Comment:** *There appears to be a typographic error in question 9. We base our comments below on the presumption that it should read '...products with a marketing authorisation...' rather than '...products without a marketing authorisation...'* *The view taken by the FPM is that none of the options 1 to 4 are likely to enable full disclosure. Whilst special cases can be made for phase I studies it is difficult to justify on the basis of safe guarding patents. The dangers of deferral for periods of up to 9 yr. could be used to prevent disclosure of data indicating serious safety concerns or important childhood datasets.* *The FPM recommends that, at a minimum, the data from a trial sub-group should be released before market authorisation, and preferably the full clinical study report, or equivalent, with appropriate anonymisation and redaction. Safety data should be made available as soon as possible after the completion of a trial, and release should not be dependent on market authorisation or discontinuation of the programme.*
704-708	38	**Question 9** **Comment:** It is difficult to select a particular proposal as they all state that the IMPD–Q will not be made public when in Question 7 we have suggested a situation where the IMPD–Q might be made public. Of the four, proposal number three would be our choice unless the trial shows no benefit, in which case publication should be immediate. Otherwise, there is the potential for a waste of

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		resources by other researchers following the same therapeutic path.
704-708	39	**Question 9** ***Refuse deferral rules that would postpone the release of information up to ten years*** We disagree with the creation of ***trial*** categories, which were not mentioned in the Clinical trials Regulation, to justify and allow "deferrals" that would grant sponsors the possibility to withhold information up to 10 years. According to the EMA, "*the period of 10 years have been chosen to give a reasonable period after the trial has been completed, before publication, 10 years corresponding, by analogy, though not actually linked to, the data protection period provided for in the EU*" (lines 718-720). The EMA seems thereby to confuse two concepts. Regulatory data protection means that generic and biosimilar producers cannot use data of the "innovator" industry during 10 years for request for a marketing authorisation even if it is publicly available. It does however not prevent for data transparency, which is needed to avoid publication bias, allow for the reanalysis of clinical trial results and cost-effectiveness assessments. **Only the proposal 1 is acceptable** and in line with the Clinical trials regulation, provided the following changes are made: "*the study specific and product specific documents are made public at the time of the decision of the trial, and the exception set out in Article 81(4)b would only apply to the IMDP-Q section,* ~~***which would not be made public at any stage***~~***, unless there is an overriding public interest in disclosure***". We urge the EMA not to introduce any deferral rules in Phase IV and low-intervention trials that would allow sponsors to avoid the timely publication of information. Similarly, no deferral rules can be accepted in phase I trials (see comment below, page 14). The other proposals (proposal two, three and four) allow deferral rules that would arbitrarily postpone the release of information up to ten years. That is unacceptable. **Outcome (if applicable): *Choose option 1 for all trials***, both pre and post- marketing authorisation and regardless of the intent of the trial (having or not a therapeutic or prophylactic intent). This entails:

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		• Amending section on 'phase I trials' to remove any deferrals; • Amending section on '*Phase IV and low-intervention trials' to remove any deferrals.* *Reject options 2, 3 and 4 which are not in line with the Clinical trials Regulation.*
704-708	40	**Question 9** It is important that study specific and product specific information is published and made available at the earliest opportunity, whilst acknowledging that it is also important to protect commercially confidential information. Proposal 1 We disagree with this proposal as it does not allow for any confidentiality of study and product specific information that should be justified for phase I, II and III trials on the grounds of protecting CCI through Article 81(4)(b) when applying the concept of MA (assuming the EMA adopts proposal 1.3 of 4.4.2, which we have previously outlined our support for). Proposal 2 We disagree with this proposal as we consider that for phase III studies, there would be overriding public interest to make the study specific information publically accessible at the time the summary of trials results is loaded into the database. Proposal 3 We support the principle behind proposal three, which takes a differential approach to the timing of the publication of study specific and product specific documents depending on the stage of product development. However, our support for this proposal should be considered alongside our support for proposal 1.3 (see answer to question 6 above) and our recommendations to amend 6.5 (see answer to question 10 below). It is right that this addendum acknowledges the higher degree of commercial confidentiality associated with products being tested in phase I and II trials, over products in phase III trials, by setting out conditions that allow for study specific information to be made publically available at a slightly earlier stage for phase III trials. Furthermore, we agree that the case for overriding public interest is likely to be stronger for phase III trials where there is wider availability of the active substance and its use is in larger subject populations for therapeutic purposes. It is therefore right that the study specific information from these trials is made publically

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		available at the same time as the summary of trial results, if not earlier. We therefore recommend that: • For phase III trials, the study specific information should be made public at the time the summary of trial results is loaded into the database ***or earlier***. • The study specific and product specific information for Phase I and II trials, and the product specific information for Phase III trials, should ~~**only**~~ be made available when the earlier of the conditions set out in 6.5 are met (assuming our recommendations to amend 6.5 are adopted). Consideration should be given to how this approach will affect Phase IV and low interventional trials as the issue of research confidentiality would still apply to these trials. Proposal 4 We disagree with this proposal. Although we agree with the principle of taking a differential approach to the timing of the publication of documents depending on the stage of product development, we are concerned over how the stage of product development would be established, particularly in the oncology setting. This proposal would require sponsors to declare the therapeutic or prophylactic intent of the trial. Given the automated nature of applying the transparency rules through the database, the extent to which this declaration could be certified would be limited. Furthermore, we have concerns that the therapeutic or prophylactic intent does not always reflect the stage of product development.
704-708	41	**Question 9** Proposal Two (6.2) is the most appropriate option described. This option provides Sponsors with confidence that they can protect their commercially confidential information during the drug development process. It is similar to the regulatory environment in the USA and would maintain a competitive environment in EU for commercial clinical research. Proposal One (6.1) provides the Sponsor with no opportunity to protect their commercially confidential information and, consequently, would trigger the demise of EU as a location for commercial clinical research. Proposals Three and Four (6.3 and 6.4 respectively) describe differential approaches to transparency, with greater protection of

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		early stage trials than later stage trials. Either of these options will disadvantage EU and its patients as a location for later stage commercial clinical trials. Sponsors will seek to minimise any risk to their confidential information by choosing to avoid conducting these clinical trials in EU altogether, or deliberately timing their implementation to the latter stages any development plan.
704-708	42	**Question 9** We agree with proposal 1 6.1. Proposal One: The study specific and product specific documents are made public at the 661 time of the decision on the trial, and the exception set out in Article 81(4)b would only apply 662 to the IMPD-Q section, which would not be made public at any stage.
704-708	46	**Question 9** **Comment:** We propose the adoption of **Proposal Two.** (6.2, Line 663-665) This is the only option which will give Sponsor's the confidence that they can adequately protect their Confidential Information during the drug development process in Europe and is in line with the regulatory environment in the USA. This is essential if Europe is to maintain a competitive environment for clinical research. Proposal One (6.1, Line 660-662) does not provide a Sponsor with any opportunity to protect their Confidential Information and therefore makes Europe an unattractive location for commercial clinical research i.e. would result in the demise of clinical trials in Europe. Proposals Three and Four (6.3, Line 666-681 and 6.4, Line 682-702 respectively) provide differential approaches to transparency, giving greater protection to early, rather than later, phase trials. Either of these options would weaken the position of Europe and therefore also disadvantage its patients by making it a less attractive location for later phase commercial clinical trials. We fear that Sponsors will avoid placing these clinical trials in Europe altogether to minimize the risk to their Confidential Information. All of the stakeholders (patients, Sponsors and service providers) would be disadvantaged if these proposals were adopted.

