2 October 2014
EMA/351881/2014
Chief Policy Adviser

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

From stakeholder 127 to stakeholder 156

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
127	96	What is a “large simple trial”?	Change “large simple trial” to “large single arm trial”
127	97	“form” should be “from”	
127	102	After the colon, the text does not form a complete sentence (this differs from how the other definitions were written).	Change “…(PD):shall mean…” to “…(PD): Personal Data is defined as…”
127	150	It is not clear if the actual datasets from a given study will be deemed “O” or “C”. They should be deemed “C” because of what could be done with these	

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		data. See our comments regarding lines 217-218 below.	
127	168	Who and how is the determination made on what data will be deemed adequate? What is the process by which the data is sent to the Agency? If this information is not available now, when will it be available?	
127	186	It is not clear why individuals given access to these data do not provide some documentation of how their analysis was performed (such as a statistical analysis plan). Without such documentation there is no way of understanding the assumptions made by investigators, nor any way of verifying the conclusions reached. This is a recipe for significant problems (see comments regarding lines 217-218).	
127	217-218	It is not clear why the Agency will not judge the competence of the requestor or the analysis plan (see comment related to line 186). How will the Agency ensure that requestors do not have conflicts of interest (competitors to the sponsor, science deniers, and individuals/organizations with ulterior motives)? For example: A possible situation in which new vaccines with high efficacy are studied and presented to the Agency for approval in Europe. With this access to clinical-trial data policy, groups who believe, a priori, in the absence of scientific proof that all vaccines are unsafe, request these data and may analyse in a biased manner. It is important that a body (potentially independent of the Agency) be created that would evaluate the professional competence of the requestor, appropriateness of the analysis plan, and possible conflicts of interest.	
128	1-35	EASL welcomes the publication of this draft policy and supports the fundamental principles on which it is based, namely, improved transparency and access to clinical trials data for the purpose of supporting public health, improving regulatory decision-making and promoting a better use of	

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		medicines. We agree that, “independent replication of CT data analysis is a legitimate scientific and societal goal.” We also take note that this policy is being developed independently of but alongside a revision of the 2001 clinical trials directive and legislation on medical devices that also includes provisions on access to CT data, a process that we also welcome and support.	
128	36-43	EASL considers that there are significant potential benefits from data mining that could lead to improvements in public health, improved treatment of patients with multiple chronic conditions and early detection of adverse events, particular with new drugs, without the need to carry out further time-consuming and expensive RCTs. However, we are also aware of the potential for such data mining to be used to undermine patient confidentiality. We would therefore like to see a continuous dialogue between the medical community, patients groups, other concerned organisations, the EMA and EU and Member State Personal Private Data (PPD) bodies as this policy evolves to ensure that unforeseen loopholes in PPD protection do not emerge.	
128	49-51	EASL agrees with the statement, “In general CT data cannot be considered CCI.” We agree that the definition of CCI should be narrowly defined in order to allow as much transparency and access to data as possible in the interests of public health, whilst protecting the reasonable need of sponsors to protect their R&D investments.	
128	77-88	EASL supports the introduction of this policy from 1 January 2014. Notwithstanding the fact that other policies are in place for access to documents submitted to EMA before this date EASL would also like to see EMA propose a timetable for publication according to these principles of CT	

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		data submitted in support of market authorisations from 2000 onwards. Some pharmaceutical companies have already agreed to do this on a voluntary basis and we see no reason for the policy to be limited to data submitted from 2014 onwards in the medium term. This cut-off date of 2000 would cover approximately 80% of the drugs currently on the EU market and would be a significant contribution to European public health.	
128	128-37	EASL supports the narrowest possible interpretation of commercially confidential information that does not prejudice the ability of the pharmaceutical and other relevant sectors to continue to innovate in the interests of public health.	
128	138-154	EASL supports the proposed timeline of publication at the time of the European Public Assessment Report or 30 days following withdrawals.	
128	176-205	As a Swiss-based organisation and given the number of clinical trials conducted in Switzerland EASL would support extending access to documents to requestors based in Switzerland and the other EFTA countries, provided this is possible under the statutes of the EMA. EASL would also like to see more clarity in the policy concerning how EMA would ensure that the requirements for access to controlled access data laid out in the legally binding data-sharing agreement are properly met and implemented by the requestors. We would also like more information on what steps will be taken by EMA to enforce the agreement should it become known that the requestor is in breach of one or more of the requirements.	
128	219-233	EASL welcomes the proposal to release information on requestors and on	

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		requests granted/refused/ withdrawn with reasons.	
128	256-261	EASL welcomes the emphasis on patient confidentiality and would be happy to provide expertise on this point to EMA if needed.	
129	Line 132	It would be helpful if the guideline clearly described the criteria according to which a document will be considered as containing CCI. What will be the responsible Authority to make this decision and what procedure will be used?	
129	Line 142	Could you please explain what is meant in the Policy by "*public-health reasons why personal data can be made public*" or give some examples of such reasons.	
129	Line 193	Could you please explain the reasoning behind the statement that the requester should "*refrain from using CT data accessed to gain a marketing authorisation in a non-EU jurisdiction*".	
129	Line 198	It is not clear in what circumstances ethics-committee approval would be required to request CT data.	
129	Lines 227-228	Since the Agency may publish the information about the requestor upon publication of the requested data, it would be expected that the requestor informs the Agency of the fact that requested data have been published.	
129	Lines 250-253	Taking into consideration the current stage of the draft, it is considered that the date when marketing-authorisation holders or sponsors applying for centralised marketing authorisation (or for variation) shall be subject to the policy should be postponed (later than 01/03/2014). The reason is to assure adequate time following publication of the policy for preparation of CT according to requirements described under 4.2 "Data standards".	

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130	General	PLOS is an open-access publisher and advocacy organisation. Since its inception the PLOS journals (http://www.plos.org/publications/journals/) have supported open access to clinical trial reports and the sharing of data from those trials, including the protocols. The PLOS journals have also strongly advocated for the publication of all trials, especially so-called negative trials. PLOS is a supporter of the AllTrials initiative (http://www.alltrials.net/). We support the draft policy as an important step forward. We specifically note and support these two points: The opinion that the interests of public health outweigh considerations of commercially confidential information (CCI). The Agency's appropriately guarded approach to the sharing of individual patient-level data.	
130	67-72	We would urge the EMA to support full open-access publications of secondary (and also primary) analyses of clinical trial data and to mention open-access specifically	
130	77-82	We would urge that past CT data are made available under the same terms as prospective data	
130	150	The agency should define open access and indicate which license if any the data are available under. Do you mean just free availability, or true open access, which implies reuse is allowed? See http://creativecommons.org/choose/ for options	
131	General	The RCP is grateful for the opportunity to comment on this draft policy. We welcome the broad principles which overall seem thoughtful, proportionate	

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		and sensible. However, we do wish to draw attention to serious concerns relating to the sharing of patient-level Category 3 data as outlined within the joint response from the Academy of Medical Sciences, the Association of Medical Research Charities, Cancer Research UK, the Medical Research Council and the Wellcome Trust. Our experts also have some concern with regard to the robustness of what the authors term 'adequate de-identification of data'. We believe that this concept should be further developed as we can envisage some potential difficulties with release of smaller trials of agents for orphan diseases which could fall within the scope of this proposal.	
132	General	The British Medical Association (BMA) is an independent trade union and voluntary professional association which represents doctors and medical students from all branches of medicine all over the UK. With a membership of over 152,000 worldwide, we promote the medical and allied sciences, seek to maintain the honour and interests of the medical profession and promote the achievement of high quality healthcare. The BMA supports the EMA's decision to maximise openness and transparency in relation to data from clinical trials, while respecting both patient confidentiality and the need, in some circumstances, to restrict access to commercially sensitive information for periods of time. In our view, the EMA's position achieves a successful balance of these considerations. On the subject of commercial confidentiality, before results are known to be positive or negative and if a truly innovative product is being researched for the first time, the BMA would accept that withholding identifiable details of such a product at an early stage could be justified. The withholding of such details involves only a tiny fraction of the data that are produced from	

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		clinical research projects and the weight that is conventionally put upon 'commercial confidentiality' as a reason for not publishing the results of clinical trials is unjustified. Commercial confidentiality does not justify withholding of data when a trial indicates that a product cannot be developed. The presumption should be that data are published with a case having to be made not to do so based upon their containing commercially confidential information. We would welcome greater clarity on who will make the decision that data are commercially confidential and on what basis. The concept of 'legitimate economic interest' is too broad and could include withholding negative trial data about a product already on the market. Decisions should also be published. The paragraph on this subject in Section 3 could be clearer. We recognise that individuals give data to researchers for the purposes of that research. Future consent from participants must include information about data publication.	
132	57-61	We welcome the acknowledgement of this issue by the Agency, and would welcome greater clarity on how it intends to put this policy into effect and any punishments it envisages, particularly if the analysis breeches the protection of personal data.	
132	62-66	We are unclear why the protection from external pressures ceases once a decision has been made. Pressure could be applied to persuade the Agency to over-turn a previous decision. We would welcome further clarification of the Agency's thinking on this matter.	
132	67-72	We welcome the proposal for greater transparency to extend to secondary uses. 'A reasonable period of time' is a vague concept and it is unclear what 'external interventions' the analysis needed protection from. Greater clarity on the Agency's thinking would be welcome.	

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133	General	The Association of Clinical Research Organizations (ACRO) represents companies that provide a variety of specialized services that support the development of new pharmaceuticals, biologics and medical devices. ACRO member companies employ approximately 95,000 professionals worldwide and annually conduct more than 11,000 clinical trials involving nearly two million participants in 115 countries. ACRO supports the concept of responsible sharing of clinical trial data, while recognizing that responsibility for the data generated in clinical trials conducted by our member companies lies with the sponsors of those trials. In commenting on the draft policy, therefore, ACRO has focused on those aspects that have potential to impact our member companies' operations in the conduct of clinical trials and seeks clarity on these issues in the final policy. Specifically, our concerns at the operational level are as follows: One relates to the lack of clarity over whether or not informed consent information provided to trial subjects will require revision in order to inform subjects that their anonymized individual data and/or aggregated data (e.g., in clinical study reports) will be published by the Agency and therefore made available for third party analysis, possibly in ways that were not envisaged in the original consent information. We note that the advisory group on legal aspects of the policy established by the Agency could not reach a consensus on this point and published divergent views in their advice to the Agency. This lack of clarity is unhelpful to organisations conducting clinical trials as, should changes to informed consent be required, considerable additional workload will be required in these organisations with regard to: Review of informed consent template language to ensure it is sufficiently robust to allow for publication and secondary use of data as proposed by the	

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		Agency Review of informed consent form language currently in use to ensure it is sufficiently robust to allow for publication and secondary use of data as proposed by the Agency Determination of whether any consent forms currently in use (or used in completed trials that will be submitted to the Agency after implementation of the policy) specifically forbid secondary use of data. Determination of the need to amend informed consent language and to re-consent patients in ongoing trials. Our second concern relates to the publication of information on company staff and investigational site staff identified in the clinical study report. This also has the potential to generate considerable additional workload for organisations managing large numbers of clinical trials with regard to: Determination if site contract template language is sufficiently robust to inform investigators and other site staff that their details and participation in the trial may be made public as proposed by the Agency Determination if current contract language in place with all sites globally is sufficiently robust to inform investigators and other site staff that their details and participation in the trial may be made public as proposed by the EMA Determination if any site contracts globally contain language that would specifically forbid publication of site staff details and participation in the trial as proposed by the EMA	

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		Determination of the need to amend site contract language for ongoing trials The need to ensure that all relevant staff at investigational sites globally are informed that their details will be made public Additionally, as some ACRO member companies perform non-clinical studies in addition to clinical trials and so may be subject to animal rights activism, we are very concerned about publication of staff names because of the potential for intimidation or worse. This could also apply to investigators and site staff who are seen to have links with companies that perform animal studies. Finally, we are concerned that by "moving the goalposts" in terms of trial subject and trial staff understanding in ongoing/completed trials about publication of their information, the Agency risks creating a general perception of concern about whether participants and investigators can "trust" the continuing value/legality of the informed consent and investigator/site contracts, which may result in discouraging future participation in clinical trials by patients and investigators alike.	
133	44-48	ACRO strongly supports the view expressed here that the policy shall not enable any other use of patient data that oversteps the boundaries of patients' informed consent. However, any publication of data contributed by patients makes the data available for analysis, potentially in ways that may not have been explained during the informed consent process. We have particular concern for clinical trials that are already underway, and trials that have been completed, but the data of which will be submitted to EMA after the policy comes into effect. This applies to trials undertaken anywhere in the world (not just in Europe), for which the data will be used	The policy should specifically identify the circumstances in which informed consent would need to explain to trial participants that their de-identified individual data and/or aggregated data (e.g., in clinical study reports) will be published by the Agency and therefore made available for third party analysis. Further, the policy should either clarify whether informed consent information currently in use in ongoing clinical trials will require amendment in these

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		to support a European marketing authorisation. The general rule (which may vary from country to country) is that the data is collected in the context of the relationship between a physician and a patient. By the very nature of this special relationship, the physician must keep data arising out of such relationship confidential unless full and informed consent is given by the patient. Full and informed consent generally requires that the informed consent must specify the person(s) to whom the information will be given and the purpose(s) for which the information will be used. The EMA draft policy to make patient data publicly available would mean that patients' data would potentially be used by unidentifiable persons in unimaginable ways. It is highly likely that the majority of existing informed consents granted by participants in current and completed clinical trials do not foresee or consent to data being made publicly accessible as proposed by the draft policy. Moreover, an analysis of whether existing informed consent is wide enough to grant permission for the public access to such data is a question to be answered under the laws of the country where the participant granted his or her consent. We have great concern that the EMA is unable to carry out such a review, especially considering that the participants' informed consents are not part of the documentation submitted to the EMA. If EMA intends to pursue its current policy of making a general assumption that patients have given informed consents for the very general reasons set out in lines 44-48 without analysing individual informed consent forms, the EMA must consider the consequences if publication does in fact exceed an individual's informed consent.	circumstances, and how informed consent considerations should be applied to the publication of data from completed trials that will be submitted to the agency after implementation of the policy, or state clearly that public health considerations for publication of data over-ride informed consents obtained during the trials. While we have concerns about the ethical and legal implications of the latter approach, we consider it essential that the policy must provide clarity on the implications of publication relative to informed consent. In our view, the approach that is most consistent with the Agency's stated commitment to respecting the boundaries of patients' informed consents in relation to current and completed clinical trials would be to make the policy applicable to data from clinical trials that are commenced after the policy comes into effect. This would allow informed consents to be appropriately widened to take into account the EMA's new policy from the beginning of new clinical trials.

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		Retrospectively re-consenting patients is not a feasible option as it would require substantial work from those who arrange clinical trials, and it is ultimately the patients' right to agree to an expansion of their informed consent. Furthermore, any attempt to re-consent retrospectively could introduce a selection bias to the data made available for analysis.	
133	144-149 And 285-292	The policy states that public health reasons over-ride the protection of personal data of clinical trial personnel. While there may be a case to argue that public health reasons over-ride the personal data protection interests of the investigator, we submit this is not so for other personnel involved with a clinical trial. Therefore, we submit that clinical trial personnel data should be subject to the same personal data protections as participants (de-identification and "controlled status"). If the EMA draft policy with regards to clinical trial personnel is not amended as we propose, the policy should clarify the implications of this with regard to investigational site contracts. Also, as noted above, as some ACRO member companies perform non-clinical studies in addition to clinical trials and so may be subject to animal rights activism, we are very concerned about publication of staff names (even of staff who have nothing to do with animal studies) because of the potential for intimidation or worse. This could also apply to investigators and site staff who are seen to have links with companies that perform animal studies.	The policy should recognize that other important issues in addition to public health reasons apply to the release of an individual's identifiable personal information, and should adopt a case by case approach to the publication of the personal details of clinical trial personnel and introduce appropriate protections to de-identify and protect such data. In particular, the policy should clarify the implications of publication with regard to investigational site contracts. Additionally, the policy should require de-identification of personal details where the individual concerned has explicitly indicated that they do not agree to such publication.
133	165-175	ACRO strongly supports the view expressed here that trial subject data must be appropriately de-identified. However, there is no standard for de-identifying data that is generally recognized by the data protection agencies of the data protection agencies in the various EU Member States and, as the draft policy notes, the proposed minimum standard may need to be	The policy should clearly establish a standard for adequate de-identification of data and, if there are circumstances in which a minimum standard may need to be supplemented by additional methods, the policy should clarify those circumstances and address who

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		supplemented by additional de-identification methods. We believe that the policy should clearly establish a standard for adequate de-identification of data and, if there are circumstances in which a minimum standard may need to be supplemented by additional methods, the policy should clarify those circumstances and address who will make this determination and what additional standards should be applied.	will make this determination and what additional standards should be applied.
133	191-192	Controlled access to category "C" data will be granted only after the requester has agreed, by way of a legally binding data-sharing agreement, to "refrain from using clinical trial data accessed for any purposes that are deemed outside the boundaries of patients' informed consent". Clarity is required on (a) who would make the determination of whether or not the purpose is considered outside the boundaries of the informed consent, and (b) how these boundaries will be defined.	Unless the policy includes a general over-ride of informed consent on public health grounds, the policy should clarify who will make the determination of whether or not the purpose is considered outside the boundaries of the informed consent, and how these boundaries will be defined.
133	248-261	As noted in our General comments, we are concerned that by "moving the goalposts" in terms of trial subject and trial staff understanding in ongoing/completed trials about publication of their information, the Agency risks creating a general perception of concern about participation in clinical trials and the continuing value/legality of informed consent and investigator/site contracts that may discourage future participation in clinical trials. In ACRO's opinion, therefore, the policy should apply only to clinical trials initiated after publication of the final policy.	Revise timelines so that publication applies only to data from clinical trials initiated after publication of the final policy.
134	61	When its product's labels were challenged, the Bio-Pharmaceutical industry has found it difficult to defend its clinical trial data in the public domain as it was claimed this would represent an act of unlawful 'direct to consumer selling'. We agree that with the new transparency, it could be considered to be as strict with the bio-pharmaceutical industry as with any other	...against claims resulting from inappropriate analyses "up to and including (civil) penalties for any proven falsified/false claims of intended or unintended public harm or proven acts of scientific negligence".

