2 October 2014
EMA/342115/2014
Chief Policy Adviser

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

From stakeholder 01 to stakeholder 88

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
01	Entire document	Norgine would like to congratulate those drafting this policy for weaving their way through a vast array of stakeholder needs to produce a policy which, in large part, seems workable and an appropriate compromise to satisfy as many of these needs as possible. We are fully supportive of the publication of all clinical data submitted to support regulatory decisions and to appropriate re-analysis and scrutiny of such data by those permitted to do so via this policy.	
01	34-35	This statement appears to suggest that re-analysis of data submitted to a regulatory authority and on which a regulatory decision has been made can	Clarification of the circumstances in which the regulator can be challenged should be included and

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		be challenged by a third party analysis. This could lead to concern amongst EU citizens regarding the competence of the regulatory authorities and could lead to uncertainty for patients, physicians and MA holders that an MA granted might be revoked or "second guessed" by multiple re-analyses of data	the rights of patients, physicians and MA holders to engage with the process of such challenges
01	60-61	Associated with the comment on 34-35, this seems to be of critical importance in advance of finalisation of this policy in order to protect the reputation of the regulatory authorities and avoid bringing the regulatory process into disrepute	Measures to protect public health and regulatory decisions should be put in place prior to the finalisation of this policy
01	64-66	Related to the comments above, these sentences appear to be contradictory. It is unclear why protection of regulatory decision making no longer applies after a regulatory decision has been made. Norgine is concerned that competing pharmaceutical companies could engage in re-analyses of each other's data leading to vexatious challenges to the regulatory process.	Further clarification is required as to how regulatory decision making can be protected
01	153-154	Companies may withdraw applications in order to re-submit at a later date with enhanced clinical (or other) data. In these circumstances, publication of already submitted clinical data would provide competitors with valuable commercial information that could give them unfair advantage. In other situations, companies may withdraw applications knowing that there is no chance of gaining approval due to failure to demonstrate appropriate efficacy, safety or quality. In the latter case, early publication of data would clearly be in the public interest.	Please consider classifying withdrawals with planned re-submission differently and maintain these data as confidential until after subsequent approval or rejection. A time limit could be applied e.g. 3 years, whereby if resubmission had not been made or was not imminent at this time, the data would be published anyway. Where applicants withdraw due to futility, these clinical data could be published as described
01	180	Further clarification of what is meant by "established in the EU" would be welcomed. For example, it could be envisaged that those wishing to gain access to data from other regulatory jurisdictions with a view to illegally applying for licences there could easily "establish" themselves within the EU for the sole purposes of gaining access to data. How will EMA guard against such illegal acts which are clearly not within the spirit of this policy	Further clarification and safeguards are needed to ensure only EU citizens or legal entities can access clinical data.

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01	193	Linked to the comment above, further information regarding the means by which regulatory agencies globally will co-operate to ensure that downloaded data are not used to gain non-EU regulatory approvals would be welcomed	Further assurance regarding protection against illegal use of downloaded data in non-EU jurisdictions would be welcomed
01	205	It would seem important to know how EMA will verify that downloaded data sets are destroyed after the original purpose for their access has been fulfilled	Additional information required to indicate how data sets will be destroyed and what proof will be requested
01	219-221	Same comment as lines 153-154 re circumstance behind withdrawal	As line 153-154
01	227	How will EMA know when analyses have been published? Will applicants be obliged to inform? Will editorial policies in journals be amended to establish publication guidelines for re-analyses of downloaded data that safeguard against inappropriate data mining, improper analytical methodology and repetitive publication of the same data without this being evident to readers	Further clarification regarding publishing safeguards would be welcomed to protect against multiple publications of the same data sets i.e. to ensure it is clear to readers that the data are the same, just the analysis is different.
01	Annex I 2.5.2	Even the overview of biopharmaceutics could contain CCI especially when dealing with novel formulations	Please consider re-classifying 2.5.2 as C
01	Annex II 16.1.4	Certain elements of this section are confidential (namely CVs) – perhaps this would be better classified as C	Consider re-classifying 16.1.4 as C
01	Annex II 16.1.6 and 16.1.7	Have these been incorrectly classified? Listings of patients and patient identification and randomisation schemes should be confidential	Consider re-classifying 16.1.6 and 16.1.7 as C
02	44-48	Boundaries should be more precisely defined. What are the researches that fall outside the boundaries of informed consent? Examples should be provided. Are the boundaries depending on what the patients are signing or are they “global”, i.e.: with an objective of advancement of science or public health? More comments on this point below (182-183)	
02	67-71	I am not sure that those who generate CT data in the first place (i.e. pharma industry) can be considered as the highest standard of transparency!	

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		Otherwise, all their analysis would already be in the public domain... Ok for transparency but saying that the public requesters should be as transparent as pharma industry might be laughable.	
02	77	Prospective: It can be understood that it would be a huge work to make this procedure retroactive. However, some clinical study reports (CSR) or other documents from the Common Technical document (CTD) have already been requested and sent to requesters. These CSR and CTD parts are thus already in an appropriate format for public domain. They should be made available as it is planned for category 2 documents (see lines 150-154). This could show that EMA has recently become more "transparency-minded" and which are the products experts are making researches on.	
02	179	How will the requester be assured that his/her name will not be known from a third party outside EMA? What process will be put in place?	
02	182-183	What is in the interest of public health and what is not? Is searching for a bias in the interest of public health? Is improving knowledge on patients' evolution in the interest of public health? Details on what is not in the interest of public health should be proposed. The decision that an analysis is in the interest of public health should be based on objective points previously described in the procedure. Spirit of informed consent: This is not acceptable as such. If, for example, the following sentences are put in the informed consent: *"to guarantee confidentiality, your personal data will only be available to the sponsor, medical team in charge of you and health authorities"* or *"your personal data will only be used for the purpose of the study"*, this would mean that data should not be made public, even with controlled access. Either a mandatory sentence should be put in any informed consent stating that de-identified data can be used for public health interest research by people not involved in the study or it should be clearly stated in the procedure that informed	

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		consent cannot limit access to the data.	
02	185-187	What does “exhaustive and detailed” mean? It is an open door to refusal of the data for subjective reasons. Requesters should only have to tick a case: for example meta-analysis, patient description, subgroup analysis, re-analysis, potential bias evaluation, other exploratory analysis, other (+ written precision). Ticking one of these cases could be mandatory but should not limit data availability.	
02	191-192	Not acceptable (as above 182-183). If, for example, the following sentences are put in the informed consent: “*to guarantee confidentiality, your personal data will only be available to the sponsor, medical team in charge of you and health authorities*” or *“your personal data will only be used for the purpose of the study”*, this would mean that data should not be made public, even with controlled access. Either a mandatory sentence should be put in any informed consent stating that de-identified data can be used for public health interest research by people not involved in the study or it should be clearly stated in the procedure that informed consent cannot limit access to the data.	
02	194	“Not share, in any way or format”: Some evaluations might need the description of few patients: for example description of specific subtypes of patients, lost for follow up, very good or very bad responders or any other specific subgroups of patients... Some publications are providing readers with a list of patients with some characteristics. Does this sentence forbid requesters to provide a list of patients in their publication? It should not. A sentence such as “no more than 30 patients and no more than 10 items could be published” could be proposed.	
02	198	Under which circumstances is approval from ethics committee needed? What about approval from organism such as CNIL in France? A global approval from CNIL or other agencies dealing with e-databases should be obtained for	

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		data de-identified by EMA. This approval is to be obtained for any clinical trial prior start. Is this approval valid for requesters?	
02	201	The agreement paper should contain the limitations described from line 222 to 231	
02	205	CT data access should be destroyed after a delay following the publication to allow the requester to answer to any discussion about the publication. Once the publication is made and the information put on the EMA website, a 6-month delay could be reasonable before data are destroyed.	
02	226	In case of combined analysis of more than one CT data, the one year delay should start after the last CT data are obtained (ex: meta-analysis)	
02	229	Why? By definition, EMA has the same set of data and can perform the analysis to solve any public health issue or need, doesn't it? Of course EMA can ask the requester to know if he/she can provide information but it is not a reason to disclose the requester's name. EMA can ask the requester to disclose his/her name but the name of the requester should not be made public by EMA for this reason.	
02	242-247	The CT data should be available in a format which is readable with non-proprietary software.	
03	General	I welcome this transparency measure and I think that EMA's doc is extremely well written and structured! Regarding the implications of this publication on Health care Professionals as investigators, I generally agree with the classification of this personal data as non PPD because of the public health responsibility of these professionals and public interest. Also, in Portugal there is a trend in disclosure this information…	
03	Page 1, line 29	Consider the use of "medicine" instead of "drug"	

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03	Page 4, line 139	Confirm that all the sentence should be in italic	
03	Page 6, line 193 and page 7 line 247	Confirm the use of hyphen (or not) of marketing authorisation	
04	General	The BioIndustry Association (BIA) welcomes the opportunity to submit these comments and observations on the European Medicines Agency's draft policy on the publication and access to clinical trial data as described in the document issued for public consultation. The BIA comments on the draft policy are outlined below. In addition we wish to provide on behalf of our members some further comments for consideration by the Agency before implementation of the policy on the publication and access to clinical trial data. Independent replication of clinical trial data is the primary reason given which will enable public scrutiny and secondary analysis of clinical trials. However it is not clear how this aim will be met since a requester asking for access to data is not required to submit a statistical analysis plan and thus could perform an inappropriate or incorrect analysis without any peer review. Indeed, the proposed approach for data access could have a significant negative impact on public health rather than the desired positive impact. The policy on access to data should include defined processes for peer review of requesters proposed re-analyses of clinical trial data to prevent any inappropriate or incorrect analyses being generated. It is not in the interest of public health or good communication practice if mixed and confusing analyses are provided to the general public that may potentially undermine the authority of the EMA or national regulatory authorities to undertake independent assessment.	

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		The stated aim of the policy is to enable the wider scientific community to make use of detailed and high quality clinical trial data to develop new knowledge in the interest of public health. A major consideration in the development of this policy was the potential that clinical trial data would be re-analyzed by third parties. To be of value the reanalysis must be appropriate and valid. As such the policy should be clear on what additional analyses would be allowed on clinical trial data including a process to peer review requests to confirm if the data can support such additional analysis objectives. Whilst we welcome that the "Agency respects and will not divulge commercially confidential data or information", we do not support the statement that "in general, however, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI", for the following reasons: 1. We feel it is difficult to express a view or to determine a priori whether or not a document contains CCI (or data are CCI) without having reviewed it and/or consulted with the "owner" of such document (and/or with persons whose interests may be affected by the wrongful disclosure of such document or the granting of access thereof). In addition this statement is not consistent with the current position adopted by the EMA and EU Heads of Medicines Agencies (HMA). Indeed, the HMA/EMA Guidance Document on the Identification of Commercially Confidential Information and Personal Data adopted in March 2012 sets out the following in section 3.2 relating to Non-Clinical and Clinical Information: "Information encompassing non-clinical and clinical development of the medicinal product and the subsequent assessment by Competent Authorities is not per se commercially confidential.	

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		[…] In the case of exceptional and substantiated cases, particularly where innovative study designs and/or innovative analytical methods have been used, consideration will be given to the need for redaction" (our emphasis). In increasingly complex research and development stages, particularly for biological medicines, certain confidential know-how in the quality or pharmaceutical testing or assay developments is intrinsically linked to the clinical development. Care should be exercised to avoid inadvertent disclosure of commercially sensitive information. 2. Under the policy which the EMA applied consistently since its implementation, access to CT data was refused on the ground that such data were precisely CCI and that it was not in the public interest to allow such access (see order of the President of the General Court in Case T-44/13 R, paragraphs 6 and 7). 3. One of the issues which the EU Court will need to examine is whether CT data benefit from a general presumption of confidentiality, in which case such data shall be considered as CCI in their entirety, unless an exemption applies; the EMA would have the burden of proof that this is the case. In addition, the issue of confidentiality of CT data may be determined in the context of the ongoing negotiations for the adoption of the EU Clinical Trials Regulation. Thus, it may be premature for the EMA to express such a view without considering the factual circumstances of a specific matter. 4. Whilst the EMA must determine whether access to CT data in marketing authorisation applications submitted to the Agency could affect the protection of commercial interests, including	

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		intellectual property, it may arguably not be within its competence (or even within the competence of any EU institution or agency) to determine the scope of trade secret protection (and of intellectual property rights). This issue is largely governed by national laws, not EU laws, and falls within the competence of the EU Member States. The EMA has a duty to avoid interfering into the rules in Member States governing the system of property ownership (see Article 345 TFEU). In view of the above, we respectfully submit that the Agency should set up an appropriate process to determine the proper basis (through engagement of the data owners) for publication and access to clinical trial data, which adequately balances all (potentially conflicting) interests concerned, including the fundamental right to protection of confidential information. We recommend the Agency refraining from expressing any view or opinion as to whether or not clinical trial data contain confidential information, since this matter is currently the subject of litigation before the General Court to determine the legality of the Agency's policy on disclosure of clinical trial data. Therefore, given this matter is under judicial consideration, the EMA may wish to consider it necessary to ensure that its policy is consistent and compatible with the judicial decisions arising from the ongoing direct actions in the General Court. For this reason, it is our respectful view that the entry into effect of the Agency's policy ought to be postponed, as far as possible. We would be happy to discuss any of the comments in this response. We look forward to continue the dialogue with the Agency in this important area of clinical trial data transparency to the ultimate benefit of both patients and the life sciences sector.	

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04	28-31	*Enabling public scrutiny and secondary analysis of CTs:* There is no evidence to suggest that this policy "will make drug development more efficient". Accordingly, the statement in the policy document should be less categorical.	Please revise this sentence as follows: ~~**It will**~~ **The policy has the potential to** make drug development more efficient by establishing a level playing field that allows all drug developers to learn from past successes and failures, and it ~~**will**~~ **may** enable the wider scientific community to make use of detailed and high-quality CT data to develop new knowledge in the interest of public health.
04	30-31 44-48 Also 183 191-192	*Enabling public scrutiny and secondary analysis of CTs:* The statement "...to make use of high-quality CT data to develop new knowledge in the interest of public health" is very wide and is potentially at odds with lines 47-48 stating that "...any other use of patient data oversteps the boundaries of the patients' informed consent, and shall not be enabled by the policy". While re-analysis may be in line with the informed consent form this is much less clear for exploratory analyses (e.g. the data from patients who have not explicitly consented to secondary/exploratory use may have to be excluded).	The policy document should indicate what kind of mechanism will be put in place to ensure that use of patient data is compatible with the informed consent, in particular the handling of situations where a patient or Ethics Committee have refused secondary or exploratory use, or alternatively, where national laws prohibit secondary or exploratory use not described in the protocol.
04	34-35	*Enabling public scrutiny and secondary analysis of CTs:* The EMA has made its position clear regarding re-analyses. Specifically, the EMA wants third parties to be able to use the raw data to verify the Agency's regulatory decisions. However, this seems misaligned with the current practice where the EMA does not receive the raw data to analyse it before it makes its decisions. Does this mean that the EMA will want to see raw data to be submitted in future marketing authorisation applications (MAAs)?	Please revise this sentence as follows: Access to CT data **submitted in a marketing authorisation application to the EMA** will enable third parties to verify (...). Clarification is requested on the EMA's analysis of raw data and consequently the inclusion of such raw data in future MAAs.
04	36-43	*Protection of personal data (PPD):*	

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		This section should include explicit reference to the need for a controlled access model that prevents the download of data, to reduce the risk of re-identification of study participants.	
04	40-41	We fully share the Agency's concern that emerging technologies will increase the potential for unlawful retroactive patient identification. We believe that such risk for identification may also depend upon the nature of the trial and the development programme for a given product. For instance, this risk may be increased particularly for orphan products, which are usually treated or studied in specialised centres and the data subjects would be easily identifiable.	It is recommended that the EMA's policy on publication and access to clinical trial data takes such a risk into consideration.
04	50-51	*Protection of commercially confidential information (CCI):* The statement that *"In general, however, CT data cannot be considered commercially confidential information"* is not supported. In particular, it does not take into consideration the timing of publication. CT data shared precociously, during development of a product or resubmission of a marketing authorisation application, can seriously harm the competitive position of the sponsor.	Please revise this sentence as follows: In general, however, CT data cannot be considered **to be** CCI **once marketing authorisation has been obtained or the product development has been abandoned**; (...).
04	52-56	*Ensuring future investment in bio-pharmaceutical R&D:* It should not be ignored that allowing third parties access to CT data held by the Agency may negatively impact on the value, competitiveness, ownership of trade secrets and intellectual property rights of undertakings, especially for SMEs, and of researchers and their ability to share information and innovate. As the European Commission recently pointed out: *"the protection of confidential business information as a trade secret is, for many businesses, often the only or the most effective way to protect their intellectual property. Such protection would allow innovators to reap the benefits from their innovations, at least for some time, and*	Please add the following: **The Agency will take into consideration risks of a negative impact on the value, competitiveness, ownership of trade secrets and intellectual property rights of undertakings, especially for SMEs, and of researchers and their ability to share information and innovate in the Union. Often SMEs have one technical platform or one product under development or marketed. Therefore it is critical for them to protect broader intellectual property rights**

