2 October 2014
EMA/354914/2014
Chief Policy Adviser

Overview of comments received on 'Publication and access to clinical-trial data' (EMA/240810/2013)

From stakeholder 157 to stakeholder 169

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
157	General	The draft Policy states that in general, clinical trial (CT) data cannot be considered commercially confidential information (CCI), the interests of public health overweighing considerations of CCI. This is in contradiction with the Agency's definition for CCI *i.e.* any information that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the owner of the information. Dissemination of CT data may impact on industry's commercial opportunity in markets outside the EU.	

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		The draft Policy also applies to withdrawn or rejected marketing authorisation (MA) application. The release of some of these data could prejudice the integrity of the regulatory process for any further resubmission and could undermine the future commercial viability of the product. Marketing Authorisation Holder (MAH) must work according to high quality international standards during the drug development. It is questionable why the same standards do not apply to the requester of data access. The draft Policy affords protection for commercial confidentiality to the requester of data access which is contradictory with the transparency and non-confidentialiy of the CT data submitted by MA applicant. All secondary analyses should also be publicly available and accessible for further scrutiny as soon as they are completed. The draft Policy states that “Access to CT data will enable third parties to verify the regulatory’s positions and challenge them where appropriate” which questions the Agency confidence in its decisions. A procedure should be established involving the MAH and described in the Policy. The MAH should have the possibility to appeal. Procedures and guarantees for the MAH should be duly established : • How contradictory results of re-analysis will be dealt with? The MAH should be aware of the requester/the request at the time of the application as well as of the results of the re-analysis to understand possible further gap. • In case CT data are used to gain a MA in a non-EU jurisdiction, despite a legally binding data-sharing agreement has been set up.	

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		The draft Policy states that the data access is provided for the sole purpose of addressing a question or conducting analysis in line with the spirit of informed consent. The reference to the 'spirit of the informed consent' implies a permissive approach to the respect of the informed consent in disclosing patient level data. Who will be responsible for determining whether the use of data are within the boundaries of the subjects' informed consent ? The procedure for data access to individual CT (one MAH concerned) and multiple CTs (several MAHs concerned) for a perspective of network meta-analyses should be clarified. The Policy should clearly state whether or not products authorised by Mutual Recognition Procedure, Decentralised Procedure are in the scope.	
157	33	Please define "Independent replication of CT data analysis". Explain why 'replication' of CT data analysis is a legitimate scientific and societal goal.	Add details or replace "independent replication of CT data analysis" by "third parties analysis fo CT data"
157	34-35	The draft Policy states that "Access to CT data will enable third parties to verify the regulatory's positions and challenge them where appropriate". This sentence questions the relevance/competence of regulatory authorities, including CHMP/PRAC and assumes that decisions are only based on individual CT analyses. Sentence to be deleted.	~~Access to CT data will enable third parties to verify the regulatory's positions and challenge them where appropriate~~
157	44-48	Nothing in the draft Policy guarantees that the analysis will not overstep patients' informed consent. To be reworded. Furthermore Informed consent for completed studies did not include any section regarding the possible secondary use of patient data. How this will be dealt with?	The analysis results must be fully compliant with the inform consent and not only 'in line' with.

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157	50-51	This section is not in agreement with the following section "Ensuring future investment in bio-pharmaceutical research and development (R&D)" since the draft Policy states that, "in general, CT data cannot be considered CCI". CT contains data which are to be considered CCI *i.e*. pharmaceutical development but also development strategy, statistical programs. Sentence to be deleted.	~~In general, however, CT data cannot be considered CCI;~~ the interest of public health outweigh considerations of CCI.
157	55-56	The draft Policy states: "it is designed to guard against unintended consequences". It is an intention, not a guarantee. There is no procedure for the consultation of the MAH and review of the data nor procedure for the MAH to appeal against Agency's decision to disclose data. Legal aspects must be put in place to match the intention stated in the draft Policy.	
157	57-59	It is not acceptable that the highest possible scientific standards including study personnel and qualifications imposed by ICH are applicable to the MAH and not for the requester of any secondary analysis. It is not acceptable that the Agency allows re-analysis of data provided by the MAH to a third party that would not perform those analyses according to the highest possible scientific standard. Sentence to be modified. Results from secondary analysis being made accessible to public, a high level of quality must be requested with at least a statistical analysis plan, a detailed analysis of CV and qualifications from personal involved in data re-analysis. An independant Committee responsible for evaluating the secondary analysis plan and results could ensure a high quality of analysis.	The Agency ~~cannot~~ should guarantee that all secondary data analyses that are enabled by the policy will be conducted and reported to the highest possible scientific standards.
157	60-61	The draft Policy states: "However, the Agency will put in place measures to ensure the best-possible protection of public health (and regulatory decisions) against claims resulting from inappropriate analyses": this	

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		sentence should be clarified by specifying the foreseen measures. The MAH should also be protected in case of inappropriate secondary analyses of data that would question the initial analysis.	
157	65-66	The draft Policy states: “Once a decision has been reached, considerations no longer applies”. Agency’s decisions are therefore at risk of being doubted by any third parties.	
157	67-68	The draft Policy states: “those who make secondary use of patient-level CT data shall be held to the same standard of transparency as those who generate CT data in first place”. The same level of transparency is to be expected for the requester of data than for the MA holder of those data.	“shall” to be replaced by “must”
157	70-72	Secondary analysis will be made public however the draft Policy states that “those who conduct secondary analysis should be allowed a reasonable period of time during which their analyses and deliberations are protected against external interventions”. This is in contradiction with the Agency’s position on transparency and the non-confidentiality status of CT data of the MAH. Sentence to be deleted. Nevertheless, opportunity should be given to the MAH to discuss secondary analyses before they are made public. In particular secondary analyses in contradiction with the original ones should be at least discussed before dissemination, with the original team and/or EMA and/or an independent ad hoc Committee.	‘~~However, those who conduct secondary analysis should also be allowed a reasonable period of time during which their analyses and deliberations are protected against external interventions.~~’
157	78-82	To avoid misunderstanding, clearly state that CT data already submitted in the frame of a Common Technical Document having obtained Marketing Authorisation before the policy came in force and included in the frame of a new application (*e.g.* extension of indication) do not enter in the scope of	

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		this policy.	
157	90-101	The definition for CT data is too large and several subcases should be foreseen. For exemple, pharmacoepidemiological studies on external datasets are performed via payed access to these datasets. The access to these individual data will pose a problem of contract/financing with respect to the structure responsible for datasets whereas statistical analyses performed on those data are performed by the MAH. It is suggested to refine the definition of CT data according to its nature (integrated or individual patient data) as the proposed CT data definition contains both integrated data (CTD overview, summary and body of the CSR) and some individual data (all sections 16.2 of the CSR, raw data) that may require a high level of protection and/or can be submitted to a different policy as indicated in the above example. See later comments.	
157	111-113	It should be stated that development strategy is part of commercial confidences. In line, statistical programs should be considered as intellectual property of the pharmaceutical company. To be added.	"CCI falls broadly into two categories: trade secrets (including formulas, programs, process or information contained or embodied in a product, etc.) and commercial confidences *including development strategy and statistical programs*."
157	118-123	What is the interest of providing individual patient line-listings and CRFs if individual data sets are provided? To be deleted. SAS statistical programs and SAS logs are part of CCI (see above comment). To be deleted.	"Raw CT data: For the purpose of the policy, raw CT data shall mean individual patients data sets~~,~~ ~~individual patient line-listings, individual CRFs~~ and documentation explaining the structure and the content of data sets ~~(e.g. annotated CRF, variable definitions, data-derivation specifications, data-set definition file).~~ It also includes supporting documents, such as test outputs (if not contained in the SAP), ~~SAS~~

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			~~logs and SAS programs if code not included in the SAP)~~."
157	129	Refer to comment for line 50-51: delete 'small'.	… a ~~small~~ number of CT data/documents can contain CCI. …
157	132	CCI should be applicable by default to points 2.7.1, 5.3.1 and 5.3.2 of Annex I, without necessity to duly justify it. Sentence to be deleted.	~~However this information will only be deemed CCI in duly justified cases.~~
157	133	Upon which criteria will a document be considered as "deemed to contain CCI"? Who will be in the position to decide that CCI are included ?	
157	136	List the procedures and guarantees that will apply if a document is deemed to contain CCI.	
157	139-143	"All documents" is too vague. Does it include blind reviews reports, individual data, reports generated during study review? List the documents considered as without PPD. The draft Policy states that any personal data should be adequately de-identified. However, it is stated later that appropriate standards, rules and procedures for de-identification will occur later, possibly not before 31 October 2014. How applicants will face de-identification in between ?	
157	150	Open Access should imply user/login creation and authentification. Else, anybody will have access, without identification of persons keeping a copy of the data. To be added.	

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157	150-154	The draft Policy states that it will be applicable “at the time of publication of EPAR for positive decision”. It is important that CT data disclosure takes place only after the product has been approved by both EMA and FDA in order not to interfere on evaluation processes. In case an application has been withdrawn or rejected, since the development program may still be ongoing, it is important not to disseminate the submitted CT data to avoid interference with the regulatory process of any further re-submission. Applicants applying for a MA should have the opportunity to duly justify that some data initially pre-identified as ‘Open access’ (O) are relevant to category 3 with ‘Controlled access’ (C) (at least for some points of CTD Module 2 listed in Annex I) : a procedure should be established for that purpose, in addition to an appeal procedure in case of disagreement. To be modified accordingly.	
157	155-231	A technical guidance should be made available - before the policy comes in force - to clarify the whole procedure about requests and provision of CT data/documents under category 3.	
157	169	The draft Policy states that the CT data to be submitted may include all the data sets … (*e.g.* the main analysis set, containing a limited number of indirect identifiers). Clarify the meaning of “limited number of indirect identifiers”. Will some specific rules/standard list be provided ?	
157	172	The proposed method (Hrynaszkiewicz) induced many CT data removal, resulting in potential loss of population regroupment. Moreover, there are several options of items to remove. The Policy should provide a defined level	

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		of de-identification required for submission.	
157	174	The draft Policy states that in some situations, the minimum standard may need to be supplemented by additional de-identification methods (e.g. statistical). The example provide “e.g. statistical” should be clarified. Will some specific rules be provided ?	
157	174-175	‘The methods of de-identification should be such that adherence will preclude subject de-identification, even when applying linkages with other data carriers (e.g. social media).’	‘The methods of de-identification should be such that adherence will preclude subject ~~de~~ re?-identification, even when applying linkages with other data carriers (e.g. social media).’
157	179	The draft Policy states that for Controlled access documents, the Agency will verify the identity of the requester. It should be added that the Agency will also verify the qualification of the requester unless this would mean that the access to Category 3 data *i.e.* controlled access data is not restrictive at all.	“requester has identified themselves, and the Agency has verified the identity *and the qualification* of the requester”
157	180	What is the protection against any requester (established in the EU) working for persons outside the EU? To be read in connection with comment on L 193.	
157	183	The reference to the “spirit of the Informed consent” is too large as regards the protection of subjects who have agreed to participate in clinical trials. The request for further analysis should be fully compliant with the Informed consent. How the Agency can guarantee that analyses will be ‘in line with the spirit of the Informed consent’ and ‘not out the boundaries of patient informed consent’ wheras the requester has not to provide a detailed plan i.e. not statistical analysis plan ?	

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		"In line with the spirit of the Informed consent" is not satisfying under the French Law and is contrary to the law. To be changed.	
157	183-187	Define the purpose of making a "re-analysis"? The draft Policy states "An exhaustive and detailed list of the aims of accessing the data (not necessarily a statistical analysis plan shall be submitted at the time of the request)". The objectives should be clearly written and the statistical analysis plan should be provided at the time of the request to have a clear idea of the request. To rewrite	
157	193	Refer to comment for L 180. The draft Policy states that the requester should agree, by the way of a legally binding data-sharing agreement, to refrain from obtaining a MA in a non-EU jurisdiction. What are the legal guarantees in case of gaining a MA outside EU? Some sentence protecting the MAH should be added.	
157	194-197	The requester should not share in any way or format CT data accessed from the Agency with anyone else. How can this be guaranteed? Will inspections be conducted? Will a legal settlement/appeal be set up in case data are provided to a non-authorised person ? To be added	
157	198	It should be specified in which situation ethics committee approval has to be obtained. If this relates to the patient consent revision, the requester should refer to ethics committees initially concerned.	

