2 October 2014
EMA/349245/2014
Chief Policy Adviser

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

From stakeholder 109 to stakeholder 126

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
109	30	Delete “and high-quality” since this is a value judgment and there is no intention to restrict disclosure based on quality of the data.	
109	32	Either replace “and” by “including”, or delete “and patients”, since patients are a subset of EU citizens.	
109	33	Add “and / or extension” after “replication”.	
109	33-34	There must be a limit on the number of times data need to be accessed for independent replication. If some have already accessed and verified, do	

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
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		others still need to?	
109	34	After “verify” add “the original analysis and conclusions, to conduct further analyses (including sensitivity analyses), and to examine”.	
109	38	“established ways and means to anonymise data” requires references.	
109	41	What is “unlawful retroactive patient identification”? Is it the use that is unlawful rather than the intent? Is it unlawful for individual patients to identify their own data?	
109	43	Delete “rare but potentially damaging instances of” unless you are specifically targeting this objective. Instances of patients identifying themselves may be more frequent than rare and may not be potentially damaging unless by finding that they can identify themselves patients become distressed.	
109	44-46	Include “improving their own knowledge of and their own treatment of disease.” As written the statement is altruistic but should also allow a justifiable selfish objective.	
109	47-48	In addition you should mention informed assent where patients do not participate in the consent process (children, unconscious patients, those with cognitive deficits including dementia, etc).	
109	51	Is this a legal judgment? Is it always true?	
109	61	Presumably not legal “claims” but “false or unjustified claims”?	
109	68-69	Replace “same” by “highest”, and delete “as those who generate CT data in the first place”. The original standards may not be known or may not be the	

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		best. 71 What constitutes “a reasonable period of time”? Who allows it and when does the period of time start?	
109	77	“CT data that will be submitted to the Agency” With both EMA and pharmaceutical companies independently releasing data from the same trial there is potential for discrepancies. How will these be avoided?	
109	97	“form” should be “from”.	
109	104	Replace “his” by “their”.	
109	118	It is not clear that raw CT data also includes X-rays, CT and MRI scans, ECG and EEG traces, photographs, photomicrographs, audio tape recordings, and video recordings, tissue samples, etc.	
109	125ff	The terminology in Section 4 is difficult to follow with the use of categories short-hands. Can this be simplified particularly to avoid confusion with the footnotes in Annexes I and II.	
109	138	Be careful about defining data category by exclusion. If all personal data are appropriately de-identified (as line 165) then all category 3 (controlled access) data become category 2 (open) data. Surely this cannot be the intention and must not be the result. Therefore definitions need to be clarified.	
109	143	What is the interpretation of “adequately de-identified”? An example may help.	
109	166	“Adequately de-identified data” is not defined. Adequate for what purpose?	

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		De-identification by distortion will make replication of results impossible. This suggests data must be de-identified by removal of directly and indirectly identifiable data, and data sharing agreements must make clear the negative consequences of using combinations of outcome measures to identify individual patients.	
109	170	What is “sufficiently low” and for what purpose? Is it conceded that patients in many trials will be able to identify themselves without difficulty? If data are de-identified to an extent that such subjects cannot identify themselves, then knowing that they are included in the dataset, some could surely request correction under Data Protection Acts. Some patients may become distressed by having their age, or even their sex, changed, for example.	
109	173	Application of the minimum standard, especially if supplemented, may render the dataset inadequate for replication of original analyses.	
109	174	What is meant by statistical de-identification? An example would help.	
109	175	Replace “de-identification” by “re-identification. Add “and other clinical trials in which the subject may have been entered.”	
109	179	The research team should be identified and properly qualified. Exacting standards are usually upheld for the original research teams and there is no reason for standards to be relaxed for either replication or secondary uses. A suitably qualified statistician should be identified to oversee analysis.	
109	180	What is the justification for establishment in the EU? What does establishment in the EU mean? This restriction appears to exclude data required for analysis conducted by a team outside of EU; how is this justified? It will be possible to acquire some data from pharmaceutical	

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		companies.	
109	181	Is the legal agreement with an individual, a team, or their employer?	
109	184	On obtaining data for meta-analysis some investigators attempt to improve on previous analysis by cross-checking with patient records, and / or extension of the follow-up period. Such activities may not be possible with de-identified data. Will such activities still be allowed under “controlled access” in some circumstances?	
109	192	Patients’ informed consent usually includes such statements as “The coordinating centre would seek information from participants’ own doctors, and from NHS and other central registries about any serious illnesses that occur. All such information would be used, in confidence, only for medical research purposes and for routine regulatory and audit purposes.” Such past consent cannot be widened to the present context without additional specific consent for disclosure. In addition EMA may need a declared policy for patients who give only partial consent for access to and release of data since this may forestall release of the entire sample entered in a specific trial.	
109	204	A one year period is too short. To allow time for understanding the data, analysing it in full, preparing and submitting reports / papers for publication, peer review, and time “in press” a minimum of two years should be allowed.	
109	205	How can data be destroyed unless stored on stand-alone computers not connected to systems, such as university networks, which are backed-up routinely for years? If data are accessed on the EMA website they would not be destroyed.	

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		Destroying data “once the analysis is completed” is ambiguous. Data must still be available to answer any issues that arise following publication.	
109	217	Some control is necessary. Data should not be used repeatedly for the same purpose. Requesting teams must have appropriate qualifications to avoid inappropriate analysis. Statistical analysis plans must acknowledge that any analysis other than the original is *posthoc*.	
109	219	Repeat EPAR in full.	
109	General	Patients/participants will need to provide full and non-negotiable consent for their data to be shared. The EMA must provide a form of words that can be applied to all trials prospectively. People must not join a trial if they do not agree. Selective non-consent to this specific point will not be acceptable because results would never be reproducible. This is one important implication of this endeavour and may damage recruitment to trials.	
109	General	There is no mention of assent and patients who cannot consent for themselves.	
109	General	The process for obtaining data needs to be clear. When should a researcher approach the originator as a collaborative and when should they bypass the originator and come to EMA? What are the implications of bypassing? How to avoid differences between datasets obtained from both sources?	
109	General	A clear process needs to be in place to handle discrepancies in the findings of replicated research with original research. A form of mediation or honest brokerage is required. If there are discrepant results, both parties cannot be right. This could attract media attention, which would undermine the public faith in clinical trials and affect our ability to undertake further research. Therefore, discrepancies will need to be handled carefully and sensibly. This	

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		may have major implications for workloads at EMA.	
109	General	An audit trail after application for data is required.	
110	General	National Voices is the national coalition of health and care charities in England. We strongly support the maximum transparency of clinical trial data. On behalf of our member organisations we signed the AllTrials petition earlier this year. Our entry is as follows: “National Voices is the national coalition of health and social care charities in England, with more than 150 member organisations. We work together to strengthen the voices of patients, service users, carers, their families and the voluntary organisations that work for them. We think it vital that patients have clear and accurate information about therapies: their relative efficacy, risks, harms and side-effects. Unless all such information is available, regulators, the NHS and doctors are not in a position to make safe, informed recommendations, nor are patients in a position to make informed decisions, or give informed consent. The incomplete availability of clinical trial data is therefore a threat to the health and safety of patients; it makes a mockery of the principles of transparency, shared decision making and evidence-based medicine. It is unethical and indefensible. The failure to register or publish the outcomes of clinical trials can also be seen as a form of abuse of those who have participated in clinical trials. Government, academia, publishers, regulators and the pharmaceutical industry all have a responsibility to ensure that this	

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		state of affairs is not allowed to persist." We support the EMA's attempts to improve transparency and deplore the efforts of some pharmaceutical companies to thwart these efforts.	
111	General	BPI generally supports the EMA's plan to disclose information about clinical trials to the general public and believes that this plan is consistent with the current legal situation in Germany and Europe. However, BPI takes the view that the Agency's plan to publish data from clinical studies generally and proactively in accordance with its Draft Policy has no basis in law. In accordance with the laws currently in force, the EMA may not publish confidential data from clinical trials, either on its own initiative or in response to requests from third parties. It is currently the practice of the EMA not to regard data from pre-clinical and clinical trials as commercially confidential information categorically, and therefore to release such data to third parties in connection with requests for information (Regulation (EC) No. 1049/2001). The Agency deems this categorization to be obvious „and derives from this its new proactive transparency policy in which data from clinical trials are to be generally available for down-load from the EMA's website without consulting the owner of the data." BPI takes the view that the EMA's proposal to publish data from clinical studies as a general rule lacks any authorizing basis. In accordance with the law currently in force, the EMA may not publish confidential data from clinical trials on its own initiative. This would infringe upon the ownership position of the manufacturer of the medicinal product, which is protected as a fundamental right. Moreover, Article 4 of Regulation 1049/2001	

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		(„Exceptions“) expressly states that confidential data may not be released. The publication of marketing authorization information at the request of third parties is also impermissible insofar as commercially confidential information is involved. Contrary to the EMA's view, the European courts view marketing authorization information, including pre-clinical and clinical data, as commercially confidential information, unless such information has already been published by the marketing authorization holder. The public has a legitimate interest in the conduct of clinical trials. The current legal situation already satisfies this interest. For example, the public is informed about the conduct of clinical trials through study registers (e.g. the EU Clinical Trial Register). Moreover, the EMA is already required by law to publish a complete scientific evaluation of marketing authorization applications for medicinal products, and this evaluation is constantly updated even after authorization (the European Public Assessment Report, EPAR). In Germany, a duty to publish the results of clinical trials has been in effect since 1 January 2011 (§ 42b of the German Medicinal Products Act). As an agency which is entrusted with medical and scientific functions, the EMA's administrative practice disregards both legal and economic aspects which can have an enormous negative impact on those affected by the consequences of its actions.	
111	General	**2. Detailed Opinion** **2.1. Implications** Interfering with existing competition and providing competitors with clinical trial data containing business and trade secrets would represent a massive transformation for the entire pharmaceutical industry of its proven economic	

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		system, which, to a large extent, is based on and sustained by the principle that investments should be encouraged through the protection of business and trade secrets. The publication of information pertaining to marketing authorization would jeopardize billions of Euros of research and development investments by the manufacturers of medicinal products. This administrative practice of the EMA can only be found in the pharmaceutical industry: in no other sector is all product information published, whether by the company or by government agencies. In the chemicals industry, for example, the sector which is most similar to the pharmaceuticals sector, Article 118 No. 2 of the REACH Regulation (EC) No. 1907/2006 expressly defines the information for which it may be assumed that disclosure would impair the protection of business interests. Such a rule, which creates confidence and clarity, does not exist in medicinal products law, however. Ex-acerbating the situation is the fact that products in the pharmaceuticals sector constitute a special category, since e.g. patents for additional indications for medicinal products which are already on the market, due to incremental innovations, are difficult to obtain once the patent for the active ingredient has expired. Many sections of the authorization file should not be made public, since many details contain information, or allow competitors to derive information, which would then enable competitors to imitate an innovation and market the product without extensive investment in research and development. The release of clinical trial data, whether or not such data contains business and trade secrets, must take place in independent fashion as a decision-making process based on scientific, legal and economic aspects, together with consideration of the public interest.	
111	General	**2.2. Existing transparency**	

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		The EMA's centralized marketing authorization procedure already provides a high degree of transparency relative to other regulated industries, as well as relative to other industries in which significant investments in scientific and technological developments are involved. The public is informed about the conduct of clinical trials through study registers. Moreover, the EMA is required by law to publish a complete scientific evaluation of applications for marketing authorization, which is constantly updated even after authorization is granted (the European Public Assessment Report, EPAR). This is not the case for other official testing of R&D-intensive products which have a relevance for public safety similar to that of medicinal products, such as type approvals for cars, (high-speed) trains and aircraft.	
111	General	**2.3. Existing legal framework** The EMA's proposed policy on publication and access to clinical trial data conflicts with existing statutory rules, such as TRIPS, EU fundamental rights, the German Freedom of Information Act, the Federal Data Protection Act, Volume X of the German Social Code, the fundamental right of self-determination concerning personal information, the European Data Protection Convention of 1981, Articles 8 and 9 of the European Charter of Fundamental Rights of 2009, the European Data Protection Directive of 1995 (in the future, the General Data Protection Regulation) and the recommendations of the OECD and UNO. Furthermore the proposed policy conflicts the regulation (EU) 726/2004, in particular article 13 paragraph 3 of the regulation: “The Agency shall immediately publish the assessment report on the medicinal product for human use drawn up by the Committee for Medicinal Products for Human Use and the reasons for its opinion in	

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		favour of granting authorisation, after deletion of any information of a commercially confidential nature. Therefore the categorization of clinical trial data as not commercial confidential by EMA is violating the statutory provisions of this regulation. Furthermore the EMA conflicts article 57 of this regulation: “Where appropriate, the database shall also include references to data on clinical trials currently being carried out or already completed, contained in the clinical trials database provided for in Article 11 of Directive 2001/20/EC. The Commission shall, in consultation with the Member States, issue guidelines on data fields which could be included and which may be accessible to the public.” That means these guidelines will be legislated by the Commission and member states and not by the EMA. The EMA proposed policy will endanger data exclusivity conflicting „NOTICE TO APPLICANTS, VOLUME 2A, Procedures for marketing authorization, CHAPTER 1 MARKETING AUTHORISATION, June 2013”: „5.4 It must be stressed that assessment reports such as the EPAR for Community marketing authorizations which are made publicly available by competent authorities for reasons of transparency cannot be considered to supply sufficient information to meet the requirements of Annex I of Directive 2001/83/EC und 6.1.6 Reliance on pre-clinical and clinical data contained in the dossier of a reference medicinal product under data exclusivity: During the period of data exclusivity of a medicinal product, the data contained in the pre-clinical and clinical file of that product and obtained through access to documents or freedom of information legislation within the EU or in third countries, cannot be relied on by other applicants or the authorities in the procedure to ascertain the safety and efficacy of other products which are shown to be bioequivalent, whether in the framework of Article 10 of Directive 2001/83/EC or under other procedures (Articles 8(3),10a or 10b).	

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		Furthermore the proposed policy is unlawful due to the fact there is no critical examination of company- and business secrets or commercial confidential data and no relevant legal basis is mentioned. According to the prevailing view in the case law and literature, unpublished study data which are submitted to approval authorities qualify as commercially confidential information. This information falls under the applicant's right of ownership and is protected on the European level in accordance with fundamental rights. A number of legal instruments already exist in the EU in this regard, such as Directive 2004/48/EC on the enforcement of intellectual property rights. The authorities are obligated, pursuant to § 30 of the Administrative Procedure Act in Germany, to maintain the secrecy of commercially confidential information which becomes known to them in the course of their activities, including unpublished study data which are presented in connection with applications for approval. This obligation has been upheld not only by the European Court of Justice, but recently by the German Federal Supreme Court as well. Insofar as approval authorities in EU member states, as well as the EMA, now take the view that unpublished study data presented to them in connection with applications for approval do not constitute commercially confidential information, this view has no basis in law. This view conflicts not only with the definition of "commercially confidential information" used by the authorities themselves, but also with the prevailing view in the case law and literature, as well as the view of the European Commission. While no single definition of „business and trade secrets“ exists in the EU, the German Federal Administrative Court defined this term in 2009, and this	

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		definition may be used on the EU level as well: “Business and trade secrets are all facts, circumstances and events relating to a company which are not known to the general public, but rather are available only to a limited group of persons, and in whose non-dissemination the legal entity has a legitimate interest. Trade secrets largely consist of technical information, while business secrets relate primarily to commercial information (Federal Administrative Court, NVwZ 2009, NVWZ Year 2009 Page 1113, following BVerfGE 115, BVERFGE Year 115 Page 205 [BVERFGE Year 115 Pages 230 et seq] = NVwZ 2006, NVWZ Year 2006 Page 1041). Accordingly, qualification as a business or trade secret requires, in addition to an absence of public knowledge of the underlying information, a legitimate interest on the part of the company in its non-dissemination. Such an interest exists if disclosure of the information has the potential to make exclusive technical or commercial information available to market competitors and thus detrimentally affect the competitive position of the company (Federal Administrative Court, NVwZ 2009, NVWZ Year 2009 Page 1114; Federal Administrative Court, NVwZ 2009, NVWZ Year 2009 Page 1113).” The EMA's view conflicts with this definition since the marketing authorization data are avail-able only to a limited group of persons and their publication has the potential to affect the company's competitive position. The publication of commercially confidential information demolishes confidentiality and destroys the protection of such information. Such an action, the greatest possible interference with a legal position protected by fundamental rights, requires an authorizing basis in law. However, such a basis is entirely absent for the publication of clinical study data.	