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704-708	47	**Question 9** EORTC is not in favour of automatic decision making based on the phase of the trial and MA status of the drug only. Taking example of oncology, multi-modality treatments are frequently used. Clinical trial may fall under CT regulation, qualify as low-intervention trial, but may include other experimental modalities or correlative research that may justify the deferral to the time of publication of results or even later. EORTC would also like to bring the attention to the fact that some trials aiming to develop companion diagnostics for already registered drugs would fall under CT regulation. For these trials drug information may not be considered as CCI anymore, but companion diagnostics information may still be CCI. Similar situation may present with devices. Studies at such an interface of regulations are to be treated with caution. **Proposed change (if any):** EORTC would suggest giving sponsors the possibility to justify an eventual CCI based on other EU regulations (e.g. IVD, devices etc…).
704-708	48	**Question 9** **Comment:** Our choice is for **Proposal Two**: The study specific and product specific documents (with the exception of the IMPD-Q section, which would not be made public at any stage) should only be made public after the earlier of the conditions set out in paragraph 6.5 are met. Indeed, a distinction between Phases from I to III would not be workable as the definitions are subject to interpretation. Also, any stage of the development there may be commercially confidential information in those documents. In order to stimulate development, there should be no distinction in any pre-MA study. The referral procedure is still considered part of the procedure for granting marketing authorisation. Publication of study results should only be possible when all appeal procedures have been exhausted, and not before the final decision of the European Commission or the Competent authority. Concerning withdrawal of applications, this should not trigger publication of study results as companies may file again this study plus others. CCI should not be disclosed from withdrawal but using the rule of the 9 years.
704-708	53	**Question 9** states: **Please comment on proposals one, two, three or four regarding clinical trials on products with a marketing**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		authorisation indicating which proposal best meets the requirements and objectives of the Regulation. Please provide a brief rationale for your choice of proposal and explain briefly disagreement with the other proposals. however the section of text referred to pertains to trials using products **WITHOUT** marketing authorisation. **Answering both questions 8 and 9 REFERRING TO THE APPROPRIATE TEXT** We believe there should be no differentiation between the processing of trials in terms of decision making on commercially sensitive information, regardless of the phase or category of the trial and the definition of the timing of release of information should be the same; ie the definition of when it is no longer commercially sensitive. Under the definition of low intervention trial, it is hard to for see a circumstance where the data can be justifiably referred to as commercially sensitive. The products will have MA and be used as such or outside the MA according to published guidelines. The document includes the statement *'There are many clinical trials carried out on non-authorised medicines, in the early phases of development prior to marketing authorisation, which are never later used in a marketing authorisation as the development of the medicines is discontinued (approximately 80% of medicines which enter trials in human subjects are discontinued) or indeed the trials may not have been conducted in preparation for a future marketing authorisation, but rather as basic research'. (line 630-634).* ..It is not clear whether it is the intention for the data from these trials to be made public. We believe that there should be a defined time-period after which such trial data should be made available. This would be consistent with the principle of ensuring that even negative results are made freely available to avoid the conduct of duplicate and futile clinical research With respect to the selection of the most suitable proposed text for inclusion in the amendment; **we would support proposal 3** as being the most appropriate. We agree with the principle that the extent of information made public could progressively increase during the development period to the marketing authorisation of a medicine. It is noted that it will be the responsibility of the sponsor to provide information on the status of the marketing authorisation of the product on submission of the application for clinical trial authorisation and that the final decision will be by the member states as part of the trial authorisation process. This should be applied to all trials, rather than a differentiated system for low intervention and phase IV trials. This would provide a clear decision point on the defining the time-points for the release of data at the onset of the trial. We feel that there are no circumstances where a trial deemed to be in the low intervention category should be deemed as having commercially sensitive information.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
704-708	54	**Question 9** Regarding Section 4.4.3 paragraph 6 and the four proposals for release of study specific and product specific documents, **we think proposal two best meets the requirements and objectives of the Regulation.** This is where the study specific and product specific documents (with the exception of the IMPD-Q section, which would not be made public at any stage) should only be made public after the earlier of the conditions set out in paragraph 6.5 are met. This is because this seems like the most sensible and easy to implement. Proposal one would have the potential to harm industry's commercial interests (as release would be before the grant of a Marketing Authorisation) and could negatively impact on the amount of research conducted in the EU. Options three and four would be difficult to apply. An approach towards different phases of development or whether there is therapeutic intent would be difficult to define and apply consistently. There are no separate and distinct phases for every trial, some trials are exploratory as well with therapeutic intent and some involve both healthy volunteers and patients. There is neither the capability nor capacity to assess release on a case by case basis, so automated release could cause may issues. Without a legal basis for this the EMA could be liable to many legal challenges for inadvertently releasing information which may have been deemed one phase when it was in fact another.
704-708	59	**Question 9** **Comment:** We believe options 2 or 3 would best meet the requirements and objectives of the regulation. The regulation supports innovation within the EU. By following the rules outlined in options 1 commercially sensitive information will be released on products still under development. This will discourage Sponsors from developing such products within the EU. We do not feel option 4 would work from a practical standpoint as it does not take into account multi-part studies which may include both non-therapeutic and therapeutic parts. This could result in commercially sensitive information being released on non-therapeutic trials despite this not being intended by the rules. **Proposed change (if any):** Section of option 2 or option 3
704-708	61	**Question 9** **Comment:** LEO Pharma is providing this answer under the assumption that the actual question reads "Please comment on proposals one, two, three or four regarding clinical trials on products ***without*** a marketing authorisation indicating which proposal

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		best meets the requirements and objectives of the Regulation". LEO Pharma does not agree with Proposal one as the released documents may contain significant confidential information and disclosure at this stage of development could truly jeopardise future investments of the developers. Proposals 3 and 4 are considered very complex and may give rise to continuous discussions and misunderstandings (how would, for instance, a combined phase 2/3 study be dealt with)? LEO Pharma is, therefore, in favour of Proposal 2.
704-708	62	**Question 9** **Comment:** Proposal Four is the preferred option because it is most likely to protect any commercial interests on a product as it ensures all therapeutic trials have study documentation posted only when results are available. Both Proposal Three and Proposal Four provide some protection from disclosure of study specific documents that may provide commercially sensitive information about drug development. Without this protection pharmaceutical research in Europe would be hampered.
704-708	63	**Question 9** **Comment:** In favour of proposal Three (6.3.), where Phase I and II is more conservatively protected and Phase III less. Proposal four (6.4) is (despite the analogy) independent on Phase of CT and targets the intent 'the therapeutic or prophylactic intent' of the CT. This is regarded as too difficult. Question is who will be in charge for decision? **Proposed change (if any):** Proposal three (6.3) supported.
704-708	67	**Question 9:** The EFPC opts for proposal 1: The study specific and product specific documents are made public at the time of the decision on the trial, and the exception set out in Article 81(4)b would only apply to the IMPD-Q section, which would not be made public at any stage. Phase II and II looking for the best dosage (II) and evaluating the real efficacy (III) are really too important to accept long delay in

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		making information available because of 'confidentiality'; at the moment EMA is evaluating pro and contra it is important that the information is also available for others: it is the only possibility to have more transparency in the evaluation process of EMA (and more transparency is really needed). We ask for very strong argumentation of the drug industry before confidentiality can be accepted (and not the opposite : that it is necessary to prove 'overriding public interest' before study data are made available)
704-708	75 76	**Question 9** **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.
704-708	77	**Question 9** **Comment:** We do not support proposal 1. Proposals two and three are acceptable, with a preference for proposal 3 because the principle of the phase of the study (I, II, III or IV) is applied and not the marketing authorisation status of the product. This is of importance to protect also the interest of the academic researcher. Proposal 4 is not supported because this is too complicated due to the (existing) different interpretation of therapeutic intent. How will the process be if there is a discussion on the therapeutic intent of a trial?
704-708	80	**Question 9** **Comment:** For phase IV trials or low-interventional trials on medicinal products with MA, no justification for a deferment of publication can be found.
704-721	69	BEUC doesn't support any of the two options 6.5.1 and 6.5.2 as there should be no triggers for timing of publication.
709-713	74	**Question 9** **Comment:** Proposal one is in accordance with the Regulation
709-721	14	**Question 10**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Referring to Question 10: comment on the proposed time points in paragraphs 6.5.1 and 6.5.2 and indicate whether they meet the requirements and objectives of the Regulation (Please provide a brief rationale for your support or disagreement.) **Comment**: In our opinion, paragraphs 6.5.1 and 6.5.2 meets the requirements and objectives of the Regulation (6.5.1 because the status of the application for marketing authorization is known and collected in the database and 6.5.2 because the proposed time is a reasonable period and protects patents).
709-721	24	**Comment**: EHA would appreciate a more thorough justification of the trigger for timing of publication formulated in 6.5.2 where nine years have elapsed from the date on which the first summary of results of the trial should have been published. The rationale given appears arbitrary.
709-721	31	**Question 10**: Please comment on the proposed time points in paragraphs 6.5.1 and 6.5.2 and indicate whether they meet the requirements and objectives of the Regulation. Please provide a brief rationale for your support or disagreement. As for question 9 above, it is important to note that the regulation foresees publication of summary study results 12 months after the end of the trial. This publication is independent of the marketing authorisation status. These results can only be interpreted appropriately if the full study protocol is available. The methodological information available in the "major characteristics of the trial" is insufficient for study assessment. Therefore, the full study protocol should be published together with the study results. Otherwise, the aims of the publication of study results as laid down in the regulation cannot be met. Therefore, neither proposal 6.5.1 nor proposal 6.5.2 is appropriate to ensure a sufficient level of transparency.
709-721	71	**Question 10** **Comment:** Proposal 6.5.2 is the preferred approach. The proposed timings are acceptable as they provide a sufficiently long time period.
709-725	10	**Question 10** **Comment:** Section 6.5.2. still refers to 10 years of data protection, even though that period is now 8 years. Except for that, we support the proposals, which seem to offer protection for a reasonable amount of time.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Proposed change: Consider changing to 8 years in section 6.5.2.
709-725	11	**Question 10** ACRO agrees that the proposed time points meet the requirements and objectives of the Regulation, and support the proposal, which provides clear and objective triggers for the timing of publication.
709-725	12	**Question 10** **Comment:** We agree with the triggers for timing of publication being: • The granting, refusal, or withdrawal of the marketing authorisation application • 10 years after the end of a trial We are concerned about the timelines for publication of (lay summary reports) for the following reasons: The issue: • The draft proposal does not allow for a distinction between development stages of the product (phases of clinical research, therapeutic/non-therapeutic trials) or marketing authorisation status where the publication of summary reports is concerned • It is inconsistent with the spirit of the document and the CTR's definition of Commercially Confidential Information that summary reports should be published in all cases within 12 months after the end of a trial • It is unclear why the draft proposal does not acknowledge that summary reports can "contain extensive detail of a commercially confidential nature" whilst it does acknowledge this e.g. for the subject information sheet and protocol We refer to a position paper by the European CRO Federation (EUCROF) dated 31 October 2014 which was submitted as part of EUCROF's response to the first consultation on the EU portal (https://www.researchgate.net/publication/272151443_EUCROF_position_paper_public_access_to_early_phase_EU_database_information_31_Oct_2014). This paper states that: *"With regards to the potential benefits of publicly accessible (lay) summary results of Phase 1 studies, we found that the benefits stated by [ClinicalTrials.gov, the WHO/International Clinical Trials Registry Platform (ICTRP) and the CTR] will not necessarily affect patients or ongoing clinical research at the time. Benefits will become relevant at*