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		organisation's public health claims: both should be solidly based on a scientific analysis of the clinical trial data. Significant harm has (possibly) occurred to public health by claims based on unscientific or inappropriate analyses, and "denialism" (e.g. claims that HIV/AiDS does not exist). It is felt that the balance of the consequences should be fair as well.	
134	149	Please clarify what is to be understood with CT personnel?	
134	203	Clinical Trial Data is obtained at high cost. In order to stimulate innovative research, the EMA could envisage allowing the owner the Clinical Trial Data to recuperate some of this cost by charging the requester of analysis a fee for access.	Add "The requester will pay a fee to the EMA, part of which will allocated to the owner of the Clinical Trial Data to cover for the Clinical Trial cost"
134	203	Clinical Trial Data is analyzed by the EMA as well as the Bio-Pharmaceutical industry with great care. It would seem cautious that the requester shares the conclusions of their analysis with the EMA and the Clinical Trial Data owner prior to making it public, so that any public debate is prepared fairly by all parties involved; and false claims are identified prior to causing possible harm.	Add "The requester will provide their analysis and conclusions to the EMA and the owner of the Clinical Trial Data "10x" business days prior to making their data public".
135	General	With reference to Declaration of Helsinki, I don't see why every investigator running a clinical trial should not register it before its beginning and report about the results, fully, in due time from the end of the trial. The ethical motivation are obvious: millions of volunteers that participated in clinical trials did that because they thought that were collaborating to find out more about the effects of treatments on disease, to help other patients and medical doctor informed decision. Unfortunately, this obvious ethical principle about reporting has been widely ignored. Withhold of valuable information from some of the clinical trials are	

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		damaging patients, as prevent clinicians from having clear figures on efficacy and side effects of a drug. This is what led me to fully support the AllTrials campaign, which is now supported by other 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. I encourage the European Medicines Agency to ensure a full access to clinical trial informations that the Agency already holds. I believe that if data is submitted to support a marketing authorisation for a medical product in Europe then this data should be available for scrutiny by researchers. More then one eye will help having safer medical products. I agree that the EMA has a role to play in the dissemination of this data. I 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 clinical trials. These information is needed to make and to scrutinise decisions about medicines and to assess published summary findings – with special reference to collaborations specifically designed for Meta-Analysis studies. 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. I 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	

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		an application for marketing authorisation is complete. I fail to see the point of it. 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. I wish the EMA to implement its new policy as soon as possible.	
136	General	The Health Disparities Research Consortium (HDRC) is writing to comment on the European Medicines Agency ("the Agency") Policy 0070, "Publication and Access to Clinical Trial Data." HDRC is a non-profit, United States-based organization whose mission is to improve the quality of life and health outcomes of women and minority patients through innovative clinical research activities. Disparities are acknowledged in a number of fields of medicine, in particular cardiology, with the impact of cardiovascular disease increasing especially in women and the elderly. HDRC is addressing health disparities that exist in medicine (with a current focus on cardiovascular diseases), through clinical research and clinical trial services that improve study design, recruitment, analysis, and reporting of findings as they relate to underserved populations. HDRC would like to commend the Agency on opening its policy draft to public comment, and wishes to provide several comments related to the Agency's plans for allowing access to clinical trials data for secondary analysis and publication. HDRC is in strong agreement with the Agency regarding the tremendous public value in the transparency of clinical trials data. HDRC agrees that public access to clinical trials data must be carefully	

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		accomplished, and that access controls, data use agreements, and statistical analysis plans are appropriate and necessary underpinnings of any approach or process for publication and access to clinical trials data. Mechanisms to assure both patient privacy and corporate intellectual property must also be implemented and should be reflected in the Policy. HDRC recommends that the Policy explicitly anticipate the need of requestors for access to multiple or pooled sets of clinical trials data. Members of the HDRC Cardiovascular Clinical Advisory Panel are renowned clinical and research experts with a strong interest in accessing clinical trial data sets in order to conduct sub analyses, furthering the mission of HDRC in a way currently unavailable, or available only through cumbersome or costly avenues, through the US regulatory agencies, registries and clinical trial sponsors. We therefore recommend: The Agency open the criteria for requestors to include those outside of the EU (as outlined in section 4.1.3 of the draft policy) so that the global population of clinical investigators are able to access this rich resource, furthering public health on a global scale. Again, HDRC would like to thank the European Medicines Agency for their progressive policies related to the transparency of clinical trials data. Such an opportunity to access trials data for scientific study would contribute significantly to HDRC's ability to achieve its mission and thereby improve patient care.	
136	180	We recommend that the Agency open the criteria for requestors to include those outside of the EU so that the global population of clinical investigators are able to access this rich resource, furthering public health on a global	

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		scale.	
137	General	The key points of response from the European Association of Hospital Pharmacists to this consultation are: One of the motivations for patient participation in clinical trials is the advancement of healthcare and science for the benefit of future generations. The regulatory arrangements for the reporting of clinical trial research results should therefore support the achievement of these goals. Improved access to clinical trial results and other information associated with the trial reduces duplication of effort, improves the basis for conducting future trials, and enhances independent scrutiny of a conducted trial. Accordingly EAHP signals its support for the EMA's proposed policy on opening access to clinical trial data submitted to the agency in relation to marketing authorisation applications. The information is of key public value and merits its place in the public domain. EAHP considers that the concerns expressed by critics of the EMA proposals can all be addressed through appropriate risk-management measures, and has confidence in the experience and expertise of the EMA to counter these risks	
137	General	**First principles of clinical trial research participation** Clinical trial research is conducted across Europe on a daily basis by thousands of dedicated professionals, including hospital pharmacists[1], and is engaged in by many more thousands of patients, all striving towards the ultimate goal of improving healthcare and scientific understanding for the	

[1] http://www.eahp.eu/sites/default/files/files/Eur%20J%20Hosp%20Pharm-2013-Frontini-ejhpharm-2013-000284%20(1).pdf

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		benefit of future generations. It is the view of the European Association of Hospital Pharmacists (EAHP) that the over-riding motivation for participation in clinical trials is an altruistic one, in the sense of the activity providing social benefit for future generations. We therefore consider that the goal in as far as regulating the clinical trial process, should seek to match this objective – to ensure the participation in trial activity delivers the maximum future benefit. **It is from consideration of these first principles of clinical trial research participation that EAHP signals its strong support for the step-change increase in clinical trial results transparency proposed by the European Medicines Agency in this consultation.** **Why clinical trial transparency matters** Greater transparency of clinical trial results is required in order: to prevent duplication of research effort and support the development of future trials by building on previously conducted work; to offer opportunities for independent scrutiny of the methodology and results of any conducted trial; and to enhance patient safety by greater knowledge sharing in relation to adverse drug reactions experienced in conducted trials to meet the expectation of participating patients that results will be well utilised and available for the purposes of progressing medicine An illustrative example of the potential harm that can occur when the reporting of clinical trial results is **not** transparent can be provided by	

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		reference to the publicised case of Vioxx™(Rofecoxib). Deficiencies in the original clinical trial methodology (e.g. none of the three Alzheimer's trials had a Data Safety Monitoring Board) and under-reporting[2] meant that the links between use of the painkiller and increased risk of heart attack and stroke were not reported or identified to the medicines regulator at the time of making an authorisation decision. Greater public transparency at the outset about the trial methodology and results may have enabled the faults in trial design to be identified at a much earlier stage, and warning signs about associated cardiovascular risk to be recognised. In summary, the need for greater transparency about clinical trial results and methodology is a 'must-have' for the protection and safeguarding of public and patient safety, not a 'nice-to-have'. EAHP consider the status quo scenario in relation to clinical trial result transparency is inadequate in the sense that: it is estimated that the results of half of all clinical trials ever conducted have never been published, and those with positive results are twice as likely to be published[3]; and, researchers are often presented with a series of demoralising obstacles in trying to secure relevant trial data in order to conduct independent scrutiny[4]; too often the impression is given that from a trial sponsor perspective commercial interests in relation to data disclosure trumps and overrides the	

[2] http://www.ahjonline.com/article/S0002-8703(12)00318-3/abstract
[3] http://www.alltrials.net/wp-content/uploads/2013/01/Missing-trials-briefing-note.pdf
[4] http://www.alltrials.net/2013/the-challenges-for-journalists-writing-about-clinical-trials/#sthash.WhjxjKt8.dpbs

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		patient and public interest[5]; Change is required and the sharing of information about clinical trial results should move from '*data-sharing 1.0'* (filing a request for information, waiting hopefully for a positive answer that does not always come) to '*data-sharing 2.0'*, where an expectation of open disclosure of information is met. This is in keeping with improved transparency in many other areas of government and public interest, enabled by the advance of technology and managed online platforms[6]. **Managing the risks** Critics of the European Medicines Agency proposals on clinical trial transparency have cited a range of concerns, including: fears about commercial confidentiality and loss of intellectual property; the potential for data-mining techniques to uncover individual patient information; and, 'unqualified' individuals misinterpreting or misusing clinical trial However, EAHP consider these fears to be misplaced, and that each of these concerns can be addressed in turn. ***The suggestion that commercial confidentiality should be the prime consideration*** The European Ombudsman has already declared in its advice to the EMA on	

[5] http://www.bmj.com/content/347/bmj.f5354
[6] http://www.theguardian.com/public-leaders-network/2012/sep/26/francis-maude-open-government-partnership

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		good administrative practice and the proper limits of commercial confidentiality that there is no commercially confidential information in trial protocols or clinical study reports[7]. Further to this, it must be understood that the public interest takes a higher priority than the commercial interest, and for reasons explained above, there is a strong public case for an expansion of trial result transparency. Finally, EAHP considers that the European Medicines Agency is the best placed 'honest broker' organisation, and mediator in the public interest, to determine what information may or may not be considered legitimately 'commercially confidential', as opposed to some current proposals that would enable each commercial company to make this determination[8] – a scenario of conflicted interest. ***The suggestion that released data might be 'mined' for patient specific information[9]*** EAHP has confidence in the ability of the EMA to manage this risk, and indeed believes the risk can be better managed through the actions of a central body tasked with authority for trial result provison, rather than the alternative model of many separate organisations releasing information in potentially variable forms[10]. ***The suggestion that 'unqualified' individuals may 'misuse' released data*** In many regards, this is a cited objection to transparency across many	

[7] http://www.ombudsman.europa.eu/cases/draftrecommendation.faces/en/4883/html.bookmark
[8] http://www.efpia.eu/mediaroom/114/43/EFPIA-and-PhRMA-Release-Joint-Principles-for-Responsible-Clinical-Trial-Data-Sharing-to-Benefit-Patients
[9] http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/04/WC500142877.pdf
[10] http://www.efpia.eu/mediaroom/114/43/EFPIA-and-PhRMA-Release-Joint-Principles-for-Responsible-Clinical-Trial-Data-Sharing-to-Benefit-Patients

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		areas: "*If we release this information 'unqualified' people will not fully understand its meaning and misuse the information".* Yet, EAHP consider that this has rarely come to pass in other areas of public policy where transparency has been extended, and is moreover a societal risk that goes beyond the remit of the EMA per se e.g. the accuracy and diligence of media reporting. Yet even without change in EMA policy on trial transparency this risk will persist, whether a small, or a large amount of information is released. More importantly, with greater information available, qualified and credible sources will always be in a position to give a well-informed opinion about any emerging issues, whereas this may not be the case currently, due to a reduced availablility of information. **In summary** EAHP consider that EMA has undergone a full consultative process in advance of publishing this consultation as to their future policy on publishing clinical trial data. Its policy is guided not only by European Ombudsman advice, but by over-riding public interest. The EMA's proposed policy on clinical trial data publication is supported by the European Association of Hospital Pharmacists (EAHP).	
137	27-35	EAHP supports the reasoning provided by EMA for its change in policy in relation to clinical trial data transparency – fundamentally, a substantial public benefit will be served.	
137	36-43	EAHP has confidence in the EMA's ability to abide by European legislation and protect patient's data, whilst at the same time making appropriately redacted information about clinical trial results more openly available.	

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137	50	EAHP supports the premise that *"CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI."* This is also supported by the European Ombudsman.	
137	57-61	In many regards, this is a cited objection to transparency across many areas: "*If we release this information 'unqualified' people will not fully understand its meaning and misuse the information".* Yet, EAHP consider that this has rarely come to pass in other areas of public policy where transparency has been extended, and is moreover a societal risk that goes beyond the remit of the EMA per se e.g. the accuracy and diligence of media reporting. Yet even without change in EMA policy on trial transparency this risk will persist, whether a small, or a large amount of information is released. More importantly, with greater information available, qualified and credible sources will always be in a position to give a well-informed opinion about any emerging issues, whereas this may not be the case currently, due to a reduced availablility of information.	
137	67-72	EAHP 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.	
137	128-136	EAHP 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.	
137	138-154	EAHP 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.	

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137	155 – 162	EAHP 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.	
137	219-221	EAHP agree that category “C” data should be made available from the time of publication of the EPAR for marketing authorisation decisions or withdrawals.	
137	235-236	EAHP support the policy that all documents listed in Annexes 1 and 2 should be fully searchable.	
137	237 – 238	EAHP 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.	
137	239-241	EAHP support the policy that the applicant should provide relevant unique study identifiers in the list.	
137	242-244	EAHP support the policy that clinical trial data should be provided in the format in which they were analysed by the applicant.	
137	251-252	EAHP 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.	
137	256-261	EAHP 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.	

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138	General	C-Path has experience in constructing unified, integrated and standardized databases comprised of patient-level clinical trial data contributed from multiple sources for the purpose of answering prospectively defined research questions. The comments we offer, therefore, focus on making data available and appropriately standardized and formatted for such analyses. In our experience, access to aggregated clinical trial data is a critical step towards the goal of enhancing the understanding of disease processes and informing scientists about informative endpoints and methods to assess therapeutic candidates. Sharing such data is indispensable for efforts to create novel methodologies and drug development tools (e.g. biomarkers, clinician-reported outcome measures, patient-reported outcome measures) and to create in silico quantitative tools such as disease progression models and clinical trial simulation tools. The public-private partnerships sponsored by C-Path have relied on aggregation of patient level clinical trial data to support the regulatory review and opinions on novel methodologies under the EMA guidance document on Qualification of novel methodologies for drug development: guidance to applicants (09 January 2012 EMA/CHMP/SAWP/72894/2008 Rev.11 Scientific Advice Working Party of CHMP) C-Path believes that it is extremely important for requestors who want to access and utilize data generated by drug developers to support appropriate and rational use under a regulatory scheme to hold themselves to the same rigorous standards as those who spend millions or billions of Euro to generate the data according to GCP and all other standards required by stringent regulatory authorities. Thank you for this opportunity to comment on this important evolving policy.	

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138	27-29	A pivotal component of data analysis is the ability to extract analysis datasets from CT data. This is enabled through the use of data standards that define how data from CT are to be represented and organized. Elsewhere in this draft policy document (lines 245-247) , EMA has indicated the plan to require the use of CDISC data standards for future MAA submissions. This is to be commended as it will enable sponsors to meet submission requirements which are standardized across U.S. FDA and EMA. Use of global standards will further enable aggregation and analyses of larger data sets that can be informative about disease progress, potential biomarkers and other methodologies	
138	29-30	We submit that learning will come from appropriate queries of the data to inform hypothesis-driven research questions and that this should be done with appropriate structural integrity in the research plan, the analysis plan and ensuing statistical scrutiny. This requires that data analyses be conducted by those who have gained the necessary expertise and experience from working with clinical trial data of a regulatory nature.	
138	36-43	C-Path also considers the possibility that emerging technologies might enable retroactive patient identification as a very real concern. Although it is not possible to absolutely ensure that retro identification of personal data will never occur, steps can be taken to ensure the highest possible level of protection of personal data, without preventing the use of such data for meaningful and useful analyses. It is recommended that a requirement that external researchers who acquire access to data sign a statement to attest that they will not seek to identify any patient from their access to the data.	
138	44-48	We propose that this be considered in the context of broader informed consent forms that allow the patient to opt-out of further and future use of	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		data. C-Path sees the greatest utility of access to large amounts of data being the ability to aggregate data into larger datasets across multiple trials in order to explore new information about a disease, trial designs, subsets, etc. as opposed to simply replicating an analysis	
138	57-61	C-Path strongly suggests that measures be put in place to guide any future analyses by external researchers and that they be held to the highest scientific, methodological and statistical standards. Consequences for patients and public health can be dire when multiple analyses of datasets lead to divergent conclusions. In such cases, it becomes incumbent upon the regulatory authority to be the arbiter and make the determination as to appropriate risk/benefit recommendations regarding safety, efficacy and quality of products.	
138	64-66	It is unclear what is meant by the last sentence cited above. C-Path fully supports that regulatory authorities be driven solely by highest integrity, rigorous science, highest quality data, benefit/risk assessments and best interests of patients and that the decision-making process be free of external pressure; however, we do not see that this need changes once a medicine has been initially authorized/licensed. The regulatory authority (as well as the sponsor) still has responsibility to continue reviewing new and emerging data to continue to assess benefit/risk of a medicine. The fact that clinical trial data will be made accessible and therefore open to analysis by other parties, should not impact decisions of regulatory authorities after approval; however, the same fact demands increased vigilance by the regulatory authorities to assure that emerging information from new analyses be considered, as appropriate based on scientific robustness and regulatory merit.	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
138	67-69	C-Path fully supports EMA's position that secondary research use and analysis of patient level clinical trial data be held to the same standard of transparency as that of the originators of the data and strongly recommend that a requirement be in place for relevant subsequent analyses to not only be published in a peer-reviewed journal but, additionally, C-Path recommends that the EMA require that the subsequent analyses be published on EMA's website.	
138	86-88	C-Path agrees with and commends the Agency for not including data based on Individual Case Safety Reports (ICSRs) in this scheme and that access to this type of data continue to be managed via the existing EudraVigilance database, system and access policy.	
138	111-112	The definition of "programs" in this context should be clarified. Specifically, we recommend that information regarding a specific medicine's development program, be excluded from this definition, as that would constitute trade secret information.	
138	118-119	It is not clear from the language if individual CRFs refers to a blank CRF serving the purpose to describe how data were to be collected during the clinical trial or if the intent is to include completed case report forms (de-identified) of each patient/subject. It is our concern that inclusion of patient specific CRFs offers an additional opportunity to re-identify individual patients and burdens the sponsors with additional requirements whereas data line listings should be adequate to accommodate the need for this purpose.	
138	180	It is unclear if this language precludes access by legitimate researchers who have no affiliation in the EU. It is recommended that the global community	

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		be included in any plans going forward.	
138	191-192	It is unclear how the requestor can determine what the “boundaries of patient’s informed consent” are. It is suggested that only those organizations which own the data and therefore followed the practices and policies of their own organization in securing consent are in a position to make this determination. Therefore, it is recommended that the sponsor/owner of the data determine if the informed consent used in a given clinical trial are adequate to allow secondary research use.	
138	193	Many, if not most, drug developers conduct global programs with the intent to use the full aggregated global database of individual patient level data to provide the necessary evidence to support marketing authorisation in multiple markets. C-Path suggests that a requirement to separate out data gained only within the EU jurisdiction is an additional and undue burden for drug sponsors. Additionally, the requestor would not gain access to a full data set for a given clinical trial and therefore, would be expected to find differing results and conclusions from those analyses. C-Path recommends that data sets remain intact as submitted by sponsors	
138	194-197	We recommend that use of data for a legally established Public-Private Partnership, or consortium, (such as those under the auspices of groups like the Innovative Medicines Initiative, TI Pharma, and Critical Path Institute) be allowed to access data by citing only the organizations and institutions (as opposed to the many individuals) which are part of the PPP or consortium based on existing legal agreements that are in place at the time	
138	199-200;207-	C-Path suggests that this language be made stronger and that the Agency require information be submitted. An “awareness of” standards for good analysis practice is, in our opinion, an insufficient requirement. We therefore	