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		On the contrary, the data submitted by the marketing authorization holder are specifically protected from third parties under the Community Code through data exclusivity. In particular, it should be stressed that, even after the data exclusivity period expires, no publication of data takes place and the disclosure of data to third parties is not permitted. Rather, manufacturers of generic drugs are only permitted to refer to the data of the original manufacturer in order to avoid additional pre-clinical and clinical trials. However, it is not possible to obtain the data and then use them, e.g. in countries where the approval process took longer and where data exclusivity may still be in effect, thus preventing a reference. • The general rules concerning access to information held by the authorities must be viewed systematically in light of the specific rules of European medicinal products law. Primacy of the Community Code: Given the particular importance of protecting development results, the handling of in-formation which is made available by an applicant to the authority for testing purposes is governed by the Community Code. The latter, as the more specific rule, takes precedence over the general rules. Accordingly, the publication of data during the data exclusivity period which can be used economically by competitors is not permitted, whether at the initiative of the authority or in response to requests from third parties. • Weighing of legitimate interests But even after data exclusivity expires, the various interests must be weighed. The general rights of access to information in accordance with	

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		Article 15 No. 3 of the Treaty on the Functioning of the European Union, the EU Access to Information Regulation and the German Freedom of Information Act are not absolute. The right of access to in-formation is limited by superior legal interests in the non-dissemination of personal da-ta, state secrets and commercially confidential information. The protection of the private and corporate sphere and intellectual property in accordance with Article 7 and Article 17 No. 2 of the Charter of Fundamental Rights of the European Union takes precedence over the right of access to information. In particular, pre-clinical or clinical data on the basis of which the original manufacturers may be able to obtain patent protection enjoy protection as long as a patent application has not yet been filed. European patent offices are requiring an increasing amount of data in support of patent applications. However, if such data are published in advance, such publications would be harmful for the development of new products and would stand in the way of the issuance of a patent. Since patents are another key incentive, serving to protect substantial investments in the development of medicinal products, this legitimate interest must also be protected. Patents are issued if the underlying invention is new and innovative. “New” means that the invention was not available to the general public prior to the application. If the invention has been discussed at conventions, shown on posters or published online or in journals, it is no longer new and a patent therefore cannot be issued. „Innovative“ means that something more than the expertise of the average specialist was required in order to make the invention.	

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		Indications as to the degree of innovative-ness may be e.g. that the invention took a particularly long time to make, that a scientific prejudice has been overcome (e.g. the belief that the invention was not even possible), etc. Routine development activity is generally not considered innovative and is therefore not patentable. In the clinical sphere, it is possible, after applying for a product patent, e.g. for an active ingredient (e.g. aspirin), to file an additional patent application for a specific indication (e.g. heart attack, if the first application related e.g. to pain). The requirement, once again, is that this indication (heart attack) must be new and innovative, i.e. was not previously published and shows innovative progress. There are decisions by the European Patent Office which relate to this subject: Case No. T158/96 related to the active ingredient sertraline, for which a patent was sought for the indication of obsessive compulsive disorder. A document published prior to the patent application contained a reference to a Phase II study for the same indication. Since the results of experimentation on animals, other pre-clinical tests and the Phase I study failed to establish the effectiveness of sertraline, the patent was issued. However, it was noted, on Page 9, that the patent would not have been issued if the pre-clinical tests or prior clinical trials would have revealed with an adequate degree of certainty to a person specializing in the field that sertraline would be effective for that indication. In Case No. T241/95, it was decided that the novelty of an invention is absent if its therapeutic effect on animals is already described, and the patent was not issued in that case. If pre-clinical and/or clinical data are published by the authorities,	

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		subsequent patents can no longer be obtained if the therapeutic effect on animals has been published (e.g. in vivo or in vitro), or if clinical trials indicate that the medicine would be effective on humans. Accordingly, the right of access to information does not justify access to data which constitute commercially confidential information and whose disclosure was not consented to by the affected person • Subordinate importance of the interest in disclosure In exceptional cases, European law allows the publication of protected information if there is an overriding public interest in its disclosure. Such an overriding interest generally does not exist in connection with study data. The interest in the protection of intellectual property, including commercially confidential information, generally outweighs the interest of the general public in disclosure in accordance with the rulings of the European Court of Justice. In particular, the ECJ has ruled that the interest in the protection of marketing authorization documents which were not made public takes precedence over the general interest in disclosure in part because the approval authorities have unlimited access to the study data and are therefore in a position to take the necessary measures to protect public interests in the course of their responsibilities. This is all the more true considering that the public interest in disclosure is already adequately served by the study registers which have been set up, and by the publication of summaries of the results of medicinal product studies as part of the des European Public Assessment Report (EPAR) pursuant to Article 13 No. 3 of Regulation (EC) No. 726/2004, as	

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		well as corresponding reports by national approval authorities. Nevertheless, the EMA generally assumes the existence of an overriding public interest in the publication of study data, which it justifies on the grounds of public health. How-ever, a finding in such general terms is not permissible. Rather, it is necessary to weigh the various interests in each individual case, and this is lacking in the EMA's approach. Even if one were to accept that the EMA is authorized to create a procedure in which, in the case of two competing fundamental rights, one is found to be generally superior, even though such a procedure would violate European law, it must be kept in mind that the confidentiality of study data also ultimately serves the public interest in health. If a generally overriding public interest in the publication of study data is affirmed, the incentive to conduct clinical trials, and with it the incentive to develop new medicinal products in the interest of protecting public health, would be lost. Accordingly, the non-dissemination of study data and the associated protection of the results of investments in the development of medicinal products serve not only the private economic interest of the pharmaceutical industry but also, and above all, the public interest in the constant improvement of the protection of health. The protection of health certainly out-weighs the interest in access to information. In accordance with the rulings of the European Court of Justice and the Federal Constitutional Court, life and health occupy the highest position in the value system of the European Union and the German Basic Law. What is involved is not hiding study data from the public. The results of clinical trials are made available, without restriction, to the approval	

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		authorities, as custodians of the public interest. On this basis, the approval authorities are in a position, without restriction, to investigate the quality, effectiveness and non-objectionable nature of medicinal products. Conducting this investigation is the responsibility of the approval authorities. On the other hand, it is not the responsibility of the scientific community and the public to make approval decisions or to render judgment about the approval decisions by the authorities as „courts of popular opinion“. • Application of the FOI Regulation, 1049/2001/weighing of interests In fact, the EMA's consultation paper calls, in a few cases, for the recognition of certain information as business and trade secrets. In those cases, however, the result is not the omission of publication, but rather a different publication procedure, namely one in accordance with the principles of Regulation 1049/2001. The uploading of all information on the EMA website without hearing the affected company, which is proposed as „proactive“ publication, would release the EMA from its responsibility to look through the documents for business and trade secrets and to revise them accordingly. In other words, the practice of assuming whenever possible that data do not have the potential to be confidential information may have the benefit of reducing bureaucratic expense, but it has nothing to do with the professed goal of improving patient safety or public health. <u>Criminal prosecution and state liability for the unauthorized publication of study data</u> If authorities publish heretofore unpublished study data which are presented	

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		to them in connection with applications for approval without the consent of the applicant, they commit a breach of the official duty of confidentiality. The office holders responsible for such publication are subject to criminal prosecution in accordance with German law, pursuant to § 203(1) and (2) of the German Penal Code. Such actions may also establish a duty to compensate the applicant for the damages caused by the publication, under the heading of state liability.	
111	General	**2.4. Findings from the study commissioned by the EU Commission on trade secrets** (Study on Trade Secrets and Confidential Business Information in the Internal Market – Final Study –April 2013 – Prepared for the European Commission, Contract Number: Markt / 2011/ 128 / D) The study examined the legal and economic structures which serve to protect business secrets in the European Union. With respect to the significance of information and discoveries, the study states as follows: „In today's economy, information and know-how - representing the result of R&D investments, creativity and business initiative – have become the key factors for developing and maintaining competitive advantage … Trade secrets are valuable business assets to both innovative and non-innovative firms. As valuable business assets, trade secrets play an important role in economic growth and fostering innovation … A consensus among economists has emerged that trade secrets play an important role in protecting the returns to innovation and that trade secret protection is an integral and important part of the overall system of protection available to EU firms to protect their intangible assets, like patents and copyrights … With specific	

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		focus on small and medium-sized enterprises (SMEs), trade secrets appear of particular importance because innovation in this segment tends to be more incremental in nature and of core significance to firm value and performance.“ The authors of this study „… conclude that there are clear economic justifications for granting legal protection to trade secrets and confidential business information“.	
111	General	**2.5. Argumentation of the EU Ombudsman concerning introduction of the policy and alteration of the EMA's transparency policy** The statements made by the Ombudsman do not create any legal obligation. In general, the Ombudsman tends to comment only on administrative issues, such as to say that the handling of a particular matter is taking too long, etc. Whether data from clinical trials constitute business and trade secrets, as well as the relationship of legal positions protected by European law to one another, are legal questions which must be interpreted not by the Ombudsman, but rather by the European courts, and only them.	
111	General	**2.6. The case of InterMune and AbbVie vs. the EMA** The two plaintiffs, InterMune and AbbVie, sued the EMA in separate cases before the EGC for releasing data from marketing authorization documents. Upon submitting the documents, the companies had been asked by the Agency for an opinion as to which data could be published by the EMA. However, the Agency failed to comply with the ban on publication. In its decision, the EGC ordered the EMA not to release InterMune's data, finding that a) the confidentiality of data cannot simply be denied without further investigation and that b) publication may cause irreparable damage. The Agency appealed this decision, and the ECJ will soon render a ruling via	

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		interlocutory proceedings. A ruling in the main action is not expected before 2015. BPI points out in this context, that the EMA should also take note of the proceedings which are currently pending. If the publication of marketing authorization documents is declared to be void in the main action in accordance with Article 264 of the Treaty on the Functioning of the European Union, this declaration would have general effect in this regard and would therefore apply erga omnes. A decision by the Agency before a final ruling is issued would be tantamount to disregarding the court. Nevertheless, the EMA's new transparency policy is scheduled to take effect on 1 January 2014.	
111	General	2.7. Damages as a consequence of the policy The implementation of the EMA's policy would have a substantial detrimental impact on Germany as a center of research, as well as the research landscape in Europe: the publication of approval information jeopardizes research and development investments in the billions, and therefore threatens to undercut the research and development of new and innovative medicinal products for the promotion of public health. As a final consequence, it may hinder the access of European patients to innovative treatments, or at least delay such ac-cess by years, if the threat to the confidentiality of research and development results in Eu-rope leads to a situation in which the approval of innovative medicinal products is sought only in places where the confidentiality of study data is protected by the approval authorities, as is the case e.g. in the US and Japan. Not insignificantly, the release of data may establish personal criminal liability for the relevant office holders on a national level. Moreover, the authorities	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		themselves may be exposed to claims based on state liability. In its Proposal for a Clinical Trials Regulation, the European Commission referred to the high and rising cost of con-ducting clinical trials and proposed ways to create more of an incentive to conduct clinical trials in the European Union in order to promote public health and medical research. It based these proposals on the fact that clinical trials are an indispensable component of clinical re-search and are, in turn, essential for the development of medicinal products and for the improvement of medical treatment, remarking that, without clinical trials, there would be no new medicines, no further development of existing medicines and no evidence-based improvement of treatment with medicines. Applications for the approval of medicinal products and publications in medical journals are based on data obtained in the course of clinical trials. These days, it takes several hundred million Euros in investments to develop a medicinal product, and the total investment can easily exceed 1 billion Euros. Such an investment will only be made if there is sufficient opportunity for an adequate return. In its Proposal for a Clinical Trials Regulation, the European Commission finds that unfavorable conditions led to a significant decrease in the number of applications for clinical trials in the European Union, and that more attractive conditions are necessary in order to give patients more rapid access to new and innovative medicinal products and counteract the loss of competitiveness in Europe. Moreover, the Recitals to the Regulation concerning the creation of a supplementary protection certificate for medicinal products state that inadequate protection has had a detrimental impact on pharmaceutical research, creating the risk that research centers located in the member	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		states will be moved to countries where more protection is offered. The EMA's plan to publish data from clinical trials and its general willingness to release data from applications for marketing authorization in response to requests from third parties make conditions for research and development even worse, rather than improve them. As a result, they run counter to the European Commission's efforts to promote the research and development of innovative medicinal products in order to improve public health. Sufficient opportunity for an adequate return means that the development results of innovative companies must be protected from being used by their competitors without incurring any cost of their own. If competitors are placed in a position where they can take over the innovative company's developments free of charge, and then undercut the innovative company on price because they did not have to incur any cost of their own, the innovative company would be robbed of the fruit of its labor. This would turn the free market principle on its head: non-achievement would be rewarded and achievement would be punished. The development of new and innovative medicinal products by private companies cannot function under such conditions. If the driving force behind the economy, economic incentives, is eliminated, private companies would no longer develop new and innovative medicinal products. This conflicts with the interest in promoting public health and medical research. The EMA has failed to consider the economic context. It ignores the fact that the publication of study data will allow not only the scientific community and the public, but competitors as well, to obtain knowledge of such data and use them freely. Publication destroys all protection of the intellectual property inherent in the study data, so that the incentive to conduct clinical	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		trials in the interest of promoting public health is lost as well. Patent protection, which could compensate for the non-protection of study data, is lacking in many cases. Moreover, the publication of approval documents itself may render it legally impossible to obtain patent protection. If study data are published, the 10-year data exclusivity period would be evaded. Through publication, the data would be exposed to unprotected access by anyone anywhere in the world, including competitors. The published study data could be used directly and at will to apply for the approval of competing preparations worldwide and without having to refer to the approval documents held by the approval authority, as would be the case in a conventional application for the approval of generic drugs. Moreover, because the data would be presented by the applicant itself, the approval authorities would not be able to refuse approval on the grounds that a reference to the documents held by the authority is permissible only after expiration of the periods pre-scribed by law in that regard. Such a reference would no longer be required: rather, the data would be presented independently. Because the EMA plans to publish data on the patient level as well, there will be a conflict between the content of the declaration of consent signed by the patient and the EMA's publication policy, as patients do not consent, in that declaration, to the publication of their data by an EU agency. Moreover, patients have no revocation option, and the EMA policy does not block publication if consent is revoked (the rights of those affected are disregarded). BPI also finds the statements concerning the recording and documentation of the process to be inadequate, as the draft policy does not specify who is responsible for monitoring the disclosure process and whether	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		an audited or certified process will be involved.	
111	General	**2.8. BPI's proposal for the scope of publication of clinical trial data** BPI deems the categorization of business and trade secrets in the EMA's draft policy to be inadequate. The Agency concedes that the system it has developed is not entirely secure. BPI therefore proposes replacing the data listed in the annexes to the draft policy, which have to be presented to the Agency by the pharmaceutical enterprise for the purpose of publication, with the CONSORT criteria (see Table 1: Suggestion for criteria for publication of results of clinical trials according to the transparency guideline of the EU). BPI points out that the publication model of PhRMA and efpia (Principles for Responsible Clinical Trial Data Sharing) is acceptable as a model, in principle, although this practice ultimately depends on the decision of the individual company, since the relevance of clinical trial data may differ substantially in some cases for large companies, on the one hand, and mid-size manufacturers on the other. The decision by individual companies to determine their own scope of publication should be distinguished from the general publication rules. A more generous practice generally does not extend the legal framework.	
111	General	**Table 1: Suggestion for criteria for publication of results of clinical trials according to the transparency guideline of the EU**	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any