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		hence to earn sufficient return on their investment in innovation. In particular, it appears that trade secrets/confidential business information are often regarded as key protecting tools by small and mid-sized companies (SMEs) and researchers in (non-profit) research institutes, who use trade secrets both to replace as well as to complement IPRs. Concerns regarding the effectiveness of the protection of trade secrets in the Internal Market are already being voiced. (…) The (current) protection would not represent a sufficiently strong deterrent against theft of such confidential business information. Therefore, this could dissuade the sharing of confidential business information across borders with business partners who could offer valuable possibilities to develop new market possibilities for innovative products (our emphasis)" http://ec.europa.eu/internal_market/consultations/docs/2012/trade-secrets/121211_trade-secrets-consultation_en.pdf	**including know-how because they represent important company assets.**
04	59-61	*Addressing the consequences of inappropriate secondary data analysis:* What measures will be put in place to protect against claims resulting from inappropriate analyses? We believe that requests for access to clinical trial data together with the statistical analysis plan should be reviewed by the Agency before access to data was granted; this would give some protection against inappropriate analyses being conducted (see lines 185-187). The broad restriction of public communication of conclusions of secondary analyses by third parties prior to interaction with the original decision maker would in our view be a sensible measure.	It is recommended that requests for access to clinical trial data together with the proposed use of the data should be subject to prior review.
04	64-66	*Protecting the Agency's and the European Commission's deliberations and decision-making process:* The statement that *"once a decision has been reached, this consideration [i.e. external pressure] no longer applies"* is not valid.	Please remove this sentence: **Once a decision has been reached, this consideration no longer applies.**

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		Many regulatory actions have taken place post authorisation further to external pressure after the initial approval decision has been made. New information may come to light about a product and risk-benefit would then be re-evaluated regardless of the source of the data.	
04	67-70	*Ensuring that transparency is a two-way street:* *"The Agency takes the view that … all secondary analyses shall also be in the public domain and accessible for further scrutiny by the scientific community."* There are no details about how to implement/enforce accessibility and scrutiny. For example, are the requesters going to be required to submit their analyses, including specifications of the analyses, any derived datasets, programmes, logs, metadata, etc. to the Agency?	Please provide details on how to ensure that the requesters are going to be held to the same standard as the sponsors in respect of data quality and integrity arising from the secondary analysis.
04	71	What is a reasonable period of time during which those conducting secondary analyses should be protected against external interventions?	Clarification is requested on the reasonable period of time; it is suggested to be "no more than 1 year after access to data was granted" to align with other timings described in the policy document.
04	77-82	The scope is not clear. It is stated that the policy only concerns data that will be submitted to the Agency after the policy comes into force. In other words, the trigger is submission after the policy enters into force. However, the paragraph goes on to state that pre-existing data submitted to the Agency (presumably post coming into force), e.g. in the context of a referral procedure, are out of scope. In addition, informed consent issues may occur during the early phase of implementation given that submissions will contain clinical trial data from studies that were conducted before the policy was in	Clarification is requested on the scope adding further details of what is within and outside the scope of this policy. Please revise this paragraph as follows: The policy is prospective in that it concerns ~~**only those**~~ CT data ~~**that will be**~~ submitted to the Agency after the policy comes into effect as outlined below **(and for any product or purpose)**. All other CT data currently held by

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		place. Therefore very few applicants would have updated their informed consent templates to accommodate the proposed data sharing measures.	the Agency (e.g. those on products already on the market) or pre-existing CT data of marketed products that will be submitted to the Agency, e.g. in the context of a referral procedure ('legacy data'), **whether such data currently exist or will be generated after such entry into effect,** continue to be made available to external requesters on a 'reactive' basis as outlined in the Agency's current policy on access to documents.
04	83-85	For a marketed product, the MAH is meant to review all emerging data on an ongoing basis regardless of source and update their periodic benefit-risk evaluation report (PBRER) if required. These updates and conclusions would at that point become transparent, although the data may not be available for public scrutiny.	Confirmation is sought as to which data submitted post-marketing authorisation is within the scope of this policy.
04	96-97	*Clinical trial data*: For some types of observational research, sponsors do not have access to the data and the analyses are conducted by third parties. Sponsors would have access to the data under strict conditions as specified in a legal contract. There will be situations where the sponsor will not be able to provide the data supporting the observational research conducted.	Clarification is requested on what is within the policy scope for observational research methodologies. The policy document should acknowledge limitations to the ability of sponsors to provide data from research conducted by third parties.
04	102-106	*Personal data*: It is not clear from the definition of personal data whether data related to deceased persons fall within or outside the scope. The Article 29 Working Party under the Data Protection Directive takes the view that the current EU law on data protection does not apply to information relating to deceased persons. The position will likely be the same under the new Data Protection Regulation.	Clarification is requested as to whether data from deceased individuals fall within the definition of personal data.

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04	109-111	*Commercially confidential information (CCI)*: In view of the ongoing dispute before the General Court of the EU, it is not possible to establish with a necessary degree of legal certainty what is to be understood as CCI. As per Regulation (EC) No 1049/2001, one of the exceptions to the principle of access to documents held by the EU institutions include the possibility that such disclosure would "*undermine the protection of commercial interests of a natural or legal person, including intellectual property, court proceedings and legal advice, the purpose of inspections, investigations and audits".* We believe the definition of CCI needs to include internal knowledge, e.g. development strategy for the compound, since Annex 1 in 2.7.3 requires an analysis of study results across studies, as well as data obtained from third parties where access/publication of such data is restricted or prohibited by contract.	Please add the following sentence: **However, in view of the court cases before the General Court which will bring legal clarification on the definition of CCI, it is not possible to unambiguously establish what is to be considered as CCI. In any event, the policy should be compatible with the decisions of the General Court.**
04	122-123	*Raw CT data*: It is not clear why the SAS logs and SAS programs are included in the definition of raw CT data. As noted in the draft policy, the statistical analysis plan (SAP) may contain code fragments for the proposed statistical analyses but will not contain full copies of final statistical programming code used to generate TFLs. Many statistical programs used to generate the statistical analyses use complex programming structures and utilities to create the TFLs and this code is considered proprietary.	Please remove reference to SAS logs and SAS code from the definition of raw CT data.
04	129-132	**Category 1-** *CT data/documents containing CCI:* Uncertainty remains as to whether all documents listed as CCI in the policy Annexes are automatically and definitely deemed to be CCI or if there needs to be an assessment of "justified cases".	Confirmation is requested that the documents designated as CCI in the Annexes are classified as such by default/automatically. For other information to be classified as CCI, a clear process should be put in place.

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04	137	We cannot agree with this statement *"CT data/documents that are not categorised as 'CCI' in Annex I are considered to contain no CCI"* - see general comments and lines 50-51 above.	Please revise this sentence as follows: CT data/documents that are not **pre-**categorised as 'CCI' in Annex I ~~**are considered to contain no CCI**~~ **may still contain certain CCI that may necessitate redaction**.
04	149 & 289	**Category 2 -** *CT data/documents without protection of personal data (PPD):* Under Regulation (EC) No 1049/2001 regarding public access to European Parliament, Council and Commission documents (this includes documents held by EMA) the public authority must refuse access if disclosure would undermine the privacy and the integrity of the individual, in particular in accordance with Community legislation regarding the protection of personal data. In other words, there is no public interest test to be applied. By advocating disclosure of personal data of CT personnel, the EMA is applying a different standard in its policy compared to the requirement under the Regulation.	The existing Regulation 1049/2001 protects study personnel information from being made public. All study personnel information should be categorised as PPD.
04	168-171	**Category 3 -** *CT data/documents with PPD concerns*: Appropriate de-identification It cannot be guaranteed that appropriately de-identified data sets will always preserve the ability to replicate the main analysis as it depends on the patient identifiers included in the main analysis and the balance to protect patient confidentiality.	Please revise this paragraph as follows: The data to be made available may include all the data sets or a relevant subset (e.g. the main analysis set, containing a limited number of indirect identifiers, so that the risk of compromising subjects' identity in case of wide publication of those data is considered to be absent or sufficiently low, while preserving the ability to replicate the main analysis **if this is at all possible**).
04			

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	172	The Hrynaszkiewicz reference provided provides a set of principles for de-identifying data but does not provide details for how data should be de-identified.	It is suggested to provide more details as to how data should be de-identified and clarify what is expected to be submitted to describe how data was de-identified; this could be described in a separate guidance document.
04	180	The statement "requester ... is established in the EU" is ambiguous and open to interpretation.	Please confirm whether the term "established in the EU" has the same meaning as that set out in the Treaty for the Functioning of the EU.
04	181	**Category 3 -** *CT data/documents with PPD concerns*: Controlled access It is stated that the requester has agreed, by way of legally binding data-sharing agreement, (...) What would the consequences be if a requester fails to adhere to the data-sharing agreement? Who, if anyone, is going to enforce these agreements? Will there be audits/monitoring? Who are going to be the parties to this agreement, the EMA and the requester? From the requesters' perspective, would they have to amend the data sharing agreement if an additional analysis of the data is included?	It is suggested that the following contractual conditions are included in the data-sharing agreement: (i) right to audit/monitor, and (ii) sanctions for noncompliance with the agreement. It is also suggested that the marketing authorisation holder/sponsor be party to the agreement, thus providing the possibility of enforcement of such agreements.
04	185-187 & 218	The requester does not need to submit a statistical analysis plan (SAP) to describe their planned re-analysis of the clinical trial data. Yet sponsors conduct their statistical analyses following strict regulations. Should requesters be held to the same standards as sponsors and have to submit a SAP when requesting access to data? The regulators can then judge whether the proposed re-analyses are valid before granting access and this will help to prevent any inappropriate or incorrect re-analyses being conducted.	It is recommended that the proposed analysis plan is uploaded and that the Agency reviews it to check the aims match any details provided.
04			

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
	205	We believe that accessed CT data must be destroyed in a secure manner.	Please revise this statement as follows: destroy **in a secure manner** CT data accessed, once the analysis is completed.
04	207-209	It is not sufficient to make requesters aware of expectations relating to good analysis and transparency. We believe it would be equitable to require third parties to adhere to good CT data analysis standards and transparency to avoid inappropriate and/or misuse of clinical trial data.	It is suggested that good analysis practices be included in the data-sharing agreement as a legal obligation.
04	220	Releasing CSRs from withdrawn marketing applications may harm resubmission and a subsequent re-assessment by the EMA.	We believe that this policy should not apply to withdrawn applications; therefore re-analysis of any raw CT data is unnecessary.
04	222-231	It is not clear what the rationale is for delaying release of the requester's details. The criteria for disclosure appear arbitrary.	We believe that the requester's details should be shared at the time of granting access to data and it would be possible to object to disclosure on reasonable grounds.
04	242-244	**Data standards** It is unclear as to who during the process would provide confirmation that data have been appropriately de-identified at the time it is submitted. If the sponsor has performed an integrated analysis in the submission, the data set containing the integrated clinical trial data should not need to be resubmitted.	Clarification is requested on the process for confirming data have been appropriately de-identified. It is suggested that integrated data sets containing multiple clinical trial data will not need to be submitted if the sponsor has conducted integrated analyses.
04	244-246	**Data standards** There are no details on how data will be submitted. FDA has released guidance on data standards which includes details of how sponsors	It is suggested to include further details on how data is to be submitted. Alternatively it should be noted that additional guidance will be developed,

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		submit CDISC compliant data sets to FDA. Will the EMA develop guidance relating to data standards?	in consultation with stakeholders, to describe the process for submitting data.
04	253-255	A duplicate set of documents from which identifying data has been removed will be made available through 'open access' ('O' data) or 'controlled access' ('C' data). However there is no reference to the possibility to also remove CCI. The draft policy states at lines 259-261 that a separate guidance document on 'C' data will be issued in 2014. Nonetheless, the draft policy in Annex II highlights a number CSR sections and Annexes that are said to become disclosable by January 2015 for new products. Additionally, what happens if there is disagreement between the Agency and the marketing authorisation holder as to the extent of the redactions of PPD?	We believe that the policy should clearly specify that the duplicate set of documents should be de-identified and CCI removed by the applicant/marketing authorisation holder. Alternatively the applicant/marketing authorisation holder must be given sufficient time after the grant of a marketing authorisation to redact CCI from the concerned documents. Clarification is requested on the process including a recourse mechanism.
04	256-261	Section 16 and Annexes I-VIII can be extremely voluminous documents. A total de-identification of each new marketing authorisation application would be a resource-intensive and expensive task. The draft policy must provide a justification why access to all these documents is considered of public health interest. We argue that access to Case Report Forms is not necessary to conduct a re-analysis and is disproportionate. There is also concern as to when it would be "practical" to make the 'C' data available. If the guidance document is finalised by the end of October 2014 as suggested, there will only be 2 months available to create the 'C' data sets for the regulatory submissions that fall within the scope of the policy. This timeframe is insufficient to get all the supporting documentation in place.	It is suggested that Case Report Forms are categorised as 'PD' (personal data) and fall outside the scope of the policy. It is recommended to revise the implementation date of the policy to enable sponsors to put in place all necessary steps to meet the new requirements of the policy, and to submit the 'C' data 6 to 9 months after finalisation of the relevant guidance document.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
04	278-281	It is unclear if marketing authorisation holders should de-identify or exclude personal data from certain sections during the preparation of CSRs (e.g. from the narratives). No post-decision redaction step seems to be foreseen for CSRs.	Clarification is requested as to whether personal data should be excluded from the original application, the duplicate set of documents or whether sufficient time will be granted after the marketing authorisation is granted to de-identify data.
04	Annexes I and II	Names of investigators and vendors etc for pre-clinical and clinical studies should be flagged for special consideration (category 4 in table) for reasons of protection from activists for example.	It is suggested that these sections in Annexes I and II are subject to protection of personal data.
05	General	**Introduction** EFPIA continues its active involvement in the important issue of responsible clinical trial data transparency and welcomes the opportunity afforded to comment on the EMA draft Policy 0070 on *Publication and access to clinical-trial data* (EMA/240810/2013, referenced as 'draft Policy' in these comments). EFPIA recognises the potential scientific and public health benefits of providing greater access to information from clinical trials. Biopharmaceutical companies are indeed committed to advancing public health goals through responsible sharing of their clinical trial data in a manner which is consistent with the following imperatives: • Safeguarding the privacy of patients; • Preserving scientific rigor and the trust in the regulatory systems; and • Maintaining incentives for investments in biomedical research. Under the draft Policy, the EMA will begin to proactively publish on its	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		website the clinical trial data submitted by applicants in marketing authorisation (MA) applications, which it designates as 'open access', and will also reactively provide 'controlled access' to those clinical trial data which may contain patient-identifiable information (patient level data), under described conditions. EFPIA has considerable concerns with several of the concepts outlined within the draft Policy, the implementation of which, in its current form, we believe would not benefit public health and would conflict with the imperatives referred to above. The published draft Policy does not adequately acknowledge or address key recommendations from stakeholders in the five advisory groups established by EMA earlier this year. Above all, we are concerned that the draft Policy presented could actually (1) weaken safeguards intended to ensure the privacy of patients and other individuals identified in MA dossiers, (2) undermine the trust in the regulatory approval system governing biopharmaceutical products and introduce risks of misinterpretation and misuse of clinical data into the process; and (3) weaken incentives for companies to invest in biomedical research by disclosing companies' commercially confidential information (CCI), without due consideration of the competing interests that may or may not justify disclosure, in each particular case. A consultation process with the MA holder (MAH) needs to be established to allow for removal of commercially confidential information (CCI). Consequences of the EMA draft Policy, as currently written, may inadvertently, but negatively impact public health. Specifically, in recognition of these stated imperatives, EFPIA is concerned that the "controlled access" proposals would not provide adequate: (1) protection of patient privacy, through appropriate de-identification of patient data and access via a controlled environment that does not allow	

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		downloading of the data or (2) review of research proposals to ensure good science. It appears from this draft policy that the EMA intends to request information from companies that is not currently required as part of an MA application (e.g. individual patient data sets, SAS logs, SAS programs) without justification based on public health need. In this respect the draft Policy goes beyond the purpose of the legislator to provide access to documents of the institutions (Art. 2 para 1 of Reg. 1049/2001). EFPIA believes that the provision of access to such additional data falls under industry's own responsibility and commitments, which are summarised below. Biopharmaceutical companies already publish their clinical research, collaborate with academic researchers, and share clinical trial information on public web sites at the time of patient recruitment, after marketing authorisation, and when investigational research programs have been discontinued. Building on those continuing efforts, EFPIA and PhRMA have recently adopted Principles for Responsible Clinical Trial Data Sharing. These set out industry's commitments to: (i) enhance data sharing with researchers; (ii) enhance public access to clinical study information; (iii) share results with patients who participate in clinical trials; (iv) certify procedures for sharing clinical trial information; and (v) reaffirm commitments to publish clinical trial results. We request that the EMA take into account the Principles for Responsible Clinical Trial Data Sharing adopted by EFPIA and PhRMA and assess the added value of its draft Policy against these broad ranging commitments. These Principles represent the consensus views of a large part of the world-wide biopharmaceutical industry, which commits to data sharing of study level and	

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		patient level data, and protocol information with researchers, to enhance public access to clinical study information. Following approval of a new medicine or new indication for an approved medicine in the US and EU, biopharmaceutical companies will make publicly available, at a minimum, the synopses of clinical study reports (CSRs) for clinical trials in patients submitted to the Food and Drug Administration (FDA), European Medicines Agency (EMA), or national competent authorities of EU Member States', and to share results with patients who participate in clinical trials. The EFPIA/PhRMA principles include responsible controls on disclosure in order to ensure that clinical trial information released is used to conduct quality research, respecting patient privacy, and is not used inappropriately for competitive commercial purposes. Release of clinical trial information under these principles will therefore be assured of serving the public health interest, while at the same time protecting personal data and CCI. **<u>Fundamental Comments</u>** **1. Protection of Patient Privacy and Personal Protected Data (PPD)** The draft Policy states that "protection of patient privacy is a paramount concern when sharing raw CT data", with which EFPIA strongly agrees. However, EFPIA is concerned that the measures set out in the draft Policy may not be sufficient to provide the necessary level of protection for patient privacy. Data should not be provided if there is a reasonable likelihood of re-identification. As stated above, the controlled provision of patient level data properly falls within the remit of the clinical trial sponsor, and the industry is committed to sharing such data in a way that effectively safeguards patient privacy, as set out in the Joint Principles. EFPIA is open to discussing with the EMA and other stakeholders the most efficient technological means of	

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		directing researchers to the relevant clinical trial sponsor/company to request the data they need. Recent studies have tested long-held assumptions that de-identifying data protects patient privacy and have shown that the risk of re-identification is particularly acute when de-identified data are made widely available. Re-identification technology is advancing rapidly, allowing re-identification of data once thought to be anonymised. Therefore, if EMA is to ensure the privacy of clinical trial participants, before implementing its proposal, the Agency should ensure that these technologies provide the necessary de-identification measures to adequately protect patients. As the Agency recognizes, it would need to consider not only the clinical data themselves, but also all other public information that could be combined with study data to deduce subject identities, including discharge data, data in public study databases, claims data, U.S. and EMA clinical trials databases, and even social media. To appropriately execute this task, EMA would need the detailed input of information security and bioinformatics experts. In any event, a controlled access model should not allow for the data to be downloaded, in order to reduce the risk of re-identification described here. EFPIA is also concerned that protection of the personal data of investigators, sponsor, and study personnel named in MA submissions is excluded in the draft policy, which states that "these personal data are considered exempt from PPD considerations". There seems to be no legal basis for this assertion – the EMA must respect and protect the privacy of *all* individuals, whether they are investigators, study personnel or patients. EU Data Protection Regulation (EC) No. 45/2001 (Data Protection Regulation),[1] which imposes on	

[1] Regulation (EC) No. 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:008:0001:0022:EN:PDF

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		the EMA requirements similar to those in the Data Protection Directive 95/46/EC (DPD),[2] defines "personal data" broadly to encompass any information relating to an "identified or identifiable natural person," which obviously includes any individuals involved in clinical trials, such as investigators as well as patients. EFPIA does not agree that this general exclusion of study personnel from personal data protection is correct or lawful. In relation to the 'open access' data category, the draft Policy requires that MA applicants provide the EMA with an additional set of documents "that are appropriately de-identified to ensure protection of personal data". Notwithstanding the efforts that would be required of MA applicants to de-identify documents, EFPIA notes that, in this case, it is the EMA that will be making the actual disclosures from its website and the Agency will therefore be responsible for the publication of any information released. Specifically, as the publisher, under Regulation (EC) No. 45/2001, EMA remains legally responsible for ensuring that any information published under open access is appropriately de-identified and for addressing any breaches of privacy or consequences from inappropriate re-identification based on information made available through its open access policy. Likewise, the EMA will have the same legal responsibility to ensure that information published under open access is appropriately de-identified in compliance with (where applicable) non-EU privacy laws - which may vary from those in the EU - given the fact that CSRs frequently include data from patients from countries outside the EU. Since the Agency is subject to the Data Protection Regulation (EC) No.	