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	218	suggest that some demonstration of technical capability and expertise be represented in order for a requestor to gain access to data. We suggest that the Agency not only make the good analysis practice document publicly available but that a checklist be requested in which the requestor acknowledge capability to deal with each element within the checklist emanating from the best practice. We also suggest that a statistical analysis plan be required in advance of allowing access to data.	
138	201-205	C-Path applauds the Agency for establishing these requirements and we fully support the collection and transparency of this information. As mentioned elsewhere in these comments, we also recommend that the Agency provide a place on the EMA website for the results of the analyses to be posted	
138	210-215	C-Path respectfully submits that the Agency require the statistical analysis plan be uploaded before data access is provided. There is no acceptable rationale for lowering the standards for those who request access with an intent to conduct further analyses than that required for the innovators that generated the data. The proposed analysis plan should be required of the new requestor.	
138	216-218	We at C-Path fully appreciate that the Agency does not have the resources (or likely the legal jurisdiction) to make a formal judgment on the requester's competency or analysis; however, in making the data accessible in the manner described in this document, we do believe that the Agency takes on the mantle of being the steward of data privacy protection and data best use practices. Therefore, as stated elsewhere in these comments, we believe that the Agency should require transparency of the requester's name and affiliation and analysis plans. If a requester declines to upload a statistical analysis plan, then we submit that they should be denied access to	

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		the data	
138	245-247	We commend the Agency for setting a clear requirement for CDISC standards in the future. Clarity for all stakeholders on use of globally accepted clinical data standards will be extremely helpful in this regard.	
138	253-255	The requirement for sponsors to provide the Agency with an additional set of "O" documents that are appropriately de-identified due to the need to make data transparent, will require additional and duplicative resource on the part of the sponsor. If the Agency moves forward with this requirement, we suggest that the provision of this additional data set be timed so as not to delay submission of or the initiation of review of a MAA (or other) and that it be accepted at a later time during the EMA review period.	
138	294 Annex 1	We strongly recommend that the overview section not be made available as the product development rationale and other sections are very likely to contain proprietary information for that sponsor and that this information does not necessarily add anything of consequence to future analyses of data by outside parties.	
138	Recommendations:	C-Path offers the following recommendations regarding the overall process for EMA to consider: 1.Provide tutorial of key concepts of clinical trials and clinical trial data analysis for regulatory purposes 2.Require uploading of names and capabilities of individuals or consortia names and sponsors to be involved in analysis by requester before data access is allowed 3.Require uploading of statistical analysis plan by requester BEFORE data access is allowed	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		4.Require results of analysis to be posted on EMA's website – at a time period to be determined but to be reasonable to allow publication by author	
138	General	Critical Path Institute (C-Path) welcomes the opportunity to comment on the EMA's draft policy on publication and access to clinical trial data, Policy/0070, dated 24June2013. We appreciate the transparent process that has included opportunities for input from expert committees, the scientific and biopharmaceutical industry stakeholders as well as the general public. C-Path agrees that transparency on clinical trials and data is very important to further establish public trust in the process for medicines oversight. However, C-Path recommends that the transparency goal be accompanied by education regarding the general principles of the clinical trial process and the requisite data required to support use of a new medicine and for the nuances of data analysis necessary to support regulatory decisions. It is also important to help educate external researchers and the public regarding the substantial gap between the type of data and data analytics necessary to support regulatory decisions and those which are utilized solely for peer reviewed publication. We suggest that after the review of the comments received by the Agency, a next step would be the issuance of a procedural document that outlines in more detail the proposed process by which clinical trial data would be made available to external researchers. General Comments: C-Path has experience in constructing unified, integrated and standardized databases comprised of patient-level clinical trial data contributed from multiple sources for the purpose of answering prospectively defined research questions. The comments we offer, therefore, focus on making data	

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		available and appropriately standardized and formatted for such analyses. In our experience, access to aggregated clinical trial data is a critical step towards the goal of enhancing the understanding of disease processes and informing scientists about informative endpoints and methods to assess therapeutic candidates. Sharing such data is indispensable for efforts to create novel methodologies and drug development tools (e.g. biomarkers, clinician-reported outcome measures, patient-reported outcome measures) and to create in silico quantitative tools such as disease progression models and clinical trial simulation tools. The public-private partnerships sponsored by C-Path have relied on aggregation of patient level clinical trial data to support the regulatory review and opinions on novel methodologies under the EMA guidance document on Qualification of novel methodologies for drug development: guidance to applicants (09 January 2012 EMA/CHMP/SAWP/72894/2008 Rev.11 Scientific Advice Working Party of CHMP) C-Path believes that it is extremely important for requestors who want to access and utilize data generated by drug developers to support appropriate and rational use under a regulatory scheme to hold themselves to the same rigorous standards as those who spend millions or billions of Euro to generate the data according to GCP and all other standards required by stringent regulatory authorities.	
139	General	European Biopharmaceutical Enterprises, EBE, a specialised group of European Federation of Pharmaceutical Industries and Associations, EFPIA, represents the voice of biopharmaceutical companies of all sizes in Europe that use biotechnology to discover, develop and bring new medicinal	

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		products to market. Majority of EBE members are micro, small and medium sized companies. EBE recognises the potential scientific and public health benefits of providing greater access to information from clinical trials. EBE Supports EFPIA's response (5 September 2013) to the EMA consultation on Draft Policy for Clinical Trials Data Sharing Policy. As highlighted by the EFPIA response to the EMA consultation, the EMA draft policy proposal raises important concerns which could put at risk the promotion of public health, both in Europe and internationally: risks of de-identification of patient data, sharing of companies' commercially confidential information, and commercial consequences of secondary analysis of data for approved products. These concerns are fully shared by EBE member companies, of which majority are small and medium biotech enterprises, and which support the EFPIA response to the EMA consultation. In addition, EBE is concerned that the SMEs will be disproportionally impacted by the proposed EMA draft policy. **"Indeed, SMEs fear that certain measures suggested in the EMA draft policy could provoke consequences on their business models and impact on their ability to continue researching in what could become an insufficiently protected / regulated landscape" stated EBE President Roberto Gradnik.** Small product portfolios, limited human resources capabilities, and fragile and delicate financial business models characterize these SMEs, which could be doubly impacted by the proposed measures and their consequences. However fragile and delicate, the capacity of SMEs to participate in Europe's	

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		growth, health and science is major. It is therefore crucial to preserve these business models and not put their growth capacities at stake because of disproportionate administrative requirements. EBE therefore wishes to hereunder illustrate its concerns regarding the potential incurred impact of specific proposed EMA measures on small and medium sized biopharmaceutical companies: (i) **Disproportionate additional financial and human resources are required to implement the policy:** small teams and limited budgets constrain SMEs' ability to implement such additional projects on top of existing very heavy EU requirements, particularly in case of responding to regulator's requests for de-identification of raw data, the redaction of commercially-confidential information, and regulator's access-driven requests for additional data. (ii) As **commercially confidential information (CCI)** varies from one company to another, and as no definition covers all companies' CCI, the likelihood of CCI being available to competitors will remain high. For companies with short pipeline and small portfolio of products inadvertent disclosure could have dramatic consequences, jeopardizing a company's unique product or indication of development opportunities, particularly as this represents large to total potential proportion of the company's revenues. Broad dissemination of clinical trial data may negatively impact upon industry's commercial opportunities in markets outside the EU which have no or different standards of regulatory data protection, and may prejudice intellectual property rights. Biopharmaceutical SMEs, and directly the patients, may be impacted by the risk of (iii) **de-identification of patient data in small patient**	

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		populations. There seems to be insufficient levels of patient privacy protection, which could be particularly consequential for smaller patient populations. In the area of rare diseases for example, with limited centers of reference in each country, and with new re-identification techniques, it will be easy to re-identify patient/personnel data. Other concerns are the following: (iv) **"Substandard" reanalysis of clinical data by third parties** which, if not regulated properly, could result in unfounded interpretations of data, again jeopardizing the sometimes unique products on the market. (v) The worldwide impact of this policy could **increase vulnerability to generic entry in third markets** and impact on licensing opportunities. (vi) **Additional data submission requirements** and (vii) the need for additional review of clinical study reports (CSR) contents prior to submission. These concerns also arise for large companies, but SME's will be particularly - challenged to address them. Furthermore EBE is concerned about the way future transparency will be driven and questions whether the regulators are rightly positioned to drive improved data sharing. Increased commitment to transparency is inevitable and welcomed, and the EFPIA/PhRMA position addresses key concerns that are also supported by EBE members. Beyond the logistical and technical issues raised by the policy, EBE believes that it would be appropriate to evaluate the consequences for the SME funding model. All of the above aspects, and the ones made previously by EFPIA and PhRMA, represent more burdensome challenges and risks for SMEs. Regulatory policy should preserve SME competitiveness in Europe, not destroy it. European legislative framework for medicinal products is essential	

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		to ensure a high level of public health protection and to stimulate a dynamic environment for continued research. Additional hurdles, which EMA's draft policy presents, risk to jeopardize the incentives Europe has put in place to innovate and develop new medicines. These issues should be properly-evaluated prior to introduction of the policy, perhaps through an impact assessment exercise, which would have been a necessary part of the policy process had the proposal been introduced by the EU institutions.	
140	General	If the policy comes into effect, it will provide extensive clinical data to the requestor on any clinical trial on the EMA database, over and above what is in the EPAR.	
140	Lines 49-51	There could be aspects of a CT that however should be considered as CCI, such as formulation aspects and potency of the IMP.	
140	Lines 219-221	Would the sponsor be made aware that such 'C' data is being requested and would the sponsor also have a say in 'declining' to share such information with the requestor?	
141	129-137	We agree with this position. While there can be some data that is genuinely commercially confidential, this should be justified. The burden of proof should lie with the company claiming the confidentiality.	
141	144-149	We understand the rationale relating to publication of personal data of CT personnel, but it is not clear if there could potentially be public health reasons that would mean personal data relating to patients could be made public, overriding considerations of PPD? This should be clarified as patients' data should be always protected against leakages that could be detrimental	

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		for their lives, e.g. potential sources of discrimination.	
141	165-175	It is not clear who will be responsible to confirm whether or not data have been adequately de-identified. In addition, it is unclear what is the difference between “C” data that has been de-identified, and category “O” data that contains personal data which has been de-identified (line 143). The former would be available only under controlled access, while the latter would be open access, but is not clear to us what is the added value of category “C” over category “O” if the de-identification method selected is appropriate and robust.	
141	210-218	Given that the Agency considers “preparation and uploading of the detailed protocol/statistical analysis plan before data access of utmost importance, to ensure the credibility of subsequent results”, we do not understand why the request as choice whether or not to upload such plan would not be a factor in the agency’s decision to grant access. Moreover, if a reason to access data is to conduct further research, then the request as professional competence would be a factor to ensure the quality of the results. However, not only researchers but stakeholders such as patient organisations and public health NGOs might wish to access clinical trials data. Possibly a way forward might be to define criteria for different reasons to request data, and different types of stakeholder, to allow equitable access while still ensuring quality as far as possible.	
141	249-261	We suggest that a **working group** should be set up to define criteria and draft guidance document on the release of different types of data, such a working group should include **a sufficient number of representatives of patient organisations** to ensure that the criteria adopted are fit for purpose and acceptable to patients.	

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141	155-233	This section raises a number of concerns and questions, importantly the following: what is considered a question that is “in the interest of public health”, and who decides this? what is considered “in line with the spirit of informed consent” or “outside the boundaries of patients’ informed consent”, and who decides this? When would ethics committee approval be needed, and who decides this? We suggest that there should be **a permanent structure**, e.g. a panel, to evaluate all requests for category 3 data, and that this structure within the agency should **include a sufficient number of patient representatives**. **Objective and transparent criteria** for access should be defined, also with the input of patient representatives.	
142	General	Cittadinanzattiva, through its Tribunal for patients’ rights and National Coalition of Associations for Patients suffering Chronic Diseases (CnAMC)[11], want to give a contribution to the public consultation promoted by EMA on publication and access to clinical trials data. First of all we do want to remark that while much attention has been paid to the point of view of different stakeholders groups (such as industry, etc.) little has been published about what patients in general as well as those who participate in the clinical trials have to say regarding the disclosure of	

[11] The CnAMC is a network of Cittadinanzattiva established in 1996, which represents an example of crosscutting alliance between associations of people with chronic and rare diseases, for the protection of their rights. It has about one hundred members.

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		clinical trials information. We believe that even in this decisions, it is necessary to protect Patients' rights. We refer to the 14 rights summarized in European patients charter rights[12], plus three rights of active citizenship. The most relevant rights to underline for this public consultation are: - Right to Privacy and Confidentiality *Every individual has the right to the confidentiality of personal information, including information regarding his or her state of health. All the data and information relative to an individual's state of health, and to the medical/surgical treatments to which he or she is subjected, must be considered private, and as such, adequately protected.* - Right to Information *Every individual has the right to access to all kind of information regarding their state of health, the health services and how to use them, and all that scientific research and technological innovation makes available.* Health care services, providers and professionals have to provide patient-tailored information, particularly taking into account the religious, ethnic or linguistic specificities of the patient. Every individual has the right of direct access to information on scientific research, pharmaceutical care and technological innovations. This information can come from either public or private sources,	

[12] www.activecitizenship.net.

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		provided that it meets the criteria of accuracy, reliability and transparency. - Right to Consent *Every individual has the right of access to all information that might enable him or her to actively participate in the decisions regarding his or her health; this information is a prerequisite for any procedure and treatment, including the participation in scientific research.* Documents, doctors, practitioners and all health professionals must use a language known to the patient and communicate in a way that is comprehensible to persons without a technical background. A patient has the right to refuse a treatment or a medical intervention and to change his or her mind during the treatment, refusing its continuation. A patient has the right to refuse information about his or her health status	
142	General	Starting from European patients charter rights, we do believe that there are some principles that should be highly considered and the consequent citizens/patients' rights protected. Patient safety and confidentiality are paramount. Clinical trials must be developed and implemented in an ethical way which includes also registration and publication of clinical trials data and their results. Clinical research must be encouraged to ensure the development of innovative treatments that lead to improved patient outcomes and that are able to answer to patients (and care givers) needs. The decisions referring to transparency of processes should consider also the principle of progressivity and balancing of rights, in which the	

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		right to privacy of the person must be weighed when deciding that the personal data of the patient (and his identifiability) may become public to everybody. The following points five points want to clarify better these guide principles. **Patient Level Data, row data and informed consent** Significant measures must be in place to prevent individual patient identification: their right to privacy must be protected. That's why we ask that Patient level data cannot be shared unless the patient has provided his or her informed consent and only when it is really essential to transparency and research progress. **The informed consent should have a specific paragraph dedicated to privacy, confidentiality, and consent for disclosure.** This paragraph should content the possibility to choose if the patient want to disclosure information concerning: His/her own health and personal data data/information related to his/her family or related to familiar condition (such as genetics information). The question should separate these two items. Patients should also have the opportunity of giving informed consent on his/her own health data, but not data/information related to his/her family or related to familiar condition (that could not respect their privacy). Patients should also have the choice to choose about giving or not giving the **consent for disclosure; this should not discriminate from the**	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		possibility of participating in the clinical trials. Patients who participate in clinical trials **must be advised on how their information is going to be used before they provide their consent for disclosure**. Health professionals giving information about the informed consent on disclosure should ensure that the patient have really understood what it means for him/her and also for his/her family (sometimes information are also related to genetic or familiar health conditions). **Retroactive Access** Retroactive access to patient data may only be allowed if the patient provided informed consent that his or her data may be accessed following the conclusion of the clinical trial. If the information are related to familiar health conditions, we suggest to make the informed consent be explicit on this point. **Clinical Trial Registration and Publication** It is in the interest of patients and their representatives that all trial results (not all the associated data but the end result), whether negative or positive, be publicly disclosed. It could also ensure a better use of public funds for research. **Research and Development** Research and development into to the creation of new and innovative treatments that lead to improved patients outcomes, as well as answer to patients' and care givers' needs in terms of a better qualy of life must be	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		encouraged. Protection of commercially sensitive information must be assured, to make also private company invest in research. **Participation by Patient and citizens organizations** Patients and citizens organizations are an important stakeholder in this issue and therefore patient groups or citizens organizations engaged in protecting patients' rights and advocacy activities must be included in decisions about information sharing and the models of informed consent to be used for this. They are a sort of guarantee of patients interests.	
143	General	Joint response from the Academy of Medical Sciences, the Association of Medical Research Charities, Cancer Research UK, the Medical Research Council, Parkinson's UK, and the Wellcome Trust Key points: We welcome the European Medicines Agency's plans to increase transparency and publish clinical trial data; however, we have serious concerns over the lack of a well-defined review process for requests relating to data in Category 3. We support a controlled access mechanism for patient-level Category 3 data, and believe that the EMA or an independent panel should judge the competence of requesters to analyse the data and review the proposed statistical analysis plan.	
143	General	We welcome the European Medicines Agency's plans to increase transparency and publish appropriately safeguarded clinical trial data. We agree that the sharing of clinical trial data for secondary analyses has great	

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		potential to be translated into significant benefits to public health. However, we have serious concerns relating to the sharing of patient-level Category 3 data, specifically the lack of a well-defined review process for requests for access to data in this category. We believe it is vitally important to put appropriate mechanisms in place to prevent inadvertent or inappropriate disclosure, to protect patient confidentiality, and to ensure the scientific and analytical robustness of the proposed data use. While the principles and intentions of the draft policy are sound, we are concerned that the lack of such a review mechanism will jeopardise its effective implementation. We consider it to be crucial to establish appropriate mechanisms to mitigate the following concerns: 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 it would be responsible to verify the requesters' data-handling competence and require that requestors provide a plan of how they will store data securely. Similarly, potential harm could result from wrongful secondary interpretation 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. Finally, requestors of Category 3 data 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	

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		different settings. We therefore support a controlled access mechanism with an appropriate review process, in line with existing data access committees that oversee data requests to, for example, genomics studies, and in line with the mechanisms in use by other organisations. As part of this review process, we believe that the EMA or an independent panel should judge the competence of data requesters to analyse the data and review the proposed statistical analysis plan in order to prevent the data from being misinterpreted or inappropriately analysed, as well as ensuring that data access requests fall within the boundaries of the original informed consent. While the EMA's proposed 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 provides the safeguards set out above. We recognise that this will have resource implications, and that further work will be needed to explore the detail of potential mechanisms and ensure appropriate oversight, such as through a 'safe haven' or 'honest broker' model – but such issues should not preclude the broader considerations set out above. 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, controlled access to patient level data should ensure that access only follows after appropriate independent review of the proposal.	
143	44-48	Broad consent for data sharing should be encouraged in order to ensure that data are used to their full potential. Some guidance from the EMA, drawing	

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		on existing guidelines, on the wording of such consent for future trials (subject to ethical review) would be helpful.	
143	57-61 & 216-218	We are concerned that the EMA will not assess the methodological robustness of the requester's proposed secondary analysis, or the requester's competence to analyse the data. We support an appropriate review mechanism that would make such assessments, as described in the main body of the response, above.	
143	109-115 & 129-132	It would be helpful to have greater clarity on who can decide whether information is classified as CCI.	
143	143, 165, 172-175 & 278-281	We would appreciate further clarity on whose responsibility it will be to carry out adequate de-identification of data, and to verify that de-identification has been carried out to an appropriate standard.	
143	149	We are concerned regarding the statement that personal data of CT personnel is not regarded as confidential. Although we agree the names of the investigators and institutions should be in the public domain, we do not think that contact details or the names of all CT personnel should be available.	
143	181	It is not clear how such a data sharing agreement would be enforced, or what the EMA would do if the requester fails to adhere to it.	
143	183 & 198	We would welcome further clarity as to who will decide that research is in the interest of public health, and who will define what is appropriate in terms of ethics committee submission.	