	Synopsis/ Report according to ICH-E3 Guideline	CONSORT Statement 2001/2010	Condensed suggestion BPI-proposal
Title + Abstract			
		Structured summary of trial design, methods, results, and conclusions	
		(Randomised trial in the title)	
	Sponsor		Sponsor
	Studientitel		Studientitel
	Study number internal		Study number internal
	Eudra-CT study number		Eudra-CT study number
Introduction		Scientific background	
		Explanation of rationale	
		Specific objectives or hypotheses	
Methods			
	Relevant amendments		Relevant amendments
	Study/test medication		Study/test medication
	Reference medication		Reference medication
	Co-ordinating investigator according to ICH-GCP		Co-ordinating investigator according to ICH-GCP

Stake-holder no.	General/ Line no.	Stakeholder comments				Proposed change by stakeholder, if any
			Investigators	Settings where the data were collected	Investigators	
			Study centres	Locations where the data were collected	Study centres	
			Study period		Study period	
			Publications		Publications	
			Clinical phase		Clinical phase	
			Objectives • Primary • Secondary	Primary and secondary outcome measures, including how and when they were assessed	Objectives • Primary • Secondary	
			Methodology	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Methodology	
				Determination of sample size, explanation of interim analysis, stopping rules		
			Number of subjects included (tabular overview)		Number of subjects included (tabular overview)	
			Diagnosis and main criteria for inclusion	Eligibility criteria for participants	Diagnosis and main criteria for inclusion	
			Test preparation (Dose, mode of administration, batch number)		Test preparation (Dose, mode of administration, batch number)	
			Control (Dose, mode of administration, batch number)		Control (Dose, mode of administration, batch number)	

Stake-holder no.	General/ Line no.	Stakeholder comments				Proposed change by stakeholder, if any
			Duration of treatment		Duration of treatment	
			Criteria for evaluation • Efficacy • Safety		Criteria for evaluation • Efficacy • Safety	
			Statistical methods	Statistical methods used to compare groups for primary and secondary out- comes	Statistical methods	
				Statistical methods for additional analyses, such as subgroup analyses and adjusted analyses		
				Method used to generate the random allocation sequence		
				Type of randomisation; details of any restriction (such as blocking and block size)		
				Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned		
				Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions		

Stake-holder no.	General/ Line no.	Stakeholder comments				Proposed change by stakeholder, if any
				If done, who was blinded after assignment to interventions (and how		
		Results				
				Participant flow (Diagramm) • For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome • For each group, losses and exclusions after randomisation, together with reasons	Participant flow (Diagramm) • For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome • For each group, losses and exclusions after randomisation, together with reasons	
				Dates defining the periods of recruitment and follow-up		
				Reason Why the trial ended or was stopped		
			Tabular overview: • Demographic data	A table showing baseline demographic and clinical characteristics for each group	Tabular overview: • Demographic data	
				For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups		

Stake-holder no.	General/ Line no.	Stakeholder comments				Proposed change by stakeholder, if any
			Tabular overview: • Results of primary and secondary efficacy parameters	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Tabular overview: • Results of primary and secondary efficacy parameters	
				Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		
			Tabular overview: • Results of Safety analysis	All important adverse events or side effects in each intervention group	Tabular overview: • Results of Safety analysis	
		Discussion				
			Conclusion	Interpretation of the results	Conclusion Efficacy	
				Generalisability (external validity, applicability) of the trial findings	Conclusion Safety	
		Other Infor-mation				
				Registration number and name of trial registry		
				Sources of funding and other support		
111	15-17	Assessors of the CTD should be aware of their responsibility towards the community and also should be confident in the decisions/recommendations they make. Therefore, no further disclosures apart from those already prodided in the EPAR are necessary				

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
111	27-31	Retrospective analyses of already collected data can never be of the same quality as prospective data analysis, where all endpoints are defined prior to data collection	
111	41-43	This should never be permitted. According to the current recommendations on the content of the informed consent form in Germany, patients only consent that the authorities have the right to view the data. Patients do not allow the authorities to make their data publically accessible.	Patient level data will not be disclosed.
111	57-59	It is not acceptable that the community is confused and worried by low quality data from scientifically inferior analyses being made public. It is also unacceptable to undermine conclusions from RCTs and EMAs decisions based on such low quality secondary data analyses.	
111	70-72	It is unacceptable to withhold information about the identity of the organisations/persons requesting access to the data. Otherwise one cannot speak about the same transparency standards applied to the MAHs and any other organisations/persons	
111	77-78	Does it mean that all clinical trial data from studies with medicinal products not subject to a centralized MAA is excluded from the scope? In this case, different standards are applied to medicinal products which must be centrally authorized and to those eligible for decentralized authorization. Also, personal data would be handled differently- it cannot be accepted however that personal data of individuals participating in trials with medicinal product subject to central MAA is less protected Same issues apply to any trials with authorized products.	
111	155	Under no circumstances access should be granted to any personal data. No matter what requirements are to be met by a requester, it will not prevent	No access to CT raw data should be permitted

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		criminal behaviour	
112	General	EMA Publication clinical Trials data policy Der Vorstand der Deutschen Gesellschaft fUr Soziale Psychiatrie e.V . - DGSP- begruBt und unterstlitzt ausdrucklich die Initiative der EMA, die Ergebnisse wissenschaftlicher Arzneimittelforschung offentlich zuganglich zu machen. Die hier eingeforderte Transparenz der Ergebnisse der Arzneimittelstudien bietet die Chance, eine optimale Versorgung von Patienten und Patientinnen mit Arzneimitteln zu erreichen und so unerwunschte Effekte wie z.B. massive Nebenwirkungen und Unvertraglichkeiten in der Anwendung der Medikamente zu verhindern. Ebenso waren die Behandler und die Patienten und Patientinnen in der Lage, neue Medikamente und die damit oftmals verbundenen Heilsversprechungen durch die Pharmaindustrie einer realistischen Einschatzung zu unterziehen . Dies konnte dazu fuhren, dass insgesamt, wie von unserer Gesellschaft in dem Memorandum zur Anwendung von Neuroleptika u.a.gefordert , in geringerem MaRe Medikamente eingesetzt werden, Wirkungen und Wechselwirkungen in der Behandlung besser berucksichtigt werden konnten, Patienten und Patientinnen vom Behandler unabhangige Informationen zu ihrer medikamentosen Behandlung zur Verfl.igung haben werden und somit uber eine bessere Entscheidungsgrundlage verfl.igen u.v.a.m. *. Auch Krankenkassen und andere Kostentrager medizinischer Behandlungen und die Gerichtsbarkeit hatten so eine solidere Grundlage fUr ihr Handeln und ihre Entscheidungen. Die politisch verantwortlichen Akteure der EMA sind aufgefordert, ihre Politik an den Interessen der Bevolkerung und an	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		deren gesundheitlichem Wahl offensiv zu orientieren . Diese Gemeinwohlorientierung ist als hoherranging gegenuber den Interessen der Pharmaindustrie und ihrer Lobbyisten zu sehen. Allen Versuchen eine maximale Transparenz zu verhindern ist eine klare Absage zu erteilen . Die DGSP setzt sich seit uber 40 Jahren fUr die Interessen und Rechte von Menschen mit psychischen Erkrankungen ein. Getragen wird die DGSP von Mitarbeitern und Mitarbeiterinnen psychiatrischer Einrichtungen, institutionellen Anbietern psychiatrischer Hilfen, Menschen mit PsychiatrieErfahrung und deren Angehorigen und psychiatrisch engagierten Burgern und Burgerinnen. Die DGSP sieht die zunehmende biologische Orientierung in der psychiatrischen Behandlung und die damit einhergehende Priorisierung medikamentoser Behandlung kritisch. *Memorandum siehe: http://www.dgsp-ev.de/fileadmin/dgsp/pdfs/Flyer_Infoblatt_KuFo-Programme_Broschueren/Broschuere_Neuroleptika_2012_web.pdf	
112	General	**Translation provided by the Stakeholder:** EMA Publication clinical trials data policy The Executive Board of the German Association for Social Psychiatry eV DGSP - welcomes and strongly supports the initiative of the EMA, providing public access to the results of scientific drug research. The collected here transparency of the results of drug trials offers the opportunity to achieve optimal care of patients and patients with medicines and so undesirable effects such as serious side effects and intolerance in the use of drugs to prevent. Similarly, the clinician and the patient, and patients	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		will be able to new drugs and the often associated promises of salvation would be subjected to by the pharmaceutical industry a realistic assessment. This could cause a whole, as others of our company, the Memorandum on the use of neuroleptics required medications are used to a lesser extent , effects and interactions in the treatment could be better taken into account , patients, and patients will have by the practitioner independent information on their medical treatment available and thus a better basis have much more * . Also, health insurance companies and other payers of medical treatments and the jurisdiction had such a solid basis for their actions and decisions. The politically responsible actors of the EMA are asked to orient their policies to the interests of the population and their sanitary well offensively. This common good is seen as hOherranging against the interests of the pharmaceutical industry and its lobbyists. All attempts to prevent a transparency is a clear refusal to grant. The DGSP has been working over 40 years for the interests and rights of people with mental illness. The DGSP is supported by staff and staff of psychiatric facilities, institutional providers of psychiatric help, people with psychiatric experience and their relatives psychiatrically and dedicated citizens. The DGSP sees the increasing biological orientation in mental health treatment and the concomitant drug treatment prioritization critical. * http://www.dgsp-ev.de/fileadm in/dgsp/pdfs/Fiyer_Infoblatt_KuFo-Programme_Broschueren/Broschuere_Neuroleptika_2012_web.pdf	
113	General	Parkinson's UK welcomes the proposals to increase transparency when publishing clinical trial data. People affected by Parkinson's are supportive of data being shared effectively, being accessible and being transparent for the	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		purposes of research. For example, Parkinson's UK has 370 local groups across the UK and we conducted seven separate events across the UK with members of these groups and staff in order to engage with them on clinical research issues. From a survey conducted with the members and staff, 90% (241 out of 256 people) reported that NHS data should be available to researchers. We therefore endorse any plans to ensure greater transparency for accessing research data.	
113	General	Although we support the sharing of research data and transparency of publishing clinical trial data, it is very important to people affected by Parkinson's that data will be kept safely and securely and a commitment to ensuring data will be anonymised, where possible, is welcomed. Therefore, it is important to have appropriate methods in place to protect confidentiality when sharing category 3 data. Currently, the process for reviewing requests to access this data lacks detail and needs to be strengthened.	
113	57-61, 216-218	To ensure that category 3 data does not have the potential to become identifiable and to ensure that it is not disclosed, a more robust process is needed to identify the competence of the requester. For example, more information should be gathered on the following: • data handling – to ensure data will be held securely, • data analysis – prevent misinterpretation and ensure accurate secondary analysis, • gain a more detailed plan of how the data will be used, • ensure that the original informed consent is still relevant for any secondary analysis.	The EMA should take responsibility for judging the requester's competence and analysis plan.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		As the UK's Parkinson's support and research charity we're leading the work to find a cure. So far we have invested over £60 million in ground breaking Parkinson's research and encourage the publication of clinical trial data if it boosts Parkinson's research. However, it is vital that we have the support of the public in this work and encourage their participation in research by ensuring the secure handling of their confidential data.	
114	#39-43	Data mining and database linkage are only mentioned as potential threads for "unlawful retroactive patient identification". This is certainly an unbalanced description as legal safeguards exist for the use of these techniques. In addition they are usually, if not always, employed with sincere scientific intentions in line with the overall objectives of EMA. In the same vein, in #43 the policy should only mention "damaging instances of patient identification" if there is some evidence from the past that this thread really exists.	
114	#44-48	The EMA's overarching long-term goal is to protect and foster public health (#13 and 75). This goal cannot be met by the proposed policy if use of patient data is restricted to analyses only pertaining to the development and assessment of a particular medicine that the patient initially consented to. With appropriate safeguards and monitoring, the policy should enable use of CT data that goes beyond the repetition of analyses aiming to only establish the benefit or harm of a given drug. For instance, CT data from several sources may be used jointly in individual patient-data or network meta-analyses in order to better understand the comparative effectiveness of a entire class of drugs. Also see #191-192 where this restriction is repeated.	
114	#77-82	If only CT data submitted to EMA in the future will be within the scope of the new policy, this will considerably restrict the use of already existing CT data	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		in new and independent analyses. It will also lead to an incomplete picture in cases where early trials have been completed already but phase III trial data have not yet been submitted to EMA. At least in the latter cases, all CT data pertaining to the development of a drug should be made available.	
114	#77-82	If only CT data submitted to EMA in the future will be within the scope of the new policy, this will considerably restrict the use of already existing CT data in new and independent analyses. It will also lead to an incomplete picture in cases where early trials have been completed already but phase III trial data have not yet been submitted to EMA. At least in the latter cases, all CT data pertaining to the development of a drug should be made available.	
114	#97	typo	studies, case control studies, or registry data. Reports ~~form~~ from such studies may sometimes differ from
114	#122-123	To avoid ambiguity, it should be clarified that “SAS” does not mean the statistical package of the same name."	
114	#128-137	Section 4.1.1 on Category 1 data (and also the classification used in Annexes I and II) does not make clear that data not deemed CCI by the EMA will automatically fall under Category 2 with open access (and not Category 3). This should be made explicit.	
114	#132	It is important to stress that there will be no automatism to consider data as CCI only because they are contained in the three respective sections of Annex I. It needs to be clarified what the criteria and procedure of accepting “duly justified cases” will be.	
114	#137	Annex II should be mentioned here, as well: “… in Annex I and II…”	CT data/documents that are not categorised as 'CCI' in Annex I and II are considered to contain no CCI.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
114	#156-158	The definition of CT data/documents with PPD concerns should also mention the documents of Annex I, point 5.4.	
114	#180	A main purpose of the policy is to enable independent analyses and research using CT data. Such analyses often take place in international scientific collaborations. The group of eligible requesters should therefore be enlarged including those in countries such as Switzerland that are formally affiliated with EU research programs such as FP7 and partners in the ECRIN network.	
114	#182	“controlled data” is an undefined term and should be replaced by “data with controlled access” or “C data”. Also, further below in this section, there is mention of ‘CT data’ (#188, 191, 193, 194) and it needs to be clarified whether all CT data or only ‘C data’ are meant.	- data with ~~access~~ controlled access ~~data~~ for the sole purpose of addressing a question or conducting analyses
114	#188-190	There is a logical short-cut here, if in general, data linkage is put on a level with retroactive identification of patients. While requesters should, of course, refrain from trying to identify individuals, data linkage per se should not be excluded. There are many valid uses of this technique that do not imply retroactive identification and that should not be banned per se.	
114	#194-197	As research collaborations do not stop at the EU borders, it needs to be clarified whether non-EU partners in international research groups will be granted access to datasets under the same conditions.	
114	#205	The obligation to destroy CT data after completion of analyses conflicts with obligations of academic researchers to store original data during a defined time. Such obligations are enshrined in regulations and recommendations aiming to ensure research integrity and good scientific conduct. For instance, the European Code of Conduct for Research Integrity recommends that “original scientific or scholarly research data should be documented and	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		archived for a substantial period (at least 5 years, and preferably 10 years)" (Section 2.3, page 13 in March 2011 version).	
114	#235	Replace "Annexes 1 and 2" by "Annexes I and II	All documents listed in Annexes ~~1~~I and ~~2~~II - whether categorised 'O' or 'C' - shall be provided in
114	#235-236	It is unclear whether this means provision of PDF documents by EMA to requesters or provision of original documents to the EMA. Will EMA convert documents (other than raw CT data) primarily submitted in other formats into PDF and make them searchable?	
114	#285-292	This list of groups of persons involved in the conduct of clinical trials should also include members of data safety monitoring boards.	4. This section contains personal 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 members of data safety monitoring boards, ~~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 overriding public interest, these personal data are considered exempt from PPD considerations.
115	General	The concept of transparency in relation to research on medicinal products is, in general, welcomed by EUCOPE, in particular, where it serves the expansion of scientific knowledge, e.g. through bona fide research, and	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		constitutes the basis for an educated risk-benefit advice to patients. However, the Agency has to strike the balance between an increased degree of transparency and the rights of the industry and patients to have their confidential information duly protected in order to stimulate research and development in new medicinal products. The sharing of clinical-trial data with qualified scientific and medical researchers for conducting legitimate research is clearly an issue that needs to be discussed and requires a solid regulatory framework. In this regard it has to be observed that, at the time being, two court cases are pending with the General Court of the European Union, which, *inter alia*, address the question of the legal definition of commercial confidentiality and whether or not EMA was entitled to give access to clinical trials documents submitted in the marketing authorisation dossiers for Humira (adalimumab) by AbbVie and Esbriet (perfidenone) by InterMune. In April, the Court granted interim injunctions to AbbVie and InterMune, preventing the disclosure of those documents to third parties. It has to be expected that the Court will give in its decision in the main proceedings of these cases general guidance on the publication of clinical-trial data by the Agency. As the Agency underlines that the Policy on publication and access to clinical-trial data complements the existing Policy on access to documents (related to medicinal products for human and veterinary use) (Policy/0043) which has been in place since 2010, it has to be observed that the lawfulness of the latter has not yet been ruled on by the European Union Courts. As the General Court has emphasised in its order of 25 April 2013 in Case T 73/13 R, **there is no existing case law whether some of the general assumptions of the EMA contained in the Policy/0043 and repeated in Policy/0070 might infringe the marketing authorisation**	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		holders' rights to professional secrecy, as guaranteed by Article 339 TFEU and Article 7 of the Charter of Fundamental Rights of the European Union, on the ground that the information at issue is confidential in nature and must therefore be protected against any disclosure. **This involved, according to the Court, a question of principle affecting the functioning of the pharmaceuticals and biotechnology sector in Europe and worldwide**. In order to avoid a situation where the EMA has to revise its Policy on the publication and access to clinical-trial data after these decisions have been taken and becomes liable to damages, **EUCOPE strongly suggests to let the new Policy only enter into force after the court proceedings are finalised taking the outcome(s) into consideration**.	
115	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 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.	
115	44	The Agency underlines the "respect for the boundaries of patients' informed consent". However, it remains unclear how the Agency will address the question of the scope of an informed consent given by the patients participating with regard to the subsequent use of their data. A general view that the informed consent also encompasses the publication of the data derived from the clinical trial in question is not acceptable and, once again, the Agency has to assess on a case-by-case basis whether or not a	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		publication of the data is lawful.	
115	49-51	Although EMA allows for exemption from this rule, the view ("in general") that CT data cannot be considered CCI and that the interests of public health outweigh considerations of CCI is not adequate and conflates the question of whether the data are confidential and the disclosure of them could damage the legitimate interests of the owner of them and the question of the public interest in overriding any such confidentiality. The confidential nature of the data has to be assessed by reference to the particular circumstances, and this broad categorisation also contradicts the argument of the European Ombudsman laid down in its draft recommendation in complaint 2560/2007/BEH against the EMA. There the ombudsman stated that a per se rule against disclosure of data package contents was not in accordance with Regulation 1049/2001. Therefore, the Agency cannot adopt an axiomatic rule the other way, in favour of disclosure unless the question whether or not clinical-trial data contains CCI is addressed in a careful, case-by-case and document-by-document analysis. Furthermore, the general assumption that the interests of public health outweigh considerations of CCI does not sufficiently take the recent findings of the Study on Trade Secrets and Confidential Business Information in the Internal Market of the Commission's DG Internal Market and Services (MARKT/2011/128/D) into consideration. According to the definition of CCI as provided for in EMA's draft Policy paper: "CCI shall mean 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. CCI falls broadly into two categories trade secrets […] and commercial confidences."	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		The above mentioned study confirmed “that the relevance of trade secrets in the new global economy is steadily growing: they are pervasive key factors for maintaining competitive advantage in all business sectors, for both innovative and non-innovative firms, regardless of their size. In this context, trade secrets protection effectively fills the gap between copyright and patent protection, the two traditional pillars of intellectual property, for purposes of appropriating the results of investments in innovation. There are straightforward economic justifications for creating a sound legal environment to protect trade secrets: empirical evidence and stakeholders' opinions converge on the conclusion that an initiative of the EU Commission in that direction would contribute to fostering economic growth, competitiveness and innovation in the Single Market” (page 151; emphases added). The study further clarifies that “economists have observed that trade secrets appear of specific importance to SMEs because innovations by SMEs tend to be more incremental in nature and of core significance to firm value and performance. The perceived higher cost of patent ownership and the material impact that disclosure may have on SME firm's value and performance encourage the use of secrecy as a protection” (page 149). Additionally, the European Court of Justice has stated in Case C 453/03 (ABNA) that the publication of detailed product data is against the principle of proportionality as far as the authorities dispose of such data. Without any protection of this value innovation might be impeded significantly. An undifferentiated approach to balancing public health and considerations of CCI does clearly not create a sound legal environment to protect trade secrets and therefore would contradict any Commission’s attempt to effectively protect trade secrets.	