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		Furthermore, if the Informed consent does not address accessing of data/re-analysis by third parties, what will be the procedure for the requester. The Policy should clarify this aspect.	
157	205	Which means will be implemented in order to ensure that CT data accessed have been destroyed once the analysis is completed, and were not distributed to any third parties ? How the requester will prove he has deleted all copies? What means “once the analysis is completed” ? Once publicly available ? To be clearly stated.	
157	208-209	The Agency will set up a document on CT data-analysis standards on its own expectations relating to good analysis and transparency. Why the requester has no legal obligations to comply with these standards? The wording “no legal obligations” is contradictory with the sentence in L 181 “by way of legally binding data-sharing agreement”.	The requester should comply with data-analysis standards .
157	210-215	Refer to comment on L 57-59. The requester should not be allowed to decline uploading a detailed protocol/statistical analysis plan before access to ‘C’ data. It is mandatory to reinforce the reliability of secondary analyses. A template for detailed protocol/statistical analysis plan should be beneficial.	
157	213	The “Agency’s interpretation of any subsequent reported results” is not detailed further.	Clarify in the Policy the objectives of the Agency.
157	216-217	The Agency should <u>at least</u> judge the requester’s professional competence to conduct analyses.	‘The Agency will ~~NOT~~, at the time of allowing access to 'C' data, judge the requester's professional

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		Should an ad-hoc Committee be responsible to check adherence of principles? What about its composition and its responsibility to review the statistical plan, the results in particular if not consistent?	competence to conduct analyses.'
157	222-225	It is not acceptable that the Agency will not immediately disclose any information about the requester/request since this may open the door to any request. To be revised.	
157	236	The draft Policy states that all documents listed in Annexes 1 and 2 – whether categories 'O' or 'C'- shall be provided in PDF and should be fully searchable.	Define "fully searchable".
157	242	The draft Policy states that wherever technically possible, analysable de-identified raw CT data shall be made available for downloading in the format they have been analysed by the applicant, submitted and evaluated.	Define "technically possible".
157	244-247	The requested format for de-identified raw CT data should be further specified since Clinical Data Interchange Standards Consortium (CDISC) is not a standard by itself, but provides multiple standards.	Define which standards are expected.
157	249	The draft Policy states that it will come into effect on 1 January 2014. The date should take into account all procedures to be made available e.g. guidance for good analysis and transparency to the attention of requester of data, procedure for de-identification …	Date in force to be postponed.
157	285-292	The draft Policy considers that the personal data of trial personnel are exempt from Protection of Personal Data (PPD) considerations. PPD should be applied to all designated personnel involved in Clinical Trials except the Principal Investigator (PI). Indeed it is difficult to understand how the	

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		disclosure of the other names has any impact on public health. Same comments for the names of company personnel. To be revised.	
157	Annexe I	There are discrepancies in Annex I and Annex II regarding the access categorisation. In Annex I, section 2.7.1. has the status of "CCI". With the same approach, section 2.5.2. should be considered "CCI" (and not "O"). The same difference is raised for Sections 5.3.3, 5.3.4 and 5.3.5 in Annex I and Sections 14.2, 16.2.6 when PK data are included in the CSR. In module 5 of Annex I, the overall CSR has the status "O" whereas individual patient data from CSR report appendices (sections 16.2, 16.3 and 16.4, if applicable) should be "C" instead of "O". Section 2.7.2. Summary of Clinical Pharmacology Studies: some studies include information which may be considered by the MAH as CCI e.g. PET studies.	To be changed to 'Controlled access'
158	General	Harvard University's *Multi-Regional Clinical Trials Center* (MRCT) respectfully submits the following comments on the EMA's proposal, 0700 (June 24, 2013), entitled Publication and Access to Clinical Trial Data" (EMA/240810/2013**),** a proposal that will complement the existing 'Policy on access to documents (related to medicinal products for human and veterinary use)' (POLICY/0043) (EMA/110196/2006). The current draft seeks to make clinical trial (CT), detailed and high-quality data available for analysis by a wider scientific community enabling third party analysis and providing opportunities to broaden our understanding of human biology. MRCT strongly supports EMA's objective to increase sharing of participant-level clinical trials data to ensure regulatory integrity and to further public	

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		health. That said, MRCT is aware of the complexities and the need to balance personal autonomy and privacy of the clinical study participant on the one hand, and wider sharing in the service of public health and scientific innovation, on the other. We should state at the outset that any approach to data-sharing generally, including the specific considerations of sharing participant-level data, should apply equally to all public and private study sponsors, whether government, foundation, academic, industry or other, and all data-generators and data-users. Formed in 2011, MRCT at Harvard is a partnership of academia, government, non-profits and industry dedicated to improving the design and conduct of multi-regional clinical trials, especially those involving sites in the developing world. Of note, MRCT does not fund, plan, conduct, or monitor clinical trials, but rather studies their regulatory, practical and ethical aspects, in order to improve design and conduct of clinical trials. MRCT has convened a number of working groups to study ways to facilitate greater access to participant-level clinical trials data while maintaining the security of private health information. One MRCT work group explored models for sharing access to participant-level data, favouring an 'independent, learned intermediary' to ensure appropriate access.[1] A second MRCT work group has studied the issues impacting informed consent, including participant privacy, confidentiality and identifiability. The comments submitted herein by MRCT focus on the highly nuanced informed consent issues offering a multi-stakeholder perspective, one which MRCT may be uniquely positioned	

[1] The models were reviewed in May and presented to a large multi-stakeholder group including experts from academia, industry, government and patient groups for feedback. The majority of the participants favored the use of an independent, learned intermediary (independent of the trial sponsor) that would review and approve individual research requests to ensure access by qualified researchers. The conference materials, including slides and a summary of the discussions from the conference are available on our website, http://mrct.globalhealth.harvard.edu

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		to represent.	
158	General	1. Protecting Personal Data The EMA has defined three categories of data: Category 1, containing elements of commercially confidential information (CCI) that will not be made available to the public, Category 2, without personal data concerns that would be released immediately, and Category 3, containing personal data that would be made available (1) after adequate de-identification and (2) through a controlled access process. Personal data includes any information relating to an identified—either directly or indirectly—or identifiable person. MRCT at Harvard agrees with the Agency's acknowledgement of the limitations of current technologies that purport to protect participants from later identification. Given advances in data mining technologies, availability of databases and the potential for linkage, and the ever-expanding information available in social media, the ability to guarantee individual participant privacy and confidentiality is limited, especially where access is more open and information can be downloaded and combined with other publically available datasets. Though participant re-identification and misuse of data may be unlikely overall, the consequences of one incident of re-identification occurring may severely threaten public trust in the scientific investigative process with potential detrimental impact on participation, volunteerism, and confidence in the clinical trial system. We therefore respectfully submit that maximal clarity with regard to ownership of personal data be provided together with the steps necessary to achieve adequate data de-identification given the current informatics environment to inform policy on the use of participant-level data.	

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158	General	2. Defining “de-identified data” The risk of identifying study participants varies depending on the underlying type of data, as different methods of de-identification accord different levels of protection. Particularly, in clinical trials, there exists an important analytical and practical distinction between key-coded, de-identified and anonymized data. In key-coding, every participant is assigned a code and the link between the coded data and the individuals, such as name, date of birth, and address, is kept separately. Investigators are the only party with access to the key, while sponsors of the clinical trial and other parties involved receive data in the coded form only, it is important to note also that sponsors apply additional controls to assure confidentiality of the key coded data related to access and storage such that the combination of the coding and the controls affords adequate levels of protection. Of note, the data has not been de-identified completely at this point, for example, some attributes such as age, dates of birth may be present. General sharing of key coded data without the aforementioned controls does not provide the most advanced level of protection for participants’ data nor does mere de-identification even if completed according to generally accepted standards and therefore has an associated risk of re-identification. On the other end of the spectrum is complete anonymization of participants’ data through such techniques as removal of indirect identifiers[2] and a second coding of this de-identified data or through aggregation of data. Individual participants are no longer identifiable and the data cannot reasonably be traced back to them. As a result, the risks posed by sharing such anonymized data are considered to be lower. MRCT is conscious of the different levels of protection afforded	

[2] Final advice to the European Medicines Agency from the clinical trial advisory group on Protecting Patient Confidentiality. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142853.pdf, accessed 26.9.2013.

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		by key-coded, de-identified and anonymized data and in referring to de-identified data through this comment, MRCT is referring to data than has been fully de-identified and anonymized. In contrast, the EMA draft Policy does not elaborate on what is meant by "de-identified" data and which de-identification standard would EMA believe provides an adequate level of protection? Is de-identification according to a particular standard acceptable or are more advanced levels of protection, such as removal of indirect identifiers and verbatim text, and a second anonymization with discarding of key code, required? Significant clarity could be gained by defining the meaning of "de-identified data" within the policy. EMA should evaluate potential ethical and practical considerations raised by methods and from a practical perspective, how these methods will be impacted by the degree to which data can be combined with other available datasets. Very lenient de-identification and accessibility increases the risk of participant privacy breach, which may in some jurisdictions be a breach of Good Clinical Practice, and could serve to discourage future clinical trials participation. On the other hand, a more rigorous approach may place undue burdens on data-generators, as well as render anonymized data useless for future researchers by stripping it of relevant identifiers.	
158	General	3. Recognizing the Role of Informed Consent Documents in Protecting Personal Data Mitigating against instances of re-identification and resulting erosion of public trust is the education and information given to the participant during the informed consent process, embodied in the informed consent document ("ICD"). There is no question that the EMA acknowledges the importance of the informed consent. The EMA states in the draft policy that it takes "*a*	

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		guarded approach to the sharing of patient level data" and further indicates that "*respect for the boundaries of patients' informed consent*" is required. However, the statement that follows in the text of the policy (reproduced below) raises some ambiguity when applied to the content of individual study site ICD and therefore has the potential to be interpreted in a number of ways: "*Patients participate in clinical drug trials in the hope that their data will support the development and assessment of a particular medicine that is useful for the treatment of their disease, and will benefit the advancement of science and public health. The Agency takes the view that any other use of patient data oversteps the boundaries of patients informed consent and shall not be enabled by the policy"* MRCT finds the clause "…and will benefit the advancement of science and public health" a potential point of confusion and broad interpretation.[3] Further elaboration would be of tremendous benefit to the research community. For example, does the EMA suggest that participants "hope that their data…will benefit the advancement of science and public health" independent of application to or treatment of their disease, or only in the more limited circumstance of application to their specific disease? Does the language above indicate the EMA only advocates data access to clinical trial data for research as related to one particular medicine and only in the narrow and specific disease area under study, and that future use of the data by third parties for any other research oversteps boundaries of the ICD? Or, does the EMA advocate that data users must only demonstrate a commitment to advance science and public health to have broad access to	

[3] Actually, most confusing is the comma that precedes the "and will benefit…" Deletion of the comma would more affirmatively lead the reader to the conclusion that both conditions (development and assessment … useful for the treatment of their disease and will benefit the advancement…) must be met.

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		data, regardless of the specifics of the ICD? MRCT also notes that the EMA refers to third party researchers respecting the "spirit of the informed consent," which may be inferred to mean that researchers must not use data for purposes which the informed consent language does not contemplate.	
158	General	4. Aligning Data Sharing with Informed Consent Documents The informed consent is a legal document, the terms protected by contract law provisions. However, there are also strong ethical concerns relating to the degree to which the study participant is informed and truly understands that which is conveyed and in turn consented to by signing the document. Patients participate in clinical trials with the knowledge and expectations as conveyed by the language of the ICD and as explained by the principal investigator. The template ICD provided by the data generator and/or sponsor of the clinical trial may well contain broad language that explains how the data will be used (e.g. that the data from the trial may be used for the current research, in future research regarding the same medicine or disease area or by third party parties in related or unrelated future research). MRCT believes that there is an ethical responsibility on the part of sponsors and data-generators, principal investigators and individuals, who have attained informed consent. Likewise, secondary data-users also have an ethical responsibility to respect the specific language and the intent as represented in the informed consent document. Thus, researchers have an obligation to act in concert with these agreed upon original commitments, whether agreed to explicitly or implicitly.[4] However, determining what	

[4] A similar conclusion pertaining to biospecimens has been reached by the Health and Human Services Secretary's Advisory Committee on Human Research Protections (SACHRP) and can be equally applied to data: "In the case where secondary use of tissue samples is not compatible with the original consent for tissues that are de-identified, coded, or anonymized and are not readily identifiable, the samples are no longer subject to human subject regulations. Thus, there is no regulatory violation. Nevertheless, the original investigator and his/her institution have made an

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		acting in concert with the original commitments entails is not a simple determination. MRCT considers the position of the research participant: on the basis of the ICD, what would the participant expect? The ICD is the understanding, albeit with varying levels of clarity, with which individuals agree to participate in clinical trials. The analysis of how to proceed depends upon whether one is discussing a study in which informed consent has already been obtained from the participant (retrospective/current studies) or prospective studies, in which the ICD will elucidate, in advance, the intent to share participant data broadly. We will discuss each in turn.	
158	General	**a. Analysing Informed Consent Documents in Prospective Studies** It is more straight-forward to analyse use-cases relating to future, prospective studies. In this case, consistent with the current regulatory requirements, the ICD should disclose to any potential participant that his or her data will be shared, how it will be de-identified and anonymized, and that every attempt will be made to protect the individual from secondary re-identification. It should also include provisions that while the risk is small, there will always be the possibility that a research participant's identity will be revealed with the potential for compromising their privacy. Thus, any participant who has been properly informed and agrees to participate in a clinical trial will be made aware of the risk of re-identification as technology advances, even though the data may be de-identified according to the requirements of applicable regulations at the time of obtaining the consent.	

agreement with the subjects about use of their specimens, and have an obligation to honor that agreement." http://www.hhs.gov/ohrp/sachrp/20110124attachmentatosecletter.html, accessed 14.9.2013.