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143	191-192	The EMA should take account of the 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).	
143	244-247	We are concerned over the requirements with regard to data formats for raw datasets, as CDISC format is not yet a universal format for data sharing outside of the pharmaceutical industry. Datasets from outside the sector will not necessarily be CDISC compliant, and many academic organisations and patient groups would not be able to use the format.	
144	General	The TMF – Technology, Methods, and Infrastructure for Networked Medical Research is the umbrella organization for networked academic medical research in Germany with currently 74 member networks. TMF's IT infrastructure and quality management working group welcomes the proposed availability of clinical research data and shares the intentions as set out in policy 0070. To be able to fully exploit and utilise CT data, there is a compelling need to have metadata – annotations about the structure of a clinical study and semantics of the data element involved – compulsory attached to all data sets. Publication without metadata will hamper the intended usage scenarios because data cannot be doubtlessly interpreted in secondary analysis. This is especially true for data integration across multiple trials for meta-analyses. The TMF is committed to open standards and recommends using standards that are wide-spread and proven. We therefore embrace the mention of CDISC's suite of standards and support any further dissemination. Furthermore, we would advise to add a recommendation to utilise medical terminologies like LOINC or SNOMED-CT as references for better explaining	

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		the “meaning” of documents and other information artefacts.	
144	118	MAJOR: “Raw CT data” is a conglomerate of different entities of data that should be defined and treated separately (see comment on line 157).	Split “raw data” into 3 groups: “Individual patient data”: individual patient data sets, individual patient line-listings, individual Case Report Forms (CRFs) “CT metadata”: documentation explaining the structure and content of data sets (e.g. annotated CRF, variable definitions, data-derivation specifications, data-set definition file, *references to medical terminologies or standardised value sets*) “Statistical supporting documents”: Statistical Analysis Software logs and SAS statistical programs (if code not included in the SAP)
144	121	MINOR: “Test output” might be ambiguous. When interpreted literally, test data are not useful to be published.	Clarify.
144	157	MAJOR: Certain documents are not related to personal data (PD) as defined in line 139 and need not to be protected. Therefore, “Raw CT data” should be redefined (see comment on line 118).	“Individual patient data” should remain in category 3 as it is. “CT Metadata” should be publicly available and placed in category 2 “open access”. “Statistical supporting documents”: should also be placed in category 2 as long as no “Individual Patient Data” is contained in these files.
144	242	MAJOR: As proposed above, “raw CT data” is considered inopportune.	“raw CT data” should be replaced with “individual

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			patient data and statistical supporting documents". After the following sentence (before "In future…"), an additional sentence should be included: "CT metadata shall also be made available for downloading, preferably in CDISC ODM or Define-XML format.
144	244	MINOR: The phrase "according to CDISC (Clinical Data Interchange Standards Consortium)" is misleading, because CDISC is a Standards Developing Organisation, not a standard itself.	Clarify which CDISC standards are referred to or if arbitrary CDISC standards are applicable.
144	245	MAJOR: The phrase "other appropriate standard" leaves much room for interpretation, especially with regards to proprietary (binary) formats that can't be read without software that might be unobtainable.	Rephrase to: "other standardised machine-readable formats like comma-separated values (CSV) files as defined in IETF RFC 4180 [http://tools.ietf.org/html/rfc4180]"
144	246	MINOR: If no conversion is recommended, it will be hard to provide data in a standard-complaint way.	Rephrase to: "Conversion should be done thoroughly to ensure accuracy and integrity of data."
145	General	We welcome the opportunity of being consulted on this draft EMA document. AESGP in principle supports the efforts of the European Medicines Agency (EMA) towards appropriate transparency within the European regulatory framework in accordance with the EU Freedom of Information Act (Regulation (EC) No 1049/2001). We understand that the EMA is under increasing demand for information from civil society and increased openness in decision making. However, we do not share the EMA's assumption that the release of all the Clinical trial data will in all cases benefit public health and will increase	

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		patients' confidence. While well-intended, the proposal could result in significant unintended consequences that may undermine consumer confidence. At minima, the defining of the type of data that will be released, appropriate standards for how the data will be used and by whom, should be established. In addition, a process to submit requests for data should be designed and include the right for the originator of the CT data to accept or deny the data request. Appropriate and enforceable safeguards to protect both Commercially Confidential Information (CCI) and personal data need to be put in place before any clinical trials data can be made available. Regulation 1049/2001 stipulates that access to a document shall be refused where disclosure would undermine the protection of: commercial interests of a natural or legal person, including intellectual property. According to the EMA policy on access to documents (ref.EMA/110196/2006), “CCI shall mean any information which is not in the public domain or publicly available and where disclosure may undermine the economic interest or competitive position of the owner of the information”. Further the EMA defined “CCI [being] generally considered to fall broadly into two categories: Confidential intellectual property, “know-how” and trade secrets (including e.g. formulas, programs, process of information contained or embodied in a product, unpublished aspects of trade marks, patents, etc.) Commercial confidences (e.g. structures and development plans of a	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		company)." The Agency contends that it will protect CCI but declares that "in general CT cannot be considered CCI; the interests of public health outweigh considerations of CCI". This is contradictory and we question the rationale for such a conclusion. Clinical trials vary and a case-by-case consideration in consultation with the owner of the data should prevail before CT data can be made accessible (under conditions). In addition, the specificities of the medicinal products should be taken into account when considering CCI. Non-prescription medicines are usually not patented and operate in a very competitive environment, including against non-medicinal products. Careful consideration should be given to the consequences the release of CT data may have i.e. negative impact on investments, on innovation and on further potential implications. In our opinion the application of such policy is in contradiction with the intention not to "negatively impact on the incentives to invest in future biopharmaceutical R&D" and on the fact that it is intended to "guard against unintended consequences, e.g. breaches of intellectual property rights that might disincentivise future investment in R&D." This is true for all companies operating in the self-care sector but particularly for smaller ones. In addition, for self-care companies that have the choice between the centralised procedure and other procedures to market their product, this policy may act as a disincentive to use the centralised procedure. Our concerns relate to authorised MA but they are also valid for negative and even more so for withdrawn applications. Information about natural persons allowing identification of the individual should not be published for reasons of PPD. This is not limited to patients	

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		but also investigators, nurses, physicians, clinical psychologists, clinical pharmacists, house staff physicians, etc. Disclosure of names and contact details of these people could potentially put them at risk. In addition, the EMA draft policy on the disclosure of sections of marketing authorisation applications including clinical study reports contains provisions to protect privacy but they are not sufficient or described in sufficient detail to be implemented. In particular sections marked as “Open Access” may contain personal information and we do not believe that the names of clinical study staff should be disclosed without consent. In the document the EMA describes the measures it intends to put in place to ensure the best possible protection of public health (and regulatory decisions) against claims resulting from inappropriate analysis. We agree with the intention but we fear that the measures are not strict enough. In particular, there is no requirement for an appropriately quality-controlled statistical analysis plan, quality control of planned and/or performed analyses and/or subsequent interpretation or assessment of the proposed science. Data is just provided directly to researchers so there are not sufficient controls to protect privacy and ensure good science. There are no enforcement measures or penalties to ensure compliance with the data sharing agreement. In addition we do not believe that the Agency has power to enforce these rules and in particular to constrain requesters of data to make their analyses public. AESGP makes proposals for a more robust process.	
145	15-16	AESGP supports appropriate transparency however the access to greater transparency should be in accordance with Regulation EC No 1049/2001 and should not undermine commercial and proprietary interests.	

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145	27-28	Thesis on the possible benefit of unregulated access to CT data publication to foster public health is doubtable. Clinical Research resulting in high-quality clinical trial data is an expensive process. Parties interested in secondary usage of such data should be obliged to respect certain rules. In addition a “redacting fee” may be thought of for requesters.	Please replace by “Access to CT data ~~in an analysable format will~~ might benefit public health in future only if access is clearly regulated and results of the secondary analyses are controlled as are the results from the primary data analyses.” And please add “Clinical Research resulting in high-quality clinical trial data is an expensive process. Parties interested in secondary usage of such data are requested to enter agreement with the EMA and the originator.”
145	28-31	The implicit reference to making data available to competitors is unfortunate here. It should certainly not be the purpose of the policy. In addition this is not correct as the scope of the document is for centrally authorised medicines.	sentence should be deleted
145	31-33	We do not believe this statement is true or accurate. The average person is not able to use or understand clinical trial data. While well-intended, the CT disclosure policy proposal could result in significant unintended consequences that undermine consumer confidence if the data are misinterpreted or wrongly analysed. This would be contrary to the ideal intent described here.	sentence should be deleted or reword to state “~~high degree~~ appropriate transparency”
145	34-35	To be able to do so third parties re-analysing the data should have the same credentials that regulatory experts who assess the application and use scientific methodology and standards. Such credentials and the intended use of the data should be required before the data could be made available. If	delete sentence

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		this is not the case the incorrect use / analysis of the data could lead to flawed conclusion which would undermine the regulatory system for approving medicinal products. This would be clearly to the disadvantage of anyone. The sentence is source of potential confusion.	
145	44-48	Patients' informed consents have a clear and well-delimited scope; by giving their informed consent, patient agree to take part in a distinct clinical trial but certainly the informed consent is not allowing any use of that distinct clinical trial's data by third parties other than specified in their signed informed consent.	please delete sentence
145	50-51	We disagree with the statement on CT never be CCI. It also contradicts the EMA later reference on CCI data in CT in chapter 4.1.1 (128-137). CT data submitted to regulatory authorities for a marketing authorisation have to be considered as trade secrets and therefore as CCI because each clinical trial is individually tailored to a medicinal product.	please delete sentence "~~In general, however, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI.~~"
145	57-61	The Agency must guarantee that all secondary data analyses that are enabled by the policy will be conducted and reported to the highest possible scientific standard, this is an essential precondition for a truly reliable approach. It is acknowledged that the Agency wants to put in place measures to ensure the best-possible quality of any secondary analysis however if it "*cannot guaranty that all secondary data analyses that are enabled by this policy will be conducted and reported to the highest possible standards*" then this defeats the whole purpose of the exercise and it is quite logical to	The SAP for a secondary analysis will be provided to EMA. EMA will forward the SAP to the originator (owner of the primary data) for check and release. In case of different opinions between the EMA and originator, the EMA will appoint an external independent qualified biometrician (fees to be paid by secondary SAP applicant) The SAP release must have been granted before the secondary data analyst will gain any access to

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		conclude that "*a truly open approach*" cannot be chosen. A clear system should be put in place to check the secondary analysis plan (SAP). A possibility of process is described below. For example, the following process would ensure an adequate quality of the secondary SAP: The SAP for a secondary analysis must be provided to EMA. EMA will forward the SAP to the originator (owner of the primary data) for check and release. In case of different opinions between the EMA and originator, the EMA will appoint an external independent qualified biometrician (fees to be paid by secondary SAP applicant) The SAP release must have been granted before the secondary data analyst will gain any access to unpublished clinical trial data.	unpublished clinical trial data. For further details on the subsequent process of data access and conducting the secondary analysis, we refer to our comments on lines 176-233.
145	67-72	We agree that everyone should be held to the same standards and therefore we question the last sentence which contradicts this logic. Why should the persons conducting secondary analysis be given additional time?	please delete last sentence.
145	109-115	This resembles more a disclaimer than a definition. In addition the last sentence is misleading and unclear: CCI are CCI regardless of the disclosure process or policy.	please replace by: **"**CCI shall mean any information which is not in the public domain or publicly available and where disclosure may undermine the economic interest or competitive position of the owner of the information.

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			Further, CCI are generally considered to fall broadly into two categories: Confidential intellectual property, "know-how" and trade secrets (including e.g. formulas, programs, process of information contained or embodied in a product, unpublished aspects of trademarks, patents, etc.) Commercial confidences (e.g. structures and development plans of a company)."
145	121-123	Neither test outputs nor Statistical Analysis Software logs nor SAS program codes are Raw CT data.	please delete the sentence in lines 121-123.
145	129-132	Data needs to be reviewed before release to allow removal of CCI data – this is a case by case approach and every case is different. We apply for the review by the originator (owner of the primary data) of the material before release. This would be aligned with processes of publishing this information on an international level e.g.: Japanese Guideline 'Handling of Disclosure of Information Concerning Approval Evaluation of New Medicinal Products, 30-Mar-2011 PMDA Notification No. 0330011'. Here the identification of commercial confidential information is up to the applicant.	It should be inserted that "prior to any release of information, the EMA will consult the originator (institution/company owning the CT data, applicant filing the CT data to be assessed). The originator will be given 15 working days to review the information and ensure that none of it is CCI. In case some data are deemed CCI, the originator will provide justification to the EMA. If the EMA argues that the CCI data should be released due to an overriding public health interest, the EMA should justify and explain the 'overriding public health interest'. Anyway, disclosure of data should not occur without explicit release in writing by the originator."

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145	139-154	this paragraph conflicts with section 2. Principles on protection of personal data (PPD) of the *EMA/HMP guidance document on the identification of commercially confidential information and personal data within the structure of the Marketing Authorisation (MA) application – release of information after the granting of a Marketing Authorisation*.	please remove the third bullet and replace by a reference to the above referred HMA/EMA guidance document.
145	153 – 154	the release of CT data from withdrawn application should not be made available as the availability of these data would undermine the integrity of the regulatory process for any future resubmission and would undermine the commercial viability of the product. With regard to negative MA, it is not uncommon to see a MA denied in one side of the Atlantic and accepted in the other, due to different benefit-risk based evaluation conclusions from regulators across jurisdictions and, therefore not to undermine the evaluation in another region, data from an application which was denied MA should not be made publicly available.	The policy should clearly exclude withdrawn marketing authorisation application and also for those for which the MA was denied.
145	176-218	Notwithstanding our objections/concerns against public disclosure of any unpublished clinical trial data beyond the synopses of clinical trial reports, the approach proposed here for regulating/controlling disclosure goes in the right direction but it is not rigorous enough. For this reason we propose a more robust procedure (explained below). The EMA is responsible for the data the company owning the data has	Line 181: add "<u>with the Agency and the applicant filing the CT data to be assessed</u>" after "data-sharing agreement" Line 193: delete "~~in a non-EU jurisdiction~~" and add

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		submitted in its marketing authorisation application. Therefore EMA has to ensure a controlled access to submitted unpublished data as well as their adequate and professional use. Therefore the requester must provide professional competences/credentials and the statistical analysis plan before data can be released. EMA has to ensure an effective protection of unpublished CT data against misuse, poor quality use, and misleading publication. To this end, the applicant filing the CT data to be assessed has to be fully informed as to the request and the requester and has to be a party to the data sharing agreement. EMA may not grant access to unpublished CT data before the originator (applicant filing the CT data to be assessed) received the data sharing agreement signed by the requester, by the originator and by EMA. The data sharing agreement shall also provide for an appropriate contractual penalty notwithstanding other judicial remedies in case of an infringement of the obligations of the requester	"and accept an appropriate contractual penalty to be defined by the competent courts and to be paid to the applicant filing the CT data to be assessed notwithstanding other judicial remedies in case of an infringement of the obligation of the requester not to use the CT data to be assessed to gain a marketing authorisation or in case of an infringement of the obligation of the requester not to share the CT data to be assessed with anyone else." Line 206: add after "Before access to ´C´ is granted, the applicant filing the CT data to be assessed will be fully informed by the Agency as to the request and the identity of the requester and shall have received the data sharing agreement signed by the requester and the Agency and ..." Lines 216-218: The Agency will not ~~at the time of~~ before allowing access to ~~'C'~~ unpublished data judge the requester's professional competence to conduct analyses judge the requester's (statistical) analysis plan ~~(if uploaded; see above)~~ have received a copy of the data transfer agreement

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			signed by all parties as described above.
145	219-233	To our view the procedure is not strict enough and would like to propose the following possible process. Another example is indicated below.	The Agency will decline access to unpublished data in case any one of the criteria is not fulfilled. For example, the requester must maintain a system for QA of the statistical analysis. This must be described in detail and submitted together with the SAP. The EMA ensures the conduct of the secondary analysis according to the released SAP To receive the results in an adequate time frame and forward the results to the originator Part of the results has to be a complete statistical report The EMA will release the results after consultation with the originator In case of different opinions by EMA and originator about the results regarding e.g. robustness, credibility, correctness, completeness, power considerations or

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			sample size considerations, the EMA will appoint an external independent qualified expert (fees to be paid by secondary SAP applicant) In case of different opinions by EMA and originator concerning reasonable evidence of potential misinterpretation an external independent group of experts shall be consulted. (fees to be paid by secondary SAP applicant).
145	219-233	**Alternative process:** To install an independent statistical analysis committee (ISAC) at the EMA to conduct the analysis according to the released SAP. The secondary analyst would not receive any clinical raw data but the results of the analysis accordingly. This would avoid any further discussion on the possible publication of CCI or trade secrets. In addition this procedure would allow for secondary analysis without disclosure of individual patient data. The release of the results of the secondary analysis according to the process proposed before (see proposed changes for lines 216-218). Publication of all secondary analyses within the database (register) shall be controlled by EMA after consultation with the originator.	The EMA ensures the conduct of the secondary analysis according to the released SAP by the ISAC an adequate time frame for the analysis and forward the results to the originator that a part of the results has to be a complete statistical report that the results will be submitted to the secondary analyst only after consultation with the originator (fees to be paid by secondary SAP applicant). For publication of the secondary analysis results in the EMA database/register the same recommendations as for those of the originator will apply.

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145	285-292	We believe this paragraph contradicts other EMA transparency policies. Names of investigators, site staff and company personnel should not be included in clinical study reports without the individuals' consent. The mention of "overriding public interest" as a rational to include is difficult to understand in this context. At contrario, these people could be put at risks (e.g. animal activists etc).	this section should be deleted and all personal data should be handled as described in footnote 1.
145	294-298	The extent of Annex I and II in the proposed draft is not acceptable. It would comprise the complete clinical parts of the application dossier. The content of module 2 in particular is particularly sensitive as it contains the basis for the MAA and is the crystallization of years of companies' planning and resources concerning the application for the given product. Making it available would seriously undermine the company's strategy with regards to the given product and would affect its competitiveness. Acceptable as categorised "open" would be: Annex I 2.7.6 Synopsis of Individual Studies Annex II 1. Title page 2. Synopsis 15. Reference List 16.1.11 Publications based on the Study	Please revise the definition for "Clinical Trial Data" in chapter 3 (line 90 to 101) as well as the tabular categorisation in Annex I and II in accordance with our comments.