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115	52	It is difficult to see how the EMA can say that the Draft Policy protects intellectual property rights and investment by industry when it does not protect valuable know-how of companies. Medicinal products are not necessarily protected by a compound patent; instead, many companies in the same position, rely more heavily on confidential information and know-how. Furthermore, patent protection may be difficult to achieve where a new therapeutic indication for a well-known substance is subject of the marketing authorisation. In these circumstances, the Draft Policy, if adopted in its current form, could dis-incentivise companies, from filing applications for marketing authorisations or variations in the EU.	
115	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.
115	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. EUCOPE 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.
115	132	The Draft Policy suggests that only a small number of CT data sets can contain CCI, and that data may be classified as CCI in "duly justified cases"; it is unclear how or when this process might occur and what the EMA will take into account. On the current drafting of the policy, it appears that the EMA has already identified, as a blanket Policy, the categories of data that may contain CCI, and there is no opportunity in practice for a company to argue that other data contain CCI and should not be disclosed.	

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115	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.	Proactive publication of data should not apply to withdrawn applications.
115	155 subseq.	The Agency states that “protection of privacy is a paramount concern when sharing raw CT data. However, there remains concerns whether the Draft Policy will provide a sufficient level of protection. In particular where rare diseases are concerned the risk of re-identification is particularly high since only few individuals may have been subject to the trials in question. In this regard, the Agency has to consider all publicly available data, including social media data, when assessing the risk of re-identification.	
115	176 subseq.	The Draft Policy identifies three categories of data. In particular, there is a controlled access category for data that contain personal data. The question arises of why this, or a similar procedure, cannot be applied to CCI. EUCOPE believes it would be possible to enter into data sharing agreements in order to protect against unjustified access to data by competitors, while allowing research organisations to access the data, in the framework of a self-governing scheme set up by the pharmaceutical industry. Such a scheme offers a proportionate alternative to wholesale public access without any safeguards against unfair competitive use of data. As the Draft Policy already envisages such a procedure for raw data containing personal data, it would be straightforward for the Policy to apply the same procedure to data containing CCI.	
115	193	EUCOPE welcomes assurance that the data-sharing agreement will specify that the requestor must “refrain from using CT data accessed to gain a marketing authorisation in a non-EU jurisdiction”. This rule, however, should	

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		be applicable to any clinical-trial data disclosed in the framework of the new EMA Policy. Furthermore, while the data-sharing agreement is stated to be legally binding, the question arises of how this will be enforced.	
115	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.
115	219-221	Same comment as lines 153-154 re circumstance behind withdrawal.	
115	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.
115	285 subseq.	The Draft Policy states that personal data from personnel involved in clinical trials are considered exempt from PPD considerations. This statement clearly contradicts the protection of individuals with regard to the processing of personal data according to Directive 95/46/EC. It is self-evident that the Agency is bound by the relevant legislation. Again, in particular where rare diseases are concerned, there might be only a few or even only one medicinal specialist in the respective field in one Member State.	
115	Annex I 2.5.2	Even the overview of biopharmaceutics could contain CCI especially when dealing with novel formulations.	No general assumption that this data is not confidential. Re-classifying 2.5.2 as C
115	Annex II 16.1.4	Certain elements of this section are confidential (namely CVs).	No general assumption that this data is not confidential. Re-classifying 16.1.4 as C
115	Annex II	Listings of patients and patient identification and randomisation schemes	No general assumption that this data is not

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	16.1.6 and 16.1.7	should be confidential	confidential. Re-classifying 16.1.6 and 16.1.7 as C
116	General	The following organisations explicitly supported the EUnetHTA position: 1. Hauptverband der Österreichishen Sozialversicherungsträger, HVB, Austria 2. Gesundheit Österreich GmbH/Geschäftsbereich BIQG/GÖG, Austria 3. Ludwig Boltzmann Institut für Health Technology Assessment, LBI, Austria 4. Belgian Health Care Knowledge Center, KCE, Belgium 5. National Centre of Public Health Protection, NCPHP, Bulgaria 6. National Council for Prices and Reimbursement of Medical Products, NCPR, Bulgaria 7. Ministry of Health of the Czech Republic, MoH Czech Republic 8. National institute for health and welfare (THL), Finland 9. Finnish Medicines Agency, Assessment of Pharmacotherapies Process, FIMEA, Finland 10. Direction générale de Santé/ Haute Autorité de Santé, HAS, France 11. Deutsches Institut für Medizinische Dokumentation und Information, DIMDI, Germany 12. Institute for Quality and Efficiency in Health Care, IQWIG, Germany	

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		13. National School of Public Health, NSPH, Greece 14. GYEMSZI (National Institute for Quality- and Organizational Development in Healthcare and Medicines), Hungary 15. Health Information and Quality Authority, HIQA, Ireland 16. Agenzia Nazionale per i Servizi Sanitari Regionali, AGENAS, Italy 17. Regional Agency for health and social care – Emilia Romagna, Italy 18. Regione Veneto, Italy 19. Ministère de la sécurité sociale Inspection générale de la securité sociale Cellule d'expertise médicale, CEM, Luxembourg 20. College voor zorgverzekeringen, CVZ, Netherlands 21. Agency for HTA in Poland, AHTAPol, Poland 22. National Authority of Medicines and Health Products, INFARMED, Portugal 23. Working group for pharmacoeconomics, clinical outcomes and HTA of the Slovak Ministry of Health, Slovakia 24. National Institute of public health, NIPH, Slovenia 25. Instituto de Salud Carlos III, ISCIII, Spain 26. Basque Office for HTA (OSTEBA), Spain 27. Andalusian Agency for HTA (AETSA), Spain 28. Galician Agency for HTA (Avalia-t), Spain	

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		29. Swedish Council on Health Technology Assessment, SBU, Sweden 30. National Institute for Health and Care Excellence, NICE, UK 31. NIHR Health Technology Assessment Programme, NETSCC, UK 32. Agency for Quality and Accreditation in Health Care and Social Welfare, AAZ, Croatia 33. Norwegian Knowledge Centre for the Health Services, NOKC	
116	27-35	EUnetHTA strongly supports improved publication and access to clinical trial data as described in EMA's draft policy. Full trial information and results (for all trials, involving medicines, devices or other healthcare interventions) are needed for HTA agencies to be able to provide appropriate and meaningful assessments of drugs and other health technologies within their remit. There is overwhelming evidence, that trial data published in scientific journals are insufficient to provide a complete and unbiased picture of a given drug. HTA needs other independent and high quality data sources. Data submitted to regulatory agencies are therefore essential for HTA agencies. A key aim of HTA is to estimate relative or comparative effectiveness. Methods used by HTA require full information about study methods, e.g. for the assessment of risk of bias. Extended information about patient populations included in clinical trials is needed, e.g. to understand to what extent the study results are relevant for real-world populations. HTA comparative effectiveness research also uses indirect comparisons. For this type of analysis full information on study methods including e.g. operationalisation of study endpoints and full information on patient populations is required to allow for assessing assumptions on similarity	

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116	36-43	EUnetHTA supports protection of personal data. The measures described in the policy are considered sufficient to ensure this protection. A guidance document should be developed	
116	44-47	It should be noted that patient data are already used for publications in scientific journals\conferences and other scientific activities aimed at knowledge evaluation and dissemination. Transparency, clinical trial data analysis and verification\appraisal of results – e.g. in HTA comparative effectiveness assessments - all work towards the “development and assessment of a particular medicine that is useful for treatment of their disease” and towards “the advancement of science and public health”.	
116	49-51 Annexes 1 and 2	EUnetHTA strongly supports the statement that clinical trial data (indeed for all trials, involving medicines, devices or other healthcare interventions) cannot be considered commercially confidential information (CCI), and that the interests of public health outweigh consideration of CCI for clinical trial data. EUnetHTA also supports the classification of documents with regard to CCI in Annexes 1 and 2, i.e. that trial information other than sections 2.7.1, 5.3.1. and 5.3.2 of the CTD are not considered CCI.	
116	77-82	Since HTA is very often comparing new interventions to currently available therapies, full information on study methods and study results is required for all drugs in current use. EUnetHTA therefore suggests that EMA re-considers making all clinical study reports available at the agency for any drug approved in Europe. Restricting the policy to data submitted after the policy comes into effect is insufficient to meet HTA requirements in comparative research.	