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		various time points during drug or drug/device combination development. This may be earlier or later than one year from the end of a trial." It goes on to say: *"The potential risks of early publication and disclosure of Phase 1 studies' […] results may outweigh its benefits for patients, health professionals and the public. During early drug development much of this information is considered commercially confidential. Regulation outside Europe does not require publication of Phase 1 studies, except after FDA approval in the US. Sponsors would therefore likely manage perceived risks by performing Phase 1 studies outside Europe. This would have a detrimental effect for European early and late phase clinical research, which would ultimately translate into disadvantages for patients and the public."* The paper provides a detailed risk/benefit as evidence and proposes that a staged approach to publication of results, depending on the relevance to the patient and commercial sensitivity. Our proposal: • The same application of commercial confidentiality should apply throughout the transparency provisions of the CTR **Proposed change (if any):** If it is decided that the publication of summary reports should be at a fixed point following the end of a trial (which we support as this is a simple process which can be automated), we propose to set this at a time much later than one year from the end of a Phase 1 study, at a point when the published information has ceased to be commercially confidential.
709-725	19	**Question 10** **Comment:** Response to Question 10. The proposed time points in paragraphs 6.5.1 and 6.5.2 meet the requirement and objectives of the Regulation (EU) No 536/2014.
709-725	55	**Question 10** **Comment:** We agree with the proposed time points for publication of the applicable information for products without a marketing authorisation. These provide appropriate justifiable delay in publication of information on studies which subsequently form part of a marketing authorisation and those which do not.
709-725	57	**Question 10**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: Paragraph 6.5 states that once a marketing authorisation has been granted (or refused, marketing authorisation application withdrawn) or 9 years from the date on which the first summary of results of the trial should have been published, whichever is the earlier, all **product specific** documents will be made public. Section 4.4.1.2 acknowledges that product specific documentation (in particular the investigator brochure and IMPD-S and E sections) contain extensive detail of a commercially confidential nature but does not provide an opportunity for identifying and redacting such information which remains commercially confidential post marketing authorisation. Disclosure could compromise sensitive and commercially confidential information in relation to indications under development, i.e. outside of the particular indication and/or pharmaceutical form of the medicinal products for which the marketing authorisation has been issued. This does not meet the requirements and objectives of the Regulation. **Proposed change:** The IB and the IMPD-S and E sections fall into the category of documents that should remain confidential, and should be subject to a redaction process, similarly to EMA's Policy 70.
709-725	65	**Question 10** **Comment:** EFPIA questions the proposed requirement to make study- and protocol-specific documents submitted to the clinical trial database public where no MAA is submitted. A compromise to consider would be to recommend the use of abstracts as a means of achieving a more minimalistic form of disclosure. In this way, transparency regarding the trials conducted would still be achieved.
709-725	70	**Question 10** **Comment:** EUCROF agrees with the EMA proposal.
709-725	81	**Question 10** **Comment:** Our members agree upon this. The proposed interval of 9 years seems to be a good balance between public interest and the sponsor's need for protection of CCI.
711-713	27	**Comment:** the proposal 6.5.1 meets the requirements of the Regulation (see art 37(4)) even if, according to the Regulation, the loading will have to be performed within 30 days starting from the MA final decision.
722-725	4	**Question 10**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		EURORDIS agrees with the proposal.
722-725	5	**Question 10** **Comment:** The proposed time points presented in sections 6.5.1 and 6.5.2 meet the requirements and objectives of the Regulation.
722-725	13	**Question 10** (triggers for timing of publication of study- and product-specific documents) The triggers seem reasonable and meet the requirements and objectives of the Regulation. The trigger described in paragraph 6.5.1 (end of the process of marketing authorisation application) is entirely reasonable. At that point, commercial confidentiality is less of a concern for sponsors, and information about clinical trials becomes much more relevant to prescribing physicians and patients. The trigger described in paragraph 6.5.2 (at least 10 years after the end of the trial) also seems reasonable.
722-725	21	**Question 10** **Comment:** Time points according to 6.5.1. This Information about a licensed medicine should be available to patients, prescribers and reimbursers. At the current pace of research, info ten years after end of trial loses major part of value for further analysis (e.g. meta-analysis). **Proposed change (if any):** The time period mentioned in 6.5.2 should be adjusted. 3 years after the first summary of results have been published deems enough time considering justified commercial interests.
722-725	28	**Question 10** Paragraph 6.5.1. No comment. Is in accordance with EMA policy. Paragraph 6.5.2. We disagree with the chosen time frame of 9 years. It is too long and should be reduced to 3 years from the date on which the first summary of results of the trial should have been uploaded, and therefore 4 years after the end of the trial. If necessary the sponsor should have the possibility to opt for a longer deferral of publication, with a maximum of 9 years.
722-725	29	**Question 10**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		We totally disagree with both proposed time points time points (paragraph 6.5.1 and 6.5.2) as they do not meet the requirements and objectives of the Regulation (see Recital 67 and 68 below). In the Regulation it is proposed that by default all information should be made public at the time of the decision on the trial. With time points like the ones suggested, the information published is no longer of any value for the scientific community. We want to draw the attention again to the Regulation which states that in general information will be made public at the time of decision on the trial. When looking at recital 67 and 68 another approach would only be an exemption. *(67)In order to ensure a sufficient level of transparency in the clinical trials, the EU database should contain all relevant information as regards the clinical trial submitted through the EU portal. The EU database should be publicly accessible and data should be presented in an easily searchable format, with related data and documents linked together by the EU trial number and with hyperlinks, for example linking together the summary, the layperson's summary, the protocol and the clinical study report of one clinical trial, as well as linking to data from other clinical trials which used the same investigational medicinal product. … The information in the EU database should be public, unless specific reasons require that a piece of information should not be published, in order to protect the right of the individual to private life and the right to the protection of personal data, recognised by Articles 7 and 8 of the Charter. Publicly available information contained in the EU database should contribute to protecting public health and fostering the innovation capacity of European medical research, while recognising the legitimate economic interests of sponsors.* *(68)For the purposes of this Regulation, in general the 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, the application for marketing authorisation has been withdrawn. In addition, the main characteristics of a clinical trial, the conclusion on Part I of the assessment report for the authorisation of a clinical trial, the decision on the authorisation of a clinical trial, the substantial modification of a clinical trial, and the clinical trial results including reasons for temporary halt and early termination, in general, should not be considered confidential.* Even if in general the data / documents should be published at the time of the decision on the clinical, there is still the possibility for a sponsor to ask for a deferral. But even if a deferral is accepted, it would not serve transparency and medical progress if by general rule publication would be postponed to a time point, where the data are no longer needed. Where is the justification to postpone the time point for more than eleven years, to a time where the information in most cases is no longer relevant for the scientific community?