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		All other data are either to be categorized as CCI or in case of 5.4 "Literature References" (Annex I) as possibly copyright protected.	
146	General	Leem welcomes the opportunity to comment on the EMA draft Policy 0070 on "Publication and access to clinical-trial data". Leem is fully in line with EFPIA comments (see comments from Stakeholder no. 05). Leem supports EFPIA commitments on clinical trial data sharing and the recently adopted "principles for responsible clinical trial data sharing". These set out industry's commitments to: Enhance data sharing with researchers Enhance public access to clinical study information, Share results with patients who participate in clinical trials, Certify procedures for sharing clinical trial information, Reaffirm commitments to publish clinical trial results. Leem main concern is the continuation of investments in biomedical research in Europe and in France. The number of Clinical trials decreased of 25% from 2007 to 2011 in Europe (see the Proposal for a Regulation for clinical trials) and it is necessary to stop this decrease not only with a regulation for clinical trial authorization process but with incentives on all the clinical trial environment. The EMA draft policy designates most elements of the clinical trial data	

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		submitted to it by Marketing authorization applicants as “open access” on its website, and that commercially confidential information (CCI) will not be disclosed, but that “in general, however, CT data cannot be considered CCI; the interest of public health outweigh consideration of CCI”. For data protection reasons, a strong procedure for the consultation of the MAH and review of the data proposed for disclosure, and for the MAH appeal against EMA’s decision to disclose, should be implemented. Clinical trials data within the MA dossier may include commercially confidential information, the majority of disclosure requests are from pharma companies. It is essential that EMA, before any disclosure decision, conducts a careful case by case analysis (balance between disclosure of CCI data and public interest), including consultation of the owner of the data, in order to determine if an information is CCI, and if yes, if its disclosure is justified for public health interest. The Principles for CT data sharing proposed by EFPIA and PhRMA answer to these concerns and meet the needs of data access for researchers.	
146	15	There is a growing demand for full transparency from certain external stakeholders in the debate. EFPIA supports responsible transparency, which recognizes that full and unfettered transparency of all information submitted as part of MA dossiers could also have unintended detrimental consequences.	
146	28-32	Here the intent is described as improving the efficiency of the drug development process by enabling competitors to benefit from access to each other’s proprietary information. This is not a proper purpose under EU law	This premise should be further considered.

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		for disclosing CCI and should not be the primary intent of the EMA's transparency initiatives. In particular, the reference to establishing a level playing field is unfortunate and open to misinterpretation. EFPIA does not share the current EMA vision that enabling untracked, uncoordinated and unsupervised secondary analysis of CT data on which MAs are based will provide substantial benefits for the public health. Ultimately, data access and enhanced, responsible transparency can only positively contribute to society if robust conditions for secondary analysis are established and enforced.	
146	32-35	Greater transparency of the regulatory decision making process is laudable and may increase confidence of patients and prescribers, if implemented responsibly. However, the contention that replicating the clinical trial analyses will improve confidence and rigour without compromising the regulatory process may be too simplistic. It could equally undermine the regulatory evaluation process and may not offer any positive benefit over a high quality review by the health authorities. In our view, and based on EU legislative framework, the regulator's core function is to ensure the validity and robustness of the clinical trial process. Indeed, the regulatory framework is designed to enable this rigorous scientific oversight for all Industry-sponsored trials to ensure scientific validity in the design and conduct of clinical trials including pre-specification of the trial protocol, associated statistical analytic plan, careful documentation of any changes in the protocol, and oversight by institutional review boards (IRBs) and data and safety monitoring committees.	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		Also, implementation of this draft Policy would require variable use of resources within the Agency (in order to validate or invalidate interpretations) inevitably diverting energy from core responsibilities – i.e., evaluating the safety and efficacy of medicines. EFPIA considers that a more robust mechanism of data sharing should be put in place, and is committed to implement a system to receive and review research proposals and provide applicable data to help facilitate such scientific and medical research.	
146	44-47	In the draft Policy, the EMA infers a far broader scope to individual patient informed consent than is given in reality. The release of patient level data can only take place within the scope of the specific informed consent given by the patient to the trial sponsor. How will the Agency ensure that the integrity of patient consent and the use of data do not overstep the boundaries of an individual patient's informed consent (e.g., informed consent specifically does not permit release, informed consent is silent on the subject of release)? Unless explicitly stated in the informed consent, it cannot be assumed that patients have consented to their information being released in order to "benefit the advancement of science and public health". Without the prospective understanding of the effectiveness of the measures that will be put in place to ensure their anonymity, it is difficult to envisage how a subject can give truly informed consent to the ongoing use of their personal data. It is unclear from the draft Policy how international studies would be managed, if informed consent forms varied across countries in relation to release of patient level data.	
146	50-51	The EMA statement "CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI" – EFPIA strongly contests the EMA's assertion in this regard. This precise issue is currently the subject of	In the light of the decision of the General Court, the draft Policy should either be revised substantially in relation to the protection of CCI, or implementation

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		litigation before the General Court of the EU. Furthermore, on 25 April 2013 the President of the General Court granted interim measures in favour of AbbVie[13] and InterMune[14] preventing the Agency from disclosing to third parties certain clinical data from these companies' MAA dossiers before the companies' respective legal challenges to the Agency's proposed actions had been fully examined by the Court. The President considered that both companies had demonstrated a prima facie case that the Agency's decisions to disclose such documents were in breach of Article 4(2) of the Transparency Regulation; the fundamental right to the protection of information covered by business secrets and information of a confidential nature under Article 7 of the EU Charter of Fundamental Rights; and the obligation by EU institutions under Article 339 of the Treaty on the Functioning of the European Union not to disclose information that is covered by the obligation of professional secrecy. The EMA's broad and unexplained contention that CT data cannot generally be considered CCI and its intention to implement this in its new proactive disclosure draft Policy in the near term, directly contradicts this ruling of the General Court. Also, this statement is inconsistent with the CCI definition adopted by the EMA and set out in line numbers 109-111 of this draft Policy. Some information in certain MA dossiers, depending on the sponsor, product at issue, competitive landscape, therapeutic area, and value of the information to competitors may, indeed, be CCI. Considerations of an overriding public health interest are relevant for the distinct purpose of determining whether in certain circumstances, public health interests in disclosure of CCI	should await the final outcome of the litigation. Otherwise, companies will be denied effective redress should their CCI or PPD be at risk of inappropriate disclosure. One approach would be to replace the statement "CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI" with the following: CT data and other information present in MA dossiers submitted by sponsors may qualify as CCI, as defined below in this Policy. If the EMA seeks to release CT data, the EMA will engage in a process with each affected sponsor to determine whether such data constitute CCI. If the data constitute CCI, a separate inquiry will be made prior to public disclosure to determine whether an overriding public health interest justifies release of the information. Also, a robust process for consultation with the MAH prior to release of information should be implemented.

[13] Case T44-13
[14] Case T73-13

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		outweigh considerations supporting non-disclosure of protected information. If information in a MA dossier meets the definition of CCI adopted by the EMA in this draft Policy at lines 109-111, and if the EMA seeks to release such information over the owner's objections, then a separate inquiry needs to be made prior to public disclosure to determine whether an overriding public health interest justifies release of the information. Please note EFPIA's Fundamental Comments, Section 3, for a detailed discussion of the topic of CCI within the draft Policy.	
146	55-56	It is stated that the draft Policy "is designed to guard against unintended consequences, e.g. breaches of intellectual property rights…." but the nature and effectiveness of these safeguards are unclear. The draft policy contains no procedure for the consultation of the MAH and review of the data, or for the MAH to appeal against the EMA's decision to disclose, in advance.	In order for EMA to provide safeguards against unintended consequences by controlled access as set out in line 176, "dissuasive, effective and proportionate sanctions" for the requester should be envisaged in the case of violation of the requester's obligations. The MAH, as the party which will suffer from breach of controlled access terms, should be able to enforce the controlled access and seek imposition of the sanctions. Also and as previously described, a robust process for consultation with the MAH prior to release of information should be implemented.
146	57-61	"It <u>should</u> be possible to "guarantee that all secondary data analyses (….) will be conducted and reported to the highest possible scientific standard". If this is not possible with a "truly open approach", then that approach should not be taken, especially given that the stated goal (according to line 75, protecting and fostering public health) can be achieved by a more controlled and responsible approach.	

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

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		public health interest.	
146	65-66	EMA's draft Policy states: "Once a decision has been reached, this consideration [= protection against external pressures in whatever direction] no longer applies." This statement does not take into account the case that EMA's final decisions are subsequently disputed.	
146	67-72	We fully support the need for two way transparency and equal level of scientific standard for all clinical studies, but it is unclear what is meant by the statement "allowed a reasonable period of time during which their analyses and deliberations are protected against external interventions". A key part of the recommendations from the Good Analysis Practice advisory group was the need for the availability and review of the analysis plan, in advance of data access to ensure a high quality analysis and the ability to determine if the analysis can be replicated by others. It appears that the draft Policy affords protection for confidentiality to third party researchers (planned analyses would not be disclosed until up to a year after accessing the data) inconsistently to the standards for MA applicants (who must disclose information on their CT's prior to commencement). All documents relating to a third party researcher's request would appear to be disclosable under Regulation 1049/2001. Regulation 1049/2001 requires an Institution to notify the third party owner of information held by the Institution prior to disclosure of the information. Based on Regulation 1049/2001, there should be a notification to the third party owner of the information that disclosure is contemplated and allow the third party the right either to contest its disclosure or review any proposed redacted version of the document.	

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146	91-98	The Annex II reference to ICH E3 format should clearly indicate that the structure is not meant to dictate E3 use as a template since this would be in direct contradiction to ICH E3 Q&A (R1) of July 2012. As the CSRs for other types of studies will differ in format, it is unclear which general principles are expected to apply.	
146	113-115	The statement "It is emphasized that categorisation of information as CCI in the policy does not limit access to documents or information under other agency policies" is inappropriate, and misleading because it suggests that standards used to designate certain information as CCI, and the consequences with respect to disclosure flowing from such designation, vary across regulatory processes administered by the EMA. The definition of CCI set forth and adopted by the EMA at lines 109-111 reflects general EU legal principles, natural and fundamental rights, and applies across all EMA purposes and policies. Access to such information is subject to the analysis set forth at Article (4)(2) of Regulation 1049/2001 Regarding Public Access to Documents, as discussed in more detail in the Fundamental Comments section of this EFPIA submission. This is true regardless of the EMA access to documents policy or transparency initiative at issue in any particular situation involving disclosure of CT data or MA dossier CCI information over the objections of a sponsor.	Remove this statement.
146	116-117	The "elements submitted as a study report" may not follow the format of the ICH E3 document.	
146	121	It is not clear what is meant by "test outputs". We would traditionally consider test output as being output that is created by a program prior to the program being peer-reviewed, validated and put in 'production' (i.e., its final read-only location). We see no purpose in storing test outputs or	Remove reference to or define what is meant by test output, as it is not clear how it relates to raw data.

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		providing them to anyone. Perhaps "test output" has a different meaning in the draft Policy.	
146	122-123	In this draft Policy, EMA appears to express its intentions to request, for the particular purpose of transparency, more information from companies than requested in the past as part of an application (e.g. SAS logs, SAS programs). In that respect, the draft Policy goes beyond the purpose of the legislation to provide access to documents of the institutions (Art. 2 para 1 of Reg. 1049/2001). Further, it is not clear how SAS code and SAS logs are covered as supporting documents. These are tools for analysis. An appropriate SAP including a description of the statistical model will qualify for repeating all analyses. Pharmaceutical companies put a lot of effort (time and money—often developed by third parties) into developing and validating macro (i.e., computer code) libraries. We believe these would be considered intellectual property.	The Statistical Analysis Plan should suffice for requesters to understand what was planned and done.
146	129-132	"CT data/documents containing CCI: a small number of CT data/documents can contain CCI. […] However, this information will only be deemed CCI in duly justified cases" Clarification is needed for the process by which companies can justify that information is CCI, and disputes resolved. This process must involve a case-by-case analysis of the relevant factors defining CCI, and a precise and careful weighing of any public interest at stake sufficient to justify release of otherwise protected information. Likewise, as stated by the President of the General Court in paragraph 69 of the interim measures case cited earlier in these EFPIA comments, judicial review of disclosure disputes that cannot be resolved between regulator and regulated must ultimately be made available	The following approach should be added and applicable to all data/documents: Any information contemplated for release by the Agency will be provided to the MA applicant of the information, prior to release, in order to ensure that no information contemplated for disclosure constitutes CCI. A reasonable time will be afforded the sponsor to confirm that information to be released by the EMA is already in the public domain, or is otherwise not information the sponsor considers confidential, or not the sort of information that, if released, could harm the competitive interests of the

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		-- “the weighing up of the various interests present will call for delicate assessments which must be a matter for the Court adjudicating on the substance of the case.”	owner of the information. Justification in support of CCI claims should be provided by the sponsor to the EMA. Such justification will be respected by the Agency, but may be rebutted by, for example, information indicating that information to be released has in fact already been made available, or is the sort of information that the owner of such information does not normally protect from disclosure, or is information that would not cause competitive injury if released. Likewise, because even CCI may be released if justified by reference to an overriding public interest, the EMA will have the opportunity to justify release of CCI by articulating such a public health interest, as warranted and appropriate under the circumstances of any particular case. Ultimately, disputes over release of purportedly CCI information that cannot be resolved by consultation between Agency and applicant will be subject to judicial resolution prior to disclosure, through well-established, fair and orderly processes regarding judicial review of regulatory Agency decision-making.
146	139-143	The draft Policy would treat certain documents as "without protection of personal data (PPD) concerns" (i.e., "open access"). This is to include documents where "any personal data in the document have been adequately de-identified". Further, the proposal indicates that all documents meeting the open-access criteria that are submitted to the Agency on or after 1 March 2014 will be subject to the new policy. Nevertheless, the proposal	

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

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146	144-149	The open-access category is proposed to also include "personal data of CT personnel" for which "there are public-health reasons why personal data can be made public, overriding considerations of [protection of personal data]". This appears to reflect a broader disclosure policy than that put forth in the March 2012 HMA/EMA Guidance Document on the Identification of Commercially Confidential Information and Personal Data within the Structure of the Marketing Authorisation (MA) Application. The March 2012 Guidance distinguishes whether personal data can be released based upon the individuals legally defined role or responsibility and indicates that the names of experts and designated personnel with legally defined roles or responsibilities can be released because "it is in the public interest to release this data". (§ 2(A).) However, with respect to names and personal details of other staff members, the Guidance indicates that such information should be considered protected personal data. We believe that no information in relation to the names, or technical or professional qualifications of any company employees or experts (whether or not directly involved with animal research) should be publicly disclosed; all such information should be classed as PPD.	
146	151-152	The draft Policy states that it will be applicable “at the time of publication of the European Public Assessment Report (EPAR) for positive decisions…” It is important that any CT data disclosure takes place only after the product has been authorised in major regions including the US, Japan and the EU, if applicable. Otherwise the information could be released in one region while the assessment for authorisation would still be ongoing in another region, which could undermine the integrity of global regulatory processes.	EMA’s policy should only apply following regulatory approval in major regions including EU, US, and Japan – participants of The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).
146	152-154	If an application is withdrawn there may still be an ongoing development program requiring more data to be generated or the exploration of, for	The policy should not apply to withdrawn or denied MA applications. Of note, the EFPIA/PhRMA principles

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	and 219-231:	example, a different indication. Proactive dissemination of the data submitted for this type of compound could prejudice the integrity of the regulatory process for any future re-submission, and undermine the future commercial viability of the product.	reaffirm that, “At a minimum, results from all phase 3 clinical trials and any clinical trial results of significant medical importance should be submitted for publication. This commitment also pertains to investigational medicines whose development programs have been discontinued.”
146	165-175	The Agency's proposal does not provide a clear definition of what will constitute "de-identified" data. It is unclear what “limited” means in the statement of limited number of identifiers. The proposed standards are minimal and more exacting standards should be developed to ensure patient confidentiality is maintained. At lines 169-170, the Agency suggests that data will be considered de-identified where "the risk of compromising subjects' identity in case of wide publication of those data is considered to be absent or sufficiently low". This suggests the Agency supports a risk-based threshold for de-identification. However, at lines 174-175, the Agency appears to support an absolute "zero-risk" standard: "The methods of de-identification should be such that adherence will preclude subject [r]e-identification, even when applying linkages with other data carriers (e.g. social media)." We contend that it will be very difficult to implement the recommendation to de-identify data in such a way that “adherence will **preclude** [emphasis added] subject de-identification” (presumably “re-identification”). Even the cited references (Hrynaszkiewicz and Norton, 2010) suggest some options that are difficult to implement such as “Consent for publication of appropriately anonymised raw data should ideally be sought from participants in clinical research” and that in some cases there should be a	A standard for de-identifying data would need to be developed that all can follow; however, complete de-identification would be difficult to achieve.

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		review by an ethics committee. Requirements and guidance would be necessary, which have the agreement of data protection authorities, to provide assurance to patients that their privacy is appropriately being protected. Finally, the proposal should make clear who is responsible for determining whether the proposed uses of the data (as proposed by the requester) are within the boundaries of the patients' informed consent or whether an oversight mechanism is envisaged. Ultimately, the EMA would be responsible as the body disclosing the data. Prior to disclosure, there should be an assessment to ensure that the proposed research use aligns with the research use of the original study (and therefore with the informed consent). When considering the possibility to provide access to clinical data involving personal data, it is necessary to address both data privacy obligations and the potential benefits that could result from the analyses.	
146	176-178	There should be a requirement for third party requesters to submit their analysis plan. In addition, the resources required to enable access to the data should be sufficiently balanced against the public health benefit expected from the analysis. Therefore, a robust review of the planned analysis for its scientific merit should be mandatory before enabling any data access.	Request should submit their analysis plan. Also, please add the clarification below: "'Controlled access' shall mean that access to 'C' data will only be granted after the requester has fulfilled **all of** the following requirements…"
146	181-183	The EMA conditions access to 'C' documents on execution of a "legally binding data sharing agreement," but it is not explained who the parties to such an agreement will be, the legal basis for the EMA entering into such an agreement, how the EMA will ensure the enforcement of such agreements, or the penalties or remedies available to a company or an individual harmed by use of data released inconsistent with such agreements. Implementation	

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		of a controlled access regime cannot be implemented until these critical questions are answered. If parties qualifying for controlled access must comply with certain contractual conditions, then the EMA must with particularity describe the enforcement mechanisms and penalties to be enforced in cases of breach or noncompliance. The MAH should likewise be a party to the agreement, so as to provide it with the possibility of enforcement of compliance with the agreement.	
146	183	The reference to the "spirit of informed consent" implies a very permissive approach to the respect of the informed consent in disclosing patient level data. Please note above EFPIA's comments on Lines 165-175.	
146	191-192	It is not clear how or by whom a particular disclosure is to be "deemed" outside the scope of patients' informed consent.	Further explanation is required.
146	193	The restriction on using CT data to gain a marketing authorisation in a non-EU jurisdiction should be extended to the EU as well.	Explicitly state that the restriction applies to the EU and non-EU.
146	221-231	Any postponement of disclosure of details about the secondary analysis seems to go to the expense of the MAH if his interests are impacted before the end of the 1-year period. The period may limit the MAH's possibilities to review the secondary analysis and impede MAH's chances to promptly and effectively challenge it.	
146	205	The draft Policy states: "destroy CT data accessed"; however, it is not stated how the Agency would ensure that the CT data is destroyed appropriately and in a way that no third party can re-use it. It would be reasonable to oblige the requester of the CT data to provide evidence about the necessary deletion of the CT data.	A secure environment, without the possibility to download, copy or otherwise remove the data, should be implemented.