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116	94-97	Taking into account international definitions (Cochrane Glossary, WHO, ClinicalTrials.gov), consider using the term “Clinical study data” since this term includes both interventional and observational studies	
116	118-22	Variable definition and data derivation specifications may be essential to understand the report and should not be considered raw data	
116	156	Should better read: “These are essentially 'raw CT data' (see definition above) which have not been adequately de-identified” This would help to be coherent with the definition in Category 2 (• any personal data in the document have been adequately de-identified (line 143)) and clarify that the main distinction between Category 2 and Category 3 is not based on aggregate versus raw/individual data, but on de-identified or not de-identified.	
116	194-196	Meta-analysis requests later on may want to include the data sets. How should this be handled?	
116	203-205	One year does not seem very “reasonable “for a Systematic Review\Meta-analysis of all studies for HTA comparative effectiveness purpose, though it might be reasonable for assessing an EMA regulatory decision (which is not the purpose of HTA). Destruction of accessed CT data risks being in conflict with best practice in scientific publishing (ensure accessibility to data for replication of analysis) which peer review journals require (some journals are considering enforcing	

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		publishing rules, which require complete CT data to be made fully accessible for articles reporting clinical trials' results).	
116	210-15	EUnetHTA agrees in requiring that a protocol of the analysis is published either as a protocol article or in a database of protocols of SR - ex. Cochrane Database, Prospero – or where relevant as a protocol of an HTA project in EUnetHTA.	
116	248-261	Since HTA is very often comparing new interventions to currently available therapies, full information on study methods and study results is required for all drugs in current use. EUnetHTA therefore suggests that EMA re-considers making all clinical study reports available at the agency for any drug approved in Europe. Restricting the policy to data submitted after the policy comes into effect is insufficient to meet HTA requirements in comparative research.	
116	278-81	The avoidance of retroactive identification of individuals particularly if many indirect identifiers appear jointly for the same individual needs to be clearly described in practical terms in a guidance document	
117	General	The Federation of European Academies of Medicine (FEAM) welcomes the European Medicines Agency's plans to increase transparency of the data and results from clinical trials on which regulatory decisions are based. We agree that the sharing of clinical trial (CT) data for secondary analyses has great potential to be translated into significant benefits to public health. We are, however, concerned about the proposals relating to the sharing of patient-level Category 3 CT data. We consider that there should be a well-defined and transparent review process for each request for access to Category 3 data. The EMA's proposed	

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		data sharing agreement requires the requester to guarantee that their analysis is 'in the interest of public health'. We argue that requesters themselves cannot objectively make this assessment, and hence that there is a need for a review process that, prior to granting access: • Ensures the scientific and analytical robustness, and appropriateness of the purpose, of the intended data use. • Ensures that potentially identifiable patient information will be stored with appropriate safeguards. • Verifies that the request is appropriate to the nature of patient consent given for the original study. **Ensuring 'good science'** We believe it important to put a mechanism in place that mitigates potential harm that could result from inappropriate secondary interpretation or misuse of clinical trial data. Whilst we agree that greater openness could put clinical trial data under productive scrutiny, the consequences of secondary analyses that wrongfully contradict the published findings could be severe, and are certainly not in the interest of public health. Any use of the outcomes of Category 3 data analysis as a background for change, for instance in regulatory approval, must also follow appropriate expert peer review. **Protecting data** We would be concerned about the security of Category 3 data that leaves the EMA in a potentially identifiable format. To prevent inadvertent and inappropriate disclosures that risks re-identification and patient privacy, the requesters' data-handling competence should be verified and their plan of	

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		how to store data securely reviewed. Other bodies that share patient data do so within a 'controlled environment', and further consideration should be given to appropriate mechanisms under which the data is accessed to ensure protection of patient privacy. **Appropriate consent** Requestors cannot necessarily be expected to understand the nature of the consent obtained for the original clinical trial, especially in cases where patients have been recruited from a number of different settings. We therefore suggest that the EMA or an independent panel take on the responsibility of ensuring that a request fall within the boundaries of the original informed consent Appropriate access to clinical trial data will be an invaluable resource for biomedical research, but public acceptability and trust are essential to its success. To enhance the integrity and ultimate benefit of research, and to minimise the risk of misinterpretation and misuse, controlled access to patient level data should only follow after appropriate independent review of the proposal. The organisation that takes on this review process will need to comply with quality standards and have a proven record of complying with standard operating procedures in this area, without administrative overload or delay. Detailed comments on the text of the draft Policy are set out below.	
117	44-48	Mechanisms whereby patients can provide broad consent for secondary analyses would be very beneficial to ensuring that data can be used to their full potential. We would welcome more explicit guidance from the EMA on how such broad consent should be worded in the future.	

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117	57-61 & 216-218	We would be concerned about patient level data being distributed to individuals who have neither been assessed as competent to handle the data appropriately nor required to demonstrate a robust methodology for how they will proceed with their study. We call for an appropriate review mechanism as outlined in the main body of the response, above.	
117	109-115 & 129-132	We consider that there should be more clarity on who decides whether information is classified as Commercially Confidential Information (CCI), as well as how the information can be 'duly justified' as being CCI.	
117	143, 165, 172-175 & 278-281	We would like further details on who will carry out the de-identification of personal data and who will ensure that the de-identification carried out is 'adequate' before it is made available. It is critical that appropriate methodologies are employed to ensure patient privacy is safeguarded.	
117	149	We are concerned with the statement that personal data of clinical trial personnel is not regarded as confidential.	
117	180	We would like to seek clarification on whether any company or organisation established in the EU would be able to apply for access.	
117	183 & 198	We do not consider that the requestor will always be in the position to determine that the purpose for which data is requested is in the interest of public health and in line with the 'sprit' of informed consent. We would also like clarity on who determines what is appropriate in terms of ethics committee submission.	
117	191-192	There is a possibility that an ethics committee could approve the secondary use of data that is outside the scope of the original consent (as is currently possible under the laws of many member states).	

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117	199-200 & 207-209	We consider that the data requestor who is going to perform an analysis should follow, rather than merely being made aware of, best practices and methodologies. We do, however, recognise that there may be cases where use of innovative analytics will be proposed that do not confirm to existing good practice.	
117	222-231	In the interest of transparency and to avoid duplication of work and facilitate collaboration, we believe that information about the requester and other key aspects relating to the secondary analysis should be made available promptly.	
117	244-245	To encourage openness, data should be shared in a format that is accessible to all requesters. CDISC (Clinical Data Interchange Standards Consortium) standard formats may not be immediately accessible to academic organisations and patient groups.	
118	General	IQWiG strongly supports the improved publication and access to clinical trial information described in EMA's draft policy. Full trial information and results are needed for HTA agencies like IQWiG to be able to provide appropriate and meaningful assessments of drugs within their remit. As drug assessments conducted by HTA agencies support evidence-based decision making in health care systems, improved access to clinical trial data is in the interest of public health. There is overwhelming evidence, that so far publicly available trial data are insufficient to provide a complete and unbiased picture of a given health care intervention. HTA needs additional independent and high quality data sources. Data submitted to regulatory agencies are therefore required by IQWiG and other HTA agencies. However, the data held by EMA are not only important for HTA agencies but also for other researchers supporting	

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		evidence-based decision making in health care and should thus in general be made publicly available. HTA performed by IQWiG and other agencies specifically is aiming to describe comparative effectiveness. The methodology used by HTA requires • information on all trials conducted with the intervention under assessment • full information about clinical trial methods, e.g. for risk of bias assessment • full information about clinical trial results, e.g. for meta-analysis • extended information about patient populations included in clinical trials, e.g. to understand to what extent the study results are relevant for real life populations In addition, comparative effectiveness research increasingly uses indirect comparisons. For this type of analysis full information on study methods including e.g. operationalization of study endpoints and on patient populations is required to allow for assessing assumptions of similarity of studies in a network for indirect comparisons. IQWiG's own work has shown that clinical trial documentation held by regulatory agencies provides substantial additional information compared to publicly available trial reports. A comparison of clinical study reports (CSR) with publicly available journal publications and reports from study registries has shown, that CSRs provided complete information on 88 % of relevant methods items, while journal publications included complete information only on 40 % of methods items and registry reports only on 31 % of	

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		methods items[1]. Concerning clinical trial results, CSRs provided complete information on 86 % of patient-relevant trial outcomes while journal publications and registry reports presented complete information on only 23 % and 22 % of patient-relevant trial outcomes, respectively (39 % in the combined publicly available sources)[2]. This additional information from CSRs can challenge published evidence on a given health care intervention or even reverse conclusions drawn based on publicly available information[3]. These data clearly describe the information gain from one part EMA's draft policy, i.e. making CSRs publicly available. Access to patient-level data will allow further research questions to be addressed. Our studies underline the relevance of improved public access to full clinical trial data according to EMA's draft policy for evidence-based decision making and thus public health. Our studies also show, that alternative proposals like the EFPIA's and PhRMA's recently adopted "Principles for Responsible Clinical Trial Data Sharing" are insufficient to solve the problems associated with an incomplete public record of information on health care interventions, e.g. because they suggest publication of only limited information (synopses of CSRs or journal publications) on a limited range of clinical trials.	
118	36 - 43	IQWiG supports protection of personal data. The measures described in the policy are considered sufficient to ensure this protection. According to IQWiG's own experience, patient-level data are required to answer specific	

[1] Wieseler, B., Kerekes, M. F., Vervoelgyi, V., McGauran, N., Kaiser, T. (2012). "Impact of document type on reporting quality of clinical drug trials: a comparison of registry reports, clinical study reports, and journal publications." BMJ 344: d8141.
[2] Wieseler B., Wolfram N., McGauran N., Kerekes M.F., Vervölgyi V., Kohlepp P., Kamphuis M., Grouven U. (2013). Completeness of reporting of patient-relevant clinical trial outcomes: comparison of unpublished clinical study reports with publicly available data. PLoS Med, in press
[3] Eyding, D., Lelgemann, M., Grouven, U., Harter, M., Kromp, M., Kaiser, T., Kerekes, M. F., Gerken, M., Wieseler, B. (2010). Reboxetine for acute treatment of major depression: systematic review and meta-analysis of published and unpublished placebo and selective serotonin reuptake inhibitor controlled trials. BMJ 341: c4737.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		questions in HTA and comparative effectiveness assessments. Therefore, patient-level data should be made available.	
118	49 – 51 Annexes I and II	IQWiG strongly supports the statement that clinical trial data cannot be considered CCI and that the interests of public health outweigh consideration of CCI for clinical trial data. IQWiG also supports the classification of documents with regard to CCI in Annexes I and II of the policy.	
118	77 - 82	Since HTA is comparing new interventions to currently available therapies, full information on study methods and study results is required for all drugs in current use. IQWiG therefore suggests that EMA makes available all clinical study reports available at the agency from past or future submissions for any drug approved in Europe. Restricting the policy to data submitted after the policy comes into effect is insufficient to meet HTA and public health requirements.	
118	83 - 85	While IQWiG appreciates the fact that EMA can only make available data submitted to the agency, the final goal of EMA's transparency initiative should be availability of all studies on a given drug (or even more on all drugs, devices or other health care interventions). Therefore, IQWiG would like to suggest that EMA expands the trial database to allow for posting of clinical study reports of all studies on a given drug (or even more on all drugs, devices or other health care interventions). The pharmaceutical industry and other trial sponsors could then also release clinical study reports of studies not submitted to EMA in this central database, thus underlining their commitment to transparency.	
118	116 - 117	Availability of full Clinical Study Reports is of paramount importance to	

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		support assessment of a clinical study and its results. To avoid any ambiguity when referring to the ICH E3 document, EMA might want to clarify, that a CSR not necessarily follows the format of the ICH E3 as outlined in Annex II but should meet the requirements of ICH E3 and that the classification of access refers to the CSR-content provided according to the classified sections of ICH E3.	
118	118 - 123	It is unclear to IQWiG, why “test outputs (if not contained in the statistical analysis plan (SAP))” are considered raw data. According to our understanding, test outputs are outputs from SAS providing the outcome of statistical test procedures. As such, test outputs would be summary data. According to our experience these test outputs include valuable information (e.g. about treatment by variable interaction) and should be provided as part of summary data.	
118	150 - 154	IQWiG agrees that the documents classified as “open access” should be made available at the time of publication of the EPAR to allow for timely assessment of a given drug.	
118	242 - 247	According to our understanding, currently EMA does not require submission of individual patient data sets and associated documentation explaining the structure and content of the data sets. It does not become clear from the policy, if and how these data sets and associated information will be required in the future. The policy should clarify that submission of data sets and associated documentation will be a mandatory requirement after a given date.	
118	249	IQWiG agrees that the policy should come into effect on 1 January 2014. Since the information that will be provided according to this policy is	

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		urgently required, any delay should be avoided.	
118	Annexes I and II	IQWiG supports the classification of categories of access as provided in Annexes I and II of the policy.	
119	General	I am writing on behalf of the European Public Health Alliance (EPHA) in response to the public consultation on the European Medicine Agency's Draft Policy on Clinical Trials. Following an internal consultation process with our members, we are pleased about the opportunity to provide you with our comments. EPHA – Europe's leading NGO advocating for better health - is the European Platform bringing together public health organisations representing professional groups, patients, health promotion and disease specific NGOs and other health associations. Overall EPHA is pleased to see the Agency's commitment to continuously extend its approach to transparency, including in the area of clinical trials. Hence we support EMA's intention to ensure proactive publication of clinical trial data for medicines. Given that participants in clinical trials act out of solidarity by offering their time and bodies for the benefit of society at large, it is an ethical obligation to make clinical trials results available, and this principle should not be compromised or overridden by reasons of commercial confidentiality. As the Agency correctly notes, not only will heightened transparency lead to more trust and confidence in the system but it will also allow individuals and researchers to undertake independent reviews of the methodology and evidence and to draw their own conclusions. The current situation, whereby many trials are not registered, and mostly only the results of positive trials are being reported, is not tolerable. This	

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		has been widely highlighted by health stakeholders and notably by the All Trials campaign which so far has gained the support of well over a hundred organisations including EPHA. We are thus especially pleased to see that, as a rule and in line with other EMA policies the Agency does not consider these data to be commercially confidential and is willing to engage in open sharing of information. In order to comply with the objective of Regulation 1049/2001, which aims at ensuring the widest possible access to documents held by EU institutions, the definition of commercial confidentiality must be interpreted and applied restrictively. Any exception to data disclosure has to be based on transparent and clearly defined criteria that delimit the scope of 'duly justified commercially confidential information' for CSRs. The Agency should also ensure that its decisions are periodically reviewed by independent experts and that such documents can be requested by individuals in line with EMA's access to documents policy. EPHA sees no problem with the Agency's planned policy of open access to Category 2 data without protection of personal data (PPD) concerns given that providing this information in a user-friendly way on the website will reduce administrative burden in a cost effective way. A 'controlled access' approach for Category 3 data, which is complex by nature, is reasonable in the sense that the requesters' data-handling competence needs to be verified to ensure they are taking an appropriate approach in interrogating the data which corresponds to the original consent patients have given. At a minimum requestors should thus be required to clearly explain their intentions and reasons for accessing and using the data they wish to analyse; this is important in order to avoid wrongful secondary	

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		interpretation of data, which can compromise patient safety and breach confidentiality. 'Controlled access' requirements should however be flexible enough to allow access for individuals not part of the scientific research community who can demonstrate a valid approach for accessing and analysing data. The EMA has to work towards the implementation of additional measures that allow to proactively disclose this data in ways that safeguard patient's confidentiality while the robustness of the data is maintained14 Moreover, the requirement to destroy the data following its analysis poses a challenge to researchers wishing to publish their results and having to comply with international publication standards that require authors to keep their records for a number of years. Finally, EPHA would like to seize the opportunity and highlight the demand of the AllTrials campaign to also make available retrospective access to trials results. This would provide for an added layer of transparency and help increase patient safety given that medicines prescribed today are based on results that often go back many years. In order to assess whether these results are relevant to the entire population – given the biological differences between men and women, and other differences based on, e.g. age and ethnicity –, this will allow for stratified analyses and help avoid adverse reactions that can harm individuals. We trust that EMA will listen to the concerns voiced by EPHA and its members and look forward to seeing how the results of the consultation will impact on the Draft Policy.	
120	General	MSF welcomes the proposed draft policy of the European Medical Agency (EMA) regarding publication and access to clinical trial data complementing	

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		the existing 'Policy on access to documents (Related to medicinal products for human and veterinary use (EMA/110196/2006). As an independent medical humanitarian organisation MSF doctors rely on being able to make informed choices about the safety and efficacy of drugs in order to choose the most beneficial treatment for the patients we treat. Already existing voluntary tools, such as the database clinicaltrials.gov, which was launched to improve transparency, have failed to deliver the level of transparency that is needed. MSF sees a growing need to provide open access to clinical data in order to prevent wasteful duplication of trials and to facilitate valuable data sharing in the scientific community to push pharmaceutical innovation forward. MSF therefore welcomes the proposal by the EMA to proactively publish the clinical study reports after market approval has been given or rejected by the Agency or if the application for market authorisation has been withdrawn. This default disclosure policy would, if implemented as it stands, be an effective means to ensure improved transparency and access. MSF largely agrees with the safeguards proposed by the EMA to meet the legitimate concerns raised about protecting personal data (PPD) in individual patient level data sets i.e. controlled access involving conditions such as a minimum standard of de-identification and a legally binding data-sharing agreement. However, we are concerned that the obligation with respect to the latter to refrain from using clinical trial data to gain a marketing authorisation in a non-EU jurisdiction (line 193) promotes repeating unnecessary scientific experimentation on human subjects in non-EU countries.	