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		On the other hand, participation in the research study is then conditional on the agreement to allow future use of data for the greater good of science and public health, a framing that, absent due care, might be interpreted by a potential subject as compromising their autonomy, or even coercive. Further, such a condition—even if approved by the ethics committee or institutional review board—may potentially introduce bias to the analyses made on the subject cohort,5 compromising the ability to generalize an interpretation from the dataset. An additional nuance and ethical consideration is raised by an analysis of when data is removed from association to a particular participant such that it is no longer "their data" and consideration of broader balancing with public interest allows for sharing of this data for further research.	
158	General	**b. Analysing Retrospective Informed Consent Documents.** ***1. Permissibility Language in Retrospective Informed Consent Documents*** A potentially more challenging scenario describes one in which a study has already been initiated, with the proper consent documents obtained, but the data not yet submitted to the EMA. MRCT believes that the intent and language of the specific ICD (such that an analysis of what the study participant would likely have understood and consented to) must be respected, thus a retrospective review of all ICDs will be necessary prior to any decisions about sharing the clinical trial data. After reviewing many informed consent documents, MRCT can categorize the documents into five broad categories:	

[5] It is well appreciated that trust in the "medical establishment" varies among different ethnic, racial and socioeconomic groups.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		1. ICD is *explicitly prohibitive*, stating clearly that 'the identifiable data will not be shared.' Example language includes, "All information collected throughout this study will remain strictly confidential." Wherein the ICD says "Records of your participation in this study will be held confidential except as disclosure is required by law," the participant fully anticipates that legal disclosure of their data will be for specific and pre-defined research purpose of the particular clinical trial and not generally released by a change in the law. 2. ICD is *explicitly permissive*, stating affirmatively that the 'identifiable data will be shared' with researchers for 'future research.' 3. ICD is *explicitly but selectively permissive*, stating affirmatively to whom the identifiable data may be released, and identifying a restricted and defined population of individuals or situations that may receive data. This type of phrasing is used with increasing frequency amongst recent ICDs. For instance, the ICD may read "your study information will be shared with the study sponsor and its representatives including companies that it works with, the study team and researchers at other sites, government health agencies (such as the FDA and the EMA). The study sponsor will use and disclose your information only for research or regulatory purposes or to prepare publications." In specifying the groups to whom identifiable data *will* be released, the participant will infer that it will *not* be released to others not mentioned. 4. ICD is silent, with no provisions or descriptions on how a participant's data will or could be shared for future research. 5. ICD is contradictory, in which varying segments of the ICD are	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		discrepant. In addition, all ICDs for applicable clinical trials initiated after March 7, 2012 comply with 21 CFR 50.25(C) and include the FDA mandated language: "A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time." This statement informs participants of the availability of their summary information on the public website. MRCT recommends that, if the EMA will allow data availability according to 150-154 ("data will be available as downloads from the Agency's website, at the time of publication of the European Public Assessment Report (EPAR)…"), then comparable mandatory language should be specified by the EMA prior to posting. Envisioning potential interpretations by participants, what the participant believes to be "his/her data" may vary[6] as does the desire to protect this data for fear of re-identification. To the extent that data is aggregated, de-identified and/or anonymized, participants may no longer view the data as his or her "own." Moreover, given the interest study participants have in advancing science and public health, whether in relation the original medicine or disease or an interest in contributing more broadly, participants may be keenly interested having data shared for use in further research when the data are no longer reasonably tied them. Conversely, as the risk of re-identification increases, study participants may be more likely to view data as their "own" in effort to maintain control and protect their privacy. While these issues can be more clearly communicated and agreed upon in	

[6] Arguably many would assume that 'your' data refers to personally identifiable information, not aggregate or de-identified data.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		ICD moving forward, clarity of the original consent communication and therefore the intent of the study participant is difficult to ascertain, retrospectively. A policy decision as to approach to use in analyzing these issues may be very helpful from a practical perspective.	
158	General	***2. Interpreting Informed Consent Documents Language on Data-Sharing*** The five categories of ICDs merit different approaches to data sharing and raise a number of considerations. In general, if there is explicit language prohibiting release of the data, the agreement within the ICD should be honoured and identifiable data should not be shared (Category 1). However, it is not clear whether the prohibition on data release should also apply to anonymized data. Arguably, since such data can no longer be connected to individual study participants, it no longer belongs to that individual. In such a circumstance there are potentially significant benefits that can be gained from future research uses of fully anonymized data, whether for further research within the specific disease area of original study or for broader research purposes. It is also unclear whether regulatory obligations of data-generators override any express prohibition on data-sharing. In situations where regulations impose a legal obligation on data-generators to share data, is sharing permitted and where does the legal responsibility to protect participant privacy fall? Similarly, the Category 2 explicitly permissive provisions create a number of challenges. The express language of ICDs affirming future use suggests that there should be no prohibition on releasing patient-derived study data.[7] In practice, however, the analysis can likely be more complicated as relevant	

[7] MRCT recommends that data that is to be shared generally be de-identified to the extent consistent with the intended use. So long as the ICD did not promise confidentiality, future use is envisioned.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		laws, regulations and ethics committees' guidelines, in multiple countries where the clinical trial has been conducted, may place significant limitations on data sharing, overriding express consent. Furthermore, there may be ethical reasons to reconsent a prior participant who required a consent by a legal representative at the time of clinical trial enrolment. For example, in pediatric trials, the parent/guardian may have consented on behalf of the research participant, but the datasets that are under consideration for sharing may now refer to an individual who has reached the age of consent. Lastly, the extent of such expressly permitted data sharing is ambiguous; it is unclear whether by agreeing to data use for future research, the patient believes his or her data would be shared within his or her specific disease context or can be used for other, unrelated research. In Category 3, the specific use of and audience to receive the data has been defined and identified in the ICD. Considering the perspective of individual participants, such language can be seen to suggest that data will only be shared to the circumscribed list included in the ICD. While such interpretation can be debated, MRCT believes that for retrospective studies, a more conservative approach strikes a better balance between participants' privacy and the public's interest in furthering scientific research and innovation. Thus, in such circumstances, data-sharing outside of the intended audience will be problematic. If the ICD has committed to sharing the data in only very specific settings, deidentifying data does not eliminate the responsibility to the participant. Is there then a point at which data is no longer reasonably associated with a participant such that it is no longer "their data" and would this allow data falling in this category to be shared? A broad policy decision may be necessary to facilitate this interpretation by stakeholders otherwise a conservative approach is more likely.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		The setting in Category 4 would perhaps allow one to de-identify and share potentially identifiable data provided such data was de-identified to the maximum extent which may involve considerable resource in the case of multi-regional trials;. In the event that the ICD is contradictory (Category 5), the more conservative commitment (i.e. most restrictive access) will most likely be honoured. In both Category 4 and 5, ethics committees and institutional review boards can provide case-by-case guidance on data-sharing where data is identifiable.	
158	General	***3. The Role of Ethics Committees and Institutional Review Boards*** MRCT suggests that ethics committees (ECs) and institutional review boards (IRBs) can play an important role in ensuring that data sharing is conducted "in line with the spirit" of pertinent ICDs. In each of the settings that raise some concern as to the permissiveness of the ICD, should ECs/IRBs review the ICD and the data tables or study documents proposed for release or posting? These committees are charged with respecting and protecting the "rights and welfare" of the participants and can assess the specific trial, the ICDs, and the potential risk of sharing data more widely. Their deliberation may consider such elements as the sensitivity of the data (e.g. disease states including mental health status; social/behavioural, demographic and reputational harms associated with potential re-identification, for instance sexually transmitted diseases, high risk activities and illegality), among other issues. The EC/IRB can determine whether, depending on the specific situations, the planned action is consistent with the ICD, the participants should reconsent to the planned use (impractical in many studies), or if a waiver of consent is permissible. MRCT is conscious of the administrative burden imposed upon the EC/IRB for which they may be neither prepared	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		nor resourced.	
158	General	***4. Addressing privacy concerns through Informed Consent Documents*** While data privacy considerations are linked to adherence to the terms of the informed consent, the two are separable. An informed consent should articulate in clear and understandable language what will and what will not happen to personally identifiable information and data that has the potential to be easily re-identified, together with the protections in place by law and additional protections put in place by sponsors and investigators. Though participants may understand that their data will be submitted to regulatory authorities, either because of explicit or implicit language, they do not likely contemplate the sharing of this data by regulators for use by external researchers. At this foundational step, an approach to data sharing that fails to adequately protect patient privacy is violative of the "spirit" their informed consent. Furthermore, participants may have heightened concerns should there be increased risk of re-identification given a particular approach to data sharing such as open access or even through a controlled access approach that is lacking true control from a practical perspective or as implemented. Control of release of data may require greater oversight of data release such as to whom and whether the data can be downloaded for future use and combined with other available data. However, when ICDs do clearly articulate data sharing for further research and data are de-identified and/or anonymized so as to adequately protect the participants' identity and then shared via an approach that adequately protects the participant from re-identification, these privacy concerns lessen and benefits to public health can be realized. Therefore, any data-sharing decision based on retrospective ICDs should carefully balance privacy obligations, International	

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		Conference on Harmonisation (ICH) of GCP ethical guidelines, and the language of ICDs in determining whether data-sharing is appropriate and expected.	
158	General	***5. Concluding comments and suggestions for further consideration*** How best to proceed with prospective and retrospective ICDs involves consideration of various complexities. Significant difficulties are also presented by situations calling for individualized determination of ICDs permissibility. Such situations can arise in a number of circumstances. For example, some authorities propose that participants be given the option as to whether, and how, they permit their data to be shared—that participants may "opt out". To complicate this situation further, even if the data generators and sponsors intend the ICD to contain broad consent for future use, some local ECs/IRBs will modify the local consent or give participants the choice of whether or not to participate in data-sharing. Broad consent language is often modified by ethics committees at the national or site level, sometimes in order to comply with local laws, resulting in restrictions to language limiting or prohibiting future research or analysis of the data. In some instances the ICD may not include such language from the outset or be silent on the subject of future research. These situations present a statistical problem for data integrity. One cannot post data tables in which subsets of subjects are deleted or not represented as the statistical precision of the interpretation may be compromised and such exclusion of data would potentially yield biased results. This could also affect the secondary analyses of such data, which lacks the statistical power needed to validate the original claims made by the sponsor and/or EMA,	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		potentially increasing the burden for the regulatory agency in defending its (appropriate) initial conclusion. If this scenario were to be realized, how would the EMA intend to address access to studies where some portion of the participants opted out of sharing their data with further research and thus the data may lack both integrity and usability? Similarly, EMA proposed approach to situations where there is an affirmative obligation to protect personal data requires further consideration. Though, appropriately, de-identification is proposed, the specifics are not delineated. As a starting point, the "controlled access" the EMA proposes is dependent on defining "de-identified" data and delineating the scope of data-sharing – whether such sharing should be permitted only in the narrow disease area or more broadly, for unrelated studies. EMA states that its "control access" analysis will be "in line with the spirit of informed consent." How will the EMA ensure the concordance of use and ICD? Presumably, EMA will review the ICD since the data generators, those most familiar with the study, will not receive the data request directly from the external researchers. One would assume that the requester will provide a protocol or study plan so that alignment with consent can be confirmed. Will EMA have legal authority to review and deny access if there is lack of alignment? Will EMA have the resources to review each ICD for concurrence to data request? Alternatively, will EMA be informed by the data-generators as to the appropriateness of sharing contributed data? Should data-generators determine whether clinical trial data can be released in compliance with national and global data privacy laws, ethical norms and the principles of both the Declaration of Helsinki and ICH GCP; they will also consider adherence to the specific ICD. Would EMA then retain authority to agree or disagree with the analysis of the data-generator? Will then EMA/data	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		generators then interpret the ICDs, the available data, and the qualifications of and specific studies proposed by the data requestors. If EMA shares data despite a recommendation not to share the data by the data-generator, is the EMA liable for subsequent use or misuse of the data, for data and privacy breaches? If EMA takes action against the data-generators, will the EMA indemnify the data generator for any third party claims in circumstances where data is released contrary to the terms of the ICD?	
158	General	MRCT strongly encourages the development and publication of practical guidance clarifying how the language of the ICD, and the requirement of the data-generator and data-user to adhere to such language. In addition to concerns about privacy and confidentiality, and risk of re-identification, the choice of the individual study participant regarding sharing of his/her data for use in further research must be balanced with the greater good of using data to speed scientific discovery, increase efficiency of clinical trials (possibility of fewer patients exposed to potential harms and more expedient trials) and the public interest of bringing beneficial medicines to patients who need them. Thoughtful and respectful approaches to situations described above are possible though far from straight-forward, as EMA contemplates moving forward from a practical standpoint. MRCT thanks the Agency for the opportunity to comment on this draft proposal, and stands ready to work the EMA on these important issues	
158	General	MRCT strongly encourages the development and publication of practical guidance clarifying how the language of the ICD, and the requirement of the data generator to adhere to such language, influences and impacts the implementation of the EMA policy.	MRCT strongly encourages the development and publication of practical guidance clarifying how the language of the ICD, and the requirement of the data generator to adhere to such language, should inform the implementation of, and data generators'