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		We would also recommend adding expectations around appropriate storage of PPD data between downloading and destroying (e.g. Access, security – Physical/logical etc…). The data should stay in a “closed secure environment” that would help ensure appropriate protection of personal data.	
146	206-215	“Before access to 'C' data is granted, the requester will be: ...however, the requester may decline to upload any documents at that time; the granting of access to 'C' documents is not influenced by the requester's choice to upload or not.” It is inconsistent to state that an analysis plan is of utmost importance, but then not require that such a plan be submitted prior to the granting of access to the data. The level of disclosure required of the requester regarding analyses and results should be the same as required of the MAH.	
146	219-221	The draft Policy states that it will be applicable “at the time of publication of the European Public Assessment Report (EPAR) for positive decisions....”	EMA’s policy should only apply following regulatory approval in major regions including EU, US, and Japan.
146	222	In the context of this policy we consider it is appropriate for the EMA to immediately disclose the identity of the requestor.	The Agency will ~~not~~ immediately disclose any information about the requester, ~~but will publish~~ **including** the identity (name, affiliation, **funding source**, and contact details provided)., **T**~~t~~he list of the aims of accessing the data provided…
146	235-244	In this section, the requirements are expressed in the passive (“shall be provided”, “shall be published”, “shall be made available”,) but there is no clarity as to who is responsible for these requirements.	Clarification is requested using active rather than passive language.

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
146	242-247	This request appears to go beyond what is normally submitted for the purpose of EMA's assessment for a marketing authorisation. Industry commits to provide - upon request - patient level data under a self-responsibility scheme. The information requested here could be provided under this scheme (Also, see comments to line 253-255 and scope of definition of raw data line 121-123).	
146	249	EMA draft Policy states that it will come into effect on 1 January 2014. EFPIA believes that there are numerous issues to resolve prior to full implementation.	Suggest an implementation date well beyond 1 January 2014 reflecting the need for additional clarification, regulation and sufficient time for implementation.
146	253-255	"MAH shall provide the Agency with an additional set of 'O' documents that are appropriately de-identified to ensure protection of personal data…." We would query the legal basis for this requirement. It is unclear how the Agency can legally implement this unilateral request if the MAH explicitly indicates that the documents might contain PPD and that EMA cannot disclose it without prior de-identification of the relevant data. In addition, it should be noted that the obligation for providing access to documents is with EMA, which means that EMA is responsible for ensuring that all data are appropriately anonymised.	
146	266-267	We fully agree that the impact of the EMA's final Policy should be thoroughly evaluated and the impact assessed in line with impact assessment rules for EU Institutions before being adopted. Specifically the impact on resources needs to be determined. In order to facilitate this assessment, EMA should provide a formal consultation process so stakeholders could provide input into the EMA's methodologies for assessing the impact (i.e., impact not only on the Agency, but also on MAH's, clinical trial participation, overall	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		investment in medicine R&D in Europe, etc.).	
146	279	It would be helpful to explain further what is meant by “key codes”.	
146	292	EMA explains that the personal data of trial personnel will be “considered exempt from PPD considerations”. The legal basis for this assertion is unclear and it seems to be inconsistent with current or recent EMA practice in making reactive disclosures of CT data. Therefore, we do not believe that the names of investigators, site staff and company personnel should be included in disclosed CSRs without the individuals’ consent. We do not agree with the statement in the draft Policy that there is an overriding public interest in the disclosure of these names. It is particularly difficult to understand how the inclusion of these names (or not) in a CSR has any impact on public health. Furthermore, the inclusion of company names poses significant risks for individuals. EFPIA member company employees have been targeted in the past by animal rights extremists even though they have not been directly involved in animal research. The EMA’s position on information on company staff is also inconsistent with their position on disclosure of information on EMA staff. In response to requests for access to documents held by EMA, names of EMA staff involved in pre- and post-authorisation activities will be redacted, on the grounds that disclosure would undermine the protection of privacy and the integrity of the individual, in particular in accordance with EU legislation regarding the protection of personal data.	
146	Annex 1	2.7.2: The clinical pharmacology studies may include PET studies (or similar) which provide receptor occupancy and kinetics of the compound target interaction which the company may feel is CCI.	

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		5.3.7: Access to patient line listings should not be within the scope of the Policy, because of the practical difficulties and significant resources associated with redaction/anonymisation, and the questionable additional value of the listings over and above the datasets.	
146	Annex 2	For Annex 2, EFPIA do not believe that patient listings in the CSR and CSR Appendices should be made available nor be included within the scope of the policy under either "open" or "controlled access". The documents would be difficult and extensively resource intensive to de-identify or redact, and the information would in any case be provided in the datasets under the industry commitments. At the very least, Annex 2 patient listings should be "controlled access". 16.1.4: We do not agree that information for all research staff should be available.	Should be controlled access.
146	General	It needs to be ensured that copyright considerations are covered appropriately. For example, Patient Reported Outcomes questionnaires may be copyrighted and therefore those Case Report Form pages should not be made publicly available.	
147	General	BIO Deutschland, the German Biotech Association, representing research-based biotech SMEs, welcomes the opportunity to submit comments on the draft 'Policy 0070 on publication and access to clinical-trial data'. The small and medium-sized research companies are the backbone of the EU. With their innovative ideas and research driven approach they are fostering the development of new product that lead to significant improvements for patients. This R&D should not be slowed down or made impossible by regulations.	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		BIO Deutschland supports responsible transparency. However, we feel that the current proposal diminishes the protection of personal data and of commercially confidential information (CCI), in a way which would be detrimental to the innovation and growth potential of European biotech companies, large and small. The data from pre-clinical and clinical development are the core value of a drug approval. To gain such data costs hundreds of millions, if not billions, and this process are therefore the most important investment in the industry. Most of the SME active in the field of pharma biotechnology Many SMEs are dependent on venture capital to fund this costly research and development. Therefore the obtained data are of great importance for these companies. By publishing this data the Agency could destroy the business model of innovative biotech SMEs. No investor would provide money if the intellectual property and know-how couldn't be protected. 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.	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		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, BIO Deutschland strongly suggests to pause the development of the new Policy until the ruling of the court are into force. In case the Agency believes that it is necessary to have a Policy in backhand we strongly suggest to let the new Policy only enter into force after the court proceedings are finalised.	
147	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 provided in the EPAR are necessary	
147	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	
147	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.	
147	41-43	This should 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.	~~The Agency therefore takes a guarded approach to the sharing of patient level data. This is done to enable the legitimate learnings from the sharing of patient-level data while preventing rare but potentially damaging instances of patient identification.~~ Therefore

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		The informed consent shall protect patients in clinical trials. Every possible use of the data gained in the trial need to be explained to and enabled by the patient. If the Agency plans to implement a guarded approach to share patient-level data the needed information for a informed consent will grow rapidly and hamper future clinical trials.	patient-level data will not be disclosed.
147	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. Therefore we strongly encourage the Agency not to disclose any patient-level data at all.	
147	49-51	In stating “in general” the Agency clearly envisages that there will be exemptions from this rule. The view 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 data owner and the question of the public interest in overriding any such confidentiality. 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 the Agency’s draft Policy paper: “CCI shall mean any	

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

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		In summary it must be noted that the protection of trade secrets could not be overruled by the public's interest in information about CT. Every request or disclosure has to be assessed on a case by case basis. An undifferentiated approach would contradict any Commission's attempt to effectively protect trade secrets.	
147	52	It is difficult to see how the Agency 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 de-incentivise companies, from filing applications for marketing authorisations or variations in the EU.	
147	57-59	The explicit goal of this policy should be to give scientific requesters an opportunity to conduct research with the obtained data. In addition, the patients and the public need the opportunity to get access to the results of CT. This could be arranged by a tiered access to the CT-data. Under no circumstances this policy may lead to distortions of competition between competitors offering the possibility to request commercial confidential data of constants.	
147	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	Measures to protect public health and regulatory decisions should be put in place prior to the finalisation of this Policy.

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		process into disrepute	
147	62-66	Decision making by the regulatory bodies rely on a clear mandate from the EU to ensure secure processes of market authorisation for new products within the European market. Every attempt to query regulatory bodies' decision or to abet other findings would weaken the position of the legally mandated regulatory bodies. 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. BIO Deutschland 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.
147	67-72	It is interesting that the Agency takes the view that third parties who make secondary use of the CT data shall also disclose their findings. But there are no legal or other obligations to secure that third parties will do so, especially if the generate the secondary analyses outside the EU.	
147	132	It implies that only a small number of CT data sets would contain CCI. But every request or disclosure has to be assessed on a case by case basis. An undifferentiated approach would contradict the aim of this policy and infringe the legal EU framework. In addition, it appears that the Agency has already identified 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.	
147	133-136	In line 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,	

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		cannot be applied to CCI. BIO Deutschland strongly 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.	
147	150-154	In case of withdrawals there are to reasons possible: it might be a strategic reasons and the company plans to re-submit it in a later stage with enhanced clinical (or other) data. Under these circumstances, publication of already submitted clinical data would provide competitors with valuable commercial information that could give them unfair advantage. Publication needs to be prevented in order not to generate any distortion of competition. On the other hand it might be withdrawn by other reasons. In this case a publication is considerable.	Proactive publication of data should not apply to withdrawn applications.
147	155 subseq.	The Agency states that “protection of privacy is a paramount concern when sharing raw CT data”. However, there remain 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.	CT data/documents with PPD concerns will not be disclosed or made public in any way. (Parts of the CT, e.g. CTD Modules 2.5 and 2.7 might be disclosed if there are no PPD in it.)

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		Stating in the introduction that “any use of the patient data oversteps the boundaries of patients’ informed consent, and shall not be enabled by the policy” (lines 47-48) in conjunction with the correct analysis that “the Agency is concerned that emerging technologies for data mining and databank linkage will increase the potential of unlawful retroactive patient identification” (lines 40-41) leads to the clear conclusion that under no circumstances access should be granted to any personal data. This is the only way to avoid unlawful use of any personal data from clinical trials and prevent patients and companies for criminal use of the disclosed data.	
147	219-221	Same comment as lines 153-154 re circumstance behind withdrawal.	
147	222 subseq.	It is unclear why the Agency does not handle the transparency of the requester like the envisaged transparency of the CT. Keeping the request “secret” up to one year is not necessary from BIO Deutschlands perspective. If needed the quantity of request-information given to the public could be reconsidered. However, it is essential that the affected sponsor of the requested data will be notified immediately.	
147	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.
147	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	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		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.	
147	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
147	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
147	Annex II 16.1.6 and 16.1.7	Listings of patients and patient identification and randomisation schemes should be confidential	No general assumption that this data is not confidential. Re-classifying 16.1.6 and 16.1.7 as C
148	General	The Medicines and Healthcare Products Regulatory Agency (MHRA) on behalf of the UK Government, welcomes the opportunity to comment on the proposals in draft 'Policy 70 on publication and access to clinical-trial data'. The question of transparency has been gaining profile at a national level here in the UK as well as at EU level. Along with other parts of Government, the MHRA recognises the importance of transparency to public health and is committed to the transparency agenda. A range of initiatives have taken place in the UK including the recent Caldicott review which reviewed how best to balance the need to keep patient information secure with the need to share it among healthcare professionals for legitimate reasons. The MHRA has carried out a great deal of work to ensure that information about clinical trials that we receive is put in the public domain. The Agency publishes public assessment reports following the approval of new medicines providing details of the information on which a decision to approve a marketing	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		authorisation was made. In addition, since July 2012, summaries of product characteristics of all UK approved medicines are published on the Agency's website. The MHRA is working closely with other parts of Government and its EU partners on the transparency agenda and will continue to do so going forward. The UK Parliament Science & Technology Committee has recently published a report into clinical trials and transparency, and has recommended continued work with the EMA and the European Parliament to ensure greater transparency in the dissemination of trials information, with suitable checks to ensure patient and to some degree commercial confidentiality, are embedded in European policy and legislation. A number of specific comments are provided below. We also wish to make the following general comments: • The UK Government is fully supportive of the broad principles of transparency. It is important for patients, the public, researchers and the NHS and can be achieved through ensuring trial registration and outcome publication as well as making data available through appropriate means. The UK Government welcomes the proposed amendments under the Clinical Trials Regulation (CTR) which provides a clear legal basis for public access to an EU database, which will include summaries of the results of all clinical trials. We will however seek clarity on what data would be considered confidential in the database to ensure that those sponsors with commercial interests, and the public, are reassured. • The MHRA has done a great deal of work to ensure that information about clinical trials that it receives is put in the public domain. It is worth stressing that, as the regulator, the MHRA does not receive all the raw	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		patient level data that results from clinical trials. This remains with the sponsor. What the MHRA does receive, in support of applications for marketing authorisations, is enough information (in the form of Clinical Study Reports) to allow a decision to be taken on the safety, efficacy and quality of a medicine. • We have carried out an exercise to establish what data the MHRA holds in relation to the EMA Annexes, and the present status of such data. This also identifies some data that MHRA as a UK regulator receives that is not held by EMA (in respect of national and decentralised procedures and inspections for example). This exercise is part of a wider programme of work carried out by the MHRA and wider Government to develop proposals for greater transparency in respect of its own data holdings. • We support the proposal for the EMA's policy to apply prospectively from 1 January 2014 and to apply only to new data submitted to the EMA on or after 1 March 2014. • We consider that several areas of definition in the draft policy need to be clarified or tightened, or set in their legal context. This applies in particular to definitions of commercially confidential and patient/personal information. We also think that the legal position on ownership of data held by sponsors and that submitted to regulators, including the EMA, and subsequently released, should be clarified, for example, how this relates to the EU wide General Data Protection Regulation being considered by the LIBE committee, which will have implications for regulators, sponsors and trialists. • We would welcome further clarification of the practical arrangements	

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		that are envisaged under the proposed policy for release of data that would fall under Category 3 and how those arrangements would apply in the case of orphan medicines, for example. • In relation to information on clinical trials (primarily Clinical Study Reports) submitted to MHRA we should emphasise i) that if the MHRA, as opposed to the Sponsor, is requested to release such information, national legislation on data protection and freedom of information also applies and ii) these data are supplied in support of requests for marketing authorisations, and do not represent the totality of clinical trials information. Therefore, we consider it important that the policy makes absolutely clear where specific responsibility lies for release of data and what requirements would apply in those cases where, for example, a national regulator is approached to release data that has been received via rapporteurship arrangements under the centralised procedure. • We are aware of concerns expressed by a number of stakeholders on some of the proposals, in particular sponsors of clinical trials and their representatives. While we remain broadly supportive of the overall drive towards transparency set out in the policy, we consider that any final policy should ideally aim to reflect a consensus across all groups involved in the clinical trials process, and not just Government and regulators. • We are aware of current legal challenges to the EMA position on disclosure of clinical trial information. We consider it is important to see what implications these cases hold for the future releases of data. A statement from the EMA on its position in the interim would be helpful.	

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148	36-49	We strongly agree with the proposition that personal data should be protected. We agree with the concern expressed that technological advances could lead to the re-identification of such data and that any policy adopted should include robust measures for the avoidance of such unlawful disclosure. The policy should say more on the status of patient data and also on the principle, of informed consent. How will the EMA satisfy itself that such consent has been sought on any data it releases. Our preference in relation to personal data would be not to release this if it has not been proven beyond doubt that the person has consented to its use.	
148	49-51	The statement in relation to commercially confidential data is over-simplified – this occurs elsewhere in the document. There may be exceptions where clinical trials data could be commercially confidential. A precise, legally underpinned definition of commercially confidential information should be included.	
148	132	A definition of 'duly justified cases' is needed in relation to CCI. This does not appear to derive either from legislation or ICH guidance	
148	165-175	The descriptions and proposals for de-identifying data could be more detailed, and include minimum standards and reference to specific methods	
148	177-218	Controlled access – there could be more specific detail in this section regarding the plans and proposals for identifying the requester, the reasons for the request, and the purposes for which the information or analysis is to be used.	
148	285	We have a number of concerns with the proposal that persons carrying out work in respect of clinical trials, such as investigators, should be exempt from PPD considerations. While we accept the view that such persons have	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		a role in public health and are acting in a professional capacity, the regulator has taken the view, in releasing data, that individual information about staff should not be released. This would be a departure from that practice, and we would need to consider it in the context of existing guidance and legislation.	
149	4	I commend the EMA on conducting an inclusive and transparent deliberative process regarding the publication and disclosure of clinical trial data. The proposed draft policy is an impressive document that sets a new standard in the transparency of clinical trial data. The introduction and purpose are particularly noteworthy and important, and the statement that clinical trial data cannot be considered commercially confidential information is a historic statement that should set a new standard for regulatory agencies worldwide.	
149	60	The document states that the Agency will put in place measure aimed at limiting the impact of inappropriate analyses, but does not say what these measures are.	Either briefly outline what the measures are or point readers to the section where they are discussed.
149	165	Is EMA planning to make available a single de-identified dataset (or sets of documents), or will multiple de-identified datasets be made available? I ask because certain types of de-identification only make sense when one knows the research question to be answered. There are multiple ways to de-identify datasets and choosing the right way depends on what research question one is trying to answer using the de-identified dataset. Presumably EMA is only intending for there to be one or a limited number of de-identified datasets available because EMA is proposing to NOT be involved in judging or reading the contents of each requestor's intended analysis.	The document should make clear the intention for how many de-identified datasets there will be, and who will do the de-identification (once the process and standards have been decided).
149	175	"subject de-identification". I think this is supposed to be "subject re-	Change "de" to "re"

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		identification"	
149	178	"fulfilled the following requirements:"	If a contract between requestors and EMA is anticipated as the form of "fulfilment", this should be explicitly stated.
149	180	The rationale for why the EMA will require requestors for 'C' data to be "established in the EU" should be stated. Otherwise it may be seen as unfairly excluding non-EU persons.	Please include rationale for limiting access to "C" data to only EU citizens
149	198	Ethics committee approval may apply differently to different requests.	I suggest the EMA ask for a statement regarding ethical board approval, allowing requestors to also say that no approval has been sought with reasons for why not.
149	297	Annex II does not include an entry for "certificate of analysis", presumably because it is not specified in ICH E3, but it is an important document that is included in many clinical study reports.	An entry for Certificate of analysis should be included and marked as "O" open access.
150	*Line 27-35*	The aim of the Agency to publish and grant access to clinical-trial (CT) data is to be endorsed. Particularly, we fully share the view expressed by the Agency in this paragraph. The uncountable value of sharing CT data will enhance their scientific value, reduce the potential for incomplete reporting of study outcomes, and improve the medical evidence base, thus clinical decision making. The purpose of our comments on this policy is to remove those obstacles that hamper the achievement of this aim.	None
150	*Line 36-43*	Standards for anonymisation or deidentification (or depersonalisation) of primary data should be recommended and implemented by the data producers. This is to minimize the possibility of re-identification.	"This is done to enable the legitimate learnings from the sharing of patient-level data while preventing rare but potentially damaging instances of patient