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		The policy should apply equally to all new trials as well as on trials conducted before the 1 January 2014 when the policy is to take effect, since access to the data about drugs we are currently using is just as important as data about drugs that are currently being developed. Finally, MSF would underline that discretion on what to make publically available should not continue to lie with pharmaceutical companies due to the obvious conflict of interest that this entails. In order to bring medical innovation forward we need to have access to both positive and negative data sets.	
121	27-34	The National Institute for Health and Care Excellence (NICE) provides national guidance and advice to improve health and social care. Our rigorous process of guidance development is centred on using the best available evidence. Public disclosure of clinical trial data is relevant to all our guidance offering advice to the NHS on clinical practice, but is especially important in two NICE programmes: technology appraisals, which make recommendations to the NHS on the clinical and cost effectiveness of new and existing medicines and other technologies; and clinical guidelines, which provide advice on clinical- and cost-effective approaches to the management of patients with specific conditions. If evidence from clinical trials is not fully disclosed, judgements about effectiveness and cost-effectiveness, such as those made by NICE, may be made on unreliable valuations of the benefits and harms of drugs and treatments, with negative consequences for public health and the efficiency of health services. We therefore strongly support the case made in this paragraph for enabling public scrutiny and secondary analysis of all clinical trials. The UK Parliament's House of Commons Science and Technology Committee has recently described the current lack of clinical trial transparency as unacceptable and argued that greater transparency, if	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		balanced against the need to protect patient privacy, would be likely to provide a number of benefits, such as improved patient outcomes, enhanced scientific knowledge, increased public trust in research, and fulfilment of basic ethical standards (House of Commons Science and Technology Committee, 'Clinical trials: Third report of session 2013-14', September 2013). The committee noted that a key motivation for making clinical trial data more transparent was to improve the evidence-base for treatments currently used by the NHS and facilitated by NICE.	
121	36-43	We support the Agency's 'guarded approach' to the sharing of patient-level data, while welcoming its recognition that there are established ways and means of anonymising data and protecting patients from retroactive identification.	
121	49-51	We welcome the statement that, in general, clinical trial data cannot be considered commercially confidential information (CCI) and that the interests of public health outweigh considerations of CCI.	
121	67-72	As a secondary user of patient-level clinical trial data, we agree that such users should be held to the same standard of transparency as those who generate the data in the first place. We also recognise the obligation to place the analyses resulting from secondary use accessibly in the public domain. This would be entirely in line with NICE's current practice.	
121	77-82	We are disappointed that the policy is to be prospective only. This will mean that the public health benefits of the policy will be slow to emerge, and also that the cumbersome policy of December 2010 on access to Agency documents related to medicinal products will remain an obstacle to easy access to clinical trial data on Agency-licensed treatments in current use. We recommend that the agency think again about whether the policy should be	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		retrospective as well as prospective. An alternative approach to meeting the same objective would be to amend the 2010 policy, which covers a wide range of types of documentation, so that there is fast-track access specifically to clinical trial data. The UK Parliament's House of Commons Science and Technology Committee recognised the particular benefits of retrospective application of clinical trial transparency, while also acknowledging practical obstacles (see the reference in our comments on lines 27-34).	
121	90-101	We welcome the inclusiveness of the definition of the term 'CT data'.	
121	133-136	It is not clear why those requesting documents deemed to contain commercially confidential information (CCI) should have to do so using mechanisms under the Agency's policy of 2010 on access to documents rather than through this policy. One of the general principles in the 2010 policy is: '[w]hen only parts of a document contain information that cannot be disclosed, access to the remaining parts of the document shall be granted' (4.1). We do not see why this general principle cannot be applied to documents deemed to be CCI in this policy, particularly when, as annexes I and II indicate, the CCI elements of such documents can be easily identified and therefore extracted or redacted.	
121	176-233	We agree with the conditions set out for 'controlled access' to documents that raise protection of personal data (PPD) concerns.	
121	248-261	These paragraphs would need amending were the policy to be made retrospective as well as prospective, as we recommend in our comments on lines 77-82.	
122	General	The Norwegian Institute of Public Health fully supports the view that	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		transparency on clinical trials, including access to clinical trial data in an analysable format, will benefit public health in the future. The policy proposed by EMA is in general endorsed	
122	59-61	Inclusion of a short description of planned measures to protect public health from claims based on inappropriate analyses would be informative	
122	159-161	Protection of patient privacy is highly important	
122	168-175	Which stakeholder will be responsible for ensuring that patient data are sufficiently de-identified to avoid the possibility of retroactive patient identification? EMA or MAH?	
123	General	The Danish Association of the Pharmaceutical Industry believes that the EMA draft Policy would weaken three essential elements for promoting public health both within Europe as well as at the global level: patient privacy; the integrity of scientific research and the regulatory systems; and incentives for investment in biomedical research. It is our concern that the draft EMA Policy will: 1. Weaken safeguards intended to ensure the privacy of patients and other individuals identified in marketing authorisation application (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; 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	

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		disclosure. The Danish Association of the Pharmaceutical Industry believes that implementation of the joint EFPIA-PhRMA Commitments to Data Sharing (launched 24th of July 2013) is the best means of advancing responsible transparency. Implementation of these principles will promote public health interests by safeguarding patient privacy; preserving the integrity of regulatory systems; and maintaining incentives for investment in biomedical research. EFPIA and PhRMA companies have committed to: 1. Share upon request from qualified scientific and medical researchers patient-level clinical trial data, study-level clinical trial data, and protocols from clinical trials in patients for medicines. 2. Enhance public access to clinical study information, by making publicly available, at a minimum, the synopses of clinical study reports (CSRs) for clinical trials submitted to the FDA and EMA. 3. Share results with patients who participate in clinical trials. 4. Certify on a publicly available web site that they have established policies and procedures to implement these data sharing commitments. 5. Consider all company-sponsored clinical trials for publication in the scientific literature irrespective of whether the results are positive or negative.	
123	General	**1. Fundamental Comment: How the EMA draft Policy threatens those safeguards intended to ensure the privacy of patients and other individuals identified in MA dossiers (Protection of Patient Privacy**	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		and Personal Protected Data (PPD)) The Danish Association of the Pharmaceutical Industry agrees with the EMA draft policy that “protection of patient privacy is a paramount concern when sharing raw clinical trial data”. However, it is our concern that the draft policy does not do enough to protect against re-identification of patients based on this data. As written in the EMA draft Policy, it appears that the Agency plans to widely release de-identified patient data. Recent studies have shown that there is particular risk of re-identification when such data are made widely available. Additionally, we must consider that re-identification technology is advancing rapidly. The EMA draft policy also neglects to address the protection of personal data of investigators and study personnel in MA submissions; the privacy of all individuals involved in clinical studies needs to be protected. In addition to considerations of personal data privacy, 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 third 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 is usually 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	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		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 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.	
123	General	**2. Fundamental Comment: How the EMA draft Policy could undermine the trust in the regulatory approval system governing biopharmaceutical products and introduce risks of misinterpretation and misuse of clinical data into the process (Providing Access to Data for Legitimate Research)** Secondary analysis and research of clinical trials data must be robust and for good scientific purposes. Data can be misunderstood, misrepresented and misused through inappropriate secondary analysis. The misuse of data can lead to public health scares and undermine confidence in regulatory systems. The EMA draft policy fails to secure the legitimacy and scientific rigour of the use of the data: • It does not require the requester to provide or publish statistical analysis plans • It does not allow for a prior review of the requestor's statistical analysis plan or qualifications The Danish Association of the Pharmaceutical Industry believes these missing elements are essential to avoiding poor secondary analyses which may threaten public health as well as trust in regulatory systems.	
123	General	**3. Fundamental Comment: How the EMA draft Policy weakens incentives for companies to invest in biomedical research by**	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		disclosing companies' CCI (Maintaining incentives for investments in biomedical research – protection of CCI – open access to clinical trials) The clinical trial data in a MA dossier may contain commercially sensitive information. The protection of this information helps to maintain the incentive for companies to continue innovating and making the enormous investments needed in medical and scientific research. The EMA's plans to release this data are therefore a threat to research and innovative medicine development. Problems with EMA's proposal include: According to the EMA draft Policy, the agency respects and will not divulge CCI; "in general, however, clinical trial data cannot be considered CCI; the interests of public health outweigh considerations of CCI". This is inconsistent with the definition of CCI stated in the EMA draft policy, 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". The EMA draft Policy's claim that "Clinical trial data cannot be considered CCI; the interests of public health outweigh considerations of CCI" is inconsistent with EU law, which requires that analysis weighing the relative CCI and public health interests be made on a case-by-case basis. The EMA draft Policy fails to give CCI and public health interests the equitable due consideration required. The draft Policy's assertion that MA data can be disclosed because it cannot be considered to include CCI has already been challenged in the recent interim decision by the General Court of the EU on EMA data release in two concrete ongoing cases.	

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		By employing terminology and conditions which are too broad, the EMA draft Policy suggests a lack of protection of CCI that not only threatens incentives to innovate, but also comes into conflict with EU law.	
124	General	Roche is supportive of greater transparency of clinical trial data and published its commitments in a policy in June 2013[4]. Roche' s policy on patient level data sharing has contributed to cross-company developments on transparency and shares many common elements with the recently adopted "Principles for Responsible Clinical Trial Data Sharing"[5] published by EFPIA and PhRMA. Since Roche believes regulatory authorities should remain the gatekeeper for releasing information submitted to them under an application for a marketing authorisation, Roche is supportive of regulatory authorities to release Clinical Study Reports upon request, where authorities have a legal mandate to do so. Such a release must take place under the provision that commercially confidential information and personal data have been redacted. In addition, Roche is supportive of the concept that qualified researchers engaged in independent scientific research should have access to anonymised patient-level, analysable data sets from clinical trials under the prior condition of submitting a meritorious study proposal and a signed data-sharing agreement. Roche is providing access to such data upon specific request. EMA's draft policy is intended to provide access but also to enable researchers to analyse patient-level data. Roche is concerned this may go beyond the EMA's remit, as EMA currently does not require submission of	

[4] **Global Policy on Sharing of Clinical Trials Data:** http://roche-trials.com/dataSharingPolicy.action
[5] **EFPIA/ PhRMA Principles:** http://transparency.efpia.eu/uploads/Modules/Documents/data-sharing-prin-final.pdf