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
			compliance with, the EMA policy.
158	44-48:	The language of the draft Policy is open to significant interpretational differences. In stating that patients "hope that their data…will benefit the advancement of science and public health," it is unclear whether the EMA believes that patients consent to a broader access to their data, independent of application to or treatment of their disease, or to the more limited access for research in the narrow disease area. Does the language indicate the EMA only advocates data access to clinical trial data for research in the narrow disease area of the clinical disease area and that future use of the data by third parties for any other research oversteps boundaries of the ICD? Or does the EMA advocate that data users must only demonstrate a commitment to advance science and public health to have broad access to data, regardless of the specifics of the ICD?	Respect for the boundaries of patients' informed consent: Patients participate in clinical drug trials in the hope that their data will support the development and assessment of a particular medicine that is useful for the treatment of their disease, and will benefit the advancement of science and public health. The Agency takes the view that any use or disclosure of patient data which oversteps the boundaries of patients' informed consent, shall not be enabled by the policy.
158	57-61:	The Agency properly recognizes the difficulties of guaranteeing that all secondary data analysis will be conducted and reported to the highest possible scientific standard. The draft Policy states that measures will be put in place to safeguard the public from inappropriate analyses. However, the specifics of such measures are not delineated. What ICD information will the third party researcher receive to ensure compatibility with the proposed project? The third party should exercise caution if the data set has been reformatted because of "opt out" clauses for use of the data beyond the protocol. Similarly, will the EMA require researchers to gain approval of local or national ethics committees to conduct studies using the data?	
158	64-65:	The responsibility for ethical and legal compliance rests with the party releasing the data and such responsibility must be executed in good faith. If	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		the regulatory agency contravenes the recommendation of the party releasing the data, it has responsibility for follow-on consequences and will indemnify the data generator from subsequent action.	
158	172-175:	Common standards, rules and procedures for deidentification and protection of patient privacy are needed. For meaningful data analysis, data can be de-identified but anonymity is, at best, challenging. Some data (e.g. genetic data, orphan diseases) may need to be excluded even if appropriate de-identification has occurred. The acceptable processes and procedures should be delineated.	
158	183:	Allowing controlled access in line with "the spirit of informed consent" raises a number of challenges. Since, at a minimum, ICDs present an ethical contract with a study participant, the release of clinical trial data must be concordant with the ICD. The ethical and legal release should tract the language in the ICD. However, the draft Policy does not address how future data releases plan to comply with existing ICDs. Is there a specific mechanism that the EMA proposes to use to ensure compatibility of the ICD with data sharing? Has the EMA considered to whom and to what extent the sharing of key coded study data is permitted under the informed consent documents for each study?	
158	244-247:	Standard data formats for existing and completed studies are imperative if aggregation and compilation of multiple datasets is desired.	
159	General	DGPharMed supports the intention of the draft policy in principle, but some details are to be changed or clarified.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		Protection of personnel data Up to now the informed consent of clinical trial (CT) data does not cover additional secondary analysis of data by third parties and it cannot be assumed, that this will change until this new policy becomes effective. But an informed consent covering this topic is a pre-requisite for legal use of CT data, otherwise the use would be illegal. Therefore the whole process can only start prospectively with CT starting at date when the policy will become effective. All other CTs are not covered by the new procedure. These facts are to be regarded and the draft has to be changed accordingly. Furthermore it is questionable whether the proposed "controlled access" would prevent the re-identification of subjects and their personnel data. **Scope of the policy** According to lines 49 – 51 only data of CT from manufacturers are subject of the draft policy due to the fact that these data are of commercial interest. But at least in Germany every CT has to be approved by the national authorities and data from CTs initiated and performed by research institutes like universities may be of commercial interest too. For these cases a clear regulation is necessary. **Standards for requesters / good analysis practice** A pre-requisite for any CT is the availability of an approved protocol, which usually contains a statistical analysis plan as a requirement of good analysis practice. This requirement must be effective also for requesters for data access. Therefore an analysis plan is a pre-requisite and has to be provided by the requester before an access may be realized. In addition the secondary research must be subject of the same standards of transparency than the	

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		originator. Therefore the research must be registered in a public registry before initiation and the results must be published within one year after completion. In addition a review of the purpose the data will be used is mandatory to avoid or minimize any abuse of the data and to ensure that the analysis is of public and / or scientific interest. An appropriate process has to be implemented. It has to be clarified how to deal with inappropriate secondary analyses. In this context it should be stated and regarded, that secondary analyses of CT data are not confirmative but only generate hypothesis. **Commercial interest** The person or organization requesting access to CT data must be obliged to declare, that the data will not be used for commercial purpose.	
160	General	1. Introduction Public Citizen generally supports the EMA's proposed policy 0070 on publication and access to clinical trial data,8 which provides for the publication of clinical-trial data submitted to the EMA in the future including de-identified patient-level data, as well as other documents held by the agency. This policy complements the existing "Policy on access to documents (related to medicinal products for human and veterinary use)"	

[8] European Medicines Agency. Publication and access to clinical-trial data POLICY/0070. June 24, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf. Accessed September 30, 2013.

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		(policy 0043), which provides for access to documents related to data previously submitted to the EMA.9 We support draft policy 0070, which will enable independent re-analysis of the benefits and risks of EMA-approved drugs. Draft policy 0070 promotes transparency and the opportunity for independent review, cornerstones of both sound medical research and good regulatory decision-making in a democratic society. The policy will adequately protect patient privacy if clarification is made to ensure appropriate implementation. The policy currently sufficiently protects legitimate commercial interests, preserves incentives to innovate, conforms to appropriate informed consent standards, and guards against data misuse. We request that the policy be clarified so as not to suggest, misleadingly, that informed consent is required for de-identified data and can be complied with “in spirit.” We also propose that the policy be strengthened by enabling access to de-identified patient-level data by research groups based outside of Europe, as research generated by international groups serves to benefit the public health, both internationally and within European member states.	
160	General	2. Summary of Specific Comments a. Protecting Patient Privacy Patient privacy is of great concern when considering use of data from clinical trials enrolling human subjects. Patients participating in clinical trials share sensitive health information, disclosure of which may harm the individuals’	

[9] European Medicines Agency. European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use) POLICY/0043.http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/11/WC500099473.pdf. Accessed September 23, 2013.

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		privacy interest. Moreover, personal information is protected under Article (4)(2) of EC Regulation 1049/2001, against disclosure that would undermine the privacy and integrity of individuals.10 With some clarifying changes, we believe that policy 0070 could adequately protect the privacy and integrity of individuals. Data from clinical trials should only be shared after appropriate steps are taken to de-identify any information applicable to specific patients. The EMA has selected a proposed minimum standard for de-identifying patient data, described in Hrynaszkiewicz,11 and has also required additional de-identification methods where appropriate. Preventing re-identification will ensure that disclosure will not undermine the privacy and integrity of individuals. When dealing with large data sets, there is sometimes a risk that data may be processed or "mined" in ways that allow individuals to be re-identified. We believe that the risk of re-identification is low, in part because few individuals or organizations with capacity to conduct such a "mining" effort have a financial or other interest in uncovering the identities of the patients who participated in clinical trials research. Nevertheless, the EMA has provided additional safeguards against this practice by requiring that the requester of patient-specific data enter into a legally binding data-sharing agreement, through which the requester agrees to refrain from any attempt	

[10] That regulation states that European Community institutions, including the EMA, "shall refuse access to a document where disclosure would undermine the protection of: ... (b) privacy and the integrity of the individual, in particular in accordance with Community legislation regarding the protection of personal data." Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001. http://www.europarl.europa.eu/register/pdf/r1049_en.pdf. Accessed September 30, 2013.

[11] Hrynaszkiewicz, I., M. L. Norton, et al. (2010). "Preparing raw clinical data for publication: guidance for journal editors, authors, and peer reviewers." *BMJ* 340:c181.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		to retroactively re-identify patients in clinical trials, including by relying on outside databases. This agreement requirement, if appropriately implemented to cover all data at risk for re-identification, would be sufficient to protect against re-identification. However, it remains unclear how this aspect of the policy will be implemented. Under the policy, some types of de-identified patient-level data will be classified as Category 2 and made available "open access" without a data-sharing agreement, while other de-identified patient data are classified as Category 3 and require an agreement. We think it is reasonable to require different levels of protection depending on the risk of re-identification. However, we do not believe the policy makes clear when and how de-identified data will receive the higher level of protection. One way to make this clearer would be to define what it means for data to be "adequately de-identified" under Category 2 (page 4, line 143), and how this differs from "appropriate de-identification" under Category 3 (page 5, lines 165-175). With clarification in place, we believe that policy 0070 can be implemented to adequately protect patient privacy.	
160	General	b. Disclosure of Clinical Trials Personnel Data In addition to patient data, information submitted to the EMA will include personal data related to the personnel involved in clinical trials (clinical investigators and other health care providers). These data, which generally relate to the identity and professional activities of the individual in the context of the clinical trial, do not implicate the same privacy interests as the health information collected from clinical trial participants.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		The protections for personal data in EC Regulation 1049/2001 are not absolute, but rather bar disclosure only where "disclosure would undermine the protection of: . . . (b) privacy and the integrity of the individual."12 Asking an investigator or health care provider to identify his or her professional involvement in a clinical trial does not undermine the privacy or integrity of that person, any more than an author's attribution on an academic publication undermines the privacy or integrity of the author. Moreover, such information is essential in order to identify potential conflicts of interest held by the investigators and understand how potential biases might have affected the integrity of the clinical trial results. The EMA therefore correctly determined that the personal data of clinical trials personnel is not protected against disclosure under EC Regulation 1049/2001, and should be made openly available to the public without restriction.	
160	General	c. Legitimate Commercial Interests The EMA is required, under Article (4)(2) of Regulation 1049/2001, to refuse access to documents where disclosure would undermine the protection of "commercial interests . . . unless there is an overriding public interest in disclosure."[13] We believe that policy 0070 appropriately protects commercial interests by preventing disclosure of commercially confidential information (CCI), which is defined under the policy as "any information that is not in	

[12] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001. http://www.europarl.europa.eu/register/pdf/r1049_en.pdf. Accessed September 30, 2013.
[13] Official Journal of the European Communities. Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001. http://www.europarl.europa.eu/register/pdf/r1049_en.pdf. Accessed September 30, 2013.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the owner of the information."[14] Some information submitted to the EMA may be proprietary in nature, including trade secrets and information from preclinical biopharmaceutical studies that could be used by other companies to identify proprietary compounds and create potential competing products. Such data are adequately protected under policy 0070, which protects pre-clinical reports from publication (except by specific request under the agency's policy 0043 on access documents). We agree with the EMA that data disclosing the methodology and results from human clinical trials cannot, as a general matter, be considered CCI. Most safety and efficacy trials rely on standard, validated techniques that are non-proprietary and well known to industry competitors. Information on the methodology from clinical trials should therefore be made widely available. Under rare circumstances, it is possible that a novel, previously undisclosed method used to established safety and efficacy during human clinical testing might be of some value to competitors. Examples offered during the EMA's recent workshop series included:[15] • Methods to pursue newly validated/devised endpoints that are persuasive to regulators: e.g., the suite of validated measurements for	

[14] European Medicines Agency. Publication and access to clinical-trial data POLICY/0070. June 24, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf. Accessed September 30, 2013.
[15] European Medicines Agency. Advice to the European Medicines Agency on rules of engagement for accessing clinical trial data. April 4, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142859.pdf. Accessed September 27, 2013.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		assessing the effects of migraine on the whole body in support of the approval of a drug • A novel trial design, streamlining and making more economical the proof of efficacy for a novel compound • A new assay methodology for biomarkers • A new validation methodology for a Patient Reported Outcome We recognize that some of these methods may qualify as "commercial interests" under Regulation 1049/2001. However, to the extent that these methods are submitted to justify a regulatory submission, there is an overriding public health interest in disclosure, both so that the data and rationale underlying the regulatory decision can be independently evaluated and so members of the medical community can understand the evidence supporting safety and efficacy and use the product appropriately. The identities of clinical trials investigators who "recruit well" may also be financially valuable, especially for rare diseases or difficult patient populations.[16] Again, the public health interest in understanding potential conflicts of interest and bias outweighs the potential commercial interest. We also recognize that disclosing results from clinical trials, including patient-level data, may help to identify previously undisclosed safety or efficacy concerns, thereby harming pharmaceutical sales, a "commercial interest." Yet we do not consider the company's interest in preventing the discovery of safety and efficacy information in order to promote sales to be a "legitimate commercial interest," or the type of interest meant to be	

[16] *Ibid.*

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		protected under Regulation 1049/2001. Likewise, we fail to see a legitimate interest in maintaining a cloak of secrecy around withdrawn or denied applications. While some have argued that disclosing such data would "undermine the future commercial viability" of the withdrawn or denied product, we believe additional scrutiny for such products is appropriate.[17] If anything, it is especially important for the EMA to publish data from withdrawn or denied applications, as in many cases the withdrawal or denial implicates a safety risk that should be fully considered upon re-submission. The mere fact that information from clinical trials may be frequently requested by competitors is not sufficient to conclude that disclosure will undermine a legitimate commercial interest. Competitors are strongly motivated to uncover and disclose potential health risks. Blocking such disclosure — regardless of whether the disclosure is financially motivated — is not a legitimate commercial interest. Moreover, we respectfully disagree with the suggestion, made in recent comments on this policy, that the mere fact that a clinical report is voluminous, or contains the "intellectual analysis and know-how" of sponsors, indicates that disclosure would undermine a legitimate commercial interest.[18] Having reviewed tens of thousands of pages of regulatory submissions for FDA new drug approval in the course of our 40 years of research, we can assert that although this information is highly technical in	

[17] European Medicines Agency. Comments on Policy 0070 submitted by the European Federation of Pharmaceutical Industries and Associations. September 5, 2013. http://www.efpia.eu/uploads/EFPIA_comments_on_EMA_draft_policy_access_to_CT_data_FINAL.pdf. Accessed September 20, 2013.
[18] *Ibid.*

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		nature, its form is non-innovative and its substance is of limited commercial value except to the extent that it provides valuable public health information on the safety and efficacy profile of a lucrative commercial product. Participants at the EMA's recent workshop series raised the concern that clinical-trial data may be used inappropriately to circumvent existing regulatory data protection rules or take advantage of the absence of such rules in other countries.[19] (For example, workshop participants asserted that data exclusivity in Australia, China, and Mexico is undermined by publication of the relevant data elsewhere in the world.)[20] We believe that such concerns are adequately addressed by the policy. First, the EMA has required data requesters to agree not to use patient-level data to gain marketing authorisation outside the EU, or share such raw data with other individuals who have not agreed to the same terms. Second, summaries of the main findings supporting a product's safety and efficacy are already made available upon request under policy 0040, and are generally also made public in many ways, including through medical review documents published on the website of the U.S. Food and Drug Administration. [21] We fail to see how the post-hoc analysis enabled through disclosure of patient-level data would provide additional value in obtaining regulatory approval. Third, even assuming that data exclusivity in Australia, China, and Mexico can be undermined with EMA data (which has not been	