[2] Directive 95/46/EC of the European Parliament and of the Council of October 24, 1995 on the protection of individuals with regards to the processing of personal data and on the free movement of such data. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1995L0046:20031120:EN:PDF

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		45/2001 concerning the processing of personal data by Community institutions, the proposed draft Policy must be submitted to the European Data Protection Supervisor for review and feedback. We also strongly recommend that the Agency submit the proposed policy to the Article 29 Working Party established under the Data Protection Directive as the policy requires the cooperation of organizations and individuals subject to Directive 95/46/EC. As part of this consultation, the Article 29 Working Party should be asked to opine on appropriate methods for anonymising clinical trial data. Without the agreement of EU data protection authorities (via the Article 29 Working Party) on when data can be deemed "anonymised", MA applicants will be forced to comply with the most conservative national privacy laws, which could mean the marking of all data containing indirect identifiers as potentially personal data. In addition to considerations of personal data privacy under the data protection legislation, there remains the imperative of respect for the terms of the informed consent given by the patients participating in clinical trials, both in the EU and 3rd countries, with regard to the subsequent or secondary use of their data (whether "anonymised" or not), as a matter of ethics and a central tenet of good clinical practice. In the draft Policy, the EMA appears to infer a broader scope to individual patient informed consent than may in fact be the case, especially historically in past clinical trials, when the current issues now being debated were not envisaged. The draft Policy ambiguously refers to the "spirit of informed consent", whereas in reality trial sponsors (and by definition, any other party handling the data, including the EMA) must respect the informed consent in its particular terms and according to the laws of the country where it was given. The release of clinical trial data – whether by the sponsor or EMA - can only ethically and lawfully take place within the scope of the specific informed consent given by the patient to the trial	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		sponsor and is not distorted so as to deprive the concept of 'informed' of its meaning, and the party releasing the data must bear this responsibility. **2. Providing Access to Data for Legitimate Research** As demonstrated by the joint PhRMA/EFPIA principles, biopharmaceutical companies are committed to enhancing public health through responsible sharing of clinical trial data to help facilitate bona fide scientific and medical research. We believe that it is in the interests of transparency and medical research that the secondary research is subject to the same standards of transparency as the original clinical trial and a proportionate review that determines whether the release of "CT data with PPD concerns" is justified in any given case. Firstly, in relation to the scheme set out in the draft Policy for controlled (reactive) access, there are inadequate controls to ensure that the research/secondary analyses for which the patient level data are used is robust and scientifically credible. Under the draft Policy, the requester is not required to provide or publish their statistical analysis plan at all, and any information that they do provide will not be published until up to one year after accessing the data, hence there is no prior review of the statistical analysis plan, nor of the qualifications of the requester to conduct the research to ensure its legitimacy and scientific rigour. Essentially, any researchers requesting controlled access to patient level data should be held to the same standard as the clinical trial sponsor in terms of transparency, namely to (i) publicly register their research before initiation and (ii) post the results of their research within 1 year of completion. Secondly, the proposed mechanism does not include any review of the	

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		purpose for which data will be used or the relevance of the proposed research to medical science or patient care. The notion that access to individual level health and clinical data should be restricted to legitimate research and subject to proportionate review (even when steps have been taken to protect individual privacy) is well established and enjoys broad support in the context of access to electronic health records and biological data in biobank-type repositories. EFPIA believes that a case-by-case assessment is necessary to determine whether access to "CT data with PPD concerns" is justified in any given case and without this review it is unclear how the proposed mechanism will meet the stated requirement that "analyses are in the interest of public health, in line with the spirit of informed consent". A recent article authored by European regulators, including the Head of the EMA, indicates that the regulators share EFPIA's concerns. In 'Open Clinical Trial Data for All? A View from the Regulators'[1], senior officials from the EMA and French, Dutch and UK national competent authorities, suggest that data sharing could occur only after receipt of a full analysis plan in order to guard against independent analyses "vulnerable to distortion." According to the regulators: *Unrestricted availability of full datasets may in some cases facilitate the publication of papers containing misleading results, which in turn lead to urgent calls for regulatory action. In a worst case, this would give rise to unfounded health scares with negative public health consequences such as patients refusing vaccinations or discontinuing drug treatment.* EFPIA agrees with the regulators' observations in this article that "independent analysis per se is no guarantee of high quality" and	

[1] Eichler H-G, Abadie E, Breckenridge A, Leufkens H, Rasi G (2012) PLoS Med 9(4):e1001202. Doi: 10.137/journal.pmed. 1001202.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		"independent analyses warrant a similar level of scrutiny as sponsor-conducted analyses do." It is a well-established principle of the scientific process that requests for access to clinical data should be subject to prior review, to help ensure appropriate use and analyses of the data. Such controls represent a step towards *responsible* transparency, better assured of serving the public health interest. Unfortunately, the draft EMA policy lacks the controls necessary to address the risks of unfettered access to clinical trial data identified in the 2012 article. EFPIA thus strongly encourages the EMA to adopt the EFPIA/PhRMA Joint Principles referred to above, which contain provisions intended to address these issues, including the requirement that third parties seeking access to clinical trial data in MA dossiers submit a plan for analysis of the data with a scientific review board that will participate in the review of these data requests. **3. Maintaining Incentives for Investments in Biomedical Research - Protection of Commercially Confidential Information (CCI) – Open Access to Clinical Trials Data** The EMA draft Policy designates most elements of the clinical trial data submitted to it by MA applicants as 'open access' suitable for proactive publication on its website. The EMA policy states that commercially confidential information (CCI) will not be divulged, but that "in general, however, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI". The EMA's assertion that clinical trial data and information in MA dossiers cannot be considered CCI is inconsistent with the definition of CCI adopted by the EMA in the draft Policy itself. More fundamentally, this assertion is inconsistent with core protections afforded to MA applicants/holders under	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		EU law. EMA should develop and implement a robust procedure for the consultation of the MAH and review of the data proposed for disclosure, and for the MAH to appeal against the EMA's decision to disclose, in advance of any disclosure of information (i.e., "open" or "controlled" access). In Section 3, Definitions, at lines 109-111 of the draft Policy, the EMA defines CCI as "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." EFPIA agrees with the general formulation of this definition, but fails to understand how, in light of the definition, EMA can then declare elsewhere in the policy that "CT data cannot be considered CCI" (Line 50). The EMA's own CCI definition requires on its face an inquiry into whether the information is in the public domain or publicly available; whether the owner of the information protects such information from disclosure; and whether, if released, disclosure could harm the competitive interests of the sponsor. Some information in certain MA dossiers, depending on the sponsor, product at issue, therapeutic area, and value of the information to competitors may, indeed, meet the EMA's definition of CCI. Clinical trials data within the MA dossier may include commercially sensitive information, the protection of which helps incentivise companies to continue innovating and investing in medical and scientific research. This appears to be evidenced by the fact that the majority of requests for disclosure are from pharmaceutical companies as opposed to healthcare professionals or members of the public.[3] Broad dissemination of clinical trial data may negatively impact upon industry's commercial opportunities in markets outside the EU which have no or	

[3] Doshi P, Jefferson T. *The first 2 years of the European Medicines Agency's policy on access to documents*: secret no longer. *Arch Intern Med*. Published online December 19, 2012. doi:10.1001/jamainternmed.2013.3838.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		different standards of regulatory data protection, and may prejudice intellectual property rights. The EMA elsewhere in its draft Policy recognizes this very point by stating that access to "controlled release" documents will be conditioned upon a commitment by the requestor to refrain from using the released information to gain an MA in a non-EU jurisdiction (Line 193). The fact that certain clinical trials data and other information in MA dossiers may, in principle, constitute CCI does not end the inquiry. EFPIA agrees with the EMA that, in particular cases, public health interests in disclosure of CCI may outweigh considerations supporting non-disclosure of protected information. If information in a MA dossier meets the definition of CCI adopted by the EMA in this draft Policy, and if the EMA seeks to release such information over the owner's objections, then a separate inquiry needs to be made prior to public disclosure to determine whether an overriding public health interest justifies release of the information. This stepwise analysis is, in fact, required by EU law pursuant to Article (4)(2) of Regulation 1049/2001 Regarding Public Access to Documents, which expressly states that EU institutions, including the EMA, will refuse public access to documents that would undermine the protection of the commercial interests of a natural or legal person unless there is an overriding public interest in disclosure. This view is also consistent with Article 39(3) of the TRIPS Agreement, which obliges the EMA to protect against release of data submitted for MA purposes, "[e]xcept where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use." Further, EFPIA believes that the required analysis cannot be avoided by collapsing the inquiry into one, all-encompassing finding that "CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI," as stated in the draft Policy. The fundamental principles of EU law	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		require that an analysis weighing the relative CCI and public health interests at stake be made on a case-by-case basis, should the EMA seek to release information over the objections of a sponsor. The European court has confirmed that the protection of confidential information is a right to privacy under the European Convention on Human Rights (Convention) and the Charter of Fundamental Rights of the EU (Charter).[4] In addition, sponsors have vested property rights in CCI information present in MA dossiers. Economically valuable confidential clinical trial information submitted to the EMA in MA dossiers is a form of possession pursuant to the Convention and the Charter,[5] to be protected according to European courts.[6] EFPIA agrees that the interference with such property rights by an EU institution may, in appropriate circumstances, be justified by reference to other rights and interests, such as the public interest, but the consequences to the owner of confidential information flowing from disclosure cannot be taken lightly - any disclosure of commercially confidential information will destroy the value in the property right. EMA is required, therefore, to conduct a careful case-by-	

[4] Article 7 of the Charter and Article 8 of the Convention, as confirmed in Case C-450/06 *Varec v Belgian State* [2008] ECR I-581

[5] Article 1 of the Protocol to the European Convention on Human Rights, as amended by Protocols Nos. 11 and 14, Council of Europe Treaty Series, No. 5 provides:

> "*Every natural or legal person is entitled to the peaceful enjoyment of his possessions. No one shall be deprived of his possessions except in the public interest and subject to the conditions provided for by law and by the general principles of international law*."

This right to the protection of possessions is repeated in Article 17 of the Charter of Fundamental Rights of the European Union, 2010/C 83/02, 2010 O.J. (C 83) 389 as follows:

> "*Everyone has the right to own, use, dispose of and bequeath his or her lawfully acquired possessions. No one may be deprived of his or her possessions, except in the public interest and in the cases and under the conditions provided for by law, subject to fair compensation being paid in good time for their loss. The use of property may be regulated by law in so far as is necessary for the general interest.*"

[6] Case C-450/06 *Varec v Belgian State* [2008] ECR I-581 and *Interseroh Scrap and Metals Trading GmbH v Sonderabfall-Management-Gesellschaft Rheinland-Pfalz mbH (SAM)* (Case-1/11, para. 43); *R (on the application of Veolia ES Nottinghamshire Ltd) v Nottinghamshire County Council (Dowen and another, interested parties)* [2010] EWCA Civ 1214, at paras. 120 and 121; *Van Marle and others v The Netherlands (Application No. 8543/79, Judgement of 26 June 1986) paras. 41-42;* [6] *Smith Kline & French Laboratories Ltd v The Netherlands* (1990) 66 DR 70 in a case relating to patents. The ECHR has also considered that licenses are a form of possession *Tre Traktörer AB v Sweden (App No 10873/84);* [6] *R (on the application of Malik) v Waltham Forest NHS Primary Care Trust* [2007] EWCA Civ 265, para. 29.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		case balancing exercise, including consultation with the owner of the confidential information, before it reaches a decision as to whether disclosure of the confidential information would be proportionate in light of the public interest. There is an element of timing and circumstance to this balance of interests that can only be accounted for through a robust process giving the MA holder the opportunity to assert and resolve a CCI claim. The EMA's draft Policy, for example, applies to clinical trial data in withdrawn or denied MA applications; EFPIA is very concerned that the release of certain data from these dossiers could prejudice the integrity of the regulatory process for any future re-submission, as well as potential MA submissions in markets outside the EU, and could therefore undermine the future commercial viability of such products. Therefore, EFPIA believes that the policy should not apply to withdrawn or denied MA applications. EFPIA believes that these situations illustrate with particularity how meaningful consultation with applicants is indispensable in order to determine whether information is CCI and whether, even if CCI, disclosure of information is justified by an overriding public health interest, in any particular case. The EMA's stated broad assertion that it may disclose MA data because MA data cannot be considered CCI is inconsistent with the recent decision on the release by the EMA of clinical data issued in the on-going litigation before the General Court of the EU.[7] As stated by the President of the General Court, who ordered the EMA not to release clinical trial information in a MA dossier that the applicants in those cases considered CCI, it is not "entirely unfounded" to conclude that the hundreds of pages in a clinical study report,	

[7] Cases T-29/13, T-44/13, T-44/13 R; T-73/13 and T-73/13 R.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		containing as they do the intellectual analysis and know-how of sponsors, contain CCI.[8] Moreover, the Court decided that " the question whether an overriding public interest might nevertheless justify disclosure of CCI will call for "delicate assessment," in the "weighing up of the applicants' commercial interest in not having the reports disclosed and the general interest intended to guarantee the broadest public access to documents held by the European Union. "[9] Clearly, the President of the Court rejected the blanket position, articulated in the draft Policy that the public interest, in all cases, prevails over the interests supporting non-disclosure of CCI. EFPIA believes, and the Court has acknowledged[10], that there are important legal questions to be resolved in this respect, and that the two elements of CCI and the public health interest both need to be considered.	
05	General	It needs to be ensured that copyright considerations are covered appropriately. For example, Patient Reported Outcomes questionnaires may be copyrighted and therefore those Case Report Form pages should not be made publicly available.	
05	15:	There is a growing demand for full transparency from certain external stakeholders in the debate. EFPIA supports responsible transparency, which recognizes that full and unfettered transparency of all information submitted as part of MA dossiers could also have unintended detrimental consequences.	
05	28- 32:	Here the intent is described as improving the efficiency of the drug development process by enabling competitors to benefit from access to each other's proprietary information. This is not a proper purpose under EU law for disclosing CCI and should not be the primary intent of the EMA's transparency initiatives. In particular, the reference to	This premise should be further considered.