Line no.	Stakeholder no.	Comment and rationale; proposed changes
722-725	30	**Question 10** • The first time point "The granting, refusal, or the withdrawal of the marketing authorisation application has triggered the loading into the EU database (and therefore publication) by the marketing authorisation applicant of the clinical study report for the same trial" is not acceptable: as correctly pointed by the same draft proposal (page 18, lines 630-634) "many clinical trials carried out on non-authorised medicines, in the early phases of development prior to marketing authorisation, which are never later used in a marketing authorisation as the development of the medicines is discontinued (approximately 80% of medicines which enter trials in human subjects are discontinued) …" • The second time point will allow the postponement of study and products documents publication for up to 10 years. This does not meet the requests of full transparency on clinical trials conducted in the European Union expressed by the Regulation. **Triggers for timing of publication should be avoided.**
722-725	32	**Question 10** Yes
722-725	33	**Question 10** Proposal 6.5.1 is acceptable as the public information is directly related to granting, refusing or withdrawing MA
722-725	36	**Question 10** **Comment:** *The FPM is in agreement with the proposed time points. The FPM believes that 12 months is an appropriate and reasonable timeframe for the publication of results from trials intended for MAA. However, we believe that the date of release of the summary results should not be reliant on the date that market authorisation was granted (or not) and should rely on when the trial itself has been completed.*
722-725	38	**Question 10** **Comment:** We would agree with paragraph 6.5.1 but consider that the 10 years specified in paragraph 6.5.2 is too long. Companies wishing to bury the results of a failed trial should not be able to defer

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		reporting the results just to avoid any adverse effects on the share price.
722-725	39	**Question 10** Option 6.5.1 mentions "*The granting, refusal or the withdrawal of the marketing authorisation application has triggered the loading into the EU database and therefore publication by the marketing authorisation applicant of the clinical study report for the same trial.*" This option is not adequate, as many clinical trials would fall outside its scope, since as pointed out in the draft proposal "*there are many clinical trials carried out on non-authorised medicines, in the early phases of development prior to marketing authorisation, which are never later used in a marketing authorisation*." The second option foresees deferrals of 9 to 10 years, which is, in our view unacceptable. (see answer above to Question 9). **Outcome (if applicable):** Do not establish triggers for timing of publication, just apply overall rule.
722-725	40	**Question 10** Assuming that the concept of MA is defined as set out in proposal 1.3, we support 6.5.1. 6.5.1 sets out that where the granting, refusal, or withdrawal of the MA application has triggered the publication of the clinical study report (CSR), the publication of the CSR should trigger the publication of study and product specific information for that trial, which has been kept confidential under Article 81(4)(b). It is important that in this addendum, the EMA recognises that many trials involve multiple IMPs (see case study on CRUK's Combinations Alliance initiative outlined in the text of our response to question 8). The EMA should therefore amend the text to clarify that where a trial involves multiple IMPs, it would be necessary for all IMPs included in that trial to have been granted or refused an MA, or had an MA application withdrawn, in order to trigger the publication of the CSR and therefore then publication of study and product specific information. It is right that the EMA has considered that an alternative trigger is necessary for the publication of study and product specific information for trials where a MA application may never be submitted. As acknowledged by the EMA, many clinical trials are carried out on non-authorised medicines, which are never used later in support of a MA application as the development of that medicine may be discontinued or the trial may not have been conducted in preparation for a MA, but as basic research. It is still important

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		that the study and product information from these trials is made publically available, but the timing of this publication needs to be carefully considered. The proposed trigger outlined in 6.5.2 is necessary in addition to 6.5.1 to ensure that data is published even if a marketing authorisation is never filed, which we support. We would ask the EMA to clarify the rationale behind the timeframe outlined in the proposal. We are unclear as to why the EMA has specified that the trigger of publication should be nine years after the date of the first summary of results of the trial are published. The EMA states that this is a 'reasonable period after the trial has been completed' (line 719), but does provide any evidence to support this presumption, except to say that it corresponds, but is not actually linked to, the data protection period provided for in the EU.
722-725	41	**Question 10** We concur with this proposal and believe it meets the requirements and objectives of the Regulations. We believe these timeframes to be reasonable and provide the Sponsor companies with sufficient time to conclude their development programmes.
722-725	46	**Question 10** **Comment:** We believe that the proposed time points in paragraphs 6.5.1 and 6.5.2 are reasonable and meet the requirements and objectives of the Regulation. They are sufficient to allow Sponsors to conclude their development programmes.
722-725	48	**Question 10** **Comment:** Our choice is for the granting, refusal of withdrawal of the marketing authorisation application; that is the end of the full procedure, taking into account our remarks regarding withdrawal posted in answers to question 9. IT should be understood that MAA refers to the set of clinical indications relevant of this application, which is for the indication and formulation/route of administration under study. Any other new clinical indication development should be considered as a new procedure, and benefit from the same timeframe for publicity of information.
722-725	53	**Question 10** We are in agreement with the proposed time-points for triggering publications
722-725	54	**Question 10**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		We support the proposed time points in paragraphs 6.5.1 and 6.5.2 and think that they meet the requirements and objectives of the Regulation. We think that the granting, refusal, or the withdrawal of the marketing authorisation application is an important point where more information can be made available. This is shown by the requirement in the Clinical Trial Regulation for the publication of the clinical study report once a Marketing Authorisation decision has been made. We feel that it is in the public interest at that point to make available the information provided in support of the Marketing Authorisation application and it is at this point where much of the commercial confidentiality which centres on commercial intent to apply for a Marketing Authorisation diminishes. We feel that nine years elapsing from the date on which the first summary of results of the trial should have been published and therefore at least 10 years after the end of the trial seems like a good figure. Although limited rationale has been provided we believe this gives ample time for any commercial intent for the trial information to have been undertaken (i.e. a marketing authorisation would have been applied for and a decision made). We also believe that those without any commercial intent would be those studies which would not be of urgency for making public (if this is the case then there may be a case for overriding public interest, which is accounted for in the document).
722-725	59	**Question 10** **Comment:** We have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
722-725	62	**Question 10** **Comment:** The timing described in Option 6.5.2 is the preferred option because this will allow for more protection of Intellectual Property across products.
722-725	73	**Question 10** **Comment:** EAHP has considered the suggested time points and believe the 10 year period described at 6.5.2 is too long. Such an elapse of time diminishes the value of the information to the scientific research community. In the intervening period it is likely that other studies in the same areas may have been conducted, unaided by information that otherwise could have been made available. This takes away from the research benefits of transparency and ultimately diminishes the value of the original trial, the assessment activity, and importantly, the patient's participation.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
722-725	76	**Question 10** **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.
722-725	77	**Question 11** **Comment:** We do support this, but do not understand that the option for deferral will not apply to phase I trials conducted in paediatric populations. This section (lines 726-744) is about phase I trials with healthy volunteers. There will be no deferral for phase I trials in patients at all (including paediatric patients). Please adapt the text as follows: Phase I trials conducted in healthy paediatric populations.
722-725	80	**Question 10** **Comment:** The time points under 6.5.1. are in line with the requirements and objectives of the Regulation. Regarding 6.5.2., no comment.
726-744	14	**Question 11** Referring to Question 11: comment and give a brief rationale for your support or disagreement with this proposal regarding Phase I trials: Information to be made public at the time of decision on the trial – possible deferral for Phase I trials in healthy volunteers: **Comment:** We agree and it must be indicated bioequivalence study (phase I trial), if it is the case.
726-746	10	**Question 11** **Comment:** We support the proposal. It is important to offer sufficient protection for information concerning early development stages, in order to encourage sponsors to conduct trials within the EU. On the other hand, it is also important to make information about trials in the EU more complete. The proposal seems to be well balanced.
726-746	11	**Question 11** We have reservations about the proposal regarding publication of information on Phase I trials, which would result in publication of