[19] Advice to the European Medicines Agency on rules of engagement for accessing clinical trial data. April 4, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142859.pdf. Accessed September 30, 2013.
[20] *Ibid.*
[21] Summaries of the methodology and results of clinical trials supporting safety and efficacy are published by the FDA following a product approval. These summaries, provided in a "medical review," are published on the FDA's website. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed September 30, 2013.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		established), we think the number of foreign markets that would be so affected is small (most countries either lack a premarket approval system or have data exclusivity provisions that would not be affected by the publication of EMA data). Any commercial interest in bolstering data exclusivity protection among a subset of foreign markets is outweighed by the public health interest in ensuring transparency of clinical trial results. Finally, critics of draft policy 0070 have suggested that the policy will harm the public health by undermining incentives to innovate.[22] Ensuring investment into future biomedical research is an important public health aim. Yet investment by the pharmaceutical industry is already amply protected by an aggressive system of intellectual property rights in place in the United States, Europe, and the world's other most lucrative pharmaceutical markets. Moreover, even assuming pharmaceutical companies could gain a hypothetical benefit from reviewing the clinical trials information submitted by competitors during the regulatory review process, this increased understanding will confer its own public health benefit by making drug development more efficient.	
160	General	d. Policy 0070 Protects Against Inappropriate Secondary Analysis As noted in the draft policy itself, the agency cannot guarantee that all secondary data analyses made possible through policy 0070 will be conducted and reported to the highest possible scientific standard (lines 58-59). The policy will appropriately encourage good analysis practice by making available a document communicating the agency's views on the	

[22] European Medicines Agency. Comments on Policy 0070 submitted by the European Federation of Pharmaceutical Industries and Associations. September 5, 2013. http://www.efpia.eu/uploads/EFPIA_comments_on_EMA_draft_policy_access_to_CT_data_FINAL.pdf. Accessed September 30, 2013.

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		subject, requiring publication of results within a reasonable period, and providing an opportunity for requesters to upload a statistical analysis plan, which will be made publicly available. Requesters are also required to report their identities and provide a detailed and exhaustive list of goals for accessing the data. We think all of these requirements serve the interest of transparency and provide appropriate safeguards against misuse. Critics have claimed that the risk of misinterpretation and misuses of clinical data will "undermine the trust" in the regulatory approval system.23 We disagree. The current lack of transparency regarding clinical-trial data itself has engendered mistrust in the regulatory approval system. Transparency is the best mechanism for restoring that trust and ensuing reliability within the regulatory system. We note that data originators are also capable of misusing data to mislead the public, and agree with EMA officials that "in an open society, trial sponsors and regulators do not have a monopoly on analysing and assessing drug trial results."24 Moreover, well-established mechanisms for peer review and further independent validation will help to ensure that only analyses based on high scientific standards gain widespread acceptance within the medical community. Open access to the underlying data sets will further facilitate this process of peer review. The agency has appropriately declined to insert itself as judge of data requesters' professional competence or plan for statistical analysis. Such a role would be logistically challenging, resource intensive, and unnecessarily restrictive of access to data. We do not believe, as some have argued, that	

[23] *Ibid.*
[24] Eichler H-G, Abadie E, Breckenridge A, Leufkens H, Rasi G (2012) Open clinical trial data for all? A view from regulators. *PLoS Med* 9(4): e1001202.

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		requests for re-analysis of clinical-trials data should be subject to the same level of "proportionate review" 25 to avoid a "double standard"26 between the original data sponsor and subsequent requesting parties. This is because the potential consequences of granting the data request are much less severe than the consequences of granting a market authorisation: An inappropriate market authorisation exposes millions of patients to a potentially harmful medical product. A poorly conducted re-analysis results in a poor quality paper that will be read and assessed on its merits by the scientific community and subject to academic debate. Though bad analysis should still be avoided, we think the safeguards recommended by the EMA take the right approach by encouraging high-quality analysis. We do not believe the public would benefit if the EMA were to restrict scientific debate by imposing a pre-approval requirement on requests for data.	
160	General	e. Informed Consent Policy 0070 requires data requesters to agree that analysis will be conducted "in the interest of public health, in line with the spirit of informed consent (line 183)." We agree that requesters should be required to declare their goals in requesting data and that these goals should be in the interest of public health. Such a requirement is appropriate in that it furthers the public health objective of the policy and helps to ensure transparency. We think this requirement will be easily satisfied by requesters seeking to engage in the type of research envisioned under the policy.	

[25] European Medicines Agency. Comments on Policy 0070 submitted by the EFPIA. September 5, 2013. http://www.efpia.eu/uploads/EFPIA_comments_on_EMA_draft_policy_access_to_CT_data_FINAL.pdf. Accessed September 30, 2013.
[26] Advice to the European Medicines Agency on rules of engagement for accessing clinical trial data. April 4, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142859.pdf. Accessed September 30, 2013.

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		However, we believe it is unnecessary and misleading to suggest that informed consent may be satisfied "in spirit." Informed consent must always be obtained prospectively, and it is generally not possible to obtain informed consent for post-hoc data re-analysis, as such analysis is designed and implemented after the research subjects have already agreed to and completed participation in the trial. In the U.S., informed consent is not required for research that involves only de-identified data sets, as such research is not considered "human subjects" research.27 Under this approach, informed consent is not required. Yet the draft policy suggests that informed consent is required even for de-identified data and that this requirement could be satisfied by requests made in line with the "spirit" of informed consent. We do not think this is the correct approach to informed consent and believe that the phrase should be eliminated to avoid confusion.	
160	General	f. Policy 0070 Should Not Restrict Access to Requesters "Established in the EU" The proposed policy 0070 currently requires that requesters of patient-level data be "established in the EU" (line 180).28 We request that this requirement be eliminated, as we believe it to hinder the public health objectives of the policy. Highly qualified researchers exist in the U.S., Canada, Japan, Australia, and other countries, and EU members are therefore likely to benefit from research conducted and published in foreign states. Foreign researchers are no more likely to violate patient privacy than researchers established in the EU. Moreover, it is unfair to restrict access to	

[27] OHRP – Guidance on research involving coded private information or biological specimens. October 16, 2008. http://www.hhs.gov/ohrp/policy/cdebiol.html. Accessed September 30, 2013.
[28] European Medicines Agency. Publication and access to clinical-trial data POLICY/0070. June 24, 2013. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf. Accessed September 30, 2013.

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		data to foreign populations when data supporting EU market authorization is often obtained through trials conducted outside of Europe. In addition, researchers based in the EU may wish to work in collaborative teams with foreign researchers, and it is not clear that such collaboration would be possible if all members of the team would be required to "individually commit themselves to the conditions for access," as required by the draft policy (lines 196-197). We therefore ask to eliminate the requirement that requesters be "established in the EU."	
160	General	3. Conclusion We support policy 0070 because it will enable independent re-analysis of the benefits and risks of EMA-approved drugs through the publication of full clinical trial reports and, where appropriate, patient-level data. Transparency and the opportunity for independent review are cornerstones of both sound medical research and good regulatory decision-making in a democratic society. We believe that draft policy 0070 will benefit the public health by promoting greater transparency while adequately protecting important privacy and commercial interests. Our chief suggestion is that the policy be modified to remove the requirement that requesters of patient-level data be based in Europe. This requirement does not serve an important public health purpose and will unnecessarily restrict access to clinical-trial data.	
160	138-218	The current language fails to make clear which types of de-identified patient data will be made available open access (Category 2), and which will require a data sharing agreement (Category 3). We think the policy should clarify to	One way to make this section clearer would be to define what it means for data to be "adequately de-identified" under Category 2 (line 143), and how this

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		require a data sharing agreement in cases where such an agreement is necessary to prevent re-identification.	differs from “appropriate de-identification” under Category 3 (lines 165-175).
160	174-175	There appears to be a typo in this sentence.	The methods of de-identification should be such that adherence will preclude subject r~~d~~e-identification, even when applying linkages with other data carriers (e.g. social media).
160	180, 196-197	The current language inappropriately restricts access to requesters “established in the EU.” We suggest that this provision be eliminated. If it is not eliminated, we recommend that the EMA craft language clarifying that an EU requester may share the data with other members of a research team even if all members of the team cannot individually commit to the requirement of being “established in the EU.”	• requester has identified themselves, and the Agency has verified the identity of the requester; ~~• requester, whether a natural or legal person, is established in the EU;~~ • requester has agreed, by way of legally binding data-sharing agreement, to:
160	182-187	We support requiring data requesters to agree to access the data for a purpose of addressing a question or conducting analyses that are in the interest of public health. However, we disagree that language should be included suggesting that requirements of informed consent may be met by taking actions “in line with the spirit of informed consent.” We propose removing this language.	access controlled data for the sole purpose of addressing a question or conducting analyses that are in the interest of public health~~, in line with the spirit of informed consent~~; this may include, inter-alia, meta-analyses, re-analysis, or exploratory analyses for additional hypothesis generation. An exhaustive and detailed list of the aims of accessing the data shall be submitted at the time of the request (though not necessarily a statistical analysis plan; see below),
161	General	The Danish Health & Medicines Authority welcomes the initiative on bringing about transparency in the data and results from clinical trials (CTs) on which regulatory decisions are based, and we thank you for this opportunity to comment on the proposal. We fully subscribe to the need for transparency in	

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		regulatory matters, and we agree that this should be reached through striking a balance between, on the one hand, the wish to give the public a reasonable access to data, and, on the other hand, the need for granting data relating to the pharmaceutical industry an appropriate level of protection. We are in general positive towards the underlying intentions of the draft policy. We do however have some concerns which we would like to elaborate: General The proposed policy will govern an overwhelming amount of data, and, as matters stand, the consequences of the policy are difficult to fully gauge. An impact assessment that sheds light on whether the policy will have the intended benefits for the scientific community and the public at large, and how the pharmaceutical industry will be affected by the policy, in Europe and globally, would be beneficial in our view. The responsibility for disclosing personal data In our opinion the responsibility for not disclosing personal data should not be delegated to the sponsor, if that is indeed the meaning of line 278. The responsibility always lies with the data controller, i.e. the EMA, and this entails that the EMA will need to go through the vast amount of data to be disclosed in order to assess whether parts of the data could directly or indirectly identify a person. Lack of clarity regarding personal data Our initial understanding of the draft policy was that no sensitive or	

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		confidential personal data would be disclosed as raw clinical data containing patient information would be appropriately de-identified. However, we find there to be significant lack of clarity on this issue as the draft uses the term 'ppd concerns'. If data is appropriately de-identified, there should be no personal data concerns. However, if data can be traced back to individuals, the de-identification has not been carried out appropriately, and as a result there is no de-identification and data can only be disclosed under the principles of directive 95/46/EC on the protection of personal data. In such case, it would also be an issue whether the clinical trials subjects, upon signing up for participation in the clinical trial, received appropriate information about the possibility of their data being disclosed. Thus, the impact on patient rights is unclear. Submission of de-identified documents We find it unclear on which legal basis the marketing-authorisation holder can be required to submit de-identified documents as proposed in line 255. Controlled Access We also have some comments on the practical arrangements of controlled access. How will compliance be monitored and how will any deviation from the conditions of controlled access be enforced, and on which legal basis? More specifically our concerns include but are not limited to: · How will the identity of the requester be confirmed? · How will it be confirmed that the requester is based in the EU? · How will it be monitored that the requester refrains from any attempt to retroactively identify patients? And what consequences, and on which	

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		legal basis, will non-compliance have? · How will it be monitored that the requester refrains from using CT data accessed for any purposes that are deemed outside the boundaries of patients' informed consent? And why is this relevant if data is appropriately de-identified? · How will it be monitored and enforced that the requester refrains from using CT data accessed to gain a marketing authorisation in a non-EU jurisdiction? · How will it be enforced that the requester does not share, in any way or format, CT data accessed from the Agency with anyone else; where research groups wish to collectively access a data set, the names of all members of the group shall be communicated to the Agency, and all members will have to individually commit themselves to the conditions for access? · How will it be enforced that data accessed is destroyed upon completion of the analysis? The impact of controlled access on resources In our view it seems that the implementation of the proposal will be rather resource demanding. Our concerns about resources are enhanced by our view that the final responsibility for disclosing personal data against the principles of the EU directive cannot be delegated to the marketing-authorisation holder. Does the EMA have an estimate on the consumption of resources if the proposal is adopted? We look forward to discussing further this important issue with EMA and the	

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		other stakeholders in the area and trying to find a solution that supports transparency in this field.	
162	102-106	The statement "P*ersonal data (PD)*: shall mean any information relating to an identified or identifiable natural person ('data subject')" not fully defined in the context of clinical trials	it would be helpful to define more specifically that personal data includes all information related to the person, not just personally identifiable data, eg, lab results, other test results, radiography, etc (or if that's not what's intended, define what is intended)
162	172	The article proposed as setting a minimum standard for deidentification (Hrynaszkiewicz et al. Preparing raw clinical data for publication: guidance for journal editors, authors, and peer reviewers. BMJ 340: c181; http://www.bmj.com/content/340/bmj.c181) raises some potential issues with transparency of altering the dataset and ethical oversight, described below:	
162		The article states, "In circumstances where it is essential for the scientific validity of the study to include dates, such as dates of treatment (a direct identifier), data must be presented in such a way that is unlikely to affect statistical analyses but preserves anonymity. For example, one could add or subtract a small, randomly chosen number of days to all dates, so that the true dates are not published. In cases where it is necessary to include dates, this fact and any supporting information should be disclosed on submission to the journal."	The article refers to disclosing "this fact" but it is unclear to what this fact refers. If dates or any other data have been systematically altered, the researchers must indicate that such alteration has taken place (with specifics as to the specific alterations, of course).
162		The article states, "The consensus of the authors, and working group members acknowledged in the current manuscript, is that a dataset including three or more indirect identifiers should be assessed by an independent researcher or ethics committee to evaluate the risk that individuals might be identifiable. If the risk of identification is considered	Indirect identifiers listed in the article include age, sex, and race, three commonly included variables in datasets. Clarification as to whether all such datasets should have independent review or ethical approval for release would be important, for researchers and for

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		non-negligible, before publication can proceed approval should be sought from a relevant advisory body (see below). An explicit justification for publication of a dataset with three or more indirect identifiers should be given by the researcher—as an annotation to the dataset and in any accompanying articles. This should include the name of any oversight bodies consulted."	journal editors.
162		The article states, "Participants who do not agree to publication of potentially identifying information may need to be removed from the dataset."	Researchers should indicate the number of individuals' datasets that were removed because of lack of consent.
163	General	Public consultations are more effective when it is possible not only to make a submission oneself but also to comment on submissions from others. This submission is therefore partly in the form of a comment on the submission from EFPIA. I agree with EFPIA that "the regulator's core function is to ensure the validity and robustness of the clinical trial process", and I believe that the approach proposed by EMA is appropriate to the fulfilment of that core function. Sharing of clinical trial data, including sharing with other companies, will over time: • Contribute to the improvement of science and medicine, • Raise standards for clinical trials in terms of design (ex-ante), execution and, in terms of science and clinical practice, the exploitation of the results. • Help to reduce the needless repetition of clinical trials and therefore reduce potential harm to trial subjects.	