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		In general, a benefit-risk based approach should be applied. The potential benefits derived from the secondary analyses of patient-level data following a legitimate request and for research purpose only usually overcome the possible (small) risk of re-identification. This should be recognized and reflected in practice on the assumption that, once the personal data protection is ensured, any members of the scientific community can access CT data. It is in the interest of the patient that more and more members of the scientific community can see the data as it normally happens for the specialist consultations in the every-day clinical practice. Of course, these concepts should be anticipated in the patients' informed consent (see Comment #3, line 44-48).	identification. The Agency recognizes that the potential benefits derived from patient-level data sharing trumph the possible small risk of re-identification, provided that all reasonable efforts have been done to protect personal data at the best with the current technical standards.
150	*Line 44-48*	If it is recognized that the more the experts that can access the data the better the advantage for patients, the informed consent should not pose any boundaries in this respect but rather promote this view. Of course the Agency is not responsible for the informed consent wording. However, it can foster this position along with the clinical investigators and the patients' associations. It is up to the ethics committee not to accept boundaries that are not in the best interest of patients.	The Agency ~~takes~~ fosters the view that ~~any~~ further~~other~~ uses of patient data can contribute information in the interest of patients and this should be recognised in the ~~oversteps the boundaries of patients'~~ informed consent~~, and shall not be enabled by the policy~~.
150	*Line 49-51*	We endorse the view that CT data cannot be considered CCI. However, the proposed definition of CCI can seriously question this interpretation (see Comment #10, line 109-115).	None
150	*Line 62-66*	The legal mandate of the Agency is to be acknowledged and respected. Due to the time constrains of the decision-making process and the legal responsibility of the Agency, it is important that the evaluation of the drug	"Regulators have a legal mandate to evaluate medicines. In doing so, they should only focus on the science and the best interests of patients. The

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		dossier is independent and not exposed to pressures “in whatever direction”. This would support the proposed policy to make information on CT data available once the decision has been reached. However, it should also be recognized that one pressure exists: drug companies talk to regulators before and during the decision-making procedure; the data the Agency evaluates are those of the company; if any outstanding issues make the CHMP final opinion difficult, an hearing is allowed to the company and its advisors before the Committee; etc. There is enough material to make the decision-making process imbalanced with regard to external pressures, which would suggest that scientific community too should be granted access to the data. It is understood that the scientific community could hardly contribute to the assessment process in the time-frame allowed. However, it could at least support the Agency on specific issues. See also Comment #24, Line 219-221.	scientific community could contribute to this aim, at least on specific issues, taking into consideration the strict time-frame allowed for ~~T~~the decision-making process ~~should be protected against external pressures in whatever direction. Once a decision has been reached, this consideration no longer applies~~.”
150	*Line 67-72*	We endorse the proposed policy of ensuring that the same standard of transparency is applied to both those generating CT data and those who re-analyze them. To this aim, we do not see the reason why secondary analysis should be “protected” against external interventions. In any case, the most effective protection is transparency itself (see Comment #25, Line 222-231).	The Agency takes the view that those who make secondary use of patient-level CT data shall be held to the same standard of transparency as those who generate CT data in the first place; hence, all secondary analyses shall also be in the public domain and accessible for further scrutiny by the scientific community. ~~However, those who conduct secondary analysis should also be allowed a reasonable period of time during which their analyses and deliberations are protected against external interventions.~~
150	*Line 73-75*	We acknowledge the effort of the Agency to reconcile different stakeholders views and interests. However, once the intellectual propriety rights are preserved, we do not see any competing objectives. The sole interests are	This policy ~~These competing objectives needed to be balanced against each other when developing the policy. The 73 Agency is aware that not all~~

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		those of patients and public health, which are pursued by all the stakeholders, including pharma companies.	~~stakeholders can be fully satisfied; it has aimed at striking a compromise 74 that it deems~~ will best ensure the overarching, long-term goal of protecting and fostering public health while preserving trade secrets and patients' personal data
150	*Line 83-88*	The limitations on CT data that can be made available by the Agency are reasonable at this stage. However, in the future the Agency should collect all the information available irrespective of the sponsor, i.e., also that from independent clinical trials and rely on it for the evaluation or, most probably, the re-evaluation of the marketing authorization applications. Once available to the Agency, these data can be dealt with as the CT data submitted by the commercial sponsors, taking advantage from further development of the EudraCT registry. The Agency's Eudravigilance access policy for medicines for human use should be consistent with the policy adopted for the CT data and comply with the principles mentioned in the paragraph on the *Protection of personal data* (see Comment #2 Line 36-43)	Data from CTs that are not held by the Agency are outside the scope of this policy. However, the Agency commits to collecting (and giving access to) all the information available on medicinal products which are being or have been authorised, i.e., also that from independent clinical trials. Pharmacovigilance data based on Individual Case Safety Reports (ICSRs) are also outside the scope of the policy. ~~Access by third parties to ICSR data is addressed in the~~The Agency's 'EudraVigilance access policy for medicines for human use' (EMA/759287/2009 corr.) will be consistent with the policy on access CT data and with the principles adopted for the protection of personal data.
150	Line 108	Point B "Other personal data..." should be deleted, in line with the footnote 4 at page 9 stating that "…personal data, such as the list of investigators; individual investigators' names, addresses, appointments, […] are considered exempt from PPD considerations." We support the view expressed of in the footnote which aims at making public the information on designed personnel involved in CTs.	~~B. Other personal data, including those from e.g. experts or designated personnel involved in CTs.~~

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150	*Line 109-115*	The present definition of CCI is too broad and open to misinterpretation. For example, a negative clinical trial result may actually undermine the legitimate economic interest of the owner of the information. However, it cannot be regarded as a CCI. CCI should only be intended as the information that regards the trade secrets of the product per se, not the consequences of the use of the product. Such trade secrets should be defended via patent laws.	For the purpose of the policy, 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: 111~~ trade secrets (including formulas, programs, process or information contained or embodied in a product, etc.)~~ and commercial confidences~~. 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 (e.g., paediatric information).
150	*Line 116-117:*	It should be made clear that the submission of CT data, including patient-level data, is mandatorily included in the section 5 of the CTD. The formal check of the marketing authorization application that is routinely run before starting the dossier evaluation should ensure that those data are present.	*Clinical Study Report (CSR)*: designates the entirety of elements submitted as study reports in CTD Module 5, following the format of the ICH E3 document (see Annex II). These elements mandatorily include raw CT data.
150	Line 129-132	In light of the considerations reported in comment #10 (line 109-115) points 2.7.1, 5.3.1 and 5.3.2 of Annex I have to be intended as open (or at most controlled) access, not just as CCI.	a small number of CT data/documents can contain CCI. This only applies to ~~information such as~~ details on the manufacturing of the investigational medicinal product itself. ~~some in vitro studies, or bioanalytical data characterising the product (points 2.7.1, 5.3.1 and 5.3.2 of Annex I)~~. However, this information will only be deemed CCI in duly justified cases.

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150	Line 150-154	Comment 5 (Line 62-66) on Protecting the Agency's and the European Commission's deliberations and decision-making process and Comment #24 (Line 219-221)	All CT data/documents without PPD concerns are 'open access' (designated 'O' in Annexes I and II); such data will be available as downloads from the Agency's website, ~~at the time of publication of the European Public Assessment Report (EPAR) for positive decisions, negative decisions or withdrawals (or 30 days following withdrawal, in case no withdrawal EPAR is published).~~as soon as possible after the marketing authorisation application, provided that the data are duly anonymised and the requester has fulfilled all the requirements mentioned above.
150	Line 165-175	Comment #2 (Line 36-43) Protection of personal data (PPD)	None
150	Line 176-205	We recognize that the access to these data should be conditional upon the fulfillment of general requirements. However, in order to avoid any possible conflict of interest, we suggest that the compliance with the requirements is assessed by an independent body established at European level (Data Access Review Board), not just by the Agency itself. This Board should be independent from any stakeholders, including the Agency, and should commit to assessing potential conflicts of interests and evaluating whether the requests are legitimate and the requesters fulfill the requirements for the controlled access. The above considerations are reflected in the proposed amendments to the list of the requirements. (see comments #16 to 22 below)	None
150	Line 179		requesters have identify themselves and submitted

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			CVs and conflict of interest declarations;~~requester has identified themselves, and the Agency has verified the identity of the requester;~~
150	Line 180	There is no apparent reason to deny access to people outside EU. Development of new treatments is a global tasks and collaboration must be stimulated the most.	requester may be either ~~whether~~ a natural or legal person; , ~~is established in the EU;~~
150	Line 182-183	See also Comment #3 Line 44-48 *Respect for the boundaries of patients' informed consent*	~~access controlled data for the sole purpose of addressing a question or conducting analyses that are in the interest of public health, in line with the spirit of informed consent ; ...~~ access controlled data for the sole purpose of addressing a question or conducting analyses that are in the interest of public health, in line with the spirit of informed consent which should promote rather than prevent further use of data; this may include, inter-alia, systematic reviews, meta-analyses, re-analysis, or exploratory analyses for additional hypothesis generation.
150	Line 191-192	See also Comment #3 Line 44-48 *Respect for the boundaries of patients' informed consent*, and Comment #18 Line 182-183	~~refrain from using CT data accessed for any purposes that are deemed outside the boundaries of patients' informed consent,~~
150	Line 198	We suggest to change this point because of the following reasons: it is not clear which should be the relevant ethics committee and who should select it.	have obtained ~~ethics committee~~ approval by the *ad hoc* established Data Access Review Board, ~~as appropriate~~,

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		in many countries ethics committees are not in charge of assessing secondary analyses/re-analyses of clinical data. ethics committees are highly heterogeneous in terms of standards and procedures: the requester's choice of the ethics committee could be driven by the aim of obtaining an easier approval. Therefore, we suggest that the same independent Data Access Review Board (see Comment #15) that is in charge of assessing the request also evaluates its ethics.	
150	Line 199-200	The document explaining the Agency's views on good analysis practice should be publicly available.	be aware of standards for good analysis practice; a document describing the Agency's views on good analysis practice will be made publicly available~~to the requester~~; this is for information only,
150	Line 203-204	The reasonable period allowed to publish the results of the re-analyses can be proposed by the requester and evaluated by the Data Access Review Board, which also monitors the fulfillment of this requirement.	make all results of their analyses public within a reasonable period of time; the soundness of the timeframe proposed by the requester will be assessed by the Data Access Review Board, which also is in charge of monitoring the fulfillment of this requirement r~~a 'reasonable 203 period' would normally be considered to be one year after accessing the data,~~
150	Line 216-218	We suggest to delete these points. These aspects will be evaluated by the Data Access Review Board.	~~The Agency will NOT, at the time of allowing access to 'C' data:~~ ~~• judge the requester's professional competence to conduct analyses;~~ ~~• judge the requester's (statistical) analysis plan (if~~

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
			~~uploaded; see above).~~
150	Line 219-221	See above comment #5, Line 62-66 Protecting the Agency's and the European Commission's deliberations and decision-making process.	'C' documents ~~will be~~ may be made available as soon as possible after the marketing authorisation application, provided that the data are duly anonymised and the requester has fulfilled all the requirements mentioned above. ~~t the time of publication of the EPAR for positive decisions, negative decisions or withdrawals (or 30 days following withdrawal in case no withdrawal EPAR is published).~~
150	Line 222-231	As already mentioned in comment #6 (line 67-72), we recommend the publication of the information about the requestor as soon as the request has been accepted. This increase the transparency which in turn may prevent possible external pressure.	The Agency will ~~not~~ immediately disclose any information about the requester, ~~but will publish~~ along with the identity (name, affiliation and contact details provided), the list of the aims of accessing the data provided, and any uploaded documents (statistical analysis plan and/or others), or the requester's decision to decline to upload documents (as applicable). ~~one year after the date of accessing the data, or;~~ ~~• upon publication, in whatever format or medium, of results, conclusions, or other communications that resulted from the requester accessing 'C' data, or;~~ ~~• in case of an urgent public health need, or;~~ ~~• upon court order,~~ ~~whichever comes first.~~

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151	General	Protecting patient confidentiality How can the Agency ensure through its policy that patient and other personal information will be adequately protected, i.e. that patients cannot be retroactively identified when clinical-trial data are released, and that applicable legislation, standards, and rules regarding personal data protection will be respected?	
151	General	Clinical-trial-data formats How can the Agency ensure through its policy that clinical-trial data can be shared, in the interests of public health, in a clear and understandable format that enables appropriate analyses and a swift implementation without undue burden to stakeholders?	
151	General	Rules of engagement Are there rules or conditions that should be in place before an external stakeholder can download clinical-trial data (e.g. formal acceptance of the need to respect personal data rules, uploading of analysis plans etc.)?	
151	General	Good analysis practice Are there good-analysis-practice guidelines that the Agency could ask external requestors of data to consider or be aware of, and that the Agency can apply when confronted with additional analyses from external parties?	
151	General	Legal aspects Are there any legal aspects other than personal data protection that need to be addressed when drafting the Agency's policy? Are there exceptional circumstances under which data can be claimed to be	

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		commercially confidential?	
151	General	The Irish Patients Association does not advocate for “all” patients nor does it present itself as the voice for all patients; however it is uniquely placed, based on its deep experience of 16 years of helping patients, and or their families and those close to them to find closure in part or full of their particular experience and create a space for learning to occur. This direct contact with individual and collective patient experiences and our involvement within the health care system empowers us to contribute from the patients’ perspective in many areas of policy development, regulatory affairs, regarding patient safety, quality improvement, and community and patient involvement in policy formation and performance monitoring. We advocate with patients, their families and or next of kin. On specific cases we are led by the patient and or family or next of kin we do not push the pace, unless we uncover issues where other patients can be at risk or a patient can be at risk. Results from advocacy efforts cannot be guaranteed.	
151	General	This is not a critique of the methodology of the consultative process but merely for consideration of future dialogues. There were 221 members on the EMA forum for 5 advisory groups, on average each member participated in 1.44 forum’s. There were 3 public health organisation listed, one of these has 4 delegates bringing the total delegates to 7 for this sector; none of the public health organizations are listed as having attended the critical advisory group on Patient Confidentiality. If public health is to be the main beneficiary of this improved transparency then engagement by all stakeholders in this domain	

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		of Patient Confidentiality may better inform all stakeholders.	
151	General	Regardless of where people live, or patients are treated, one of their common needs is access to innovation to protect their health. This calls for a balanced and fair relationship with providers and facilitators of innovation with patients and society. **At a recent multi stakeholder workshop, held at the European Parliament Sep 2013, organized by the European Alliance for personalized Medicine dealing with Data Protection Regulation, I said a number of things of importance are.,** That the patient is at the center of all decision making not any of the other vested interests It is not just a one-way street, because stakeholders (patients, researchers, health-care planners, medical professionals and industry) need to get together and ensure that the right governance is in place to ensure that trust given by the patients can be guarantee. That the fragile domain of trust by patients and citizens with their health systems ad institutions of the states, within Europe is protected Quoting from a report by the Irish Council of Bio Ethics on which I was a member of **Data Management** "Ethical and data protection issues associated with the principles of autonomy and informed consent as well as the rights of privacy and confidentiality becomes fundamental considerations of Good Research Practices" **Authorship and publication** "Failing to publish the results of such research	

Stake-holder no.	General / Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		would effectively, mean that the participants were paced at risk without any benefit to arise which is unethical – It is important that information at agreed milestones is made public. **Uncovering Identity**, with the advent of cloud computing and big data management it is possible for algorithms (which some experts believe some are un-auditable) to uncover individual information. Should financial institutions get access to even anomised patient data in order to build actuarial tables to match with other mined purchasable data. Personal protections must be robust following stringent Risk Assessments, such assessments should be made public mindful of not educating hackers. Reviewing the composition of the experts and this is not a critique, we wonder if sufficient consultation with what patients need has been made. It may be of interest to consider that on occasion a specific group of patients are an equally vested interest for access to innovation and financial resources, it is important to consider that the circle of inclusivity includes cross disease advocacy. It is important that a patient centered ethical approach is within the framework of what is to be released to be shared with personkind and still protects other interest; the EMA hasing a multi-stakeholder HTA of certain difficult data releases. It will be no surprise to the EMA or Irish Health care system that we would call for patient advocates be involved in all decision that affect them or their peers. A real challenge to release data from legacy research is consent. To "assume" retrospective consent could be in conflict with new legal informed consent processes. It is therefore best practice to obtain the consent from	

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		the patient in the primary trail for release . The Bottom line is that with these much needed directives , to ensure that every patient has better access to clinical trials if they need to , that they are informed and their consent obtained, that they are informed about the outcomes, and that their privacy is protected. In the final analysis these proposals will stand or fall if the public and stakeholders have trust in the system, it calls for sound Governance to deliver the framework for trust to foster, supported by appropriate Audit of the agreed processes.	
152	16-17	The scope of this policy only covers 'data from CTs on which regulatory decisions are based'. While we note this is an important step in the right direction, this policy does only cover trials that go forward for consideration in support of the licensing process. There are therefore large numbers of trials that fall out of scope, and for which accessing data will remain a challenge. As a regulator, and as a central point for trial registry, we would consider that EMA could have a larger role to work toward transparency of trial results. BPS is keen to highlight that it is largely supportive of this initiative.	
152	39/41-2	The policy notes 'established ways and means to anonymise data and protect patients from retroactive identification' will be put into place, and that EMA have stated there will be further work in this regard (258/9 i.e. plans for a guidance document). In response to this BPS would highlight the importance of a robust approach to protecting patients and ensuring de-identification of data. There need to be clear standards in place to enable data de-identification, particularly in the case of trials on rare diseases.	
152	69-70	BPS is supportive that researchers undertaking secondary analysis are held to the same standards on openness and transparency as those submitting	

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		for licensing approval. However, we note that it is not clear how researchers should make their research public other than via publication in a journal. The secondary analyses, or links to published versions, could be held by the EMA. This would enable monitoring of adherence to the policy.	
152	81/2	Considering the issues experienced by our members of accessing information via this reactive process, there is a need for EMA to review this position and undertake to determine the feasibility of making legacy data available on the same basis as covered in this policy.	
152	112/3	BPS members are not convinced by claims that such clinical trial data does contain commercially sensitive information. We therefore look forward to the outcomes of the court cases regarding the Agency's 2010 access to documents policy and clarification of the concept of commercially confidential information. Given the position of both the EU Ombudsman and European Parliament's Committee on Environment, Public Health and Food Safety that data included in clinical trial reports should not be considered commercially confidential, BPS is cautiously optimistic that there will be strictly limited - if any - need for data to be classified under category 1.	
152	121-3	It would be useful to have access, under category 2, to SASA dataset files, coding and programming files. This will allow others to check data analysis against the analysis plan and identify any errors in SAS coding.	
152	126-7	While the different treatment of data is appropriate and proportionate, BPS consider that there also must be transparency around the process for assigning types of data to specific categories, in order that concerns about where the balance between patient confidentially and public health stands can be addressed.	