[8] Paragraphs 59-61 & 68 of the Decision.
[9] Paragraph 69 of the Decision.
[10] Interim measures rulings in T-44/13 R and T-73/13 R, 25 April 2013.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		establishing a level playing field is unfortunate and open to misinterpretation. EFPIA does not share the current EMA vision that enabling untracked, uncoordinated and unsupervised secondary analysis of CT data on which MAs are based will provide substantial benefits for the public health. Ultimately, data access and enhanced, responsible transparency can only positively contribute to society if robust conditions for secondary analysis are established and enforced.	
05	32-35:	Greater transparency of the regulatory decision making process is laudable and may increase confidence of patients and prescribers, if implemented responsibly. However, the contention that replicating the clinical trial analyses will improve confidence and rigour without compromising the regulatory process may be too simplistic. It could equally undermine the regulatory evaluation process and may not offer any positive benefit over a high quality review by the health authorities. In our view, and based on EU legislative framework, the regulator's core function is to ensure the validity and robustness of the clinical trial process. Indeed, the regulatory framework is designed to enable this rigorous scientific oversight for all Industry-sponsored trials to ensure scientific validity in the design and conduct of clinical trials including pre-specification of the trial protocol, associated statistical analytic plan, careful documentation of any changes in the protocol, and oversight by institutional review boards (IRBs) and data and safety monitoring committees. Also, implementation of this draft Policy would require variable use of resources within the Agency (in order to validate or invalidate	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		interpretations) inevitably diverting energy from core responsibilities – i.e., evaluating the safety and efficacy of medicines. EFPIA considers that a more robust mechanism of data sharing should be put in place, and is committed to implement a system to receive and review research proposals and provide applicable data to help facilitate such scientific and medical research.	
05	44-47:	In the draft Policy, the EMA infers a far broader scope to individual patient informed consent than is given in reality. The release of patient level data can only take place within the scope of the specific informed consent given by the patient to the trial sponsor. How will the Agency ensure that the integrity of patient consent and the use of data do not overstep the boundaries of an individual patient's informed consent (e.g., informed consent specifically does not permit release, informed consent is silent on the subject of release)? Unless explicitly stated in the informed consent, it cannot be assumed that patients have consented to their information being released in order to "benefit the advancement of science and public health". Without the prospective understanding of the effectiveness of the measures that will be put in place to ensure their anonymity, it is difficult to envisage how a subject can give truly informed consent to the ongoing use of their personal data. It is unclear from the draft Policy how international studies would be managed, if informed consent forms varied across countries in relation to release of patient level data.	
05	50-51:	The EMA statement "CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI" – EFPIA strongly contests the EMA's assertion in this regard. This precise issue is currently the subject of litigation before the General Court of the EU.	In the light of the decision of the General Court, the draft Policy should either be revised substantially in relation to the protection of CCI, or implementation should await the final outcome

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		Furthermore, on 25 April 2013 the President of the General Court granted interim measures in favour of AbbVie[11] and InterMune[12] preventing the Agency from disclosing to third parties certain clinical data from these companies' MAA dossiers before the companies' respective legal challenges to the Agency's proposed actions had been fully examined by the Court. The President considered that both companies had demonstrated a prima facie case that the Agency's decisions to disclose such documents were in breach of Article 4(2) of the Transparency Regulation; the fundamental right to the protection of information covered by business secrets and information of a confidential nature under Article 7 of the EU Charter of Fundamental Rights; and the obligation by EU institutions under Article 339 of the Treaty on the Functioning of the European Union not to disclose information that is covered by the obligation of professional secrecy. The EMA's broad and unexplained contention that CT data cannot generally be considered CCI and its intention to implement this in its new proactive disclosure draft Policy in the near term, directly contradicts this ruling of the General Court. Also, this statement is inconsistent with the CCI definition adopted by the EMA and set out in line numbers 109-111 of this draft Policy. Some information in certain MA dossiers, depending on the sponsor, product at issue, competitive landscape, therapeutic area, and value of the information to competitors may, indeed, be CCI. Considerations of an overriding public health interest are relevant for the distinct purpose of determining whether in certain circumstances, public health interests in disclosure of CCI outweigh considerations	of the litigation. Otherwise, companies will be denied effective redress should their CCI or PPD be at risk of inappropriate disclosure. One approach would be to replace the statement "CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI" with the following: CT data and other information present in MA dossiers submitted by sponsors may qualify as CCI, as defined below in this Policy. If the EMA seeks to release CT data, the EMA will engage in a process with each affected sponsor to determine whether such data constitute CCI. If the data constitute CCI, a separate inquiry will be made prior to public disclosure to determine whether an overriding public health interest justifies release of the information. Also, a robust process for consultation with the MAH prior to release of information should be implemented.

[11] Case T44-13
[12] Case T73-13

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		supporting non-disclosure of protected information. If information in a MA dossier meets the definition of CCI adopted by the EMA in this draft Policy at lines 109-111, and if the EMA seeks to release such information over the owner's objections, then a separate inquiry needs to be made prior to public disclosure to determine whether an overriding public health interest justifies release of the information. Please note EFPIA's Fundamental Comments, Section 3, for a detailed discussion of the topic of CCI within the draft Policy.	
05	55-56:	It is stated that the draft Policy "is designed to guard against unintended consequences, e.g. breaches of intellectual property rights…." but the nature and effectiveness of these safeguards are unclear. The draft policy contains no procedure for the consultation of the MAH and review of the data, or for the MAH to appeal against the EMA's decision to disclose, in advance.	In order for EMA to provide safeguards against unintended consequences by controlled access as set out in line 176, "dissuasive, effective and proportionate sanctions" for the requester should be envisaged in the case of violation of the requester's obligations. The MAH, as the party which will suffer from breach of controlled access terms, should be able to enforce the controlled access and seek imposition of the sanctions. Also and as previously described, a robust process for consultation with the MAH prior to release of information should be implemented.
05	57-61:	"It <u>should</u> be possible to "guarantee that all secondary data analyses (….) will be conducted and reported to the highest possible scientific standard". If this is not possible with a "truly open approach", then that approach should not be taken, especially given that the stated goal (according to line 75, protecting and fostering public health) can be achieved by a more controlled and responsible approach. The EMA asserts application of the best safeguards to achieve the highest possible scientific standard, to protect public health and	

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		regulatory decisions. However, EFPIA strongly believes that the safeguards are insufficient, e.g. • Why are there no legal obligations resulting from the document on CT data-analysis standards (see line nr. 207/209)? • Why is it not mandatory to upload a statistical analysis plan (see 210)? Is it actually possible to review/challenge the secondary analysis without a SAP? • Why is the granting of access to "C" documents not influenced by the requester's decision to upload a SAP or not? (see 214/215) Does the upload of a SAP have an impact on EMA's goal to enable independent replication of CT data analysis? (see 33) • Why are there no requirements with regard to the requester's professional competence or inclusion of a qualified statistician to conduct analyses, etc.? (see 216-218) What are the measures to ensure the best-possible protection of public health against claims resulting from inappropriate analyses EMA is referring to in line 60? When would such measures be put in place? Unless these measures are appropriate, comprehensive, effective, and enforceable then there will continue to be substantive public health concerns around inappropriate analyses and false hopes or concerns from patients based on improper research. These measures will need to be detailed and validated with particularity before legitimate determinations can be made as to whether the public disclosure of otherwise protected information is in the public	

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		health interest.	
05	65-66:	EMA's draft Policy states: "Once a decision has been reached, this consideration [= protection against external pressures in whatever direction] no longer applies." This statement does not take into account the case that EMA's final decisions are subsequently disputed.	
05	67-72:	We fully support the need for two way transparency and equal level of scientific standard for all clinical studies, but it is unclear what is meant by the statement "allowed a reasonable period of time during which their analyses and deliberations are protected against external interventions". A key part of the recommendations from the Good Analysis Practice advisory group was the need for the availability and review of the analysis plan, in advance of data access to ensure a high quality analysis and the ability to determine if the analysis can be replicated by others. It appears that the draft Policy affords protection for confidentiality to third party researchers (planned analyses would not be disclosed until up to a year after accessing the data) inconsistently to the standards for MA applicants (who must disclose information on their CT's prior to commencement). All documents relating to a third party researcher's request would appear to be disclosable under Regulation 1049/2001. Regulation 1049/2001 requires an Institution to notify the third party owner of information held by the Institution prior to disclosure of the information. Based on Regulation 1049/2001, there should be a notification to the third party owner of the information that disclosure is contemplated and allow the third party the right either	

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		to contest its disclosure or review any proposed redacted version of the document.	
05	91-98:	The Annex II reference to ICH E3 format should clearly indicate that the structure is not meant to dictate E3 use as a template since this would be in direct contradiction to ICH E3 Q&A (R1) of July 2012. As the CSRs for other types of studies will differ in format, it is unclear which general principles are expected to apply.	
05	113-115:	The statement "It is emphasized that categorisation of information as CCI in the policy does not limit access to documents or information under other agency policies" is inappropriate, and misleading because it suggests that standards used to designate certain information as CCI, and the consequences with respect to disclosure flowing from such designation, vary across regulatory processes administered by the EMA. The definition of CCI set forth and adopted by the EMA at lines 109-111 reflects general EU legal principles, natural and fundamental rights, and applies across all EMA purposes and policies. Access to such information is subject to the analysis set forth at Article (4)(2) of Regulation 1049/2001 Regarding Public Access to Documents, as discussed in more detail in the Fundamental Comments section of this EFPIA submission. This is true regardless of the EMA access to documents policy or transparency initiative at issue in any particular situation involving disclosure of CT data or MA dossier CCI information over the objections of a sponsor.	Remove this statement.
05	116-117:	The "elements submitted as a study report" may not follow the format of the ICH E3 document.	
05	121:	It is not clear what is meant by "test outputs". We would traditionally consider test output as being output that is created by a program prior to the program being peer-reviewed, validated and put in 'production' (i.e., its final read-only location). We see no purpose in storing test outputs or providing them to anyone.	Remove reference to or define what is meant by test output, as it is not clear how it relates to raw data.

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		Perhaps “test output” has a different meaning in the draft Policy.	
05	122-123:	In this draft Policy, EMA appears to express its intentions to request, for the particular purpose of transparency, more information from companies than requested in the past as part of an application (e.g. SAS logs, SAS programs). In that respect, the draft Policy goes beyond the purpose of the legislation to provide access to documents of the institutions (Art. 2 para 1 of Reg. 1049/2001). Further, it is not clear how SAS code and SAS logs are covered as supporting documents. These are tools for analysis. An appropriate SAP including a description of the statistical model will qualify for repeating all analyses. Pharmaceutical companies put a lot of effort (time and money—often developed by third parties) into developing and validating macro (i.e., computer code) libraries. We believe these would be considered intellectual property.	The Statistical Analysis Plan should suffice for requesters to understand what was planned and done.
05	129-132:	“CT data/documents containing CCI: a small number of CT data/documents can contain CCI. […] However, this information will only be deemed CCI in duly justified cases” Clarification is needed for the process by which companies can justify that information is CCI, and disputes resolved. This process must involve a case-by-case analysis of the relevant factors defining CCI, and a precise and careful weighing of any public interest at stake sufficient to justify release of otherwise protected information. Likewise, as stated by the President of the General Court in paragraph 69 of the interim measures case cited earlier in these EFPIA comments, judicial review of disclosure disputes that cannot be resolved between regulator and regulated must ultimately be made available -- “the weighing up of the various interests present will call for delicate assessments which must be a matter for the Court adjudicating on the substance of the case.”	The following approach should be added and applicable to all data/documents: Any information contemplated for release by the Agency will be provided to the MA applicant of the information, prior to release, in order to ensure that no information contemplated for disclosure constitutes CCI. A reasonable time will be afforded the sponsor to confirm that information to be released by the EMA is already in the public domain, or is otherwise not information the sponsor considers confidential, or not the sort of information that, if released, could harm the competitive interests of the owner of the information. Justification in support of CCI claims should be provided by the sponsor to the

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			EMA. Such justification will be respected by the Agency, but may be rebutted by, for example, information indicating that information to be released has in fact already been made available, or is the sort of information that the owner of such information does not normally protect from disclosure, or is information that would not cause competitive injury if released. Likewise, because even CCI may be released if justified by reference to an overriding public interest, the EMA will have the opportunity to justify release of CCI by articulating such a public health interest, as warranted and appropriate under the circumstances of any particular case. Ultimately, disputes over release of purportedly CCI information that cannot be resolved by consultation between Agency and applicant will be subject to judicial resolution prior to disclosure, through well-established, fair and orderly processes regarding judicial review of regulatory Agency decision-making.
05	139-143:	The draft Policy would treat certain documents as "without protection of personal data (PPD) concerns" (i.e., "open access"). This is to include documents where "any personal data in the document have been adequately de-identified". Further, the proposal indicates that all documents meeting the open-access criteria that are submitted to the Agency on or after 1 March 2014 will be subject to the new policy. Nevertheless, the proposal also indicates that the Agency's timeframe for publishing guidance concerning "appropriate	

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		standards, rules and procedures for de-identification" will occur much later - possibly not before 31 October 2014. This presents marketing authorisation applicants with a paradox: Until clear guidelines are issued for what constitutes "adequately de-identified" data, applicants will be unable to determine when this criterion has been met; yet, the proposal would require applicants to make these determinations starting in March 2014, prior to the promulgation of the guidelines. We presume that the Agency intends for the term "de-identified" to be synonymous with "anonymised". The Data Protection Directive 95/46/EC specifies that it will not apply to "data rendered anonymous in such a way that the data subject is no longer identifiable" (Recital 26). To determine whether data has been properly anonymised, "account should be taken of all the means likely reasonably to be used either by the controller or by any other person to identify the said person". Unfortunately, there is no commonly accepted definition across the EU of what it means for data to be anonymised. There are two competing views - one, that "anonymised" means the risk of re-identification is very low; the other, that "anonymised" means there is no risk of re-identification. Providing certainty about re-identification of a patient is not possible today. This is likely to become increasingly the case in the future as technologies and publicly available data increase. It is therefore recommended that the term de-identified is used to indicate that a level of risk exists but is actively managed. Finally, the policy should acknowledge that there are situations where even aggregated data can still be considered PPD (e.g., rare diseases with very small populations).	At a minimum, the Agency should discuss this topic with industry and other major regions to determine a definition for “de-identified” that is approved by the relevant data protection authorities and indicate which of these views it is adopting.
05	144-149:	The open-access category is proposed to also include "personal data of CT personnel" for which "there are public-health reasons why personal data can be made public, overriding considerations of	

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		[protection of personal data]". This appears to reflect a broader disclosure policy than that put forth in the March 2012 HMA/EMA Guidance Document on the Identification of Commercially Confidential Information and Personal Data within the Structure of the Marketing Authorisation (MA) Application. The March 2012 Guidance distinguishes whether personal data can be released based upon the individuals legally defined role or responsibility and indicates that the names of experts and designated personnel with legally defined roles or responsibilities can be released because "it is in the public interest to release this data". (§ 2(A).) However, with respect to names and personal details of other staff members, the Guidance indicates that such information should be considered protected personal data. We believe that no information in relation to the names, or technical or professional qualifications of any company employees or experts (whether or not directly involved with animal research) should be publicly disclosed; all such information should be classed as PPD.	
05	151-152:	The draft Policy states that it will be applicable "at the time of publication of the European Public Assessment Report (EPAR) for positive decisions..." It is important that any CT data disclosure takes place only after the product has been authorised in major regions including the US, Japan and the EU, if applicable. Otherwise the information could be released in one region while the assessment for authorisation would still be ongoing in another region, which could undermine the integrity of global regulatory processes.	EMA's policy should only apply following regulatory approval in major regions including EU, US, and Japan – participants of The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).
05	152-154 and 219-231:	If an application is withdrawn there may still be an ongoing development program requiring more data to be generated or the exploration of, for example, a different indication. Proactive dissemination of the data submitted for this type of compound could prejudice the integrity of the regulatory process for any future re-submission, and undermine the future commercial viability of the product.	The policy should not apply to withdrawn or denied MA applications. Of note, the EFPIA/PhRMA principles reaffirm that, "At a minimum, results from all phase 3 clinical trials and any clinical trial results of significant medical importance should be submitted for publication. This commitment also pertains to investigational

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			medicines whose development programs have been discontinued."
05	165-175:	The Agency's proposal does not provide a clear definition of what will constitute "de-identified" data. It is unclear what "limited" means in the statement of limited number of identifiers. The proposed standards are minimal and more exacting standards should be developed to ensure patient confidentiality is maintained. At lines 169-170, the Agency suggests that data will be considered de-identified where "the risk of compromising subjects' identity in case of wide publication of those data is considered to be absent or sufficiently low". This suggests the Agency supports a risk-based threshold for de-identification. However, at lines 174-175, the Agency appears to support an absolute "zero-risk" standard: "The methods of de-identification should be such that adherence will preclude subject [r]e-identification, even when applying linkages with other data carriers (e.g. social media)." We contend that it will be very difficult to implement the recommendation to de-identify data in such a way that "adherence will **preclude** [emphasis added] subject de-identification" (presumably "re-identification"). Even the cited references (Hrynaszkiewicz and Norton, 2010) suggest some options that are difficult to implement such as "Consent for publication of appropriately anonymised raw data should ideally be sought from participants in clinical research" and that in some cases there should be a review by an ethics committee. Requirements and guidance would be necessary, which have the agreement of data protection authorities, to provide assurance to patients that their privacy is appropriately being protected. Finally, the proposal should make clear who is responsible for	A standard for de-identifying data would need to be developed that all can follow; however, complete de-identification would be difficult to achieve.