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		• Improve scrutiny and performance of regulators. While acknowledging that sharing of CT data with “independent” researchers may be useful, EFPIA seem particularly opposed to the sharing of such data with competitors. This position seems to imply a low opinion of their own industry – an assumption that competitors’ use of data will not drive science forward but will rather be abused for narrow commercial gain. All industry research is driven by the prospect of commercial gain. The industry would argue that such research contributes to the advancement of science; I submit that science will be advanced if CT data is accessible to competitors, and others, to the extent envisaged by the EMA. Indeed it would be wildly unrealistic to expect that much CT data could be subject to robust scrutiny by independent researchers alone. Competition can be beneficial, not only in economic terms but also in terms of science and ideas. A wider disclosure, including disclosure to competitors, may also have important clinical benefits. Trials may show that that a medicine is safe but also that there are limits to its efficacy – for example that it just does not work very well for some groups of patients. This is important clinical information that should be available to all, even if it may be “exploited” by a competitor. Indeed, this is precisely the kind of information that may spur a competitor to try to develop a better product, and thus contribute to the greater public good. The industry argues that more disclosure would discourage investment in research. If the effect of transparency were to reduce needed investment in research, this would certainly give pause for thought but I submit this will not be the case. There may be some reduction in investment, for example in the needless repetition of certain but this would be a good thing, since it	

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		would avoid exposing new trial subjects to potential risk. The core industry argument however, is that companies would simply not carry out many trials at all if they thought that they would have to share the results. This is to place far too much importance on secrecy in relation to CT data as a factor in protecting the legitimate economic interests of a pharmaceutical company. Companies have many legitimate weapons in their armoury to this end, including patents and other IP rights, manufacturing secrets, first mover advantage etc. Furthermore, the disclosure envisaged by the EMA is, with a few exceptions, to occur only after the granting of an MA. The EMA also, and rightly in my view, envisages access in the case of discontinued trials and withdrawn authorisations. It is precisely these trials that are most often hidden under a cloak of secrecy and they may often be of high scientific value. The fact that they sometimes may not show the sponsor's products in the best light does not detract from their scientific or clinical value. Furthermore disclosure will avoid the repetition of the same trials on new subjects, thus reducing potential harm. This is specially the case for trials that have been discontinued for adverse outcomes – such trials should never be repeated. The industry have argued in their submission and elsewhere that their property rights may be infringed by the kind of disclosure envisaged by the EMA. I can see some merit in this argument as applied to, say, mobile phone manufacturers but medicines and clinical trials are a special case. Clinical trials are licenses to experiment on human beings, albeit with their consent. Without an official authorisation, many clinical trials would amount to common assault, even with the consent of the subjects. It is right and in the public interest that clinical trials be authorised in proper cases, but the public interest must be paramount. In that context, it is not in the public	

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		interest that a company can simply claim that clinical trial results are “mine, mine, mine”. Such a claim is to ignore the fact that trials require official autorisation, that they subject human beings to some degree of potential harm, and that they are allowed at all only in the hope that they will serve an important public interest. Medicines are not mobile phones. The industry propose a number of procedural obstacles, such as requiring the EMA itself to produce a “de-identified” version of data, to consult with CT sponsors at length and at different stages before disclosure etc. This would have the practical effect of delaying disclosure for an inordinate time or even preventing disclosure at all, to the detriment of science and public health. Given the EMA’S core function of ensuring the validity and robustness of the clinical trial process the agency is perfectly entitled to require that CT data be submitted in a form that would facilitate disclosure in proper cases and ease the process of distinguishing between disclosable and non-disclosable information. The views of the CT sponsor as to what is and what is not CCI can also be canvassed at this stage. The agency should then proceed on the basis of a clear and well-founded set of transparency principles. The transparency principles must be founded on relevant EU law and, as it may be, case law but without having to check back and await the views of the sponsor at each stage. Sponsors who feel aggrieved have always the option of judicial review but the prospect, if there is such a prospect, of numerous spoiling actions from industry should not be a deterrent to moving forward towards the desired and appropriate level of transparency. In its overall transparency policy the EMA may properly, and in my opinion should, take account of the immense internal pressures that can exist within	

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		companies to conceal, manipulate or delay the release of CT data. Some cases of disclosure may cause great economic damage to a company, and in such cases the temptation to find reasons for non-disclosure or to give undue weight to arguments against disclosure may be overwhelming. We have seen numerous examples of this, including in the fines and penalties levied, mainly in the US, on many prominent companies in recent years. This is not to denigrate everyone in the pharmaceutical industry but simply to point out that some very bad things have happened at times; such facts must be taken into account and given due weight by a prudent regulator. The Industry Code Finally, industry have put forward their own Code or principles of transparency, as an alternative to what the EMA has in mind. There are many reasons why this initiative may be disregarded, including the following: 1. The Code contains no effective sanction for any company that does not implement it, even a company that does not even pretend to implement it, apart perhaps from the publication of that company's name after a lengthy intra-industry procedure and finding by the company's national association. 2. The Code leaves far too much, indeed almost total, discretion to an individual company to decide for itself how much or how little data to disclose and to whom, subject only to a review body set up by that company itself. In support of this point I put in evidence the intervention by Mr Neal Parker of AbbVie at a meeting in Brussels on 27th August, which may be found at: http://www.youtube.com/watch?v=54OY1auPQgU&list=PLBLfw2LH5apfj6gljc	

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		O8XV3bmo9QhlXOu I attach at the end of this submission the slide to which Mr Parker refers in his intervention. 3. The proposal to limit data sharing to “independent” researchers would not contribute in any substantial way to the advancement of science and public health because the number of such researchers able and willing to take on the task, or indeed with the capacity to challenge a company’s refusal, is tiny in comparison to the totality of CT trials. (This is to leave aside the fact that the company will decide who is and who is not “independent” in any given case. For example, will a company accept as independent an institute that has done research for a competitor in the same field in recent times?) 4. As implied above there are cases where a company will have huge incentives not to disclose certain data that should be disclosed. A voluntary code is no proof against such incentives.	
164	General	The European Consumers Organization (BEUC) welcomes and fully supports the EMA draft policy 70 concerning the publication and the access to clinical trials data held by the Agency. BEUC also welcomes all the efforts made by the Agency over the last years to improve transparency and to better communicate and engage with the general public (e.g. involvement of patients and consumers organizations, public consultations, stakeholders meetings etc.). BEUC was pleased to be involved in the advisory groups organized by the Agency between January and April 2013 in view of the development of the draft policy despite the discussions were often dominated by representatives of the pharmaceutical industry and focused on legal details rather than on public health	

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		arguments. The development of the draft policy has been and will be influenced by two processes currently ongoing, namely the pending cases before the European Court of Justice brought against EMA by the pharmaceutical companies AbbVie and InterMune and the revision of the EU legislation on clinical trials. AbbVie and InterMune challenged in Court the Agency's decisions to grant access to non-clinical and clinical information submitted by companies as part of marketing-authorisation applications in accordance with its 2010 access to documents policy. Unfortunately this already had a negative impact on EMA work on transparency as the President of the General Court ordered the Agency not to release the concerned documents until the final judgment. In September 2013 the European Court of Justice granted BEUC leave to intervene in the cases and we are determined to lend EMA all our support to ensure the transparency policy is upheld and reinforced in the interest of public health. The Commission Proposal for a Regulation on clinical trials published in 2012 is being debated between the EU institutions and so far the European Parliament (ENVI Committee) supported the European Medicines Agency approach on the publication of clinical trials data, stating that "*in general the data included in clinical-trial study reports should not be considered commercially confidential once a marketing authorisation has been granted or the decision-making process on an application for marketing authorisation has been completed"*. Moreover the ENVI Committee highlighted that "*the Agency continues to extend its transparency policy to proactive publication of clinical trial data for medicinal products once the decision-making process on an application for a Union-wide marketing authorization has been*	

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		completed. Those standards on transparency and access to documents should be upheld and reinforced"[29]*.*	
164	*Lines 13-75*	Openness and transparency are pivotal elements in building public trust and confidence in the European Medicines Agency operations and in addition they fulfill the right of all EMA stakeholders for impartial and comprehensible information about the medicines regulated by the Agency and their use for the benefit of public health. The EMA draft policy 70 on publication and access to clinical trials data provides more clarity on how the Agency conceives its responsibility as a public body in the field of medicines regulation. Moreover, the policy should be considered as an important step to fulfill EMA obligation to be accountable towards those who are most affected by its decisions, namely the users of medicines. Recent scandals like the one linked to the weight loss drug Mediator undermined consumers' confidence in regulators and it is urgent to restore trust. Granting access to clinical trials data is a necessary tool to restore trust in the work of medicines regulatory agencies and ultimately in the safety of the medicines on the market. Consumers, as users and potential users of prescription and non-prescription medicines and also as carers, want to be more and more involved in the decisions regarding their health. Information about medicines is essential to empower consumers and to help them make an informed choice about their	

[29] European Parliament ENVI Committee "Report on the proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (COM(2012)0369 – C7-0194/2012 – 2012/0192(COD)). 10 June 2013. http://www.europarl.europa.eu/sides/getDoc.do?type=REPORT&mode=XML&reference=A7-2013-208&language=EN

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		treatments. Granting public access to clinical studies reports, EPARs and other associated documents is useful both for “expert’ and “non-expert” patients. “Expert patients” such as those affected by chronic conditions have become in certain cases as knowledgeable as their physicians with regard to their own disease and they gained the skills to digest highly technical and scientific information: those patients want and have the right to have access to all relevant information that can help them to have a better understanding of their treatment options. “Non-experts” patients mostly rely on the information provided to them by health care professionals and nowadays also by less reliable sources for example on the internet. To ensure the consistency and the quality of the information that ultimately reaches the patient and the integrity of the information flow it is necessary that the original information is made public from an authoritative and independent source, which in this case is EMA. Overall, all citizens have the right to access information which can have a substantial impact on their health. Lines 57-61 refer to the consequences of potential inappropriate secondary data analysis. At present there is no evidence about the risks of health scares or other problems resulting from the publication of clinical trials data. On the contrary, there is significant evidence on the risk of non-disclosure. Recent medicines scandals like rofecoxib (Vioxx°) or rimonabant (Acomplia°), etc.) could have been prevented if public access to clinical data had been granted. Disclosing key information allows for timely and independent scrutiny by the scientific community and public scrutiny of regulatory decisions. Secondary independent analysis is needed to ensure	

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		that regulators do not exclusively rely on the manufacturer own analysis of their products benefit-harm balance30. At present only half of clinical trials results are published and some trials are not even registered. Information on what was done and what was found in these trials could be lost forever to doctors and researchers, leading to bad treatment decisions, missed opportunities for evidence based medicine and trials being repeated. Clinical trials' results belong to the volunteers who take part to clinical trials put their life at risk of unexpected adverse drug reactions and they do so in the spirit of altruism and for the benefit of society therefore the results of the trials belong to them and to society at large31. Data collected in clinical trials are useful and relevant not only for the purpose of a marketing authorisation and they can be helpful for the scientific progress providing insights on the diseases, on patients' behaviour and clinical practice etc. Others than those who sell the medicine tested in the trial can benefit of the information.	
164	*Lines 77-88*	Consumers have the right to access clinical trials data for all medicines on the market, both if they have been authorized via a centralized and a decentralized procedure. Different policies on publication and access to clinical trials data by medicines regulators are not justified and justifiable provided they all have an obligation to be open and transparent and they all have the same mandate and goals. While we understand that this goes	

[30] Wieseler B et al. (Institute for Quality and Efficiency in Health Care) "Access to regulatory data from the European Medicines Agency: the times they are a-changing" Systematic Reviews 2012, 1:50 doi:10.1186/2046-4053-1-50