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		raw patient level datasets for re-analysis. Consistent with Roche' s aforementioned policy, Roche is, in principle, supportive of EMA to provide access to Clinical Study Reports upon request and to establish more detailed guidance on the conceptual and procedural matters through its draft policy. However, Roche has the following specific concerns on several of the provisions proposed, in particular concerning EMA's intention to provide third party access to patient level data.	
124	General	1. Clinical Study Reports (CSR) When providing access to information, particular needs by stakeholders should be balanced against potential risks associated with any unintended and potentially harmful use, also taking into account the impact on business and resources. Roche is convinced that experience over time will provide more insight and allow an evolution of transparency systems. However, in an evolving situation, where not all risks with unrestricted access have been assessed and resource impact on regulatory authorities and companies may be substantial, certain safeguards should be maintained: a. Access to CSR should be provided upon request only and not, as proposed by EMA, as fully open downloads. EMA's policy has to take into account both social and economic impacts of the policy, including on resources. Preparation and redaction of all study reports for the purpose of being downloaded would require substantial resources by companies. On the other hand, research interest may focus on specific products and indications and, to our experience, mostly refers to CSRs of late stage drug development (Phase II and III studies). Roche is convinced that a more tailored requirement, which provides access to CSRs on request, is better manageable for all parties and still addresses the need by	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		researchers. This is notwithstanding the existing requirement to make summary results of all clinical studies available through EudraCT. b. Line listings and patient narratives in Appendices 16.2, 16.3, 16.4 should not be made subject to open access due to the risk of re-identification of patients when applying linkage with other data carriers (e.g. social media). c. Need for redaction for "commercially confidential information" (CCI) consistent with Regulation Art. 4(2) of 1049/2001: Roche strongly believes that the proposed concept, which is under the assumption that a CSR does not include CCI, could imply that companies adjust how they will draft CSRs in the future. This may include elimination of CCI upfront in situations where such information may still be of interest to competent authorities in their assessment of an application for a marketing authorisation. Finally, consistent with Art. 4 (4) of Regulation 1049/2001, the question as to whether information should be considered CCI or not should be subject to consultation with the marketing authorisation holder prior to release of such information in each case.	
124	General	2. Access to patient level data Roche is committed to provide access to patient level data to researchers who have the intention to address scientifically valid research request under a company/ industry self-responsibility scheme. For the following reasons Roche has strong concerns with the scheme proposed by EMA according to which such information should be made available by the Agency and not directly by companies:	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		a. <u>The scheme goes beyond the information EMA normally has been requesting as part of an application for a marketing authorisation.</u> Under the proposed scheme EMA intends to request more information than normally submitted with an application, solely for the purpose of transparency on anonymised patient level data. This request for additional information goes beyond the original intention of the EU access to documents legislation (Regulation (EC) 1049/2001). Roche strongly believes that information not actively used in the assessment on a routine basis by the Agency itself should not be requested as part of the proposed scheme. Such additional requests would imply a shift of paradigm with the Agency developing the capacity to store and manage large complex datasets for analysis as part of its routine assessment. This is likely to create significant resource implications for the Agency and companies. Consistent with EU procedures a robust assessment of socio-economic impacts should be conducted before any decision for such an approach is taken. b. <u>Substantial resource implications to fulfil request to submit statistical programs</u> The above mentioned (point 2a) additional request concerns in particular statistical programs which may be part of intellectual property by companies, especially when analyses have been generated by highly sophisticated reporting systems. Statistical Analysis log files are unlikely to provide additional information but to request them from companies would generate a substantial workload. Test outputs contain only output displays and no further information on the analyses performed; they have never been requested as part of submissions. As already highlighted by the data formats advisory group – the generation of such	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		additional information is a complex and labour intensive activity with questionable value for the third party researchers. c. EMA' s concept does not include sufficient safeguards that are deemed absolutely important to ensure the current regulatory system is not intentionally or unintentionally undermined through false or low quality third party analysis, a concern which has been expressed by EMA itself. The management of potentially poor quality third party analysis may require substantial resources both by EMA and the companies. The process outlined in various policies from industry which involve a third party review by an independent review panel to assess the scientific merit is the most appropriate way to put in place such safeguards. Given the complexity and substantial resource impact behind requests for access to patient level data, Roche is re-assured that the aforementioned industry self-responsibility scheme currently being established, as opposed to EMA's scheme, is the most appropriate way to address researcher's needs for access to patient level data. EMA should therefore focus on access to CSRs submitted in the dossier for regulatory review and encourage companies to respond to the need for provision of patient level data for meritorious scientific requests through independent review panels.	
124	General	3. Aspects related to data protection Roche agrees in principle with the reference to the proposed minimum standards for de-identification and the fact that the methods should take into account linkages with other data carriers (e.g. social media). This will require a careful monitoring and review of appropriateness of standards over time. Consultation of the European Data Protection Supervisor (EDPS) in	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		preparation of finalisation of the policy is highly recommended. Roche would like to re-emphasize the following important aspects relevant to data protection: a. The Agency determines the use of documents in relation to an access to documents request on the basis of Regulation (EC) 1049/2001 and is responsible for any such release. This includes liability in case of non-compliance with any relevant provisions, such as EU data protection law. While it is understood that companies will prepare anonymisation through their submissions for any release of information/ data under the EMA scheme, the Agency will be responsible for the completeness of the anonymisation. b. Principles for data protection must not only apply to study participants but also to personnel involved in the clinical trial (sponsor and investigational site staff) to prevent potential harassment of company employees. c. Particular attention should be given to the fact that CSRs from global studies most frequently include data from patients outside the EU. Other regions in the world may have different transparency cultures and provisions. At this stage, it may be difficult to assess the impact of transparency provisions in the EU on the feasibility of obtaining future informed consent in patients outside the EU. On the other hand, different cultural settings and different levels of informed consent may also imply different redaction principles within the CSR for non-EU patients. d. Any use of data should be within the informed consent for each specific	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		trial.	
124	General	4. Principles for secondary analysis In order not to undermine our current regulatory system through intentionally or unintentionally false or poor-quality third party analysis the below safeguards should be established. Furthermore, the following aspects in addition to those mentioned under Point 2 support the industry concept of a self-responsibility scheme as being currently set up: a. For any patient level data access scheme established by EMA, further legislation is needed to establish solid provisions for secondary analyses and their enforcement e.g. detailing I. principles for Good Analyses Practices, II. principles for qualification of third party researchers, including disclosure of potential conflict of interest, III. information obligations by third party researchers to EMA and the marketing authorisation holder, IV. transparency of information related to the third party analysis within a reasonable period. However, it is understood that there may be limitations under the current regulatory framework to establish such a system. b. Under a company/ industry self-responsibility scheme Roche and other companies are establishing the above (under point 4a) mentioned appropriate conditions for third party analysis. This includes an independent review panel for review of any requests. Any conditions will	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		be detailed further in bilateral agreements with third party researchers. In addition, reference will be made to publicly agreed Good Analyses Practices and standards as those evolve. Roche is willing to actively contribute to the further development of such industry-wide standards.	
124	General	5. Timing of release of information Roche acknowledges the principle of release of information after the product in question has been authorised. However, the following specific aspects are important as not to undermine biomedical research: a. As to ensure researchers involved in a clinical trial have the priority right of publishing on the data on studies in which they contributed, release of information should take place earliest 18 months after completion of the study. b. To ensure an appropriate time window, in which authorisations in other regions in the world usually take place, Roche proposes that information should be released earliest 12 months after approval in the EU. Any prior release bears the risk of undermining the principle of protection before authorisation in other specific regions. c. For any negative decision and withdrawn applications, any information release should take place after companies have ultimately terminated the development program including back-up molecules, or, formulations. Prior to program termination, clinical development is considered to be ongoing, and premature release of information would inhibit scientific innovation and pre-empt appropriate regulatory review.	
124	General	For the line-by-line comments Roche supports and refers to the comments	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		submitted by EFPIA (see comments from Stakeholder no. 05)	
125	General	The AllTrials campaign is an initiative of Bad Science, BMJ, Centre for Evidence-based Medicine, Cochrane Collaboration, James Lind Initiative, PLOS and Sense About Science and is being led in the US by Dartmouth's Geisel School of Medicine and the Dartmouth Institute for Health Policy & Clinical Practice. It was launched in January 2013 to call for all clinical trials to be registered and results reported. Clinical trials are investigations designed to assess the effects – wanted and unwanted - of healthcare interventions in people. The Declaration of Helsinki, which is the World Medical Association's statement of principles for medical research involving people, states that every investigator running a clinical trial should register it and report its results. Millions of volunteers have participated in clinical trials to help find out more about the effects of treatments on disease, yet that important ethical principle about reporting has been widely ignored. Information on what was done and what was found in these trials could be lost forever to doctors and researchers, leading to bad treatment decisions, missed opportunities for good medicine, and trials being repeated. This is what led to the AllTrials which is now supported by 57,700 people and over 400 organisations worldwide, including research funders, regulatory bodies, consumer organisations, medical Royal Colleges, professional and learned societies, journals, pharmaceutical company GSK and more than 200 patient groups. We support the European Medicines Agency's aim to ensure full access to clinical trial information the Agency holds. We believe that if data is submitted to support a marketing authorisation for a medical product in	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		Europe then this data should be available for scrutiny by researchers. We agree that the EMA has a role to play in the dissemination of this data. We welcome the EMA's proposal to proactively publish clinical study reports from clinical trials submitted in support of a marketing authorisation application. Clinical study reports contain a large amount of detailed information about the methods, analysis, results and conclusions of a clinical trial, information which is needed to make and to scrutinise decisions about medicines and to assess published summary findings. This information should be publicly available. Individual patient data in a report can be redacted and should be available on request to researchers with a commitment that no reasonable request will be refused. We support the EMA's policy that in general the data included in clinical trial study reports should not be considered commercially confidential once a marketing authorisation has been granted or the decision making process on an application for marketing authorisation is complete. There is no good reason to delay full reporting of clinical trial results. It will have huge benefits for patients, health workers, doctors, pharmacists, regulators and researchers. It will benefit treatment decisions now and research into future options. We urge the EMA to implement its new policy as soon as possible	
125	27-35	We support this position. With full information about effects and side effects, a better risk/benefit calculation can be made by doctors, and individual patients. Healthcare commissioners and regulators can make a more accurate cost/benefit assessment which ensures that the treatments available are those that are truly the most effective.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
125	36-43	We support this position. We agree with the need for a different approach to sharing patient data. We believe this draft policy protects personal data.	
125	52-56	We support this position. The effect of publishing the full reports of clinical trials will be to provide a richer research base for both industry and academia. This means greater potential for collaboration and interdisciplinary work, more productive research, and potential value from unused Intellectual Property.	
125	67-72	We support this position. Those requesting access to clinical trial data should be held to the same standards of transparency as the researchers who produced the data.	
125	78-82	We support the Agency's policy to continue to reactively release clinical trial data already held as outlined in the Agency's current policy on access to documents.	
125	128 – 136	We support this categorisation. We agree that clinical trial data should not be assumed to be commercially confidential information and should be deemed CCI only in duly justified cases.	
125	138 - 154	We support this categorisation. We support the policy to designate all clinical trial documents without personal data "open access" and to make them available to download from the Agency's website from the time of publication of the EPAR for marketing authorisation decisions or withdrawals.	
125	155 – 162	We support this categorisation. We agree that raw personal data should not be handled in the same way as category 2 documents and should not be pro-actively publicly released. We recommend that this data is available to researchers on request with no reasonable request refused.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
125	219 – 221	We agree that “C” data should be made available from the time of publication of the EPAR for marketing authorisation decisions or withdrawals.	
125	235-236	We support the policy that all documents listed in Annexes 1 and 2 should be fully searchable.	
125	237 – 238	We support the policy to publish a cumulative list of clinical trials for each product including a unique study identifier and basic information about each trial.	
125	239 – 241	We support the policy that the applicant should provide relevant unique study identifiers in the list.	
125	242-244	We support the policy that clinical trial data should be provided in the format in which they were analysed by the applicant.	
125	250 – 253	We support this policy coming into effect on 1st January 2014 and the proposal to advise trial sponsors that clinical trial data submitted to the agency on or after 1st March 2014 and designated open access shall be subject to the policy.	
125	256 – 261	We support the proposal to work with trial sponsors and other concerned parties to put in place appropriate standards, rules and procedures for de-identification of patient data. We urge you not to delay implementation of the policy any longer than necessary to do that.	
126	General	Despite efforts by the European Medicines Agency in its 2010 policy, there is still - at present - a lack of full public access to the body of available scientific evidence about the effects of medicines on human health. This prevents informed choice and leaves European citizens at greater risk for otherwise preventable harm.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		We welcome the opportunity to contribute to the public consultation on the European Medicines Agency (EMA) draft policy on the publication and access to clinical-trial data aiming to improve the current situation (i). "*The proactive publication of data from clinical trials submitted in support of a marketing-authorisation application"* proposed by the EMA represents a first and very welcomed step towards greater clinical data transparency. The annex I of the draft policy, detailing the elements relating to clinical trials contained in the common technical documents as well as their access status, indicates EMA's commitment to proactively publish several elements from the clinical study reports (CSRs). Nevertheless, staff resources at the EMA must be sufficient to avoid that the proactive publication of clinical study reports delays the publication of European public assessments reports (EPARs) or in the case of variations, the publication of assessment reports. Advances in transparency should be maintained and strengthened (publishing proactively and in a timely manner). Classifying information into three categories (category 1 "may contain commercially confidential information (CCI)"; category 2 "Open access" for "data without protection of personal data (PPD) concerns"; and category 3 "controlled access" for "data with PPD concerns") is a pragmatic approach. However, according to the current EU law (article 4.6 of Regulation No 1049/2001), any exception to disclosure should only involve the removal of specific elements of information within a document and never be applied to an entire section or certain types of documents. The "category" descriptions within the policy should therefore refer to "data" but not to "documents".	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		In our response: • We highlight that access to clinical data (efficacy and safety data) protects the public from preventable harm, and therefore call on the EMA to: - Retrospectively provide access to clinical-trial data to all drugs approved over the last 10 years (period 2004 to 2014) either centrally (at EMA), or via decentralised procedure or through mutual recognition (CMDh); - Encompass access to CT data in other EMA processes particularly into pharmacovigilance and safety issues. European public assessments reports (EPARs) should be immediately updated, particularly when a variation is prompted by a safety issue; - Encourage national Drug Regulatory Agencies to apply the best transparency practices, particularly when acting as rapporteur or reference member states. • We call for a more stringent definition of "commercially confidential information", to ensure that transparency remains the rule rather than the exception. • We caution about the use of patient data protection as a pretext to prevent clinical data disclosure.	
126	Introduction and purpose	Preamble: A consultation amidst a particularly sensitive context In May 2012, seizing the opportunity granted by the ongoing discussions on the European Commission's proposal for a new regulation on clinical trials, the European Parliament (ENVI Committee) made an effort to align the	The 24 June 2013 EMA press release mentions that the legislative proposal on the Regulation of Clinical Trials which is currently under discussion at the EU

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		legislative proposal with the EMA's 2010 policy and published in its report that "in general the data included in clinical-trial study reports should not be considered commercially confidential once a marketing authorisation has been granted or the decision-making process on an application for marketing authorisation has been completed (…)"(ii). In addition, the ENVI Committee supported EMA's commitment to transparency: "the Agency continues to extend its transparency policy to proactive publication of clinical trial data for medicinal products once the decision-making process on an application for a Union-wide marketing authorisation has been completed. Those standards on transparency and access to documents should be upheld and reinforced" (amendment 30 creating a new recital 20a). On 22 November 2012, building on its transparency efforts initiated in 2010, the EMA organized a workshop on clinical-trial data and transparency. Following that workshop, the Agency established advisory groups on different topics to inform the policy's development. These groups met between January and April 2013. Our organisations – the International Society of Drug Bulletins (ISDB), the Medicines in Health Forum (MiEF), and Health Action International (HAI) Europe – participated actively in this policy development process. Unfortunately, due to the large over-representation of the pharmaceutical industry, or third-parties working on its behalf - such as legal advisers - working group discussions mainly revolved around exceptions, rather than on the implementation of overarching principles to facilitate a policy of access to data, as foreseen by the Agency as early as 2010. The pharmaceutical industry has been fighting heavily against EMA's transparency commitments:	Parliament and Council and the court cases that are currently challenging the Agency's 2010 access to documents policy are likely to impact on this new draft policy. We encourage the European Medicines Agency to commit to the active implementation of its access to data policy in a way that ensures full access to clinical data, putting public health ahead of commercial interests. The EMA should strive towards this aim, rather than responding reactively or passively awaiting future developments.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		• In March 2013, two pharmaceutical companies, AbbVie and InterMune, supported by European and US pharmaceutical industries trade associations (EFPIA and PhRMA), brought cases against the EMA and its 2010 policy at the European Court of Justice. These court cases have led to a regression in EMA's disclosure practices (iii,iv); • In July 2013, EFPIA and PhRMA published their "joint principles for responsible clinical trial data" which are very insufficient (with no access to clinical study reports, demands for applications to be reviewed by a "scientific board" to be appointed by the company in question), and are unlikely to be implemented by their members. • In addition, in July 2013, EFPIA and PhRMA have made concrete proposals for a lobbying strategy that entailed "mobilising patient groups to express concern about the risk to public health by non-scientific re-use of data".(v) • In a recent intervention in August 2013, an Abbvie representative asserted that some adverse drug reaction data should be considered commercially confidential (vi) This public consultation provides another opportunity to reiterate the need for a policy of full transparency and access to clinical data – both data submitted during the marketing authorization procedure and once authorization has been granted – collated through post-marketing surveillance activities by regulatory agencies.	
126	Scope	**1. Access to clinical data (efficacy and safety data) protects public health from preventable harm** Public access to full clinical data, including raw data, is particularly important	The scope of the proactive disclosure has to be broadened to include all clinical data held by the Agency and the CMDh on medicines which are already

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		to protect public health as it allows for independent analysis, enhancing knowledge about the real effects of medicines and allowing comparative effectiveness reviews (vii). For instance, the identification of cardiovascular risks associated with rosiglitazone (Avandia°) in 2007 relied mostly on unpublished data. (viii) Similarly, published summary-level data, research abstracts and data submitted to the FDA were used to demonstrate an increased risk of heart attacks among rofecoxib (formerly Vioxx°) users.(ix) In contrast, the manufacturer had re-classified fatal events in several peer-review publications. (x) This policy should further amplify the scope and spirit of the current policy on access to documents (Policy /0043) (xi). In parallel to making all post-2014 clinical data available on the database, the EMA and the CMDh (Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human) must progressively publish all the clinical data they hold on medicines that are already on the market (xii). This should be done in a timely manner. While this data is not published, access must be provided upon request in a timely manner (current regulations foresee a response timeline of 2 months for information requests and 15 days for documentation requests (with an extension possibility of another 15 days). Yet, these deadlines are often extended. All information made available online should be in a legible, easily usable and searchable format, so that users can retrieve it easily using key words. To a large extent the EMA's activities and decision-making rely on the opinion of experts from different member states. Any divergences in the application of access to data policies should be avoided, and an alignment should take place among regulatory agencies in the EU. The priority for any	on the market. As a first step, to provide **retrospective access to clinical-trial data part of the common technical documents provided to the EMA and the CMDh over the 10 last years (period 2004-2014).** In order to increase the transparency of older drugs and improve patients' safety**, the harmonisation procedures coordinated by the EMA (CHMP) should be used to reassess thoroughly the harm-benefit balance** (re-analysing all clinical trials results, publishing an assessment report, and publishing an harmonised package leaflet and harmonised summary of product characteristics (SPC)). Clarification is needed on the policy implementation and its **consequences to national DRAs particularly for decentralised and mutual recognition procedures** (e.g. as regards variations to extend therapeutics indications). Encompass access to CT data in other EMA processes, particularly in the pharmacovigilance field: add **variations, referrals and pharmacovigilance data disclosure** (PSURs, PSURs assessment reports, consumption data) **as components of the policy** (category 2 "Open access" with proactive publication). Moreover**, the Agency's 'Eudravigilance access policy for medicines for human use'**

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		medicines' regulatory agency shall be to ensure the highest standards of medicines quality, efficacy and safety. **Harmonisation of procedures amongst the EMA and national medicines agencies should apply the highest existing standard.** The convergence of transparency and access to data policies must also be applied according to this principle. The best existing standards should be used as a point of reference. The EMA's policy on access to data should also go beyond its current scope, and not just apply for approval of centrally approved medicines but also for other decision making process such as **variations, referrals and work-sharing procedures (such as the PSUR centralised analyses).** Moreover, the CMDh should also proactively publish data from clinical trials submitted in support of a marketing-authorisation application through the decentralised or the mutual recognition procedure.	(EMA/759287/2009 corr.) **should be revised** to include individual detailed anonymised case reports (ICRs). Detailed ICRs are needed to be able to analyse and interpret accurately the data. Eudravigilance is a centralised 'mega-database' where suspected adverse drug reactions (ADRs) are coded using ICH terminology (MedRA dictionary). In practice, spontaneous reports can be stripped of clinical significance, by reducing the available information by coding, resulting in the significance of the data being minimised. (xiii) (xiv)
126	Introduction and purpose Line 35 Lines 113 to 115	**2. The EU Legislative framework governing access to documents also applies to the EMA** The European Medicines Agency transparency requirements are defined in the European (freedom of information) Regulation (Regulation (EC) 1049/2001) adopted in 2001 (xv); as well as in the medicines legislative framework (Directive 2001/83/EC as consolidated by Directive 2004/27/EC (xvi) and consolidated Regulation (EC) 726/2004/EC) and in Article 15 of the Treaty on the Functioning of the EU, as well as in the Charter of Fundamental Rights of the European Union (article 11).(xvii) In particular, European citizens are entitled to access any documents produced or received by European institutions, especially where an overriding public interest is at stake (article 2.3 of EC Regulation	**Align the EMA's policy to the legislative framework and transparency requirements** i.e. to Regulation (EC) 1049/2001 and,article 11 of the Charter of Fundamental Rights of the *European* Union and Article 15 of the Treaty on the Functioning of the EU(e.g. before the paragraph on "protection of personal data" at line 35 "Protection of citizens right to freedom of information" (NEW)).