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		determining whether the proposed uses of the data (as proposed by the requester) are within the boundaries of the patients' informed consent or whether an oversight mechanism is envisaged. Ultimately, the EMA would be responsible as the body disclosing the data. Prior to disclosure, there should be an assessment to ensure that the proposed research use aligns with the research use of the original study (and therefore with the informed consent). When considering the possibility to provide access to clinical data involving personal data, it is necessary to address both data privacy obligations and the potential benefits that could result from the analyses.	
05	176-178:	There should be a requirement for third party requesters to submit their analysis plan. In addition, the resources required to enable access to the data should be sufficiently balanced against the public health benefit expected from the analysis. Therefore, a robust review of the planned analysis for its scientific merit should be mandatory before enabling any data access.	Request should submit their analysis plan. Also, please add the clarification below: "'Controlled access' shall mean that access to 'C' data will only be granted after the requester has fulfilled **all of** the following requirements…"
05	181-183:	The EMA conditions access to 'C' documents on execution of a "legally binding data sharing agreement," but it is not explained who the parties to such an agreement will be, the legal basis for the EMA entering into such an agreement, how the EMA will ensure the enforcement of such agreements, or the penalties or remedies available to a company or an individual harmed by use of data released inconsistent with such agreements. Implementation of a controlled access regime cannot be implemented until these critical questions are answered. If parties qualifying for controlled access must comply with certain contractual conditions, then the EMA must with particularity describe the enforcement mechanisms and penalties to be enforced in cases of breach or noncompliance. The MAH should likewise be a party to the agreement, so as to provide it with the possibility of enforcement of compliance with the	

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		agreement.	
05	183	The reference to the “spirit of informed consent” implies a very permissive approach to the respect of the informed consent in disclosing patient level data. Please note above EFPIA’s comments on Lines 165-175.	
05	191-192:	It is not clear how or by whom a particular disclosure is to be “deemed” outside the scope of patients’ informed consent.	Further explanation is required.
05	193	The restriction on using CT data to gain a marketing authorisation in a non-EU jurisdiction should be extended to the EU as well.	Explicitly state that the restriction applies to the EU and non-EU.
05	222-231:	Any postponement of disclosure of details about the secondary analysis seems to go to the expense of the MAH if his interests are impacted before the end of the 1-year period. The period may limit the MAH’s possibilities to review the secondary analysis and impede MAH’s chances to promptly and effectively challenge it.	
05	205:	The draft Policy states: “destroy CT data accessed”; however, it is not stated how the Agency would ensure that the CT data is destroyed appropriately and in a way that no third party can re-use it. It would be reasonable to oblige the requester of the CT data to provide evidence about the necessary deletion of the CT data. We would also recommend adding expectations around appropriate storage of PPD data between downloading and destroying (e.g. Access, security – Physical/logical etc…). The data should stay in a “closed secure environment” that would help ensure appropriate protection of personal data.	A secure environment, without the possibility to download, copy or otherwise remove the data, should be implemented.
05	206-215	“Before access to 'C' data is granted, the requester will be: …however, the requester may decline to upload any documents at that time; the granting of access to 'C' documents is not influenced	

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		by the requester's choice to upload or not." It is inconsistent to state that an analysis plan is of utmost importance, but then not require that such a plan be submitted prior to the granting of access to the data. The level of disclosure required of the requester regarding analyses and results should be the same as required of the MAH.	
05	219-221:	The draft Policy states that it will be applicable "at the time of publication of the European Public Assessment Report (EPAR) for positive decisions...."	EMA's policy should only apply following regulatory approval in major regions including EU, US, and Japan.
05	222:	In the context of this policy we consider it is appropriate for the EMA to immediately disclose the identity of the requestor.	The Agency will ~~not~~ immediately disclose any information about the requester, ~~but will publish~~ **including** the identity (name, affiliation, **funding source**, and contact details provided)~~.~~, **T**~~t~~he list of the aims of accessing the data provided…
05	235 – 244:	In this section, the requirements are expressed in the passive ("shall be provided", "shall be published", "shall be made available",) but there is no clarity as to who is responsible for these requirements.	Clarification is requested using active rather than passive language.
05	242-247:	This request appears to go beyond what is normally submitted for the purpose of EMA's assessment for a marketing authorisation. Industry commits to provide - upon request - patient level data under a self-responsibility scheme. The information requested here could be provided under this scheme (Also, see comments to line 253-255 and scope of definition of raw data line 121-123).	
05	249:	EMA draft Policy states that it will come into effect on 1 January 2014. EFPIA believes that there are numerous issues to resolve prior to full implementation.	Suggest an implementation date well beyond 1 January 2014 reflecting the need for additional clarification, regulation and sufficient time for

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			implementation.
05	253-255:	"MAH shall provide the Agency with an additional set of 'O' documents that are appropriately de-identified to ensure protection of personal data…." We would query the legal basis for this requirement. It is unclear how the Agency can legally implement this unilateral request if the MAH explicitly indicates that the documents might contain PPD and that EMA cannot disclose it without prior de-identification of the relevant data. In addition, it should be noted that the obligation for providing access to documents is with EMA, which means that EMA is responsible for ensuring that all data are appropriately anonymised.	
05	266-267:	We fully agree that the impact of the EMA's final Policy should be thoroughly evaluated and the impact assessed in line with impact assessment rules for EU Institutions before being adopted. Specifically the impact on resources needs to be determined. In order to facilitate this assessment, EMA should provide a formal consultation process so stakeholders could provide input into the EMA's methodologies for assessing the impact (i.e., impact not only on the Agency, but also on MAH's, clinical trial participation, overall investment in medicine R&D in Europe, etc.).	
05	279:	It would be helpful to explain further what is meant by "key codes".	
05	292:	EMA explains that the personal data of trial personnel will be "considered exempt from PPD considerations". The legal basis for this assertion is unclear and it seems to be inconsistent with current or recent EMA practice in making reactive disclosures of CT data. Therefore, we do not believe that the names of investigators, site staff and company personnel should be included in disclosed CSRs without the individuals' consent. We do not agree with the statement	

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		in the draft Policy that there is an overriding public interest in the disclosure of these names. It is particularly difficult to understand how the inclusion of these names (or not) in a CSR has any impact on public health. Furthermore, the inclusion of company names poses significant risks for individuals. EFPIA member company employees have been targeted in the past by animal rights extremists even though they have not been directly involved in animal research. The EMA's position on information on company staff is also inconsistent with their position on disclosure of information on EMA staff. In response to requests for access to documents held by EMA, names of EMA staff involved in pre- and post-authorisation activities will be redacted, on the grounds that disclosure would undermine the protection of privacy and the integrity of the individual, in particular in accordance with EU legislation regarding the protection of personal data.	
05	Annex 1:	2.7.2: The clinical pharmacology studies may include PET studies (or similar) which provide receptor occupancy and kinetics of the compound target interaction which the company may feel is CCI. 5.3.7: Access to patient line listings should not be within the scope of the Policy, because of the practical difficulties and significant resources associated with redaction/anonymisation, and the questionable additional value of the listings over and above the datasets.	
05	Annex 2:	For Annex 2, EFPIA do not believe that patient listings in the CSR and CSR Appendices should be made available nor be included within the scope of the policy under either "open" or "controlled access". The documents would be difficult and extensively resource intensive to de-identify or redact, and the information would in any case be provided in the datasets under the industry commitments. At the very least, Annex 2 patient listings should be "controlled access". 16.1.4: We do not agree that information for all research staff should	Should be controlled access.

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		be available.	
06	General	**Introduction** vfa is the German Association of Research-Based Pharmaceutical Companies (vfa) representing the interests of these companies in Germany. 45 leading research-based pharmaceutical companies are organized in the vfa. Together with their more than 100 subsidiaries and affiliated companies, they employ nearly 90,000 people in Germany. In Germany alone more than 18,000 of their employees work in the field of research and development of pharmaceuticals. Here, the research-based pharmaceutical companies invest EUR 5.2 billion per year in pharmaceutical research. **vfa is a member association of EFPIA and therefore supports the major aspects from the EFPIA comments on the draft EMA policy.** Furthermore and on behalf of its member companies vfa would like to raise the following critical points in the draft EMA policy – see below. In the past the pharmaceutical industry has contributed much to the transparency regarding clinical trials by registering trials at their inception and by publishing summaries of the results. This should be respected within the discussion on clinical trial transparency.vfa welcomes that the EMA policy foresees a tiered access scheme depending on patient privacy and the protection of commercially sensitive information. It is also positive that the identification of the requester and contractual safeguards to protect the data in category 3 are provided. In addition, the new policy shall apply prospectively and so a time- and cost-consuming reformatting of data by the	

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		companies is not required. Overall the draft policy represents a compromise to go forward with regard to clinical trial transparency. However vfa misses some important elements and some aspects still need to be more concrete.	
06	28 - 32	*- Study sponsor must be involved in the release of clinical trial data* vfa and its member companies are committed to enhancing public health through responsible sharing of clinical trial data to help facilitate scientific and medical research – proven in various efforts by industry. We believe that it is in the interests of transparency and medical research that secondary research is subject to similar standards of transparency as the original clinical trial and a proportionate review that determines whether the release of clinical trial data with concerns regarding personal data or commercial confidential data is justified in any given case. So there needs to be a prior review of the requester's analysis plan and its qualifications - and this process must include also the study sponsor. This process must e. g. give the study sponsor the opportunity to blind commercial confidential information (CCI). Also it must be ensured that personal patient data (PPD) are not given to third parties. Furthermore the requester must sign a commitment that the data will not be distributed any further and that the requester will not use the data for any commercial purposes. Therefore it must be clear that the EMA policy ensures a fair mechanism to request and receive such data, while also ensuring that the data given to third parties are not misused.	

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		- Ensure *"Good Analysis Practice"* Secondary analysis and research of clinical trials data must be robust and for good scientific purposes. Therefore vfa considers that clear quality standards for the study data analysis need to be defined, which must valid for and respected by all players including third parties for any analysis of results from clinical trials. No one would benefit if arbitrary or inadequate evaluations regarding risks or shortcomings of efficacy be claimed based on incorrect analysis findings. Therefore vfa would like to propose to create an expert dialogue involving all players to set up a common ground for a *"Good Analysis Practice"*. Based on such a *"Good Analysis Practice"* vfa also sees the need that a requester of data need to provide the basic statistical analysis plan prior to the handover of any data by EMA or the study sponsor. Also there need to be a prior review of the requester's statistical analysis plan and the qualifications of the requestor. This process must include the study sponsor as already stated.	
	44-47	- *Data Privacy and scope of the informed consent by patients* The legal framework for data protection in the European Union (EC Directive 95/46/EC) and the relevant data protection laws of the EU Member States prohibit the disclosure of personal data without the consent of the patient. Raw data from clinical trials are not completely anonymised, but are provided with pseudonyms. This is always achieved in such a way that the record of the patient's name are removed by a code (pseudonym) so that	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		the record cannot be reassigned to a specific patient without the knowledge of an assignment list remaining with the attending physician - this is called "pseudonymous data". However, these date retain the possibility to re-identify an individual patient in principle. The patient informed consent allows explicitly access to personal data exclusively for the purpose of inspections by authorities and study monitors appointed by the study sponsor - in order to check the validity of the data. Furthermore the patient informed consent allows a handling of pseudonymous data in order to be used by the study sponsor for scientific analysis and for the marketing authorisation procedure. A disclosure of personal data or pseudonymous data (whose deployment options are explicitly mentioned in the informed consent text - only to authorities, the study sponsor, ethics committees, EU database on pharmacovigilance) to third parties is in most cases not covered by the current wording of the informed consent forms and any further distribution to third parties not mentioned in the informed consent so would be a violation of the given informed consent by the patient. This would undermine the trust of study participants and may have a negative impact on their willingness to participate in future clinical trials. To ensure the protection of personal data of the patient the EMA foresees in its draft that these data – including pseudonymous data - are released upon specific request and only after the applicant/requester meets a number of requirements, including the signing of a data-sharing agreement and the obligation to maintain the anonymity of patient data. In principle this is a correct approach.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		But in view of the wording in the current informed consent forms by the study participants, it is the view of the vfa that this approach by EMA is not in line with the consent given by the study participants. So the upcoming requirements in regard to this new EMA policy cannot be directly implement in all cases. The additional transfer of data to third parties can only be changed prospectively by necessary adjustments to the informed consent forms used in clinical trials. The study sponsor will have to decide for some years in each individual case on the basis of the respective informed consent used whether a disclosure of pseudonymous data is possible or not. Some companies have already provided appropriate wording in their consent forms that would also allow a transfer under the new policy of EMA. However, others have currently not. These aspects need to be made very clear in the EMA policy and thus, in our view, the new policy of the EMA can have its full effect only in the course of time. Prospectively appropriate formulations need to be included in the informed consent forms in clinical trials, which inform the participants thoroughly about this possible data transfer to third parties. With regard to anonymised data, Directive 95/46/EC does not apply from our view. Therefore it is possible, to pass certain anonymised data to external requesters for a transitional period until on the long term the informed consent forms are changed. The process of anonymisation of patient data would, however, require ultimatively the EMA to take over responsibility for a secure anonymity of patient data, as they put such data forward to the requestor. Possibly to ensure this anonymisation will be difficult to ensure in clinical trials in rare indications. So there is yet another need for discussion to ensure safe anonymisation also in these cases.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
	67-72	*- Prevent commercial use of data in third countries* From the perspective of the vfa it is also of high importance that the EMA policy will not be misused for any commercial purposes. This has to be ensured not only on the EU-level but also in third countries. In the past, some generic companies had attempted to use publicly available data for getting marketing approvals before the data protection period for the reference product had run out. In Germany some generic firms were successful with this approach. Meanwhile court decisions have confirmed that the provision in Article 10 of Directive 2001/83/EC and Article 14, Section 11 of Regulation (EC) 726 /2004 does not allow this. Yet the same level of protection is not given in most third countries Based on the data that was provided by the EMA on the basis of the planned transparency policy in combination with their own bioequivalence studies, generic companies might try to obtain authorisations in third countries. Therefore it is welcomed that the EMA policy does foresee should ensure that the requesters commit themselves not to use these data for any commercial purposes and that they will not make these data available to third parties. Should the data not be used accordingly e. g. for commercial purposes, EMA and the manufacturer of the originator should jointly sue the requester and exclude them for the future from all future data disclosures.	
07	General	I support this proposal, everyone will benefit from the publication of clinical trial data. This policy is important; it is time that all clinical trials are reported.	
08	General	This is just a generalised "Thank you" for tackling this important issue. The	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		present situation is unsatisfactory and needs reform.	
09	General	It is vital for evidence based science to have all evidence known and not just a portion with a desired outcome. It is only for the greater good of humanity. Sadly, the greater good is now days rarely the driving force behind research. This has to change if we want to improve the existence of humanity today and in the future. Science is very dear to me. But some powerful forces with too much of monetary leverage seek to corrupt science by excluding valid data from the public/professional eye. This has to stop if we want to build an existence that is good for us, our children and their children. Please make all research publicly accessible. It is only the right thing to do.	Make all research publicly accessible.
10	General	If the aim of the European Medicines Agency is to protect and foster public health and transparency is a key consideration, then full access should be given to all clinical trial data. Regardless who planned, financed, analysed or published the trial. Protection of personal data is an important issue but should not be used by anyone as an argument to deny or limit access. As stated in the draft policy, there are established ways and means to anonymise data and protect patients from retroactive identification. 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. This objective can only be accomplished when full access to all clinical trial data is established. It is not in the interest of trial participants that disclosure of data is used to bias research data in a way is it has evidently happened in the past - causing inestimable harm to many	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		patients. Clinical trial data is an public interest and always outweights commercially confidential information. The later has been used to often in the past to disguise hidden agendas and mislead the public. A sustained and high level of bio-pharmaceutical research has been and will always be insured by public funded universities and research institutions. The pharmaceutical industry brings ideas to the market but is rarely responsible for high level research. If full transparency is accomplished then inappropriate data analysis can and will always be openly criticised by others. Even regulators are not error free. Therefore the decision-making process should be transparent and discussable. However, of course the decision-making process should be protected against external pressures in whatever direction. The same should be true for the decision-making process on the future policy on the publication and access to clinical-trial data.	
11	General	This is clearly a major step in the right direction. In my view the legal clarification of “commercially confidential information” is essential, since in many jurisdictions (eg USA) the notion of trade secret=intellectual property, trumps all other considerations, including the public health. Therefore, currently, the FDA is prevented from releasing any such information. If, as seems likely, the EU court upholds the EU Ombudsman views, this will furnish an invaluable, world wide, precedent.	
12	General	It is imperative for public health that ALL data be accessible so that health care professionals can make completely informed decisions regarding the	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		health and well-being of their patients.	
13	General	My comments are not about changes to the document. In fact, the opposite. Having watched AbbVie's Lawyer, Neal Parker, and read the EFPIA documents, I'm writing to urge you not to change the document in response to their requests. What you're doing is right, long overdue, and their attempts at trying to undermine your efforts are shameful. Patients here, in Europe, and indeed the world have paid a dear price for the industry sheenanigans, as have doctors like me. Do everything in your power to let us see the actual data that our prescriptions are being based on!	
14	83-85	It is vital that *all* trial data be made publicly available in order to enable wide scope metastudies that aggregate all measurements ever made, especially in a field like pharmacology where biological variation makes large statistics essential.	
14	77-82	All historical data held by the agency should also be released.	
14	Rest of document	Having said all that, release of future submitted data that the Agency does have is part of that whole, and is certainly worthwhile. In summary, I think the policy is good, but needs to go further – I am certainly in favour of these first steps. Release the data! For Science!	
15	General	This policy is sensible and balanced. The priority is to ensure that clinically useful trial data is at all times open access, to maximise safety and utility for patient. We support the AllTrials campaign	
16	General	I fully support the move to clarity and openness. I remain concerned that commercial interests will maximise use of the restricted access section by reconfiguring data to limit access to negative results.	
17	General	I am informed that the following is a fact: In the UK, the Health Research Authority is about to implement its new policy to ensure all UK clinical trials are registered in a publicly accessible	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		database. From 30th September it will be a breach of good research practice to fail to register a clinical trial I hope the European policy takes this as a good start and makes it as difficult as possible for organisations to hide trials results that do not meet with their expectations.	
18	General	I would like to briefly comment on the draft policy on the publication and access to clinical-trial data. **I strongly support regulation to ensure that all trials are registered and all results reported.** I support the EMA's proposals which will help to make that happen. On the principles used by the EMA, I have some additional comments. "*The Agency has committed to the proactive publication of data from clinical trials submitted in support of a marketing-authorisation application, once the decision-making process has ended.*" I support regulation ensuring that all clinical trials are registered in advance, and fully reported as soon as they are completed, whether or not they are in support of a marketing-authorisation application. *"The Agency has embarked on this process because it believes that the release of data is about establishing trust and confidence in the system."* The purpose of releasing data is to make sure that doctors can prescribe the right drugs for their patients. It has nothing to do with establishing trust, or any other matter of perception. *"The draft policy has been designed to balance out the commitment to give widest possible access to data for independent scrutiny with the need to protect personal data as well as legitimate commercially confidential*	