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		information on these trials at a much earlier stage than required in any other regulatory jurisdiction – we anticipate that this will be of significant concern to sponsors and would significantly damage the attractiveness of the EU for Phase I clinical research.
726-746	12	**Question 11** **Comment:** We support that the sponsor will have the possibility **"to opt to have only very minimal public information at the time of decision on the trial" and for the "remainder to be made public at the point when the summary of trial results is published"**. Justification: • Commercially confidential information is protected • The proposed minimal information to be published is not commercially sensitive • The registration of all trials will assure the public that trials are bona-fide and authorised and that further information will be made available We refer to the aforementioned position paper by the European CRO Federation (EUCROF) dated 31 October 2014 which was submitted as part of EUCROF's response to the first consultation on the EU portal (https://www.researchgate.net/publication/272151443_EUCROF_position_paper_public_access_to_early_phase_EU_database_information_31_Oct_2014). This paper states that *"Following a detailed review of the potential benefits of publicly accessible registration of trials stated by ClinicalTrials.gov, the WHO/International Clinical Trials Registry Platform (ICTRP) and the CTR we found that most are not applicable to Phase 1 non-therapeutic, non-paediatric, non-publicly funded clinical trials. An argument can however be made for release of relevant Phase 1 registration information in pre-determined stages and on a need-to-know basis."* It goes on to say that *"the potential risks of early publication and disclosure of Phase 1 studies' registration information […] may outweigh its benefits for patients, health professionals and the public. During early drug development much of this information is considered commercially confidential. Regulation outside Europe does not require publication of Phase 1 studies, except after FDA approval in the US. Sponsors would therefore likely manage perceived risks by performing Phase 1 studies outside Europe. This would have a detrimental effect for European early and late phase clinical research, which would ultimately translate into disadvantages for patients and the public."*

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		The paper provides a detailed risk/benefit as evidence and proposes that a "limited amount of non-commercially confidential registration information is made publicly accessible via the EU database following clinical trial authorisation and prior to study commencement". The proposed information to be made publicly available is in line with the EMA's proposal which we therefore fully and strongly support. In this context the **definition of the term "Phase 1"** is critical. The draft proposal appears to limit the definition of "Phase 1" to trials in healthy volunteers. It is our view that this definition is not in line with current clinical research practice and will hinder innovation in the EU. Our proposed definition of "Phase 1" is as follows: Phase 1 trials are clinical trials • using IMP, device & IMP/device combinations • performed in healthy volunteers and/or patients without therapeutic (or prophylactic) intent Justification: • An increasing number of innovative, non-therapeutic/prophylactic early phase (including First Time in Human) studies are conducted in patients with the target disease and/or a combination of healthy volunteers and patients • Our definition of "Phase 1" is in line with current relevant legislation in the UK and Belgium. It would be very disappointing and against the objectives of the EU CTR, if its implementation would use a definition of "Phase 1" which is very out-dated and which would hinder research and innovation in the EU. • During this phase of drug development there is particular sensitivity about the commercial confidentiality of information on the trial • In the draft proposal, the definition of "Phase 1" impacts on the whether or not sponsors will have the possibility to opt to have only very minimal public information at the time of decision on the trial

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		• Most potential benefits of public access to information at the time of decision on a trial are not applicable to non-therapeutic trials, whether in adult healthy volunteers or patients (see above) • Publication of details of trials in patients without therapeutic intent may even be misleading as the potential indications mentioned in the protocol may raise unrealistic hope especially in end-stage diseases • The limitation to healthy volunteers will lead to a decrease in innovative non-therapeutic trial designs being conducted in the EU. The conduct of innovative, adaptive and complex non-therapeutic Phase 1 studies is one of Europe's key skills and advantages. It would be a great shame if the CTR would lead to a decline of this type of research in the EU. **Proposed change (if any)**: We propose to change the definition of "Phase 1" to clinical trials Phase 1 trials are clinical trials • using IMP, device & IMP/device combinations • performed in healthy volunteers and/or patients without therapeutic (or prophylactic) intent.
726-746	19	**Question 11** **Comment:** The proposal for Phase I trials is supported as it appropriately balances the interest of the public to information regarding Phase I trials taking place at a particular site via the publication of a minimal dataset with sponsors interests in deferring full publication of the full dataset until the trial results are published; the minimal published dataset would allow additional information to be requested from the sponsor and for this to be shared outside of the database if and where appropriate.
726-746	26	We concur with the proposal to give the sponsor the option to have only very minimal public information at the time of decision on the Phase I trial (EU number of the trial, sponsor, investigator site, phase of trial [Phase I], number of trial subjects, population under study [healthy volunteers], decision on trial). However, we do not agree that the summary results of the Phase I trials should be released due to concerns regarding potential commercially confidential information, whose sensitivity and commercial importance may be highest during this early product development stage and propose sponsors have the option to defer for these reasons. **Proposed change (if any):** lines 739-744 740 The decision on the trial would also be made public, but identifying the trial only by this minimum set of information. The

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		information that would 741 usually have been made public at the start of the trial and during the trial will, in case of a 742 deferral, be made public at the point when the summary of trial results is published **only in cases in which serious and unexpected adverse events have occurred in healthy volunteers** 12 months 743 after the end of the trial. This option for deferral will not apply to Phase I trials conducted in 744 paediatric populations.
726-746	35	**Question 11** Due to the sensitivity data of Phase I clinical trials, EUCOPE agrees to EMA's view that these data are CCI and that the sponsor will be given the possibility to opt for a deferral. In addition, it should be acknowledged that also the summary of the results of Phase I studies can contain CCI and therefore a deferral for an extended period of 6 years for these summary results should be laid down in the addendum.
726-746	55	**Question 11** **Comment:** We agree with the proposal for sponsors to be able to opt for disclosure of only minimal public information at the time of decision on the trial, with the remaining information deferred, to be made public when summary trial results are published (12 months after the end of the trial). This balances protection of innovation with legitimate public disclosure. It is acceptable that this option will not apply to Phase 1 trials conducted in paediatric populations.
726-746	57	**Question 11** **Comment:** EuropaBio agrees with the EMA that there is particular sensitivity about the commercial confidentiality of information on Phase I clinical trials. It is important to emphasise that these trials usually involve healthy volunteers or sometimes patients (see footnote 1, page 4 of the consultation document). The proposal for an option for the sponsor to defer the publication of information on Phase I trials is welcomed. However we are concerned that a 12 month time period to disclose the summary results of Phase I trials would significantly narrow the window for filing and securing patents for new inventions. Indeed a company or researcher may require longer than 12 months to prepare and file appropriate patent applications for innovative approaches or uses discovered during early stages of development, as the results of the Phase I trial may be needed to support these applications. Therefore, even though the EU Clinical Trial Regulation does not make an explicit exclusion for Phase I trial summary results, their release within 12 months after the end of the

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		trial could compromise the EU competitive position for early clinical research. In this regard consideration should be given to the need to defer the disclosure of detailed information on Phase I trials. Consequently, due to the particularly sensitive commercial nature distinguishing Phase I trials, we recommend the application of a mechanism whereby the sponsor can seek a deferral for disclosure until the time of marketing authorisation decision or 7 years upon completion of the Phase I trial, whichever is the earlier.
726-746	60	Approach to Phase 1 Studies **Comment**: We recommend that the option for deferral should not only be limited to trials with healthy volunteers (HV). The deferral should also cover first in human studies in patients (e.g. oncology) and first in human studies in paediatrics (i.e. if there were no prior trials in adults). Given the proprietary nature of drug development in the early stages, this deferral option is believed to be fully aligned with the objectives of the Regulation, while encouraging innovation, one of the key objectives of this proposal. **Proposed change (if any):** Proposed change to line 743 as follows: "This option for deferral will **also apply to first in human studies in patients and in paediatric populations where there has been no prior development in adults.**"
726-746	65	**Question 11** **Comment:** As explained in EFPIA's Major Comments under the heading of 'Proposed Timeline for Disclosure of Phase I Information and Results', EFPIA appreciates EMA's acknowledgement of the potential for particular commercial sensitivity of Phase I trials and the possibility to defer the disclosure of information to be made public at the time of decision on the trial. As outlined, EFPIA also proposes a path forward.
726-746	70	**Question 11** **Comment:** We strongly support that, for Phase 1 trials (i.e. trials without therapeutic or prophylactic intent) the sponsor will have the possibility "**to opt to have only very minimal public information at the time of decision on the trial" and for the "remainder to be made public at the point when the summary of trial results is published"**. Rationale:

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		We refer to our position paper (http://www.eucrof.eu/images/EUCROF_Position_Paper_Public_Access_to_Early_Phase_EU_database_information_31_OCT_2014.pdf). This paper states that *"Following a detailed review of the potential benefits of publicly accessible registration of trials stated by ClinicalTrials.gov, the WHO/International Clinical Trials Registry Platform (ICTRP) and the CTR we found that most are not applicable to Phase 1 non-therapeutic, non-paediatric, non-publicly funded clinical trials. An argument can however be made for release of relevant Phase 1 registration information in pre-determined stages and on a need-to-know basis."* It goes on to say that "*the potential risks of early publication and disclosure of Phase 1 studies' registration information […] may outweigh its benefits for patients, health professionals and the public. During early drug development much of this information is considered commercially confidential. Regulation outside Europe does not require publication of Phase 1 studies, except after FDA approval in the US. Sponsors would therefore likely manage perceived risks by performing Phase 1 studies outside Europe. This would have a detrimental effect for European early and late phase clinical research, which would ultimately translate into disadvantages for patients and the public."* We support publicly accessible registration of all trials, with a minimal amount for Phase 1 trials being published initially as proposed by the EMA. This will assure the public that trials are bona-fide and authorised, and that further information will be made available when it becomes relevant and at a predetermined time. At the same time, the option to "have only very minimal public information at the time of decision on the trial" and for the "remainder to be made public at the point when the summary of trial results is published" will protect legitimate commercial interests of the sponsors and the interests of researchers involved in early phase clinical trials.
728-730	49	**Comment:** The information proposed to be made public for every clinical trial seems reasonable, unless commercial confidentiality needs to be upheld.
728-744	37	(Phase I studies) **Comment:** agree with this suggestions, but we would like to stress that the same should apply for phase I studies in patients (as for healthy volunteers) as many new biologic and advanced therapies can only be tested in patients.
728-744	71	**Question 11** **Comment:** The proposal is acceptable as it gives the sponsor the possibility to opt for a deferral of information, especially in

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		competition-sensitive generic medicines development. However, Phase I trials should also include trials in patients, not only in healthy volunteers, especially if related to a generic development. There may be cases where a medication is not safe for application in healthy volunteers, e.g. in case of cancer treatments, but a PK Phase I trial is nevertheless needed for marketing authorization. Therefore, the extension to all Phase I trials is proposed. **Proposed change (if any):** Information to be made public at the time of decision on the trial – possible deferral for Phase I trials (see 4.2.)
731-739	81	**Question 11** **Comment:** There are Phase I trials including patients which come with the same exceptional commercial sensitivity than those exclusively conducted in healthy volunteers. **Proposed change (if any):** Please delete "(in healthy volunteers)" in Line 731 and "(i.e. healthy volunteers)" in Line 739.
731-746	49	**Comment:** As a tertiary specialist cancer centre, we do not host phase I trials in healthy volunteers and thus cannot comment.
740-743	81	**Question 11** **Comment:** The period of 12 months after the end of the first Phase I clinical trial is much too short for the deferral of publication of information including the summary of clinical trial results. In most cases there are needed several Phase I clinical trials for a new active substance which are conducted over an average period of 3-5 years. Moreover, obtaining of patents could be a very time-consuming process for the originator. **Proposed change (if any):** Please replace the sentence in Lines 740-743 by "Publication of study result summaries, as well as study and product related information of Phase I trials should be deferrable until the decision on the first Phase II trial – or until 5 years after completion of the respective Phase I trial (whichever is earlier)."
745	72	**Question 11** The plan for deferral for phase 1 trials, we would mostly agree with; however, this could also be extended to phase 2 trials and

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		Phase 1 trials in a patient population.
745-746	4	**Question 11** EURORDIS agrees with the proposal. Data on trials on healthy volunteers are rarely discussed among patients' organisations, and the same is true for their results. The only information that may be of importance is the global conclusion (i.e. next clinical phase can start or development should be interrupted), but details on the trials and on the products are not clearly needed at this stage.
745-746	5	**Question 11** **Comment:** In general, we agree with proposal regarding phase I studies. The proposal should, however, not be restricted to phase I studies conducted only in healthy volunteers but should also cover phase I studies in patients. (Please refer to our comment for Lines 345, 727, 731 and 739 above.)
745-746	9	**Question 11** **Comment:** For Phase I clinical trials with healthy volunteers, any deferrals to making information public must be justified, and those justifications should be independently audited and policed. If a Phase I trial in healthy volunteers is stopped because of safety concerns, information about that trial should be made public immediately.
745-746	13	**Question 11** (deferral of publication for phase I trials) We welcome moves towards increasing transparency in clinical development of new medicines, and recognise the benefits it can have to public health. However, until there are globally accepted positions on registration and publication where there is little to gain and much to lose from transparency – ie research that has little or no impact on patient care, and is commercially sensitive – there must be adequate protection of sponsors' commercial confidentiality to ensure continued innovation and investment in new medicines. Having considered the following, we believe that there should be an option to defer publication of phase I studies, to protect the commercial interests of the sponsor. • There is little to gain from publication of results of phase I clinical trials, which have no direct impact on patient care. The only

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		results of wider value are important adverse reactions, because they affect safety of healthy volunteers in future clinical trials. However, those reactions are already reported to the regulators who assess the safety of proposed clinical trials. • Those who volunteer to take part in these early phase trials should be reassured that the studies will ultimately be registered and published at a time that protects industry and the interests of patients and the wider public. • Given the high attrition rate among new medicines, premature disclosure of phase I trials may give patients false hope of new treatments. • The pharmaceutical industry is fiercely competitive, and information about phase I trials is highly commercially sensitive. Premature disclosure of information, such as the identity and mechanism of action of a new medicine, could give competitors an unfair advantage and threaten investment in new medicines. • EU contract research organisations compete in a global marketplace. Threats to the commercial protection of sponsors will be a disincentive to place early phase clinical trials in the EU, as there is no requirement to do so elsewhere (eg USA, Canada, Australia, New Zealand). In the UK, clinical trials must be registered in a publicly accessible database, but registration of phase I trials may be deferred until the start of phase II. The deferral process has worked well, and has given sponsors confidence that their commercially confidential information is protected. Some UK CROs report that over 30% of sponsors request deferral for reasons of commercial sensitivity that include: • patent application outstanding • protection of intellectual property concerning new class of medicine • global publication policy of international sponsor • unwillingness to disclose strategic information (eg development of a generic product, investigation of a new formulation/route of delivery, development stage of new medicine) A survey of a sample of deferrals by the UK Health Research Authority revealed that more than half of the sponsors requesting

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		deferral were based outside the EU. Thus, without a deferral process for phase I trials, sponsors would be likely to do their early phase research outside of the EU. So, we very much welcome the option for the Sponsor to opt to publish only very minimal information at the time of the decision of a phase I trial. It would help ensure appropriate balance in meeting the needs of all stakeholders. The information that is proposed to be made public at the time of the decision of the trial is acceptable. However, we have 2 important concerns about the proposal, as follows. 1. Publication of the summary of trial results at 12 months after the end of the trial. This is too early. According to Annex IV and V of the Regulation, the summary of results will be detailed and specific. Their publication at 12 months after the end of the trial may not allow sponsors to progress development of their IMP sufficiently to reduce the impact of disclosure on commercial competitiveness. Also, publication would be disadvantageous to a sponsor wishing to make or amend a patent application on the basis of the results. It can take up to 12 months from the end of a phase I trial to analyse and report the results. Patent applications must be made on the basis of *unpublished* information, so the Regulation may drive sponsors to apply for patents prematurely, thereby increasing the cost of drug development in the EU, and increasing the risk of either rejection of the patent, owing to lack of data, or narrowing of its scope. Also, within 1 year after filing an application, a patent application can be amended in the light of new information. But if the new information is *published* during that time it could undermine the amended patent. So, publication of trial results could prevent sponsors from maximising the commercial potential of their products. In addition, phase I trials done to support a 'use patent' for an IMP in a new indication would have to be done outside of the EU because of the risk to the patent process. Therefore, we propose that the summary of trial results be posted into the portal at 12 months after the end of the trial, but not published until at least 2 years after the end of the trial, and ideally not until the first results from therapeutic trials are available. That would ensure that the sponsor or researcher has appropriate time to protect any patent application. 2. The proposed deferral applies only to Phase I trials in healthy volunteers.

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		Some Phase I 'first in human' trials include one or more very small groups of patients with the target indication (eg asthmatics), in addition to healthy volunteers. Those studies test single ascending doses in healthy volunteers first, then in patients. The studies are not therapeutic – patients are not expected to get any medical benefit. That innovative approach allows the sponsor to obtain early information about the safety and effects of the new medicine in patients and can speed development, ultimately benefitting patients. Limiting the deferral process to trials in healthy volunteers would only drive those innovative very early clinical studies outside the EU. In addition, some first in human trials are done entirely in patients with the target indication (eg cancer). Those trials are non-therapeutic but are as commercially sensitive as phase I trials in healthy volunteers. Therefore, we propose that the deferral process apply to all non-therapeutic studies, including studies that enrol both healthy volunteers and patients, and those that enrol patients only.
745-746	28	**Question 11** The proposal is only acceptable if at the time of decision the minimum amount of trial information that must appear in a register in order for a given trial to be considered fully registered, will be made public. The WHO Trial Registration Data Set represents the minimum amount of trial information required.
745-746	29	**Question 11** We agree with the proposal, as these are non-therapeutic trials, where pharmacokinetics and pharmacodynamics in healthy volunteers are to be investigated. Phase I trials are very early development. There is not yet proof that the products works in patients, so it is justifiable to postpone the time point for the publication of the full information and reduce the amount of minimal information which is made public at the time of decision on the clinical trial. There is no need to publish a lot of data for those trials at the time of the decision on the clinical trial as it is still not known whether the product is of any therapeutic value. We also agree that this is commercially confidential information.
745-746	30	**Question 11** All the items of the WHO ICTRP should be available at the time of the decision on the trial for all trials, including phase I on healthy volunteers.