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		1049/2001). We therefore welcome the mention that “It is emphasised that categorisation of information as CCI in the policy does not limit access to documents or information under other Agency policies, e.g. access to documents or other transparency initiatives (…)” (lines 113 to 115). Since "all rules concerning access to documents of the institutions should be in conformity with this Regulation[EC N°1049/2001]” (Article 12 of the recital), any guidance document adopted by the EMA and/or national regulatory agencies concerning disclosure of information must abide by current regulations on access to documents.	
126		**3. Clinical data belongs to the public, not to pharmaceutical companies** The clinical data held by medicines regulatory authorities is related mainly to clinical trials conducted under the auspices of the Declaration of Helsinki. The Declaration of Helsinki explicitly refers to the ethical obligation to disclose the results from research and insists on the completeness and accuracy of the reports (articles 30 and 33). (xviii) In fact, patients accept to put themselves at risk, taking part in clinical trials, notably in the hope that their participation will benefit society through the advancement of science. The WHO Informed Consent Form Template for Clinical Studies clearly divides benefits into: “benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question.” (xix) Yet science is hampered when data from these studies are never made	Emphasize in the policy that clinical data is scientific data of an overriding public interest and therefore public good (and adapt CCI definition – read below).

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		public, which is often the case especially when their results do not favour the sponsor's product- "publication bias") . Since publication bias and the selective reporting of positive study results are widespread practices in biomedical research, (xx) failure to make all the data available greatly diminishes the social value of research. Moreover, industry-funded research often benefits from publicly funded research bodies (access to investigators and research teams at publicly research sites; public funding for basic research through EU grants and member state funding, etc.). It is therefore more than reasonable to expect that all data from biomedical research is made publicly available. Granting public access to detailed clinical data, including raw data, is crucial to minimise dangerous practices of reporting bias, which overrate the benefits of a drug while underestimating its harm. (xxi)	
126	Definitions CCI Line 49 Lines 109-115	***4. A precise and narrow definition of commercial confidentiality is needed*** The policy mentions that "*In general, however, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI*." (line 49). We welcome this statement, which should also be added to the definition of commercially confidential information in order for the **EMA to fully comply with the Regulation on access to documents and the TFEU, which identifies the "protection of health and life of humans'' as an overriding public interest. ([xxii])** Under Regulation No 1049/2001 on access to documents, **confidentiality is an exception**: *"In principle, all documents of the institutions should be accessible to the public. However, certain public and private interests should*	Redefine CCI as follow: ***"(…) CCI shall mean ~~any~~ information that is not in the public domain or publicly available and where disclosure ~~may~~ is duly justified to undermine the legitimate economic interest of the ~~owner of the information~~ clinical trial sponsor during a period of time that should be specified to the requesting person. In general, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI.*** ***If only parts of a requested document contain CCI, the remaining parts of the document shall***

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		be protected by way of exceptions'" (Regulation 1049/2001, recital 11). In general, EMA's default position must be that information is not commercially confidential and companies should have to prove otherwise. **A redefinition and narrowing of the notion of *commercially confidential information* (line 109) is essential to prevent the EMA from relying solely on the self-classification by the company of the information that may undermine the company's economic interest or competitive position** (read right column). Companies must be required to provide detailed information that shows that the release of information that they claim to be commercially confidential would truly harm their interests and that non-disclosure would not be detrimental to public health. In light of the objectives pursued in Regulation No 1049/2001 (article 4(2)), CCI can be overturned whenever there is an "overriding public interest in disclosure". All data with a bearing on human health, notably clinical data, should be excluded from the definition of "commercial confidentiality". This includes pre-clinical laboratory and animal data, pre-market clinical trial data, and post-market safety and effectiveness data, as well as the sales volume (needed to assess exposure levels in adverse drug reactions). An assessment from the European Ombudsman concerning a complaint lodged against the EMA for its refusal to disclosure clinical trial data found that neither trial protocols nor clinical study reports contained CCI. ([xxiii]) The same conclusion applies to another assessment concerning the disclosure of ADR reports. ([xxiv])	***be released**."*

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		In addition, **any exception to disclosure rules should only involve the removal of specific elements of information within a document and never be applied to an entire section or certain types of documents**. As clearly stated in article 4.6 in Regulation No 1049/2001: "If only parts of the requested document are covered by any of the exceptions, the remaining parts of the document shall be released." The Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals adopted in 18 December 2006, establishes in its article 118.2 a list of items deemed to undermine the protection of the commercial interests.[xxv] Nevertheless, should urgent action be needed to protect human health, safety and the environment, the Agency may disclose the information referred to in this paragraph. **The European Medicines Agency could envisage applying a similar positive listing**, in which details of the manufacturing or the finishing process, links between a manufacturer or importer and raw material providers or distributors would be considered to be commercially confidential information.	
126	Definitions Personal data Lines 36 and 102	**5. Patient confidentiality should not be used as a pretext to prevent clinical data disclosure** The protection of personal data in the EU is safeguarded by Regulation (EC) 45/2001 ([xxvi]) with regard to the processing of personal data by the Community institutions and by national data protection laws implementing Directive 95/46/EC. ( ) EU regulations establish that clinical trial data submitted to regulatory authorities has to be anonymised. According to good clinical practice, codes are used to protect patients' identity. ( )	Rephrase policy to mitigate "myths" on patient confidentiality (line 36). Restrict the definition of "personal data" by replacing "one or more factors" by "several" and precise that "*a mere hypothetical possibility to single out the individual is not enough to consider the person as identifiable".*

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		A recent study published in *BMJ Open* confirms that clinical study reports contain only anonymised individual data achieved by means of identification numbers and that patient confidentiality is safeguarded when this information is disclosed.(xxix)This is in line with previous findings from the European Ombudsman. ([xxx]) These findings show that applied de-identification methods uphold the protection of participants' data – as the EMA notes in lines 38-39 of this proposal - *"there are established ways and means to anonymise data and protect patients from retroactive identification"*. In order to allow for re-analysis, anonymisation methods have to be applied in ways that protect patients' confidentiality while the robustness of the data is preserved. In very specific cases (rare diseases), when, after all available means, re-identification is possible, additional measures should be implemented it to prevent this from occurring. Taking into account that rare diseases are often under-researched, it is all the more important to make sure that available scientific data is shared. ([xxxi]) A mere hypothetical scenario cannot be invoked against the disclosure of anonymised patient-level data. "Unlikely to happen" events need to take into consideration the current situation, where millions of otherwise avoidable adverse drug reactions are taking place because anonymised data is not disclosed.([xxxii]) As noted by the EMA, established ways to anonymise participant-level data safeguard patient confidentiality (lines 38-39). In spite of this statement, the EMA goes on by referring to concerns based on hypothetical scenarios. It is important to note that the Data Protection Working Party in its Opinion 4/2007 established that: "(…) a mere hypothetical possibility to single out	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		the individual is not enough to consider the person as “identifiable”. If, taking into account “all the means likely reasonably to be used by the controller or any other person”, that possibility does not exist or is negligible, the person should not be considered as “identifiable”, and the information would not be considered as “personal data” (…).	
126	Introduction and purpose Line 57	**6. Claims of data misuse and misinterpretation are unfounded** Claims that the disclosure of clinical trial data would lead to the misinterpretation of data and to the dissemination of skewed information that would scare the public reflect outdated paternalism and are not evidence-based. Again, proportionality in ethics has to be taken into account. There is overwhelming evidence of drug-induced harm being routinely hidden by pharmaceutical companies to the detriment of public health, while there is no example of misinterpretation of data and misuse from the last 2.5 years during which the European Medicines Agency released clinical data on request. There is no evidence of data manipulation from data sharing/open data. On the contrary, if data are publicly available, full scientific evaluation of any analysis is possible, and the reasons for differences between a primary and secondary analysis can be discussed openly. Open science stimulates advances in methods. Everyone is better protected against data manipulation when a climate of openness prevails. The publication of individual-patient data has become a reality. Some authors want to promote transparency and opt to publish the individual-patient raw data along with the scientific article. This is done currently done	Rephrase paragraph (line 57) to bear into account the proactive role of the EMA and the need to ensure robust evaluation procedures.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		on a voluntary basis but should ultimately apply to all clinical trials. ([xxxiii]) Rather than "*addressing the consequences of inappropriate secondary data analysis*" (as referred in line 57), the Agency should protect public health by making sure that new medicines being authorized into the European market have an added therapeutic value, when compared to the existing drugs, either in terms of efficacy, safety or convenience. Decisions of the EMA should be based on evidence, guided by science, in the absence of conflicts of interest, so that medicines can be adequately evaluated, and benefit public health. Access to the full evidence on which EMA decisions are based, and to the rationale that has lead to those decisions is vital. According to Prescrire's analysis, the majority of new medicines (52%) entering the EU market over the last 10 years were nothing new (copies) which did not respond to unmet clinical needs. Another sixteen percent were considered unacceptable and brought nothing else but disadvantages. (xxxiv)	
126		**7. Following up the policy's implementation and tracking progress** We would strongly encourage the EMA to: • Publish on an annual basis a report describing - access to clinical data requests - quantitatively and qualitatively (type of documents requested); as well as - the Agency responses to those requests, including difficulties faced; - overall rate of acceptance and refusal of access to document requests (including for those in controlled access by type of document and requesting entity – competitor company,	To be added to the policy.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		academia/researchers, healthcare professionals, citizens) - quantitatively (numbers) and qualitatively (document types) the information deemed CCI; - the data proactively shared online by the Agency during that given year; - a list of the documents being withheld, including an abridged summary of their contents, when information is not being disclosed by the EMA . While the disclosure of clinical trial data should be an obligation for all marketing authorisation holders, we would encourage the EMA to develop an incentive strategy and establish a Transparency Recognition system, which acknowledges the most proactive and transparent pharmaceutical companies, and highlights others with persistent shortcomings in disclosure (that unduly classify documents as CCI in order to prevent access).	
126	Use of patient data within the boundaries of patients' informed consent 47 and	It is not clear what the Agency means by mentioning: "any other use of patient data oversteps the boundaries of patients' informed consent". What are the other uses beyond public scrutiny and secondary analysis that would not be contemplated? Sometimes patients' informed consent procedures are not concrete enough in delimiting those boundaries. Moreover, pharmaceutical companies could add restrictive statements in the informed consent forms to avoid secondary analysis of CTs. A reference should be made to the Helsinki Declaration.	Line 47: Provide list of other uses. Clarification is needed. Line 192: Add reference to the Helsinki Declaration.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
	192		
126	CCI definition : Trade secrets 112	According to the European Ombudsman (decision 2560/2007/BEH) neither study protocols nor clinical study reports can be classified as trade secrets and/or commercial confidences. A medicine's qualitative and quantitative composition cannot be considered a trade secret (this principle should apply to excipients). Back in 1926 in France, medicines were granted the status of industrial pharmaceutical products only if their chemical components were included in the label. Further clarification is needed on what the Agency would consider to be a "formula".	Clarification is needed, rewording.
126	Access to information classified as category 1 133	"If a document is deemed to contain CCI, it will not be made available under the policy." According to the current regulation, any exception to disclosure should only involve the removal of specific elements of information within a document (for example when individual privacy protection is required) and never be applied to an entire section or certain types of documents. As clearly stated in article 4.6 in Regulation No 1049/2001: "*If only parts of the requested document are covered by any of the exceptions, the remaining parts of the document shall be released.*"	Clarification is needed, rewording as follows: "If ~~**a document**~~ **an information** is deemed to contain CCI, it will not be made available under the policy."
126	Category 2 150	It is important that proactive access to clinical trial data and related documents does not impair the timely access to the European Public Assessment Reports and their updates. All disclosed data needs to be easily accessible by the general public.	
126	Category 3	The proactive publication of duly anonymised raw data following established anonymisation methods must be the rule, as it does not compromise patient	Not consistent with EMA's statement in lines 38-39

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
	161	confidentiality.	
126	Category 3 179	How will the EMA verify the identity of the requester? Which means will be used?	Clarification is needed.
126	Category 3 184	Public scrutiny should be added to the list.	Add public scrutiny.
126	Category 3 198	"…have obtained ethics-committee approval, as appropriate". This requires further clarification, since it not clear whether the appropriateness will be deemed necessary by the EMA or by the requester.	Clarification needed.
126	Category 3 "destroy CT data accessed" 205	This sentence should be deleted. There is no rationale in asking for the accessed CT data to be destroyed. First, because duly anonymised raw data does not jeopardise patients' confidentiality. Second, requesters are committed to act in good conduct, following the provisions set up by the EMA (lines 182-204) Third, it is against good scientific practice to destroy the material on which assumptions are based. In addition, these data might still be relevant for research purposes long after they have been released (follow up studies, etc.).	Delete sentence.
126	4.2. Data standards 242	Delete "wherever possible". The use of this terminology opens the door to interpretation and can be abused.	Delete "wherever possible".
126	Making available	According to EU regulations, data submitted to regulatory authorities for marketing authorisation is submitted in non-identifiable form. Currently	There is a problem with the whole paragraph, as it refers to an administrative burden that in general does

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
	of category 3 ("C" data) 256	applied anonymisation methods safeguard patient confidentiality. Only in very specific cases (e.g., rare diseases) additional measures might be required to prevent re-identification. Nevertheless, this might only be necessary in very limited cases.	not exist.
126	Annex 1 5.3.1 Reports of Biopharmaceutic Studies 5.3.2 Reports of Studies pertinent to pharmacokinetics using human biomaterials	There is no public health rationale in withholding this information. At best, 5.3.1.4. "Reports of bioanalytical and analytical methods for Human studies" could be considered "may contain commercially confidential information". All the other points are very relevant to the protection of public health (information on bioavailability, biokinetics, drug interactions, etc.) and as such, there is an overriding public interest in disclosure. The EMA has to comply with Regulation 1049/2001 on access to documents and apply the exception of commercial confidentiality restrictively. The access to documents request by one of the ISDB members when conducting a study on the interaction of Clopidogrel and proton-pump inhibitors is a good example. This request resulted in a complaint to the EU Ombudsman and eventually all the documents received from the EMA after the complaint contained no commercially confidential information.	Replace CCI by O.
126	Annex 2	Provided that the data is duly anonymised, there is no rationale to justify not making that information publicly accessible.	Replace C by O.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
	16.2 Patient Data Listings		
126	Annex 2 16.3 Case Report Forms	Provided that the data is duly anonymised, there is no rationale to justify not making this information publicly accessible.	Replace C by O.
126	Annex 2 16.4 Case Report Forms	Provided that the data is duly anonymised, there is no rationale to justify not making this information publicly accessible.	Replace C by O.
126	Annex VI Listing of Patients and Observations excluded from Efficacy	Provided that the data is duly anonymised, there is no rationale to justify not making this information should publicly accessible.	Replace C by O.

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed change by stakeholder, if any
	Analysis		

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[xiii]- Prescrire Editorial Staff *"Patient reporting improves pharmacovigilance"* Prescrire International 2008 ; 17 (98) : 241-242.

[xiv]- ISDB & MIEF *"Pharmacovigilance in Europe: the European Commission's proposals endanger the population"* Joint analysis; October 2009.

[xv]- Article 73 of Regulation (EC) 726/2004 foresees that Regulation (EC) 1049/2001 applies to EMEA.

[xvi]- "Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use" Consolidated version dated 30 December 2009.

[xvii]- CHARTER OF FUNDAMENTAL RIGHTS OF THE EUROPEAN UNION (2000/C 364/01) available at: http://www.europarl.europa.eu/charter/pdf/text_en.pdf

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