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		information." Once *all* pharmaceutical companies are required to abide by the same rules of disclosure, none will be harmed by them. Therefore there is *no* legitimate commercially confidential information as far as clinical trials are concerned. The protection of personal data is worthwhile, but should *not* be allowed to impede disclosure of information that researchers need, or cause bureaucratic delays.	
19	General	I support any action that will ensure all trials are registered and all results are reported openly and transparently. Please help to end all hidden and distorted information that emerges from the current reporting system.	
20	General	It is in the benefit of patients and that is it !	
21	General	My comments are general rather than related to specific lines. As an individual affected by how the pharmaceutical industry operates I consider it essential that all trials on all drugs or potential drugs should be comprehensive and published in full. That includes: • The purpose of any trial should be published in advance; • The methodology of any trial should be published in advance; • The proposed timing of any trial should be published in advance; • The results should be published in full; • The publication of selective results should be prohibited; • The publication of meta results should be limited to independent bodies	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		such as the Cochrane Collaboration; • It should be required that any trial compare a medicine to the best available alternatives and not just to a placebo; • It should be required that all subsequent publicity, marketing or selling of a medicine by the supplier or any subsequent supplier should include: o Its ranking against other medicines, such as: ▪ Better than all others; ▪ Same as x, y and z; ▪ Barely beats placebo; o Any distortion of the ranking to cost ratio should constitute a criminal offence both for the supplier and all individuals involved in the sales and marketing process; Where a drug becomes used for a non-licensed purpose the supplier should have to perform and publish appropriate trials on the basis described above within a set time.	
22	General	All medical trials must be transparent and public. That includes: • publishing information about trial before it is started in a public registry (including procedures, doses. proposed trial methodologies, where and when results will be published.) • after end of trial, all data from trial must be published, including raw data, cases dropped from trial (including reasons), and official trial results.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		• public trial registry and trial results data must be freely accessible for everyone using Internet without the need to give any reason or registration. • failing to disclose any data from trial should be a criminal offense with penalties ranging from huge fines (payed always by companies and by researches when they're proven guilty) and/or jail time (for company managers and researchers) if there is a loss of life.	
23	General	I was born in 1976 with [*omissis*]. My mother was prescribed the [*omissis*]. I am in contact with a large amount of other people affected with disabilities that range from minor to horrific. We all feel that data was not fully reported by Merrell Dow Pharmaceutical and as a result people's lives have been destroyed.	
24	General	I wanted to write in support of a policy that all trials, regardless of outcome, be published. Ethically it is the most logical way forward. Negative outcomes are just as important as positive and will help combat false statistics.	
25	General	I am a lay person passionately interested in this subject following [*omissis*] by the administration of a drug. After reading a book on the practices of the pharmaceutical industry worldwide, I realised that [*omissis*] was far from alone in having suffered this fate. I do not want what has happened to [*omissis*], and to [*omissis*], to be suffered by anyone else and so I want to make myself heard loud and clear - the data collected from all clinical trials, be they completed or abandoned, must be published and shared among all interested bodies. This is particularly important in the case of abandoned	

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		trials, which may have been dropped because of unfortunate side effects or non-compliance indicating that the drug is possibly going to do more harm than good.	
26	General	I am writing in support of the EMA's proposed policy on access to clinical trial data. As a former health researcher [*omissis*], I am only too aware of the loss to society that arises when such data is not available. It is not acceptable to keep data hidden. Such a practice skews any assessment of the efficacy and safety of any intervention and puts health and lives at risk.	
27	General	I simply wish to express my strong support for the proposal to publish all clinical trial data. I spent several years being prescribed a drug that had much of its trial data hidden, and once that trial data was revealed it became clear the drug was not effective and may be harmful. To do anything other than publish all trials is to put commercial interests above safety and health.	
28	General	1. I whole-heartedly support this initiative and any others to ensure that all significant details and the results of ALL clinical trials are made freely available. Public health and the proper use of public funds require this. 2. Though personal data should be protected, this should not be used as an excuse for not disclosing trials or results. At an absolute minimum, the fact of the occurrence of any trial should be published together with the research team's assessment of the result. 3. Trial details should not be withheld because reasons come to light (or are claimed) which appear to make the trial invalid. This applies even if a trial is	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		not completed.	
29	Draft Section 2 Line 83 et seq. refers.	A major problem in evaluating clinical trials is that the outcomes and indeed the very existence of trials conducted but not submitted as part of the support documentation are excluded. This allows the applicant to 'cherry-pick' evidence. Scientifically, this is completely wrong because it skews the data. It is akin to seeking to show that the average height of European adults is more than two metres, while permitting the exclusion from the data set of all adults below a height of 1.99 metres. Clinical trials should be pre-registered before being conducted. Any trials not so pre-registered should not be permitted to be included in support documentation. Any relevant pre-registered trials not so included should be listed with the application and the results should be accessible to bona-fide stakeholders, so that the possibility of 'cherry-picking' is minimised.	
30	General	I work as an Anaesthesiologist and this policy clearly has a long term impact on my job. Clinical trials -especially 'negative' ones- should be immediately publicly available after completion and all clinical trials should be registered in a public database. Without having access to the full knowledge gained through these trials doctors, regulators and patients alike will have a **distorted view of a drug's true effects**. Not only that, but when one considers the **ever growing costs of medical care**, it becomes crystal clear that we absolutely need to know as much as possible about the adverse side effects of a 'new' drug. I hope you will not cave in under the pressure exercised by the powerful pharma lobby and you will pursue this policy of transparency and access to	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		knowledge. After all, you will be a patient too! (if you are not already...).	
31	General	I strongly support the full publishing and public sharing of all clinical trial data for any medicine or medical device. The only way for doctors and patients to make good, safe decisions about suitable medication is for them to have full access to every piece of information that exists about a product. I believe the withholding of any such knowledge should be a criminal offence.	
32	General	There is a strong need of transparency to respect both the patients' rights and the researchers/clinicians' role in development of knowledge.	
33	General	The European Medicines Agency's proposed policy on publishing and sharing information from drug clinical trials is immensely hopeful and necessary. The current lack of transparency regarding drug trials that is legally acceptable in Canada and elsewhere has personally affected my health and that of many others I know or know of through the media. The debilitation and harms that results from present drug retailing practices would be categorized as criminal if they were inflicted by individuals rather than on a corporate basis.	
34	General	I had a look at your draft and have to comment that I don't consent in the point of different access-groups. It's important for scientific transparency that all trials are registered, reported and open for everyone. Personal data of study-participants can be protected while the results can be spred freely. The All Trials-campaign (http://www.alltrials.net) gives a good example how this can be done.	
35	General	In general we support this advance in transparency.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
35	185	Who decides whether the reasons for access given are sufficiently 'exhaustive'? We are concerned that sponsors may put pressure on the Agency to demand excessive requirements of bonafide researchers. By its very nature, the transparency afforded by this policy should allow exploration of the data sets. Such exploration cannot be prespecified.	
35	198	Who decides whether ethical approval is appropriate? Secondary analysis of data and metaanalysis does not usually require ethical approval. It should of course be the agency who decides this, but reference should not be made to the sponsor in making this decision as it is possible to envisage that data owners will demand ethical approval as a way of delaying access.	
36	General	ALL trials should be published!	
37	General	Very pleased to see this new policy, but with the majority of medicines in current use having been licensed for many years, shouldn't this apply retroactively to the greatest possible extent? All trial data that the EMA holds for currently licensed medicines should be published as per this guidance, not just applications from 2014 onwards.	
38	General	I am writing to thank and applaud the European Medicines Agency for their proposed policy to publish and share Clinical Trial data. How we arrived at a point where such information would NOT be shared, reveals just how far afield the medical industry has strayed from serving public health and patient welfare. Clearly, clinical trial data must be shared if there is to be any credibility or validity to the trials--especially given that most clinical trials are funded by the very pharmaceutical companies that would most gain from favourable study outcomes.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		Thank you for your work.	
39	General	Excellent moves forward in the right direction. As a healthcare professional it is difficult to make clinical decisions without all of the relevant information.	
40	General	I fully support full disclosure of all trials and their results (subject to patient and other safeguards) as being essential for the future health of European citizens. Pharmaceutical companies should not be allowed to selectively publish only the most favourable results – this distorts our view of medicine effectiveness and potential side effects.	
41	General	We fully support the proposal for disclosure of clinical trial data. These data are not “owned” by the company, because public funding is the basis of most drugs in their early stage of development and during clinical testing, e.g. when hospital infrastructures are used. Patients participate in these studies with the expectation to contribute to medical progress and are usually not aware, that the data are often hidden by companies after completion of the study.	
42	General	Patient Safety is essential in the provision of patient care and should be the goal of all health care professionals regardless of the sector in which they work. To provide the best possible patient care **it is imperative that we use an evidence based approach to patient care.** This cannot be achieved without access to **all of the data.** Therefore, all data must be published and available in the public domain. The absence of evidence impedes good decision making and prevents the	

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		identification of best practice in patient care. **Research and Development** is a very **<u>expensive business</u>** and making all data available will ensure that our resources are directed to treatments that give yield genuine benefit to patients as well as prevent the waste of valuable resources.	
43	General	I support your policy of sharing all clinical trial information. I was sent here through an AllTrials email.	
44	General	As a GP a have to make many decisions every day. Therefore I need every day the best possible database. It is essential to know whether our intervention has a benefit for our patients. We and especially people helping us to make good decisions (through research, developing guidelines etc.) need access to all clinical trials, whether positive or negative. All trials have to be registered in advance. Please help us to practice good medicine beyond economic interests.	
45	General	Please add my voice towards backing up free access to all clinical trials.	
46	General	I am glad that you are working on transparency in research. This is necessary to reduce bias so that we can find better care for people.	
47	General	As a retired industrial pharmacist and [*omissis*] I feel strongly that the results of all clinical trials should be made available to the public as well as to regulatory bodies. I therefore hope that you will increase the transparency of clinical studies. Keeping results confidential just delays scientific progress and increases overall costs of medicines to the public.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		My reasons are as follows; • It can be difficult recruiting an adequate number of patients in a clinical trial. Sufficient numbers are required to get statistically meaningful results. One way to encourage patients to participate is for them to know that the results of the clinical trial will be published. In this way patients feel they are doing their bit to help the advancement of science. • Both positive and negative results should be published. Both are equally useful. Unexpected results can often give clues to help researchers find better drugs. • Publication of all results will avoid duplication of similar studies. • We all want the best use of limited resources and to treat patients in the best way possible. This is not always possible with the current situation where information provided is selective.	
48	General	[*omissis*] and my mom took the DEBENDOX. II ask that all pharmaceutical companies to make public all the results of research and experimentation and that nothing is omitted, so that the reality is clear!	
49	General	I want you to Support an Open Access to all The Data of clinical Trials.	
50	General	It is of utter importance to pass this bill, and the reason is simple: In order to have valid data on what treatments are effective on patients, we need open clinical trials, and such ones should not be hidden when a negative result appear. Therefore we need to register all clinical trials in advance, giving us hints on ineffective treatment. It's not about big pharma really, it's about the patients.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
51	77-82	The policy should also include CT data on products already on the market because there are many examples of drugs that are used off-label (e.g. gabapentin for neuropathic pain) or drugs that have been in use for a long time but have meanwhile been shown to be ineffective and/or dangerous/unsafe in certain conditions (e.g. morphine-like drugs or nonsteroidal anti-inflammatory analgesics/coxibs in chronic non-cancer pain; influenza medication such as Tamiflu; blood pressure medication such as valsartan; antidepressants such as Prozac/Paxil)	
52	General	I strongly support openness and transparency of clinical trial data. Every patient I've met in clinical trials does has the intention of helping others and the implicit understanding that the trial information would be accessible.	
53	27	In the interest of preserving the integrity of the scientific method, the EMA should take steps to establish a publicly accessible clinical trial registration database. Proper assessment of the efficacy of a treatment requires knowledge of both favourable and unfavourable findings. Requiring registration would ensure that trials whose results conflict with the short-term financial interests of pharmaceutical companies will not be buried. Therefore I propose that this policy draft acknowledge the critical urgency of establishing a clinical trials registration database, and of making registration a condition for accepting clinical trials as evidence in support of marketing-authorisation applications.	*Ensuring accurate assessments of treatment efficacy:* To ensure that assessments of treatment efficacy are based on all studies of the treatment in question, the EMA shall take steps to establish a publicly accessible clinical trials registration database, to which all clinical trials presented in support of marketing-authorisation applications shall be submitted. The aim is to create a regime in which clinical trials not registered shall not be considered by the EMA.
	47-48	Since patients participate in clinical trials in the hope that their contribution will further understanding of medicine, the proposed policy should acknowledge patients' contributions by emphasizing that data produced during clinical trials shall be made available for public scrutiny, immediately after marketing-authorisation deliberations are concluded. The policy should make it absolutely clear that failing to make clinical trial data available in the	*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.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		absence of a reasonable justification is a gross violation of patients' trust, and that preventing such violations is one of the primary concerns of this policy. I therefore propose that a paragraph of text be added between lines 46 and 47 of the draft.	The Agency takes the view that failure to make clinical trial data available for public scrutiny once the marketing-authorisation process is complete represents a violation of patients' trust, and shall not be condoned by the EMA except where a compelling reason to do so can be shown. 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.
54	General	All trials should be published in per reviewed journals to allow for proper understanding of drugs and there effectiveness.	
55	General	I believe it is vital that all clinical trials are registered in advance, stick to their originally published objectives and report all their findings in full; ESPECIALLY when these are not what they wanted to hear.	
56	General	Je crois qu'il est indispensable que tous les essais cliniques, positifs ou non, soient publiés. (I believe it is indispensable that all clinical trial data, positives or none positives, are published)	
57	General	I'm a Resident of Psychiatry in Chile, and a just want to briefly comment and support the initiative for a more open access to clinical data. I really think this will be a big step on Evidence-Based Medicine and ethics. It will allow health care professionals to make the best patient-focus decisions.	
58	44-48	Participants expect their involvement to progress science. If the trial they are in is unpublished due to null or negative results then not only does science miss out, but individuals have had their time wasted and have been	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		deceived.	
58	General	I would like to also comment on the practice by pharmaceutical companies of adding non-beneficial ingredients to already tested medicines in order to extend patents. Unless there is reasonable support for this and trials prove its effectiveness, then such practices should be open to overt criticism	
59	General	The access to all clinical trials is vital for the future of a transparent medicine. What benefit is there, if a so called “evidence based” medicine just makes a fraction of this evidence visible for the public, doctors and medical professionals? This way there is an incomplete information transmitted which is hindering finding the best possible treatment for patients and at the same time not academically impeccable as the evidence based medicine understands itself. For everybody who might ever get in contact with medicaments, in what way so ever, I hope that the alltrials-campaign will be successful, so that there is complete information and transparency when it comes to health issues.	
60	General	I do not have the technical expertise to comment on the precise wording of this proposal but I am keen to express my opinion on the principles involved. I am a UK family doctor and prescribe medicines for my patients every working day. When I prescribe, I need to weigh up the likely benefits and harms for my patient. Knowing that a drug has been licensed is not enough, since that simply means it is safe enough to give to some people in some situations. I need to look at the available evidence on safety and efficacy in the light of my patient's particular situation. If clinical trial data is deliberately hidden,	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		then the information available to me and my patients will be biased. It is essential therefore for patient safety that all clinical trials are published. The EMA has a moral duty to play their part in this by insisting that clinical trials used for licensing purposes are published. More than that, the EMA must insist that these trials are published in a way that fairly reflects the information on which licensing decisions are based. Also, suitably anonymised data on individual patients must be made available to legitimate medical scientists to facilitate the compilation of systematic reviews. Pharmaceutical companies may protest that greater openness threatens them commercially. This will only be true if they are selling inferior drugs. The EMA's first duty must be to the European public, not the pharmaceutical industry.	
61	General	**Study and protocol registration** Planned clinical trials should be registered, with a summary of the trial protocol, before the first participant is recruited. Past trials that were not registered should now be registered retrospectively. This is essential if the trial was on medicines or interventions that we currently use (this includes some trials conducted before registries were established). **Summary results reporting** A summary of results should be publicly available where the trial was registered, within one year of completion of the trial. Summary results from all past trials of medicines currently in use should be made publicly available on a register now. Summary results include information on the primary and any secondary outcomes measured and statistical analysis. This is part of	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		the structured information that global registries should support. **A full report** Trial sponsors or others who produce a full report for marketing authorisation or any other purpose should make this publicly available. The narrative reports of adverse events and individual patient data in a full report can be redacted and available on request to researchers, in the same way that reports of adverse incidents currently are, with a commitment that no reasonable request will be refused.	
62	General	Following the "All Trials" campaign, I completely support any decision allowing access and analysis of all available data concerning medical trials. The situation we have today does not allow to draw valuable conclusions on medications' utility and risks. The only way to improve this situation is to allow researchers to have access to all available data concerning published and unpublished trials.	
63	General	The Standing Committee of European Doctors (CPME)[13] represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues. CPME is thankful to the European Medicines Agency (EMA) for opening a public consultation on its "Publication and access to clinical-trial data" policy paper. Transparency of clinical-trial data and results is essential to the good	

[13] CPME is registered in the Transparency Register with the ID number 9276943405-41.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		conduct of medical research and for the amelioration of public health outcomes. CPME welcomes the general approach of the Agency to guarantee better transparency of clinical-trial data together with the highest level of patients' data protection. These transparency endeavours are all the more necessary when society expects the Agency's evaluation of medicines to be free of any undue influence. CPME would like to comment on two issues highlighted in the EMA policy:	
63	L. 44-48	Informed consent: CPME agrees with the statement made on lines 44 to 48. According to all international standards on bioethics and research on human beings, the conduct of a study cannot start before the patient gives his full informed and express consent[14]. The data can only be used for the case for which the consent has been given. Further processing of the patient's data without due consent, e.g. for epidemiological or translational studies, may be possible in exceptional situations where consent would be impossible or impracticable to obtain but must be subject to very strict scrutiny including consideration and approval of a research ethics committee. CPME highly welcomes that the Agency foresees the use of patient's data for any other purposes than the	

[14] World Medical Association's Declaration of Helsinki, 2008, Articles 24 and 25:
http://www.wma.net/en/30publications/10policies/b3/index.html
Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo Convention), 1997, Article 5: http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm
Charter of fundamental rights in the European Union, 2000, Article 3:
http://www.europarl.europa.eu/charter/pdf/text_en.pdf
International Ethical Guidelines for Biomedical Research Involving Human (CIOM Guidelines), 2002, Guideline 4:
http://www.cioms.ch/images/stories/CIOMS/guidelines/guidelines_nov_2002_blurb.htm
Universal Declaration on bioethics and human rights, UNESCO, 2005, Article 6:
http://portal.unesco.org/en/ev.php-URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		one for which it has been collected as overstepping *"the boundaries of informed consent".* Indeed, one cannot claim that the patient will be fully informed of the risks and benefits of a study that does not yet exist and for which no protocol has even been defined at the time when he gives consent. The principle of informed consent as defined in the World Medical Association's Declaration of Helsinki must always apply.	
63	Point 16.1.4. of the Clinical Study Reports' ICH guidelines	Data of clinical-trial personnel: CPME agrees that the data of the personnel taking part in a clinical investigation should be made public. Considering the high responsibilities that professionals involved in trials have towards patients, society and public health as a whole, these data should be accessible to anyone. CPME therefore agrees with the categorisation as "open data" foreseen by the Agency for point 16.1.4. of the Clinical Study Reports' ICH guidelines[15] and suggests the following: *"The list of principal investigators; ~~individual investigators' names, addresses, appointments and clinical duties; similar information of other persons carrying out observations of primary or other major efficacy variables, such as a nurse, physician's assistant, clinical psychologist, clinical pharmacist or house staff physician~~; the author(s) of the report, including the biostatistician(s)"* should be published.	"The list of principal investigators; ~~individual investigators' names, addresses, appointments and clinical duties; similar information of other persons carrying out observations of primary or other major efficacy variables, such as a nurse, physician's assistant, clinical psychologist, clinical pharmacist or house staff physician~~; the author(s) of the report, including the biostatistician(s)"
64	118	Individual level longitudinal data is required when aiming to develop longitudinal drug-independent disease progression models based on historical data, which can help to inform new trial designs and treatment optimization in patients. However, the current definition of "Raw CT data" and "individual patient datasets" is not sufficiently specific in this respect.	