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745-746	32	**Question 11** We support this proposal
745-746	36	**Question 11** Comment: *The FPM realises that in order to maintain commercial confidentiality and International competitiveness a system of deferral could be established. We believe that the proposals outlined represent a reasonable balance between the public and legitimate third party interest in trials and legitimate company needs over confidentiality in early stages of trials and development plans, where intellectual property rights may not be firmly established.* *However, we recommend that deferral not be made on an automatic basis but that the decision resides with the EMA and requires a case for justifying deferral to be made by the sponsor. Sponsors should be required to provide information as to why deferral is appropriate and reasonable. An example would be phase I studies on patients. The objective is that as much non-CCI should be released as possible and deferrals be time limited to 1 yr. We also believe that, similarly to the rules proposed for trials in paediatric populations, any data where safety concerns have been raised with an investigational product (IMP) (especially if first in class) may not be deferred. Information on safety must be accessible. These caveats are in the interests of public health.*
745-746	38	**Question 11** **Comment:** We agree with the proposal
745-746	39	**Question 11** The proposal on Phase I trials foresees the possibility for sponsors to "*opt to have only a very minimal public information at the time of decision on the trial*". If sponsors are given such an opportunity, they will certainly seize it and delay the publication of information. Yet at Phase I, there might be very little information available about a new drug or active substance. This is therefore inadequate. Also, in it is unclear whether these exceptions will also apply to those Phase I trials conducted on actual patients (for instance to test drugs against cancer). **Outcome (if applicable):** Do not grant sponsors of Phase I the possibility to "*opt to have only a very minimal public information at*

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		the time of decision on the trial."
745-746	41	**Question 11** The inclusion of the proposal to allow the Sponsor to opt to have only a very minimal public information (as described in lines 734 to 744) made public at the time of the decision of the trial is welcomed and would be a positive step toward ensuring there is an appropriate balance in meeting the needs of all parties involved. Should such a "deferral" be taken then the information that is proposed to be made public at the time of the decision of the trial, is acceptable. We believe that Phase I studies and their results should be *registered* in the EU database but, in line with current global standards, their *publication* must be delayed to protect the commercial interests of the Sponsor. Key factors to be taken into consideration on this point are:- • There is little to gain from publication of results of Phase I clinical trials, which have no direct impact on patient care. The only results of wider value are important adverse reactions, because they affect safety of healthy volunteers in future clinical trials. However, those reactions are already reported to the regulators who assess the safety of proposed clinical trials. • Given the high attrition rate among new medicines, premature disclosure of Phase I trials may give patients false hope of new treatments. • The pharmaceutical industry is fiercely competitive, and information about Phase I trials is highly commercially sensitive. Premature disclosure of information, such as the identity and mechanism of action of a new medicine, could give competitors an unfair advantage and threaten investment in new medicines. • EU contract research organisations (CROs) compete in a global marketplace. Threats to the commercial protection of Sponsors will be a disincentive to place early Phase clinical trials in the EU, as there is currently no requirement to do so elsewhere (e.g. USA, Canada, Australia and New Zealand). The current option for deferral of registration and publication implemented in the UK by the Health Research Authority has proved invaluable to many of our Sponsors. Data since October 2013 indicates that 46% (19 out of 41) of Quotient Clinical's Sponsors have requested and been granted a deferral to the publication of the research summary. Of these 19 Sponsors, 15 (79%) were based in the USA with the remainder based in the EU. All of these Sponsors cite concerns around commercial interest and competitive advantage with two more specific issues emerging namely, it is not possible because of Sponsor policies and outstanding patent

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		applications. If the option to defer is not incorporated into the final version of the Regulation then a proportionate loss in our business is anticipated, which is of course a great concern to our business model and subsequent impact on the EU as a permissive environment for clinical research. However, there are two significant concerns relating to this proposal in that the publication of the summary of trial results at 12 months is considered too early. Although the specific requirements of the portal are to be finalised, based on the detail listed in Annex IV and V of the Regulation, then the summary of results could be very revealing and, as a consequence, disadvantageous to a Sponsor looking to patent any intellectual property/know-how from their Phase I trials. On average it can take 6 months following Last Subject Last Visit (LSLV) to analyse and report the results. Any amendment to a patent application made on the basis of the results would be invalidated if the results were published within one year of the patent application so any release of results after only 12 months would undermine a Sponsor's patent process. **Proposed Change:** Therefore, it is proposed that the deferred information (the main characteristics of a clinical trial) from the 'time of decision on the trial and during the trial' noted in Section 4.2, be released 12 months after LSLV as proposed and that the summary of clinical trial results be posted into the EU portal **but** not released to the public for at least a further 12 months i.e. at least 24 months after the LSLV. This would achieve the agency's objective of ensuring that studies are fully registered and available to the public at the appropriate time, which we are in favour of, but would also ensure that the Sponsor and/or researcher has an appropriate length of time to protect any patent application, where necessary. However, since all of the data is owned by the Sponsors we would urge the EMA continues to consult closely with the Sponsors and their Trade Associations e.g. EFPIA to establish an appropriate timeline for release of results. **Comment:** The second concern is that the proposed deferral applies only to Phase I trials in healthy volunteers. However, some Phase I 'first in human' trials include one or more groups of patients with the target indication (e.g. asthmatics) in addition to healthy volunteers. These studies test single ascending doses in healthy volunteers first, then in patients. The studies are not therapeutic – patients are not expected to get any medical benefit. This innovative approach allows the Sponsor to obtain early information about the safety and effects of the new medicine in patients and can speed development ultimately benefiting patients.

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		Limiting the deferral process to trials in healthy volunteers would only drive these innovative studies outside the EU. **Proposed Change:** Deferral should also apply to non-therapeutic studies in patients, not just Phase I studies in healthy volunteers. It is therefore proposed that the text "(in healthy volunteers) is removed
745-746	46	**Question 11** **Comment:** We believe that the proposal to allow the Sponsor to opt to have only a very minimal public information at the time of decision on a Phase I trial is an essential one. This would be a welcome and positive step towards meeting the needs of all interested parties. If such a 'deferral' is taken then the information that is proposed to be divulged at the time of the decision of a trial, is acceptable. We believe that while Phase I studies and their results should be **registered** on the EU Database (as per current global standards) their **publication** must be delayed to protect the Sponsor's commercial interests. We would like the following key points to be considered: • There is little advantage to anyone (except competitors) in publishing Phase I results. There are indeed some important results of wider value, such as serious adverse events, but these are already reported to the regulators who assess the safety of future trials. • Premature disclosure of Phase I trials is likely to offer false hope to patients of new treatments. • Premature disclosure of information, such as the identity and mode of action of a new medicine, could give an unfair advantage to competitors and even threaten investment in new medicines. • Threats to the protection of Sponsor's commercially confidential information will render European contract research organisations (CROs) uncompetitive in a global market place. The threat imposed by premature disclosure does not exist in, for example, USA, Canada, Australia and New Zealand. • In the UK there is currently an option for deferral of registration and publication implemented by the Health Research Authority (HRA) and members report that this is indispensable to them in continuing to attract business particularly, but not exclusively,

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		from the USA.
745-746	48	**Question 11** **Comment:** We agree with the possibility to opt (by indicating this in the clinical trial application form) to have only a very minimal public information at the time of decision on the trial. **Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014. In fact, we ask for the systematic minimal information for Phases I trials, as an early disclosure of Phase I trial results after completion of the trial may compromise commercially confidential information. However, this paragraph only refers to possible deferral for Phase I trials in healthy volunteers for the Information to be made public at the time of decision on the trial. This should also be true for Phase I trials when done in patient populations.
745-746	51	**Question 11** **Comment:** Phase I-studies also include commercially confidential information, just like Phase II, III and IV – studies. It should not matter to what extend such information is contained in the data and what commercial value the information has. Therefore, the proposal to treat Phase I studies differently than phase II, III or IV-studies is not convincing in terms of protecting confidential information. Proposed change (if any): Removal of the proposal
745-746	53	**Question 11** There is no clear justification given in the consultation document for the proposal made for phase I trials in healthy volunteers and the commercial sensitivity of data and therefore timing of release of data should be evaluated by the same criteria as other studies
745-746	54	**Question 11** We support this proposal regarding Phase I trials in healthy volunteers. As you are probably already aware there has been growing concern regarding the transparency provision in the Clinical Trials Regulation and how these would apply to phase I trials which are deemed particularly commercially confidential as they are at such an early and crucial stage of drug development. Having normal disclosure as intended for other phases of clinical trials may deter sponsors from conducting clinical trials in the EU. We feel that the