[31] Lemmens T and Telfer C "Access to Information and the Right to Health: The Human Rights Case for Clinical Trials Transparency" (September 22, 2011). *American Journal of Law and Medicine* 2012; 38 : 63-112. http://ssrn.com/abstract=1932436

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		beyond EMA competences we believe that ensure coherency and avoid discrepancies the draft policy should be consistently applied by all medicines agency across the EU. As it stands, the draft policy only applies to clinical trials data that are submitted to the Agency after it enters into force, i.e. as of 1st of January 2014. BEUC is of the view that scope of the policy should be extended as to cover progressively also clinical trials data concerning medicines that are already on the market. The Agency should be provided with adequate resources to perform these tasks.	
164	*Lines 50-51* *Lines 109-105*	BEUC firmly agrees with the principle that clinical trials data cannot be consider commercially confidential information and that the interest of public health override considerations of commercial confidentiality. This principle is in line with the European Ombudsman assessment of two cases[32] related to the disclosure of data by EMA and with the report voted in June 2013 by the European Parliament ENVI committee (see above). Clinical trials data cannot be considered trade secrets, nor they can be compared to cars' prototypes[33], as they are generated "using" human beings, volunteers who put their life at risk for medical progress and for the benefit of humanity. The definition of Commercially Confidential Information should be further narrowed down as to prevent extensive and abusive interpretations by the	

[32] European Ombudsman. Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency (November 24, 2010).
European Ombudsman. Decision of the European Ombudsman closing his inquiry into complaint 3106/2007/(TS)FOR against the European Medicines Agency (December 14, 2011)

[33] Clinical trials data is not a public good, EFPIA, September 2013 http://www.efpia.eu/blog/93/51/Clinical-trial-data-is-not-a-public-good

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		trial sponsor that could for example consider commercially confidential information on adverse drug reactions[34].	
164	Line 47	The wording "*any other use of patient data oversteps the boundaries of patients' informed consent*" is too vague and subject to interpretations. It should be clarified bearing in mind that those who participate in clinical trials do so for the benefit of medical progress and humanity. Those taking part in a trial should do so in full conscience and only if they gave a truly informed consent. However informed consent forms should not be drafted by sponsors in such a way that they would make secondary analysis impossible.	
164	*Lines 125-127*	Overall BEUC supports the classification of clinical trials data in three categories (Category 1: commercially confidential information; Category 2: open access information; and Category 3: controlled access' information) and the general principle that information is deemed commercially confidential only if this is duly justified.	
164	**Category 1**	The paragraph regarding data classified as Category 1 should be better aligned with point 4.6 of Regulation No 1049/2001 according to which "*If only parts of the requested document are covered by any of the exceptions, the remaining parts of the document shall be released.*" The exception to the disclosure should not be applied to an entire category of documents and should only cover the information classified as CCI.	
164	**Category 2**	All information made available online should be in a presented in a reader/user friendly and searchable format. Researchers, health care	

[34] AbbVie representative, August 2013 http://www.youtube.com/watch?v=54OY1auPQqU&feature=youtu.be&t=11m30s

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	Lines 150 - 154	professionals and members of the general public should be involved (e.g. via the EMA health care professionals and the patients and consumers working parties)in a user testing exercise/pilot to define the final format of the information.	
164	**Category 3** *Lines 159 - 164* *Line 198* *Lines 256-261*	Also for BEUC the protection of consumer privacy is a "paramount concern" when sharing raw clinical trials data. "C" data shall be anonymised or pseudonymised to the highest possible standards, and all possible measures shall be taken to prevent re-identification of the data subjects. In the light of this we welcome the two complementing levels of protection described in the draft policy to "provide best-possible assurance against retroactive patient identification". The requester of "controlled access data" is required to obtain the approval of an ethics committee "as appropriate". BEUC welcomes this provision however further clarifications are needs with regard to the meaning of the wording "as appropriate". Consumers' organizations should be involved in the drafting of the guidance document on the release of "C" information.	
165	General	**Patient identification** In many sections of the document, it is mentioned that the data should be anonymised (e.g. do not contain date of birth…), that some sections of some documents could be CCI, such as sections containing PK results. The following should be clarified: -all the mentioned documents (clinical study reports, overview and summary) are part of CTD that has to be submitted in full to the Agency. Some issues can be anticipated in the documents (such as no date of birth in	

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	242 259-261	individual patient data) but this means that, for other data, in the purpose of the transparency policy, these documents would have to be later modified in some sections to put some anonymisation, to replace some sections in the document by the mention CCI section before it could be released to the public/third party…. How does the Agency plan to manage such important issues in final version of documents provided as pdf. -for example, what is planned in the context of phase II or III studies including PK results where the ICHE3 synopsis and the body of the clinical study report include a summary of these PK results? Please define “technically possible” in order to comply. A guidance document including rules and procedures for de-identification should be produced, but our understanding is that it will be published 10 months after the policy becomes effective, whereas it should be available BEFORE.	
165	General	**Request for Access to multiple studies from different MAH** The procedure to access raw data from multiple studies and multiple MAH in the perspective of meta-analysis should be clarified for raw individual data access to individual CT (one MAH is concerned) and multiple CTs (several MAH should be concerned). For a perspective of network meta-analyses, data centralisation is required.	
165	95-97	Pharmacoepidemiological studies on external datasets may be performed via payable access under agreement. The free publication of these data will be a concern from a contractual and legal point of view with respect to the owner	

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		of the datasets. Furthermore, in practice, this kind of studies usually does not follow the same standards as conventional controlled trials ; so, formatting them to the same CDISC model - as specified line 245 - will represent additional time and cost for pharmaceutical companies	
165	118-123	Interest of individual patient line-listings and CRFs if individual data sets are provided?	
165	125	Categories of CT data: these categories should be refined by taking into account the nature of the CT data (individual/raw or aggregated data). For example, the clinical study report cannot be simply allocated to category 1, 2, or 3. The body of the clinical study report contains mainly aggregated data whereas annex 16.2 and 16.4 (if applicable) contain individual patient data.	
165	244-247	Requested format for de-identified raw Clinical Trials data should be further specified since Clinical Data Interchange Standards Consortium (CDISC) is not precise enough. CDISC is not a standard by itself, but provides multiple standards. Please define which standards are expected.	
166	General	Novo Nordisk response to EMA re. its draft policy on publication and access to clinical trial data As a proponent of transparency in clinical research, Novo Nordisk welcomes the opportunity to comment on EMA's Draft Policy 70 on Publication and access to clinical-trial data. NN supports and has contributed to the consultation response submitted by	

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		EFPIA on behalf of the research-based pharmaceutical industry on 5 September 2013. In addition to stating our overall support of EFPIA's response, including the principles surrounding the protection of personal data and respect for the boundaries of patients' informed consent, Novo Nordisk would like to underline three additional viewpoints of our company, as follows: **1. Company publication of clinical study reports** Novo Nordisk welcomes EMA's commitment to address the important issue of responsible disclosure of clinical trial data. We encourage EMA to take into consideration the practices on data disclosure that already exist and function well in many pharmaceutical companies such as Novo Nordisk. We also urge EMA to examine the new initiatives on data sharing and disclosure that we are currently developing. These aim to ensure that data disclosure will meet the interests of patients, regulators and industry while promoting science and overall public health. As such, we recommend for EMA to consider Novo Nordisk's approach as a possible future framework. Novo Nordisk has a long-standing record of systematically sharing and publishing clinical trial results and related data regardless of study outcomes. We share results from our trials on Clinicaltrials.gov, NovoNordisk-Trials.com and also in scientific publications and symposia, subject to acceptance by respective governing bodies. Moreover, completed trials investigating the use of a drug, are included in the registration package for the respective therapeutic use, and the results are included in the summaries of the trial program in the European public assessment reports (EPAR), in FDA and advisory committee briefing documents, and in the drug approval packages on Drugs@FDA. These information packages are	

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		all made publicly available by the regulatory authorities. Further extending these existing practices and subject to compliance with current legal frameworks concerning information to the public on prescription drugs in the EU and United States, Novo Nordisk is planning to launch a new system through which we will make available the ICH-defined Clinical Study Reports (CSR) in addition to the other information we already make public. Novo Nordisk finds that systematically publishing all CSRs following approval is the most relevant way of making clinical trial information available to the public. The CSR is a document prepared for and used by the regulatory authorities according to ICH guidelines and is therefore, the best document to demonstrate completeness, representativeness, and comparability, thus pre-empting any concerns of selective or biased communication of data. We intend to publish the CSRs without appendices so as to avoid disclosure of information that can be traced back to individuals or individual research sites, such as lists of investigators, individual demographic data and adverse event listings by patient, etc. which may potentially compromise personal data protection. For the same reason, the content of the CSRs will also be redacted to remove any person- or site-identifiable information before publication in the interest of personal data protection. Further information will only be removed from the CSRs if considered commercially confidential or if essential for protecting intellectual property rights. Regarding commercial confidential information, please see point 2 below. In terms of timelines, the CSRs from trials included in the marketing	

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		authorisation application leading toan approved use of the compound are intended to be published 30 days after approval in the EU and the United States or 12 months after study finalisation (to allow for scientific publications), whichever date comes last. Summary reports from discontinued development projects will be published within 12 months of the public announcement of discontinuation. With this background, we suggest that EMA assesses the objectives behind the draft EMA Policy against these intended actions. **2. Redaction of commercial confidential information** Novo Nordisk opposes EMA's proposed classification of individual sections of the submitted CSRs and appendices, which in some cases classifies company sensitive data as Open Access or Controlled Access, and the notion that not much information will be considered as Commercially Confidential after marketing authorisation. We find that CSRs indeed contain limited information for which disclosure may undermine the legitimate economic interest of the owner of the information, including trade secrets and commercial confidences, i.e. commercial confidential information, even after marketing authorisation. In this respect, Novo Nordisk is concerned about the possible disclosure of detailed strategic and operational information revealing general company know-how about the efficient and competitive set-up of clinical studies, such as trial site performance, that is included in the CSRs and other materials submitted as part of the marketing authorisation applications. We strongly believe that our competitiveness in clinical development could be compromised, to the detriment of innovation, if this information could be readily accessed by competitor companies. In particular, the above applies	

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		to manufacturing data included in the introduction and discussion sections, as well as to parts of section 14 (subject data listings) regarding trial sites. Insight into these strategic decisions and considerations are valuable, as disclosure of such information could provide competitors with a roadmap to facilitate their own product development programs. Furthermore, such information, e.g. data on trial site performance, is arguably not of direct interest or relevance to the public or to third party analyses of clinical trial data sets and, therefore, can be legitimately redacted from the CSRs prior to public disclosure without compromising the intent of the transparency measures. In light of the fact that CSRs and other information submitted as part of the marketing authorisation applications can, in fact, contain commercially-sensitive information, Novo Nordisk believes that companies must be given the option to redact any such sensitive information when it is not directly related to the study results or the clinical interpretation of study results before public disclosure. In this context it should be noted that Novo Nordisk considers that study results in the CSRs do not represent commercially-confidential information once marketing authorisation/ approval has been obtained. **3. Further data access for scientific researchers conducting secondary analyses** Novo Nordisk agrees with EMA that the main objective of the clinical trial data sharing is to advance scientific understanding and, potentially, benefit patient care. However, we are concerned, along with EFPIA, about the potential personal, commercial and public health implications of EMA's	

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		proposed procedure for granting third parties access to Controlled Access data, which does not sufficiently safeguard the protection of personal data, commercial confidential data (see above point) or the scientific integrity of the secondary analyses of proprietary data. Nor would EMA have sufficient control over third parties use and dissemination of the data including attempts to identify study subjects and commercial use. Moreover, the proposed procedure lacks transparency, as access will be granted without any communication of the decision until 12 months later. We do recognise the challenge in setting up a system that will allow access to data with the purpose of furthering science and serve public health while ensuring the necessary safeguards. Therefore, Novo Nordisk, along with a number of other companies, is working to set-up an alternative system that in a scientifically valid and company-independent form will allow scientific researchers to test pre-defined hypotheses using raw data sets. The system will work to ensure that the proposed secondary analyses have a legitimate scientific purpose and are conducted by qualified researchers, and are intent of serving the interests of public health. In order to conduct the necessary quality controls of secondary analyses, Novo Nordisk advocates, along with EFPIA, the appointment of an independent review board responsible for receiving and reviewing research proposals. As part of this policy we are working to establish: • A detailed and transparent process for qualified researchers to obtain access to trial raw data-sets based on a scientific hypothesis and an analysis plan made by such researchers. • An independent review board to ensure that strong scientific rationale and methods are reflected in the research applications as a condition of	

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		approval. This Board will include independent subject matter experts. • Guidelines on good scientific practice designed to increase the likelihood of scientific integrity of secondary research analyses of clinical trial data. • A uniform approach to de-identification of patient, research site and other sensitive information that is sophisticated and flexible enough to adapt to any new data mining tools that may be developed. • Standards for publication of data that will allow for 'big data' aggregation via uniform meta-data levels, terminology and comparative trial methodologies, etc. • Two-way transparency by establishing a system for ensuring legitimate use of information and publication of findings, irrespective of outcomes. Therefore again, we request that EMA assesses the objectives behind the draft EMA Policy against these already on-going actions.	
167	General	It is appreciated that this policy paper will only apply to new CTs after this policy comes into effect and not retrospectively. 1. The ENCePP Survey of EU Member States national legal requirements on data protection (EMA/420313/2013) of 10 July 2013 should be taken into consideration. 2. Building trust is a key factor in recruitment of patients for clinical trials. Personal data protection plays a central role in clinical trials. Article 16(1) of Treaty on the Functioning of the European Union (TFEU) as introduced in the Lisbon Treaty establishes the principle that everyone has the right to the protection of personal data concerning him or her.	