[15] Point 16.1.4 concerns the "list and description of investigators and other important participants in the study, including brief (1 page) CVs or equivalent summaries of training and experience relevant to the performance of the clinical study"

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		The definitions should specifically include that “Raw CT data” includes **longitudinal** data over the course of treatment, as recorded in the clinical trial for individual patients. The type of individual longitudinal data should include not only efficacy variables, but also general patient characteristics, safety/toxicity variables, biochemical and/or hematology laboratory measurements (e.g. blood cell counts, organ function etc) and raw efficacy variables (e.g. biomarkers for disease progression or drug effect). If drug concentrations have been determined to assess pharmacokinetics, all individual concentration versus time values should be reported, not only summary level metrics for each patient. Also, the individual dose amounts given to each patient for each occasion, if available, should be provided.	
65	General	This comment applies to the whole movement of public clinical data. I am in full support of this progression for reasons to numerous to list. In short, public assess to clinical data will save lives from developing new cures faster to avoiding repeat mistakes and waste experiments.	
66	General	As much detail about trials, their registration, their methodology, the statistical analysis, results and conclusions must be published. One can patent a synthesised molecule, so long as it does not occur in nature. Only patient identifiable data need remain confidential.	
67	General	I support compulsory publication of clinical trial data and open access to it. I also support the manifesto at http://www.alltrials.net/2013/all-trials-registered-and-results-reported/	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
68	1-35	The wording “clinical trials” may be understood to include interventions that do not involve drugs or devices. The text refers only to drugs though. Manualised psychological therapy without drugs is also evaluated using RCTs. It should be subject to the same policy. Probably other policy changes would be required to forestall marketing abuses such as “Emotional Freedom Technique”/Tapping, but for this and forthcoming policy there is no reason to hold psychology to a different standard than psychiatry or medicine in general.	Formulate so that it is clear that psychological therapy is also included.
69	General	As a doctor I need to know all the clinical trials that exist to make the right decision for my patients. We know that evidence-based medicine is the best we have to offer for our patients. However evidence-based medicine is not possible if you don’t take all the data into account. Toss a coin a 100 times and publish only the ones with the head up will make everybody believe that this coin has a head on both sides. It sounds a dull example but that is what happens in medicine right now. That is why I do fully support your suggested policy about publication and access to clinical-trial data.	
70	General	Thank you for the opportunity to comment on your draft policy on data transparency. The proposed changes are welcome, and should result in improved knowledge about medicines, and therefore improved outcomes for patients, once it is no longer possible to bury inconvenient trial results. I have read your consultation document carefully, and feel that it addresses the issues well.	
70	180	However, I would query the need to restrict access to EMA data to 'those established in the EU only' (line 180). It is not clear to me why it is necessary to limit access to those established in the European Union. The scientific knowledge derived from clinical trials on humans is not the	

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		property of Europeans alone, but of all humanity. It is easy to imagine valuable secondary analyses of European data being done by researchers on other continents. Plainly such researchers would have to deal with 'C' (=controlled access) data in a responsible manner; contracts to enforce this worldwide are perfectly envisageable.	
71	General	I support the full disclosure of trial results to allow medical personnel to make fully informed decisions and to prevent pharmaceutical companies from withholding pertinent data on drug safety and effectiveness.	
72	General	I think it's fantastic that you are drafting a policy that will allow more transparency for clinical trials and pharmaceutical companies. It will contribute towards better medicine, a good for the entire medical and patient population.	
73	General	Please publish and share information on clinical research. This will empower the public to make more informed decisions regarding their health and help fuel innovation for a better tomorrow.	
74	210-218	Evaluating the requester's (statistical) analysis plan is a good way to ensure that the (statistical) analysis is in the interest of public health and in line with the informed consent, as stated in line 183.	asked to upload a (statistical) analysis plan (and/or other relevant documents); the Agency considers preparation and uploading of a detailed protocol/statistical analysis plan before data access of utmost importance, to ensure the credibility of subsequent results; evaluation of the analysis plan will influence the Agency's interpretation of any subsequent reported results.
75	General	The policy strikes the right balance for all stakeholders. How will the disclosure of data be ensured?	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
76	General	I strongly support the policy covered by this document. My only concerns are • that the privacy protection scheme might be used to circumvent full publication of relevant data • that the policy only works prospectively. I think further policy is needed to open existing clinical trial datasets	
77	General	Please consider the patient suffering and cost to the Taxpayer for any delays in your project to improve the transparency of medical trials. Sodium Valproate causes birth defects in 40% of babies exposed in the womb. Greater trial transparency would have reduced the number of people affected as women would have been given an informed choice on whether to become pregnant. Regulators are still not giving adequate warnings and women and clinicians continue in ignorance with the misleading information given to them. Please tighten legislation to avoid such preventable atrocities from happening again. The current system looks corrupt as it is not economically viable and is not in the interest of the health and wellbeing of the patient. The reputation of the EMA is at stake if the patient is not the number one priority. Please Prevent Suffering and Improve Lives.	
78	50	I welcome the recognition and clear statement that clinical trial (CT) data	

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		should not be considered confidential – this is helpful and important.	
78	61	I feel the phrase 'protection of public health (and regulatory decisions) against claims resulting from inappropriate analyses' is unclear. I suggest the problem lies in the word 'claims' which could suggest legal action, as in 'claiming damages' (although I assume this is not the meaning intended). Drug company promotion is already heavily regulated to prevent misleading advertisements, unfounded claims about product efficacy, and off-label promotion. Scientific freedom of speech is an important principle which should be upheld. I suggest that defence from false claims arising from inappropriate analyses is the responsibility of peer-reviewed journals (who may publish or reject such analyses), regulatory authorities (who control drug labelling and licensed indications), and the scientific community. Vigorous debate should be encouraged. It should not be the EMA's role to protect anybody from such claims.	
78	71-2	I found this sentence ('However, those who conduct …. interventions') incomprehensible. Why should those who conduct secondary analyses be 'protected' and what kind of 'external interventions' does the Agency have in mind? I think consideration might be given to allowing those who generated the original data a time period to allow them to perform additional analyses, since they may be best qualified to do it. But such a period should not be too long. I also believe that researchers who generate data need to be properly acknowledged in later analyses, but I do not understand why those performing secondary analyses require any type of protection.	
78	77-82	(Scope) While I welcome the EMA's new position on future data, I strongly urge the Agency to find ways to make CT data on all marketed products available. Based on the reported problems with Tamiflu (described in	

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		http://www.bmj.com/tamiflu) I am not reassured that the Agency's 'current policy' encourages or facilitates this. I very much hope the question of 'legacy data' will be given due consideration as it has important public health implications since it relates to the majority of medicines currently in use.	
79		The European Crohn's and Colitis Organisation (ECCO) main mission is to improve the care of patients with Inflammatory Bowel Disease in all its aspects. It is, therefore, a key perspective to share opinions and common strategies with the European Medicines Agency (the Agency) with the aim of delivering a better service to patients with IBD in Europe. With regard to the Agency's policy views and position, ECCO generally favors the idea of the Agency concerning proactive transparency of CT data. At the same time, ECCO recognizes, as does the Agency, the fundamental right of EU citizens and patients to receive protection of personal data. Therefore data anonymisation to avoid retrospective identification of individuals is fundamental. On the other hand, ECCO sees substantial benefit in pooling anonymised demographic and outcome data from different CTs designed to recruit patients with similar patterns of disease. This is because it enables large subsets of patients with specific locations or behaviour of disease to be collected, that will enable insight into pathogenesis and patient selection for specific therapies. From patients' rights and perspectives, ECCO completely agrees with the Agency on the need to avoid exceeding the boundaries of patients' informed consent. With regard to the consequences of inappropriate data analyses, the Agency proposals do not guarantee that secondary data analyses will be reported to the highest possible scientific standards. However, measures to ensure the best protection of public health will be adopted. In view of sharing opinions	

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		and possible common strategies, before accessibility in the public domain, ECCO is in a position to provide the Agency with expert scientific advice on inflammatory bowel disease in reviewing secondary analyses of CT to ensure the highest possible scientific standards.	
79		ECCO agrees with the views of the Agency, although research on the safety or efficacy of already authorized medicinal products will continue to improve CT design and influence clinical practice.	
79		ECCO agrees with these Agency definitions. The Agency should consider providing appropriate guidance to investigators about reporting data from non-conventional CTs (proof of concept trials, cohort studies, case-control studies, registry data), since this would facilitate appropriate reporting of efficacy and safety. This information can certainly be useful and is now not shared since most often not accepted for publication if at all submitted for review.	
79		ECCO agrees with the Agency's policy statements. Category 1 data (industry related) are beyond the remit of ECCO. Category 2 and 3 data with regard to both CT data without protection of PPD concerns (de-identification of subject personal data and allowance of publication of personal data of CT personnel) and CT data with PPD concerns (the so called "controlled access" data upon requesters' identification and all related procedures) are appropriate from ECCO"s perspective	
79		ECCO agrees with the Agency	
79		The Agency's deadlines are appropriate ECCO would be happy to collaborate with the Agency in drawing up a guidance document with regard to "C" data.	
80	General	This is a very important initiative; as an epidemiologist appraising the	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		quality of studies that are part of the body of evidence evaluated for issuing scientific opinions or in the context of applications in the EFSA domains I do believe that independent scrutiny is key; as a scientist dealing with the implementation of systematic reviews as an approach to synthesize scientific evidence I am aware of the importance of analysing all available scientific results to avoid biased conclusions.	
81	General	The Faculty of Pharmaceutical Medicine ('The Faculty') is a professional membership organisation and standard-setting body. The Faculty has 1,500 members, who are practising pharmaceutical physicians or those with a professional interest in the speciality. It was founded in 1989, and is a Faculty of the Royal Colleges of Physicians of the UK. Pharmaceutical medicine is a medical specialty concerned with the discovery, development, evaluation, licensing and monitoring of medicines and the medical aspects of their marketing. The Faculty's members work in diverse environments; from front line clinical trials, to medical affairs and medicines regulation. Our mission is to advance the science and practice of pharmaceutical medicine by working to develop and maintain competence, ethics and integrity and the highest professional standards in the specialty for the benefit of the public. Like the EMA, the Faculty seeks, through its activities, to protect the public and to foster public health. The Faculty is broadly supportive of the proposals contained within the draft policy. We have been vocal in our calls for increased transparency and have previously engaged with the EMA through the clinical trials advisory groups, and have also worked with a number of other stakeholders on these issues,	

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		including the House of Commons Science and Technology Select Committee. While we are strongly supportive of the direction of travel by the EMA, we have some concerns that the systems designed to encourage transparency are complex and will be challenging to implement. We feel that in some instances, the practicalities of how these processes will operate are still poorly defined in the draft policy. It would be helpful if the kinds of pharmaceutical products and trials that are within the scope of this document were more clearly specified, and particularly what is not in the scope e.g. clinical trials that are not included in a marketing authorisation application or variation, also documented. Our comments below provide more details regarding these concerns.	
81	Lines 27-35	The Faculty agrees with the sentiment expressed, however we have concerns about the manner in which secondary analyses are performed, and their potential effect on previous regulatory decisions. It is anticipated that some secondary analyses could be generated by direct, or indirect, competitors of the marketing authorisation holder. The draft document states that the policy will render the public better able to challenge regulators decisions from a technical standpoint – however, at present no procedure exists for formally making such a challenge and the Faculty recommends that such a procedure should be put in place to ensure consistency in the Agency's responses to matters raised by the public. The Agency will also need to put in place a defined procedural system to permit the marketing authorisation holder enough time to address any issues raised by secondary analyses that could impact upon the validity of the original marketing authorisation. It is anticipated that the current procedures in place to handle pharmacovigilance generated safety issues will not be adequate or appropriate to handle questions or issues raised through third	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		party secondary analyses of data.	
81	Lines 44-51	The Faculty agrees with the draft policy here. However, we urge the Agency to consider how the management of provision of data, directly or indirectly, to persons or corporations in jurisdictions that have a poor record of compliance with international laws governing trademarks, patents and industrial espionage, will be handled.	
81	Lines 57-61	The Agency should be more specific about its intentions regarding protection against claims resulting from inappropriate analyses. In particular, the Agency should state: a) what powers it possesses to provide such protection, b) whether it will provide expert witnesses in support of such litigation, c) whether it will provide the latter free, or at cost, and d) upon which standards or jurisdiction it will judge the provision of such protection.	
81	Lines 67-72	The Faculty agrees that, fundamentally, the same principles of openness and public interest must apply to both the original generators of clinical trial data and those using such data for secondary analyses. However, we are concerned that the Agency provides no feasible measures for ensuring the same standards of transparency on the part of data requestors. The Faculty recommends that a reasonable time limit for publication of secondary analyses would be 12-18 months from the time of access to the data.	
81	Lines 86-88	If access to pharmacovigilance data is outside the scope of this policy and governed by different considerations, the Faculty would seek clarification as to what safeguards will be put in place to determine whether or not either (i) data sets used for third party secondary analyses are as complete as is possible; and/or (ii) data pooling from CTs and pharmacovigilance monitoring are combined in a scientifically valid manner in secondary	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		analyses.	
81	Lines 109-115	The Faculty recommends that there should be recognition that valid patent rights can be generated from CT data and early disclosure will prejudice such patent filings. It should be recognised that not only patents related to the medicine itself have value to the owner of the CT data. There is a concern that it will form a valid consideration for companies as regards the relative timings of their global marketing authorisation filings. However, we also recognise that often CT data will not be subject to such data mining possibilities. Currently, safeguards are built into the EU document disclosure system, which requires the owner of the commercially confidential information to justify non-disclosure on a case by case basis. Hence we recommend this possibility should explicitly be acknowledged and recognised in the Agency's policy.	
81	Lines 150-154	The Faculty agrees with this policy, but we would suggest that, in line our response to lines 67-72 (above) of this submission, we recommend that the downloading of data requires the requester to make a declaration that all secondary analyses be published within 12-18 months of the download. As a minimum level of accountability, all requesters should have their identity published as for "C" category data requesters (lines 222-231), to allow the marketing authorisation holder to monitor publication of any secondary analyses.	
81	Lines 181-205	The requirement to enter into a data-sharing agreement is welcomed. The Faculty recommends that the Agency outlines the possible sanctions that might apply should the requester, for example, use the data to obtain marketing authorisations in ex-EU jurisdictions.	
81	Lines	The Faculty believes that the w.e.f. date of 1 January 2014 conflicts with the	

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	249-261	time needed for proper consultation and implementation as per due process. We recommend that the w.e.f. date should be whenever the consultation process etc. is completed, as per the normal procedure.	
81	Annex 2, point 16.1.4	Whilst the Faculty agrees with this information being made public, we anticipate that the Agency may encounter resistance to the provision of detailed information about personnel.	
82	General	The Drug Commission of the German Medical Association (DCGMA) is grateful for the opportunity to comment on the EMA policy “Publication and access to clinical trial data”. The DCGMA is taking the opportunity to make some general comments on the policy, followed by a detailed proposed change of the text. The DCGMA concurs with the Agency that “access to CT data in an analysable format will benefit public health in future” and commends the Agency’s initiative with this policy for transparency. The DCGMA also lauds the commitment of the Agency for the protection of patient personal data and is keen on the exact protocols and specifications for de-identification of said data, as it is of paramount importance. In regards to the purpose of this guidance document as outlined in Chapter 1, the DCGMA assumes that clinical trial study reports in the format of the ICH E3 guideline will probably cover most of the interests from external parties on access to clinical trial documents and data. There will be only a small number of requesters who wish to have ‘controlled’ access to raw data beyond the full study reports. Performing a proper re-analysis on the basis of raw-data will need much expertise, high skills and technical equipment	