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		option of deferral with minimum data requirements for publication until the summary of trial results are published (12 months after end of trial at the latest) would address these concerns.
745-746	59	**Question 11** **Comment:** We have no concerns about the proposal this question relates to. Phase I trials are of particular commercial concern. The information proposed to be released is similar to that already released by companies in clinical trial registries for these studies (a requirement of UK ethics approvals). This therefore minimises any negative impact on the EU as a centre for innovation relating to this proposal. Publishing the full information at the time the summary report is released ensures that the required information is speedily made available to the public after the end of the trial. **Proposed change (if any):** Not applicable
745-746	61	**Question 11** **Comment:** LEO Pharma is in agreement with the proposal for Phase 1 trials and in particular with the possibility for the sponsor to defer making information of trials in healthy volunteers publicly available at the decision of the trial. Leo Pharma's position is to have all clinical trials registered on a public accessible register before trial initiation, irrespectively of development phase and population.
745-746	62	**Question 11** **Comment:** Agree with the proposal for the Sponsor to be given the option to opt to have only very minimal information available at the time of the decision.
745-746	63	**Question 11** Deferral Phase I **Comment:** An optional deferral for Phase I in healthy volunteers is foreseen. It might be to be discussed about similar CT in patient population, which is by nature or IMP not possible in healthy participant e.g. FIH in oncology. **Proposed change (if any):** Phase one in patients might also be matter of an optional deferral.

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745-746	67	**Question 11:** Phase I (first in man and toxicity) not relevant for evidence based appraisal (but later sometimes very interesting) and of course commercially spoken very 'sensible'
745-746	78	**Comment:** The deferral for phase I trials in healthy volunteers without expected benefit is supported provided that the waived information is published in case of a safety concern.
745-746	80	**Question 11** **Comment:** ESMO is supporting this proposal. It gives the phase 0 scenario a greater chance of being established/used.
747-750	14	**Question 12** Referring to Question 12: comment on whether this proposal meets the requirements and objectives of the Regulation: **Comment:** The arrangements for payment of investigators and sites as set out in Annex I (P) (69-71) of the Regulation, should not be published as they relate in all cases to the commercial financial arrangements between the parties and the exception set out under Article 81(4)(b) should apply in all cases, because this information can be considered to be commercially confidential. We agree. Nothing to add.
747-750	27	**Question 12** **Comment:** we suggest to made public the arrangements of payment to sites in order to be in line with EFPIA code (see *EFPIA CODE ON DISCLOSURE OF TRANSFERS OF VALUE FROM PHARMACEUTICAL COMPANIES TO HEALTHCARE PROFESSIONALS AND HEALTHCARE ORGANISATIONS*) **Proposed change (if any):** The arrangements for payment of investigators and sites as set out in Annex I (P) (69-71) of the Regulation, should ~~not~~ be published ~~as they relate in all cases to the commercial financial arrangements between the parties and the exception set out under Article 81(4)(b) should apply in all cases, because this information can be considered to be commercially confidential.~~
747-750	51	**Question 12**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
401-403		**Comment:** It is agreed that the financial arrangements between the sponsor and the investigator should not be disclosed and any economic interests impairing the impartiality of the investigator should be made public instead.
747-750	71	**Question 12** **Comment:** The EGA is in agreement with this approach.
747-752	10	**Question 12** **Comment:** We support the proposal for the reasons mentioned in the document.
747-752	11	**Question 12** ACRO agrees that the proposal meets the requirements and objectives of the Regulation.
747-752	12	**Question 12** **Comment:** We agree that this proposal meets the requirements and objectives of the regulation. **Proposed change (if any):** None
747-752	19	**Question 12** **Comment:** The proposals meet the requirement and objectives of the Regulation (EU) No 536/2014.
747-752	35	**Question 12** EUCOPE strongly agrees to EMA's suggestion not to publish any arrangements for payments of investigators.
747-752	55	**Question 12** **Comment:** The sponsor agrees with the proposal as described in lines 747-750. Arrangements for payment are commercial confidential information and therefore this meets the requirements and objectives of the regulation.
747-752	57	**Question 12**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		Comment: EuropaBio supports the proposal that the arrangements for payment of investigators should not be published.
747-752	60	CCI of Investigator Payments **Comment**: We agree with the proposal in this addendum as stated. **Proposed change (if any):** None
747-752	65	**Question 12** **Comment:** EFPIA believes that the proposal meets the requirements that this information should not be published and agrees with the rationale provided by the EMA in its proposal. Furthermore, it is also worth noting that the aggregated compensation data collected and published as per the HCP EFPIA code or Member states national specific requirements on transparency (or rules of publication of contracts) should provide adequate information in this respect.
747-752	70	**Question 12** **Comment:** EUCROF agrees with the EMA proposal.
747-752	81	**Question 12** **Comment:** Our members agree upon this. Payments to investigators should not be made public as this information may contain commercially sensitive information.
747-777	49	**Comment:** Agree.
751-752	4	**Question 12** EURORDIS disagrees with the proposal. These financial arrangements are not to be confused with the commercial interests of the sponsor/company. They relate to the financial interests of the investigators/sites. To make this information public can only inform on the revenues of the investigators/sites, one's can hardly oppose the commercially confidential nature of that information for the sponsor/company.

Line no.	Stakeholder no.	Comment and rationale; proposed changes
751-752	5	**Question 12** **Comment:** The proposal meets the requirements and objectives of the Regulation.
751-752	13	**Question 12** (payments to investigators) This proposal meets the requirements and objectives of the Regulation. Details of payments to commercial phase I units are commercially confidential. Their disclosure would unfairly advantage the units' competitors.
751-752	21	**Question 12** **Comment:** Disagree. The payment will be reported (Annex I (P) (69-71). The amount depends on the going rate in each country. **Proposed change:** Payments to publicly funded institutions and persons (investigators) should be public. Payment to exclusively commercial research organisations need not.
751-752	28	**Question 12** The proposal is only acceptable if 'any conditions such as economic interests and institutional affiliations that might influence the impartiality of the investigators which are submitted, as part of the application dossier [will] be made public'.
751-752	29	**Question 12** We agree that information on payment arrangements between sponsor and investigators should not be published, especially as most people will not be able to judge the reasonability of the payments.
751-752	30	**Question 12** Any financial arrangements between the sponsors and sites should be published. This will enhance the transparency around potential suspicious partnership and incentives.
751-752	32	**Question 12** Yes

Line no.	Stakeholder no.	Comment and rationale; proposed changes
751-752	36	**Question 12** **Comment:** *The FPM agrees with this proposal.*
751-752	38	**Question 12** **Comment:** We agree with the proposal
751-752	39	**Question 12** The proposal mentions "*The arrangements for payment of investigators and sites as set out in Annex I (P) (69-71) of the Regulation, should not be published as they relate in all cases to the commercial financial arrangements between the parties and the exception set out under Article 81(4)(b) should apply in all 749 cases, because this information can be considered to be commercially confidential."* Any arrangements to fund investigators per patient recruited could be considered a perverse incentive and should therefore not be considered confidential.
751-752	41	**Question 12** We concur with this proposal and believe it meets the requirements and objectives of the Regulation.
751-752	46	**Question 12** **Comment:** We agree with this proposal and believe it meets the requirements and objectives of the Regulation.
751-752	48	**Question 12** **Comment: Yes**, this proposal does meet the requirements and objectives of the Regulation (EU) No 536/2014.
751-752	53	**Question 12** this proposal is appropriate
751-752	54	**Question 12**

Line no.	Stakeholder no.	Comment and rationale; proposed changes
		We feel that these proposals meet the requirements and objectives of the Regulation.
751-752	59	**Question 12** **Comment:** We have no concerns about the proposal this question relates to **Proposed change (if any):** Not applicable
751-752	62	**Question 12** **Comment:** Agree with the proposal not to publish arrangements of payments to investigators and sites. Note: This information is already reported elsewhere in accordance with ABPI.
751-752	67	**Question 12:** The EFPC supports as much as possible transparency, also on the level of arrangements for payment of investigators.
751-752	80	**Question 12** **Comment:** Yes, it does meet the spirit of the Regulation.