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		3. The current proposal does not sufficiently account for response to challenges posed by development of new technologies for back-identification of involved individuals. This in particular refers to orphan indications where the number of subjects with a particular disease are scarce (per definition of an orphan disease). 4. The EU CT Database and the published EPARs are already existing tools of transparency to the public. Furthermore the ENCePP Register of Studies aims to provide publicly accessible ressource for pharmacovigilance and pharmacoepidemiological studies in Europe and should prevent unnecessesary duplication of research. While only ENCePP studies are mandatory, all other studies might be entered voluntarily. 5. This proposal does not address the risk of decreasing European competiveness, reduction of investments into EU CTs bringing European patients at risk when less data within the European population is generated. 6. The policy of increased transparency and information of CT should not open the door for general publication of data within a MA (scientific discussion and summary is already included in EPARs). EMA should not disclose CT data prior to granting a MA (positive opinion / Licence). 7. Furthermore the possibility of transfer of data from the EU to other parts of the world should be considered. Also the use of information by requestors to get non-EU licenses invulges the commercial interest of the originator / sponsor of CT. 8. The interpretation of the measures to protect public health should be	

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		clarified in context with the TRIPS and DOHA Declaration. Transparency of CT from Marketing Authorisations to any requestor could lead to breach of copyright of applicant´s documents. 9. EMA should introduce a system of in-house hearing / meeting with originator – in case of different views of interpretation of commercial confidential information. 10. Transparency is a two way road. Consequently the requester who intends to perform secondary data analysis should be held responsible to come back to the Agency in a reasonable time (e.g. 1 year similar to the sponsor´s responsibility to provide a clinical study report) and present the outcome of his analysis. These results will also be of interest for the MAH and sponsor of the CT. 11. A definition of “data requestor” is missing 12. The same principles should also apply to studies not sponsored by industry.	
167	38	Reference to the European “Regulation on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation)” is recommended.	The policy has to ensure adequate PPD: it must be compliant with applicable regulations in the EU, in particular Regulation (EC) No 45/2001 and Directive 95/46/EC and ***General Data Protection Regulation COM(2012) 11***
167	67	Ensuring that transparency is a two-way street: It is recognized that requesters need time for their secondary analyses and that they should be in the public domain. However there should be a time commitment to the requester, that he has to come back to the Agency with	*Ensuring that transparency is a two-way street*: The Agency takes the view that those who make secondary use of patient-level CT data shall be held to the same standard of transparency as those who generate CT data in the first place; hence, all secondary analyses

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		the results of the additional analysis within 1 year. This is in line with the requirement for sponsors to provide clinical study reports within 1 year after closure of the clinical trial.	shall also be in the public domain and accessible for further scrutiny by the scientific community. However, those who conduct secondary analysis should also be allowed a reasonable period of time during which their analyses and deliberations are protected against external interventions. The sponsor should provide the Agency with results of the secondary analyses within 1 year.
167	88	CT for orphan indications should be outside of the scope of this policy since the limited number of available patients might easily result into identification of individuals which is not in line with the General Data Protection Regulation	Clinical trials for drugs for which orphan designation has been recognized by EMA are outside of the scope of this policy.
167	112	A more clear definition of CCI regarding investigational medicinal products CMC would be appreciated.	CCI falls broadly into two categories: trade secrets (including formulas, developmental programs, ***manufacturing process, analytical data*** ....and commercial confidences.
167	150	Disclosure of CT data relating to the conduct of the clinical trial (e.g. investigators CV and investigational sites) are not deemed necessary for additional analysis of data.--> see also comments on Annex	
167	193	Information on CT is submitted by sponsors as part of an application for granting a Marketing authorisation. Sponsors expect that regulatory Authorities regard the submitted information as confidential part of the License. Article 10 of Directive 2001/83 says" Following the granting of a marketing authorisation, the authorisation holder may allow the use of the pharmaceutical, pre-clinical and clinical documentation contained in the file	

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		on the medicinal product, with a view to examining subsequent applications relating to other medicinal products possessing the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form." 1. With the current proposal the commercial interests of the originator and a co-company are invulged. **2. How will the Agency ensure that the requestor "will refrain from using CT data accessed to gain a marketing authorisation in a non-EU jurisdiction"?**	
167	219	The Agency shall inform the sponsor of a CT or Marketing Authorisation holder of a request for disclosure of C-documents.	
167	222	The Agency will inform the sponsor of the CT and/or the MAH of any request to disclose C documents.	The Agency will inform the sponsor of the CT and/or the MAH of any request to disclose C documents including the details of the requestor, the list of aims and the requester´s statistical analysis plan. The Agency will disclose information about the requestor to the originator / sponsor of the CT. The Agency will not immediately disclose any information about the requester to the public, but will publish the identity (name, affiliates and contact details provided), the list of aims of accessing the data provided, any uploaded documents (statistical analysis plan and/or others), or the requestor´s decision to decline the uploaded documents (as applicable=

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167	285	It is acknowledged that investigators, nurse and other trial staff have a key role in the conduct of the clinical trial. We disagree with the view that investigators are exempted from PPD. Information on clinical staff is not deemed necessary for secondary data analysis by a requester.	
167	Annex II section 16.1.4 and 16.1.5	Information about investigators like CVs should be considered confidential and listed as “C”. This information is deemed not necessary for retrospective secondary data analysis.	16.1.4 and 16.1.5 “C”
167	Annex II section 16.1.6	16.1.6 Listing of patients receiving test drug(s)/investigational product(s) from specific batches, where more than one batch was used should not be classified as “O”, but rather as C” in light of the protection of personal data.	16.1.6. “C”
168	General	I strongly recommend that results of all the clinical trials must be transparent and should be published (irrespective of what the result is).	
169	General	EUROTARGET - European collaborative project on Targeted therapy in renal cell cancer: genetic and tumor-related biomarkers for response and toxicity is a collaborative project supported by the European Union under the Health Cooperation Work programme of the 7th Framework programme (grant agreement number 259939) http://www.eurotargetproject.eu The EUROTARGET project brings together 12 partner organisations (10 research institutes and 2 companies) from 8 European countries. It is coordinated by L.A. Kiemeney, Radboud University Nijmegen Medical Centre (RUNMC), Netherlands. The EUROTARGET project aims to identify and characterize host and tumour related biomarkers and to predict responders and/or adverse responders from non-responders for targeted therapy in	

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		mRCC. The overall concept is to focus on germline genome and tumour transcriptome, methylome and kinome-related biomarkers using a hypothesis free and integrative approach and to evaluate promising findings via replication as well as functional assays. Several Work packages deal with clinical trials and they are thus interested by the public consultation on “publication and access to clinical-trial data”. One work package led by Dr Anne Cambon-Thomsen, Inserm and University of Toulouse III Paul Sabatier, UMR 1027, Toulouse, France is dealing with bioethical aspects and more generally the ethical, legal and social aspects of this project. As part of this work a regular survey of public consultations of relevance for the project is performed. The present Consultation has been signalled, explained and circulated to all members of the project and contributions solicited. The draft answer has been prepared by Velizara Anastasova, jurist in Inserm UMR 1027 in collaboration with other members of the team, especially Aurélie Mahalatchimy and Emmanuelle Rial-Sebbag, jurists, under the supervision of Dr Anne Cambon-Thomsen, MD, research director. A discussion between persons interested was then organised and the attached answer circulated to all participants before submission. EUROTARGET is grateful to the European Medicines Agency to have been given the opportunity to contribute to this consultation.	
169	General	The EMA draft policy on the publication and access to clinical-trial data is a very good initiative in order to establish a uniform and clear frame for the EU members and sponsors. The policy is a very relevant and practical document for stakeholders and European bodies. Moreover, we strongly appreciate the attention paid to the data protection legal frame.	

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169	17- 23	We also appreciate that the EMA is planning to align the present policy with the existing one on access to documents to ensure consistency. Indeed, given the high numbers of EMA guidelines/policies, to link them where appropriate contributes to enhance the clarity of the whole frame.	
169	44-48	During the decision making process, it is necessary to raise patient awareness of the fact that only anonymized data will be shared.	**Please add this aspect in the paragraph about patients' informed consent.**
169	65- 66	The interest of the sentence "Once a decision has been reached, this consideration no longer applies" is unclear. If "this consideration" refers to the previous sentence (i.e. "the decision- making process should be protected against external pressures in whatever direction"), what is meant by permitting external pressures once a decision has been reached? Pressures on whom?	**Please delete or clarify this sentence**
169	69- 70	What is meant by "all secondary analyses shall also be in the public domain and accessible for further scrutiny by the scientific community"? Is publication in scientific journals sufficient or does it involve sending to the EMA for publication on its website and linking to CT primary data?	**Please clarify**
169	76	Please specify whether this policy impacts on the CT data of the EudraCT database.	**CT Data included in EudraCT are outside the scope of this policy as these data are not held by the Agency.**
169	83- 85	This sentence is confusing as it is mixing two different reasons for scope exclusions: 1- Data from CTs that are not held by the Agency, i.e. data from CTs that are not part of the CTD of a product submitted for centralised marketing authorisation or for variation of a centralised marketing authorisation.	**Please delete or clarify this sentence**

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		2- CT data of a medicinal product that has been authorised by the Agency before this policy comes into effect or pre-existing CT data of marketed products that will be submitted to the Agency in the context of a referral procedure. Moreover, the given example ("CTs on an authorised product […] not submitted to the Agency") is even more confusing as it seems it illustrates the second part of the sentence ("a medicinal product that has been authorised by the Agency", i. e. the second reason for exclusion), whereas it refers to the first part of the sentence (i.e. the first reason for exclusion)	
169	102- 106	Definition of personal data. It shall be taken into account that the directive 95/46/CE which includes the definition of personal data is under revision and that the proposed definition may change.	**It should be added a sentence such as: The definition of article 2 (a) of regulation (EC) n°45/2001 should be used until the adoption of the future regulation which will repeal and replace directive 95/46/CE.**
169	115	Regarding the other Agencies policies on access to documents or other transparency initiatives, please specify as much as possible what the other documents are at the moment in order to enhance the transparency of the whole frame. - Paediatric information in accordance with Regulation (EC) No 1901/2006 and Guidance on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency. - Do you include "The list of fields contained in the 'Eudract' Clinical Trials Database to be made public" provided by the European Commission? Probably not as it is not an agency policy and as CT data of EudraCT do	**please specify as much as possible what other documents are at the moment:** - **Paediatric information *in accordance with Regulation (EC) No 1901/2006 and Guidance on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency.*** - **If other please specify**

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		not seem to be included in the scope of this policy although it would be necessary to specify it in its scope.	
169	128	For more visibility, specify in the title the content of category 1	**4.1.1 Category 1 *'commercially confidential information'***
169	132	Please specify who has to justify the cases where this information will be deemed CCI: the marketing authorisation applicant?	**"This information will only be deemed CCI *in cases duly justified by the marketing authorisation/variations applicant.*"**
169	138	For more visibility, specify in the title the content of category 2	**4.1.2 Category 2 *'open access'***
169	155	For more visibility, specify in the title the content of category 3	**4.1.3 Category 3 *'controlled access'***
169	175	Please correct: "The methods of de-identification should be such that adherence will preclude subject ~~de-~~identification, even when applying linkages with other data carriers".	**Please change by:** **"The methods of de-identification should be such that adherence will preclude subject *identification*, even when applying linkages with other data carriers".**
169	182-183	The expression "in line with the spirit of informed consent" seems to be steadfast regarding its importance. Indeed, controlled access for addressing a question or conducting analyses should be done only according to the research plan described in the informed consent. This is necessary in order to preserve the transparency in the relationship between the patients and researchers.	**To change the expression** "in line with the spirit of informed consent" with "according to the research plan described in the informed consent".
169	176-231	We suggest to include the adequacy of the level of data protection as a condition to grant controlled access for a third country. According to the data protection Directive and the proposal for data protection regulation this condition remains essential in order to grant transfer of personal data to	

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		third countries.	
169	203	Please specify how the requester should make results of its analysis public within a reasonable period of time: publication in scientific journals? sending to the EMA for publication on its website and linking to CT primary data?	
169	214	Please specify whether a requester who declines to upload any documents “at that time”, may upload them later. If yes, for how long? Or has he to send a new request of access?	
169	249	Given the fact that Directive 2001/20/EC on clinical trials and Directive 95/46 on protection of personal data are under current revision, it may be relevant to specify that this policy is provisory as its conformity to EU law will have to be verified soon, notably regarding the definition of personal data.	
169	265	Please complete the list of related documents by including all the documents cited in the policy: regulation (EC) 45/2001, Directive 95/46/EC, Eudravigilance access policy EMA/759287/2009 corr., regulation (EC) 1049/2001, Regulation (EC) No 1901/2006 and Guidance on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency as well as any other Agency policy on access to documents	*regulation (EC) 45/2001, Directive 95/46/EC, Eudravigilance access policy EMA/759287/2009 corr., regulation (EC) 1049/2001*,…
169	291-292	“In the light of the overriding public interest, these personal data are considered exempt from PPD considerations”. This sentence should be changed for compliance with directive 95/46/EC and protection of personal data. The data relating to investigators and administrative staff are not health data but still remain personal data. Therefore, even though there is	

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		an overriding public interest, guaranties should be established to make these data available : one solution could be controlled access	