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		usually not available to interested clinicians. The DCGMA suggests establishing an active tool to monitor whether requesters have in fact published results from re-analyses based on raw-data obtained from EMA within a reasonable timeframe. There is currently no mention of measures by the EMA in case the requester has not or cannot publish study results derived from his re-analysis (e.g. lack of staff, no funding, manuscript not accepted by any journal etc.). The DCGMA suggests establishing a special expert group at the EMA to regularly evaluate requests for full clinical data sets (including raw data; Category 3-data) and to give an opinion on acceptance or rejection of the request. By this means, scientifically unsubstantiated or sub-standard requests could be rejected. The DCGMA looks forward to the implementation of the policy and the analyses that will result from it.	
82	285-292	The DCGMA agrees with the categorization in Section 4 'Policy Statement'. However, Category 2-documents will contain data on CT personnel. In context with Annex II and its footnote 4, these documents may contain 'data, such as the list of investigators; individual investigators' names, addresses, appointments, qualifications and clinical duties; similar information of other persons carrying out observations of primary or other major efficacy variables, such as a nurse, physician's assistant, clinical psychologist, clinical pharmacist or house staff physician; the author(s) of the report, including the responsible biostatistician(s).' The DCGMA holds the view that making public 'addresses, appointments, qualifications and clinical duties' of investigators is not acceptable. This would publicly provide sensitive information of investigators which could be	This section contains personal data, such as the list of principal investigators; ~~individual investigators' names, addresses, appointments, qualifications and clinical duties; similar information of other persons carrying out observations of primary or other major efficacy variables, such as a nurse, physician's assistant, clinical psychologist, clinical pharmacist or house staff physician;~~ the author(s) of the report, including the responsible biostatistician(s). The Agency takes the view that these persons have a role and responsibility for public health in ensuring the integrity of trial data and protecting patients' welfare. ~~In light of the~~

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		problematic, e.g. in psychiatry. Moreover, the DCGMA is of the opinion that 'names, addresses, appointments' of nurses, physician's assistants etc. involved in a clinical trial are not needed nor acceptable in terms of transparency. The knowledge of such data will not have impact on the evaluation of a study's validity. Also, there will be a huge fluctuation of personnel (investigators, nurses and others) during the study period (maybe even within one year), and many of these persons will be 'lost to follow up'. We do not see an 'overriding public interest' for publication. The DCGMA recommends to focus on making public only data about principal investigators, biostatisticians and other key personnel (e.g. laboratory personnel) and abstain from regulating such data from other non-academic study personnel. The same argument is valid for Category 3-data, with reference to Annex II, item '6: Investigators and study administrative structure' (access: 'Open, 4') and to footnote 4 of the Annex document (see above). The DCGMA is of the opinion that such data are not needed and not acceptable to ensure transparency.	~~overriding public interest, these personal data are considered exempt from PPD considerations.~~
83	General	This policy is excellent. It covers all necessary aspects and represents a smart compromise between all demands from various interested parties. In particular, it respects well the International Society for Pharmaco-Epidemiology (ISPE) principles: "Overall in health research, cultivate an atmosphere of respect for the privacy of the people whose health experience is being studied" to which Eurordis subscribes fully. Even though data from patients with rare diseases are often considered to be more sensitive than data from patients with common diseases, we are particularly satisfied to see the policy is the same for all data from all	

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		patients, ensuring the same level of data protection, with no exception. One concern we may have is about the timelines: it will come into place on 1 January 2014, however guidance for 'C' data will be agreed upon and available at a second stage, by 31 October 2014, for 'C' data to be published in January 2015. The complexity of the matter explains it all, however by that time the adoption of the Regulation on Clinical Trials and the revision of the legislation on data protection may render the 'C' data guidance obsolete (or not), or confusing.	
83	General and lines 15-17	Although the policy applies for products which received positive or negative opinion for a marketing authorisation, or in case the application has been withdrawn, it is not explicitly written. For example the sentence "There is growing demand from external stakeholders for full transparency, not only about the Agency's deliberations and actions, but also about the data and results from clinical trials (CTs) on which regulatory decisions are based". One could consider this applies to e.g. deliberations for orphan product designations, and once an orphan product designation has been granted (the regulatory decision), this person could request access to data submitted at this stage, including CT data when they exist. Although it was clear from the beginning that this exercise is only for products which benefited from a benefit/risk evaluation for a marketing authorisation, once the decision is made, this is not clearly stated in the scope of the policy.	

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83	36-43	It should take less information to identify rare disease patients and special care should be given to PPD when data from clinical trials in rare diseases are shared with third parties, i.e. strict de-identification rules.	
83	41-43	The policy is well in line with ISPE recommendation to “Enforce a policy of "No access to personally identifiable information" as the default - then base exceptional access on need-to-know” and Eurordis fully supports this approach.	
83	44-48	Eurordis fully supports this view. It is crucial to respect the informed consent, cornerstone of clinical trials’ subjects’ protection. However not all informed consent for clinical trials that are currently running or planned are clear and explicit about the possibility that third party may access key-coded or de-identified data. The EMA policy should recommend sponsors and investigators, and institutions in charge or proposing templates for informed consent, to revise the clauses for all future informed consent documents.	To add: “Informed consent for current and future trials should be explicit and clear regarding the possible access to key-coded or de-identified data by others parties than the sponsor, the study team and the regulatory authorities”.
83	57-61	Eurordis is particularly satisfied by this provision, as this risk was outlined by its representative during the workshop in November 2012. Whilst acknowledging the nature of the scientific debate, it is important to prevent “bad-science” and misleading behaviours as much as possible.	
83	89-101	As restrictions exist on the types of trials that can be publicised on the EUDRACT register (type I trials are excluded), it could be useful to explain this policy applies to all CTs, including first-in-men studies or studies in health volunteers, unlike EUDRACT register, for clarification.	
83	95-97		To add: “including compassionate use programmes”.

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83	166-67	This is in line with ISPE recommendations: ”Remove data-subjects’ personal identifiability as thoroughly as is compatible with research needs. If key-coding, aggregating, or otherwise removing personally identifying information, do so with adequate rigor”.	
83	172-175	One de-identification method is proposed, based on the work published by Hrynaszkiewicz et al. It is not indicated if this is a consensus minimum standard, or one amongst many. But if it occurs that the proposed method rises too great difficulties and the marketing authorisation holders finally decide to derive from them, then the public may wonder why the guidance referenced in this policy is not respected. More guidance will be published in 2014 and this is welcome.	
83	181-187	If the access controlled data is only in line with the spirit of informed consent, then the room for interpretation of the informed consent can make this provision having no effect.	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 informed consent
83	198	This is in line with ISPE recommendations “Urge Institutional Review Boards and other ethics review bodies to become fully engaged with the privacy, confidentiality, and security aspects of subject protection, in secondary research on data as well as in direct experimentation” and Eurordis fully supports the proposal to request ethics-committee approval for obtaining and processing type ‘C’ data.	
83	243	It should be clarified who the applicant is.	To write: “by the marketing authorisation applicant”
84	Line 36	Although we generally support protection of personal data and the measures suggested to protect personal data we have a concern that the "guarded approach to the sharing of patient level data" may be abused and	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		unnecessary restrictions placed on potentially useful data	
84	Line 49	We support this as long as the data is obviously commercially sensitive. We also support the premise that CT data cannot be considered CCI.	
84	Line 57	We would suggest that if data from secondary analyses are to be used, the quality of the analyses should at least be scrutinised.	
84	Line 67	It would be helpful to have a definition of the "reasonable period of time" mentioned on line 71 as this is open to abuse by companies not willing to open their secondary analyses to scrutiny. The same phrase is defined in line 204 as "normally .. ..considered to be one year after accessing the data". Will the same definition apply?	
84	Line 83	We are concerned that data not held by the EMA are outside the scope of the policy. This brings us back to the comment above about what requirements are placed on companies to submit all trial data they have for a product as part of their submission.	
84	Line 109	It is important that non-disclosure of CCI is not solely due to the possibility of undermining legitimate economic interests of the owner of the information. If a product does not work it should not be possible to hide the fact merely because the company producing it will see its share price fall on the stock market – a situation not usually in the economic interest of the owner.	
84	Line 150	We support the overall statements	
84	Line 162	We support the overall statements	
84	Section 2	It is disappointing that the policy is not retrospective and that previous	

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	(Scope)	difficulties in obtaining data from completed trials will continue.	
84	Section 3 (Definitions)	It is helpful that the proactive publication of CT data is not limited to randomised controlled trials alone.	
84	General	Although most of the policy appears to be good on paper, the real test will not be until it is actually in force. Data has been difficult to access in the past, where the regulations seemed to be more protective of the pharmaceutical companies rather than the public. Will this change? Overall we support the position of making CT data used in the decision making process accessible to the public. We note this position is for data held by the EMA when a decision about a drug is made. We would question if, as part of a submission to the EMA, the drug company has to submit all the CT data they hold (incl. negative trial data) to the EMA.	
85	General	I support the aims of the EMA to increase access to clinical trial data and welcome this draft policy	
85	49-51	Commercial interests do need to be respected, however this must not be used as an excuse to limit data access without good reason.	
85	109-115	Clear processes for defining information as CCI must be put in place	
86	191	It is not clearly stated who will be in a position to determine “purposes that are deemed outside the boundaries of patients’ informed consent”; who is “deeming” here?	~~refrain from using CT data accessed for any purposes that are deemed outside the boundaries of patients' informed consent~~ explicitly state how the use of CT data accesses is within the boundaries of patients’ informed consent

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86	General	The use of data for any purpose not previously foreseen could be of the greatest relevance to public health; however, respect for patients' ownership and limited release of information should be granted. Possibly a review committee could intervene, or a more general and relaxed policy could be set in advance, in the best interest of research.	
87	28	It should be clear that transparency of CT data mentioned here refer not only to drugs but also to pertinent devices used to answer similar therapeutic needs (deep brain stimulation/levodopa is just one example).	
88	Comment summary	• The Austrian Medicines & Medical Devices Agency fully supports transparency as an important means to inform the EU population, especially patients, making the decisions by the Agency traceable, and to promote the work done by the National Competent Authorities (NCA). Making trial data publicly available after regulatory decision making bears several chances but also risks for patients and health systems. Several issues are discussed in the detailed comments below. • NCAs are a key player in regulatory assessment. The roles and responsibilities of NCAs in the context of the initiative need clarification. • De-identification of data is a very relevant and sensitive topic. The policy should make limitations of data protection explicit. • To secure the scientific value of data analyses, a statistical analysis plan should be made available before data are provided to requester. However, methodological approaches would be required to be implemented to protect against false (additional) claims. • Binding rules on the methodological qualification of the requester should be established. • Potential conflicts between different raw-data transparency initiatives worldwide might become evident in the future.	

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88	32	Ad 'take decision-making one step closer to EU citizens/patients': It is questionable whether sole replication of clinical trials' data analyses would be sufficient to (fully) understand the regulator's decision. The decision making process in relation to licensure of a new drug is becoming more and more complex, and decisions are based on risk-benefit evaluations covering all sources of evidence brought up during the drug development program. Other/additional measures (than granting access to raw data) might be required to increase and support transparency. This could be achieved by means which are accessible to a broader population, for example the EPAR or the study reports. Ad 'take decision-making one step closer to EU citizens/patients': AGES agrees to the general aim to bring decision making closer to the citizens/patients. This is beyond any doubt a noble aim worthwhile to be followed. We feel however, that this wording suggests more than can be accomplished. The benefit to the EU population and patients will not be direct, but indirect only. Individual patients will not have the capacity to process data and set these into the context of a complex decision making system. This is only feasible through the responsible work by third party experts. Therefore, the true benefit will be that further, hopefully independent, opinions become available to the public. A broader offer of opinions will therefore be available to the consumer, but generally he will again need to rely on one or the other channel. We think that a policy on transparency should clearly set its benefits into a fair perspective of what it can achieve and should not promise more than it will likely be capable to accomplish. The current policy somehow gives the flavour that the Agency and/or NCAs (i.e. the major independent channel available so far) do not do a good job. We allow to respectfully disagree. With this respect, AGES as a	

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		National Competent Authority, wants to stress that it always has and will further provide offers of premium choice. Certainly we all strive for doing even better in the future.	
	32-33	Ad 'promote better informed use of medicines': In case clinical raw data from registration trials for licensed products would be (re-)analysed in the public domain, it is likely that (potentially conflicting) results from such analyses will be published and communicated via many different communication channels, most of the time outside the control of regulatory bodies. It appears to be of paramount importance (and needs to be understood as current responsibility of EMA and NCAs) that, in such a scenario, the question of responsibility for adequate patient information and corresponding risk communication would be adequately addressed within the framework of a transparency policy.	
	35; 57-61	See, also comment for lines 32-33; From a NCA perspective, it is important to define the NCA's role and responsibilities when talking about 'measures to ensure the best possible protection of public health'. Rapporteurs' assessment teams at the NCAs will have the best scientific overview of a drug dossier, and if a CHMP decision (positive or negative) will be challenged by third parties, the extent of resources expected from NCA staff/resources to be provided to EMA remains unclear. It seems important to involve heads of NCA to clarify this point.	
	39; 165-167	"There are established ways and means to anonymise data and protect patients from retroactive patient identification"; "appropriate de-identification". Data protection and de-identification is a very sensible topic for the public.	

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		To our best knowledge there is no truly secure method for the latter and there will likely never be. All approaches to de-identification can only approach the ultimate goal of data protection. We therefore think that it is more transparent if the policy states that full protection against identification is not finally achievable and does not give the impression of secure protection. Instead, the policy should stress that state of the art methods for data protection are applied, providing best prevention of data identification. The above refers to de-identification of the whole dataset. On a second level, individual patients could also be identified by some individual subject characteristics, or with relation to study centres, timing of assessments or others. Also, on that level de-identification is not always possible, e.g. in rare diseases, but in principle this applies to all types of clinical trials. This represents an inherent risk to future willingness of patients to participate in a clinical trial, especially in the European Union. This could impact on patients, the duration of drug development and Europe's role in drug development worldwide.	
	166-167	The wording used indicates that de-identification will compromise analytical utility in some situations; this is agreed to, but would this be dealt with in practice? Who will decide if efforts of de-identification will be worthwhile under the scope of the policy? If data are de-identified, how to deal with seemingly different results identified through secondary assessment, resulting from the lack of such information? Who will decide on further steps (whom to believe? Need to assess the relevance of differences? Need to react, in case such differences were assessed as relevant?)	
	195-197	It appears advisable to add requirements on the qualification of the group members given access to the data. In our opinion it is dangerous if no	

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		qualified statistician is included in that team. It is unthinkable to us, that all the requirements mandated within this policy can be accomplished without such a team-member. Therefore we propose to specifically request inclusion of a qualified statistician in that team. The same standard should be required for regulatory assessment teams.	
	210-212	Timely availability of SAPs will principally not guarantee adequate control of trial-specific type-I-error probability, especially in cases of additional post-hoc third-party analyses of one specific clinical trial's data set. The first SAP (as developed by the Sponsor) will always remain most important, as if appropriately written, it will be the only one which is not influenced by the data. All further analysis plans can (and most likely will) be influenced by the trial data through several channels, be it the regulatory decision, trial data publications in trial registries or scientific journals, presentations at conferences, or others. Thus, with such analyses there is always an inherent risk of bias in either direction, even when applying the highest levels of integrity to the secondary analyst. The associated multiplicity problem is not addressed in the policy. Sophisticated methodological approaches would be required to be implemented to protect against false (additional) claims, but as discussed this will always carry the risk for bias.	
	203; 213	"Agency's interpretation" of subsequent results is mentioned: Clarification with NCAs is suggested, in how far rapporteurs' teams will have to contribute to the work of interpreting new upcoming results from third parties' analyses in relation to an existing CHMP opinion; similarly the call for 'all results are made available' leaves open whether and who of the regulators should take these into consideration, respectively for what purpose and under which procedure. Who has the (internal/external) mandate to trigger such a procedure? It might be that quite a lot of	

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		additional (but not necessarily new or different) data become available in this way.	
	214	"The requester may decline to upload any documents at that time" This is not clear to us. We think that pre-specification of these secondary analyses is a very important step in this policy. Secondary analysis can contribute a lot of suitable alternative analyses, but can also trigger many inferior analyses. It is our opinion that, if not predefined, the risk of inferior analyses increases substantially. If this is refrained from, the analysis will not have the power it could have and results could leave open more additional (un-raised) questions than giving answers. It is clear that it will be difficult to the requester to specify in advance what he will exactly do, before he sees which data he gets. However, this can be approached in a first loop, where the requestor would be provided only with information regarding data structure, size and others. In addition, the requestor must have an aim of what to address with the data, before he can even think of requesting the data (as is also recognised in 185-186).	
	General comment 1	It seems important to mention/identify NCAs as stakeholders in the execution of the policy. It is suggested that roles and responsibilities of NCAs and rapporteurs' assessment teams are clarified, either in the policy document or in accompanying documents.	
	General comment 2	Potential conflicts between different raw-data transparency initiatives worldwide might become evident in the future. Whereas in some regions (e.g. the EU) a quite liberal data access system might be established, regulatory bodies of other regions may opt for more restricted access systems (e.g. FDA proposal to make masked data available). This issue can be exaggerated, in case dossiers are submitted sequentially in different	

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		regions. In this case third party analyses could even already be available from one region, before the dossier is submitted in another region. This could introduce external pressure, which in line with line 65 needs to be protected against. Conflicts could especially appear in relation to data transparency for multiregional trials, e.g. trials with recruiting centres in the EU and the US, where these trials would be relevant for licensing in both regions. Also, similar initiatives by other organisations, such as scientific journals (e.g. British Medical Journal) or pharmaceutical companies (e.g. GSK) would need to be considered in this context.	
	General comment 3	Further, it is important to note that none of the consequences of the policy can replace the work as is done so far by the NCAs, however it has the potential to generate much additional work at the NCAs. Sooner or later, clarification is needed on who is to carry the costs of such additional work. Is it the community, who is to benefit from the policy? Is it the third party, who may also benefit from data access? Or should it be the Sponsor through an increase in fees?	