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152	132	In classing data as category 1 BPS note the EMA has stated that data will 'only be deemed CCI in duly justified cases'. This is a vague statement. While dependent on the outcome of the ongoing legal cases, we would expect that further information be provided on the criteria/justification for commercial confidentiality, and who would be taking this decision.	
152	176-218	BPS is supportive that the Agency will grant access to category 3 data once specific criteria are met; we consider it appropriate that researchers must demonstrate a valid scientific question and legally bound to ethical use of the data. Line 217 states that EMA will not judge the requester's professional competence to conduct analyses; however, BPS consider that it would be appropriate to assess those requesting the data to ensure those applicants have the knowledge and ability to manage and use the data in the public interest. In addition, we see the importance of appeals mechanisms to ensure equitable application of the access policy.	
152	236	It would be useful to provide category 2 information in Excel format, rather than PDF alone.	
152		Patients must be informed of this new process, and any updates to consent forms must follow accordingly, as patients willing to participate in trials should be confident that appropriate bodies will protect their interests.	
152		BPS members have raised concerns about the potential for charges for accessing this data. We would welcome a clear statement that the process to access category 3 data will not incur additional charges to researchers. The resource implications to EMA of putting this policy into practice will not be insignificant so there will need to be consideration of long-term funding sources.	

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153	General	InterMune would like to make clear that in general, it is comfortable with data relating to clinical trials it has sponsored being made available. However, any such disclosure must protect the fundamental rights of companies and be done within the framework of the legislation. InterMune sets out its concerns about the approach taken by the EMA in the draft policy below. In addition, InterMune notes that the landscape in this area is changing. As the Clinical Trial Advisory Group on Legal Aspects of the Draft Policy stated, there is no legal basis for introducing the proposed changes (line 288 of the Advice to the EMA); the Draft Policy does not address this issue and the basis upon which it has been determined that the point made is invalid. The draft Clinical Trials Regulation is currently being debated in the European Parliament, and although some proposed amendments are similar to the position taken in the Draft Policy, others are not, and the final wording of the Regulation is far from clear. The cases pending before the General Court relating to the recent Policy of the EMA (Policy/0043) on disclosure in relation to requests under EU freedom of information legislation will also clarify the definition of CCI and other circumstances surrounding disclosure and should be taken into account before draft Policy/0070 is finalised. InterMune believes it makes little sense to make such a sweeping – and controversial - change of policy while these cases are being decided, and the Parliament is debating relevant legislative amendments.	
153	Line 49, Line 137	The Draft Policy proceeds on the premise that “CT data cannot be considered as CCI; the interest of public health outweigh considerations of CCI”.	The Policy should include a procedure for assessing the confidentiality and the balance of any public interest in

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		Therefore, clinical study reports are categorised as “O” (Open access) – see part 5.3 of Annex I. Similarly, the draft states that, as a blanket policy, data that are not categorised as CCI in the policy “are considered to contain no CCI.” InterMune does not agree with these assertions, which conflate the question of whether the data are confidential and disclosure 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 is not in line with the true position; clinical trial data may contain confidential information, disclosure of which could harm the legitimate interests of the Marketing Authorisation Holder (MAH). Where the disclosure of documents held by an EU institution would undermine any of the interests set out in Regulation 1049/2001, the institution is obliged not to disclose them unless it has properly satisfied itself that there is a specific and compelling overriding public interest in disclosure. With respect to third party data, the institution is required to consult the third party in order to establish whether any of the interests identified in the Regulation would be undermined unless it is clear that the document should or should not be disclosed. However, the Draft Policy would mean disclosure would take place without any detailed consideration or assessment of the arguments and evidence of the confidentiality of the data, or of the damage that could be caused by their release. It would also preclude the balancing assessment which the EMA is required to conduct under Article 4.2 of Regulation 1049/2001, in order to assess whether there is, in fact, any public interest in disclosure of	disclosure in any given case.

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		the specific data which overrides the need to protect a company's legitimate commercial interests. This is particularly so in light of the publication of very detailed summaries of clinical trials and the data contained in the EPAR. Both Regulation 1049/2001 and Regulation 726/2004 require a balance to be struck between the general public interest in transparency and the protection of commercially sensitive information. Where the Draft Policy adopts general presumptions in favour of or against disclosure of categories of documents, such presumptions must not be absolute and must allow for a fact-specific balancing of rights and proportionality analysis.	
153	Line 52	We disagree with EMA's assertion that the Draft Policy protects intellectual property rights and investment by industry. The current wording of the Draft Policy disregards the need to protect know-how of companies (including trial methodologies and approaches to the analysis of data) which are associated with substantial value. This is particularly the case for orphan products, such as InterMune's product Esbriet, which is not protected by a compound patent; instead, InterMune and many companies in the same position, rely more heavily on confidential information and know-how. In these circumstances, the current version of the Draft Policy, could act as a deterrent to companies, such as InterMune, from filing applications for marketing authorisations or variations in the EU before receiving authorisations in other countries. In addition, InterMune believes that the Draft Policy should take account of the recent 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), which confirmed the importance of providing adequate protection to trade secrets (filling the gap between copyright and	

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		patent protection) as a mechanism to support innovation, competition and economic growth. The Study particularly recognised the importance of trade secrets to smaller companies, where innovations tend to be more incremental in nature and where disclosure is likely to exert a disproportionate effect on the company's value and performance.	
153	Line 132	The Draft Policy suggests that the EMA has pre-determined the categories of data that may contain CCI and that EMA's processes include no opportunity for this view to be altered on the facts of any individual case. InterMune strongly disagrees with this approach which is, in any event, inconsistent with EMA's statement that CT data may be classified as CCI in "duly justified cases". However, as currently worded the Draft Policy provides no process whereby companies may justify the confidentiality of data and explain why this should not be disclosed.	At a minimum, the policy should include a fair procedure for determining whether classification of data as CIC in any individual case, has been justified. Such a procedure should involve consultation with the marketing authorisation holder/ data owner and a mechanism for resolution of disputes.
153	Line 176	The Draft Policy identifies various categories of data, including a controlled access category, for data that contain personal information. This controlled access procedure seems reasonable, and appropriate protections are in place. It is therefore unclear why a similar arrangement should not be used in relation to CCI. Data sharing agreements could be used to allow genuine researchers access to data while ensuring that CCI was not exploited or inappropriately used by competitor organisations. InterMune refers to the proposals by EFPIA and PhRMA, which would allow controlled access to information (on the basis of undertakings of confidentiality and limited use) to third party academics and researchers (see recent protocol agreed, Principles for Responsible Clinical Trial Data Sharing, Our Commitment to Patients and Researchers (July 2013)). The Association of the British Pharmaceutical Industry ("ABPI") has	A form of controlled access should be introduced in relation to access to CCI, similar to the controlled access currently proposed for data containing personal data.

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		also recently published a “toolkit” for disclosure of information on clinical trials, including results (ABPI clinical trial disclosure toolkit, 14 August 2013). Such schemes offer a proportionate alternative to wholesale public access without any safeguards against unfair competitive use of data. In circumstances where the Draft Policy proposes such an arrangement in relation to CT data containing personal data, InterMune believes there would be no difficulty applying the same process to CCI.	
153	Line 57	InterMune also notes that the Draft Policy states that the EMA will put measures in place to ensure the protection of public health and against claims resulting from inappropriate analyses, but there are no details about how this will be done in practice. These concerns also apply in relation to data containing CCI. The regulatory data protection period in Article 14.11 Regulation 726/2004/EC (and the equivalent provision in Article 10.1 of Directive 2001/83/EC), and the steps taken by the Commission to avoid its circumvention, means that a balance has been struck between confidentiality in a data package and avoiding duplicative testing for generic products. The regulatory data protection period allows use of the data after the specified time period. However, at all times the contents of the reference product’s data package remains confidential. The Draft Policy will cut through this legislative compromise, making the data available for: (a) all commercial use within the EU within the protection period other than for marketing approval applications; (b) all uses following expiry of the protection period in the EU; and (c) all uses outside the EU from the moment of disclosure.	
153	Line 193	InterMune notes the assurance in the Draft Policy that the data-sharing agreement will specify that the requestor must “refrain from using CT data	

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		accessed to gain a marketing authorisation in a non-EU jurisdiction". However, while the Draft Policy states that the data-sharing agreement will be legally binding, it is unclear how its provisions will be enforced and what sanctions will be imposed, including in relation to requestors who do misuse CT data in non-EU jurisdictions (or researchers who pass secondary analyses of CT data to competitor organisations).	
154	Line 27-35	We support and share EMA's policy aimed at making clinical-trial data accessible to the public (information about methods and results of clinical trials) and to researchers (personal patient data) protecting patient privacy through the de-identification of personal data. Sharing and making clinical trial data accessible represents an important step towards achieving the transparency of clinical trials and contributing to the growth and progress of research. Above all, it strengthens the possibility to guarantee citizens and patients healthcare, providing data to researchers independent of those conducting the clinical trials submitted to EMA, to assess benefits and harms of the drug under evaluation. In this direction, we think that some critical points have to be re-considered.	
154	Line 109-115	The definition should be more detailed in order to avoid interpretations that could be contrary to the patients' interest: even negative results of clinical trials could be considered commercially confidential as they could damage the commercial interests of the manufacturing of the drug.	
154	Line 150	Open access information on the EMA website has to be clearly written and easily accessible also for citizens, patients and citizen or patient groups not expert in the research field.	

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154	Line 150-154; 219-221.	Open access data and controlled access data should be made available soon after the submission of the request of authorisation from the manufacturer of the drug, without waiting for EMA decisions.	
154	Line 159-162; 191-192.	It is important, as underlined by EMA policy, to guarantee patient privacy applying all the necessary methods to de-indentify patient data. Considering this as a mandatory point, and the fact that methods are available to make the risk of re-indentifying patient data very small, we think that it is very important to give access to clinical trial data, including patient data, to other researchers to carry out further analysis and studies, in the interest of patients. The informed consent should clarify this point, support the sharing of data, not restricting the use of personal data opportunely de-identified for further research studies, in the interest of patients.	
155	General	ISoP and DDMoRe support responsible data access. Providing access to patient-level clinical trial data will be a great value for the community. This will enable pharmacometricians to leverage all available data and develop models (e.g. systems pharmacology, disease progression) which are not necessarily specific to a particular drug and which link biomarkers to clinical outcomes. These models could be used to support decisions (e.g. drug development, individual patient care) as well as lead to better scientific understanding of disease and drug mechanisms.	
155	General	ISoP and DDMoRe recognize that this should be done with appropriate respect to patient privacy and commercially confidential information. ISoP and DDMoRe, representing part of the modeling community, do not believe it is in their remit to comment on those aspects of the policy.	

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155	General	ISoP and DDMoRe would like to comment on the proposed definition of “raw CT data” in order to ensure that those data will be suitable for future modeling and simulation analyses. In the interest of reproducibility, it would be important to ensure that the analysis-ready data is available, as well as the raw data.	
155	General	ISoP and DDMoRe recognize that principles of model-based approaches are nowadays widely used to inform quantitative decision making in a regulatory context. Therefore, some of the points pertaining to the provision of data and potential analyses results presented in the European Federation of Statisticians in the pharmaceutical Industry (EFSPI) response to the policy also apply when model based approaches are used by a requestor. (see proposals for lines 059-061)	
155	118	Policy should be more specific on what EMEA intends by “raw CT data” and “individual patient data sets”. In a model based context it’s important to distinguish landmark data from longitudinal data, with only the longitudinal data providing the necessary information to build drug disease models.	… raw CT data shall mean all individual longitudinal (collected over time) patient data entered in the database ~~sets~~, …
155	122-123	Policy should not be limited to mention SAS program, but all program code and related meta-data and annotations to generate raw data, derived data, and analysis datasets.	Statistical Analysis Software logs and ~~SAS statistical~~ program code used to generate the raw data files (e.g. SAS, S-plus, R if code not included in the SAP).
155	243-244	Should be more specific and mention format	…in the format in which they have been analysed by the applicant, submitted and evaluated (e.g. flat format files used by NONMEM, Monolix, Phoenix NLME, R). To make the best use of the analysis ready datasets, codes, assumptions and exclusions, if any, will also be made available in order to be able to trace

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			the analysis dataset back to the raw clinical data.
155	059-061	ISoP and DDMoRe support EMA's plan to put measures in place to protect against assertions resulting from inappropriate analyses. In our view, these measures should include: • Scientific rationale • Pre-specified model based analysis plan (defining specific research question to be addressed, analysis assumptions, model evaluation and inferences) • Qualified personnel • Independent review of the research proposal • Collaboration between the researcher and owner of the data	The measures to protect against assertions resulting from inappropriate analyses should be stated. These measures should be mandatory and not optional as in the current draft policy. It should be stated also that due to multiplicity principles any additional analyses will likely be exploratory and not confirmatory.
156	General	**PHARMIG comments on 'Policy 0070 on publication and access to clinical-trial data'** PHARMIG generally welcomes the EMA approach of more transparency in relation to clinical trial data, in particular, where it increases trust in the conduction of clinical trials and drug development process, serves the expansion of scientific knowledge, and constitutes the basis for an educated and evidence based benefit-risk advice to patients, medical staff and physicians. However, we are of the opinion that the Agency has not developed a balanced and responsible proposal between a valuable increase of transparency and the rights of the industry to have their business critical information and patients to have their private and personal data duly	

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		protected. PHARMIG therefore urges the EMA to reconsider its transparency approach in particular concerning following issues: **<u>Protection of personal data (PPD)</u>** We strongly agree with the policy statement that "protection of patient privacy is a **paramount concern when sharing raw CT data**". We therefore believe that the disclosure of patient level data needs a careful case by case assessment involving all concerned parties – including patient representatives and the MAH. Clinical trial participants must have the right to decline disclosure of their data to third parties (outside agencies, inspectors and sponsor). • The Agency itself is indicating in its draft policy concerns that emerging technologies for data mining and database linkage will increase the potential for unlawful retroactive patient identification, especially for clinical trials in rare diseases or in regions with low inhabitants' density. **Re-identification technology is advancing**, and as the agency recognizes, it would need to consider not only the clinical data themselves, but also other public information (from registries to social media) that could be combined to deduce subject identities. The policy statement that "potentially damaging instances of patient identification will be rare" is therefore very questionable. EMA has to be aware that if it will make disclosures of patient level data from its website, it will therefore be responsible and may be held liable. • We also like to point out that the exclusion of the **protection of the personal data of investigators, sponsor, and study personnel**	

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		named in submissions in the draft policy - “these personal data are considered exempt from PPD considerations” - clearly meets our disapproval. **<u>Know-how and trade secrets – referred to as commercially confidential information (CCI)</u>** It is necessary to acknowledge that clinical trial data has to be considered commercially confidential information not only in exceptional circumstances. • Disclosure of clinical trial data – including commercially confidential information - would doubtlessly **undermine and damage the interests of the proprietor of such information**. Competitors would benefit from access to this data by avoiding the investment in own experiments. Hence, broad dissemination of clinical trial data may negatively impact upon industry’s commercial opportunities in **markets outside the EU, which have no or different standards of regulatory data protection**, and may prejudice intellectual property rights. • That clinical trial data have to be considered commercially confidential information appears to be further evidenced by the fact that the **majority of requests for disclosure**, after EMAs policy on access to documents came into effect in Dec.2010, **are from pharmaceutical companies** as opposed to healthcare professionals or members of the public. • The EMA elsewhere in its draft policy recognizes this very point by stating that access to “controlled release” documents will be conditioned upon a commitment by the requestor to refrain from using the released	

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		information to gain an MA in a non-EU jurisdiction. • Finally, the perception that **clinical data may contain commercially confidential information which should be protected** from disclosure has been recently underlined by a **preliminary decision of the European Court** in two cases, clearly showing the strong legal doubts of the Court. Furthermore, EMA's unilateral decision would seriously undermine the – pending – decision-making process of the democratic and representative Union institutions in relation to the framework of clinical trials and transparency (Commission proposal for clinical trials regulation). **Therefore, a general view that clinical trial data are per se not commercially confidential information is not justified.** **<u>No per se overriding public interest in disclosure of clinical trial data</u>** It has to be taken into consideration that the publication of commercially confidential information is not generally justified by an overriding public interest in disclosure. **Publication as such does not necessarily lead to any improvement of public health.** The use of such data by competitors of the MAH can never establish an overriding public interest in the publication of these data due to its pure commercial intent. Far more, the **improvement of the conditions for research and development** of innovative medicinal products **has to be taken into account as an important public interes**t when assessing whether or not clinical trial data may be disclosed. • **Know-how and trade secrets** in the development of an innovative	

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		medicinal product are of **crucial value for the development of new medicinal products**. Without any protection of this value, essential incentives for investments in biomedical research will be cut/weakened and innovation might be impeded significantly. Clinical trials would be - even more than today - conducted in third countries in order to safeguard the innovation and the intellectual property. This **would contradict the main objective of the current Commission proposal on clinical trials** (COM(2012) 369), namely to improve the legal framework for clinical trials within the EU in order to increase the number of trials performed within the Union and to support clinical research and development. • The **European Court** also recently decided (cases T-44/13 and T-73/13) that "the question whether an overriding public interest might nevertheless justify disclosure of **CCI will call for "delicate assessment,"** in the "weighing up of the applicants' commercial interest in not having the reports disclosed and the general interest intended to guarantee the broadest public access to documents held by the European Union. " We also like to state that the **risks of misinterpretation and misuse of clinical data** by inappropriate research, which is also undermining the trust in the regulatory approval system, poses **a substantive public health concern rather than an overriding public interest.** Furthermore, disclosure of clinical trial data before marketing authorisation, within or outside the EU, could lead to inappropriate assessments and compromises application submission and evaluation. • The EMA asserts in its draft policy the implementation of the best	

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		safeguards to achieve the highest possible scientific standard, to protect public health and regulatory decisions from inappropriate secondary data analysis. We strongly believe there **could be a more controlled and responsible approach** than proposed in the Agencies draft policy. • There should **be legal obligations possible from the document on CT data-analysis standards**, which EMA is planning to include in its "controlled access" process to communicate its expectations relating to good analysis and transparency. The upload of a **statistical analysis plan has to be mandatory**, otherwise a review or challenge of secondary analysis would not be possible. Requirements with the regard to the **requester´s professional competence** or inclusion of a qualified statistician to conduct analyses need to be set up. These standards are requested from sponsors as part of an application and **should therefore be standards for requesters as well**. **Two way transparency** We fully support the need for two way transparency and equal level of scientific standard for all clinical studies, but it appears that the draft policy affords **protection for confidentiality to third party researchers inconsistently to the standards for MA applicants**. Disclosure of any information of the requester one year after the date of accessing the data or upon publication of the results of their analyses, as stated in the draft policy, clearly differs from the transparency standards of the MA applicant, who must disclose information prior to commencement. **Involvement of the MAH in the process of disclosing clinical trial data**	

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		Consequently, for a balanced, responsible and robust process the Agency has to **assess the disclosure of clinical trial data on a case-by-case basis** whether or not a disclosure of patient level data and commercially confidential data is justified and requesters meet appropriate standards. Article 4(4) of Regulation No. 1049/2001 *regarding public access to European Parliament, Council and Commission documents* stipulates that "as regards third-party documents, the institution shall consult the third party with a view to assessing whether an exception in paragraph 1 or 2 is applicable, unless it is clear that the document shall or shall not be disclosed." In this regard, **an involvement and a detailed debate with the MAH before dissemination should be compulsory to enable the Agency to consider all relevant facts and matters when reaching a decision**, especially when assessing whether or not data submitted in the authorisation process contain commercially confidential information that was previously unpublished and would be valuable in the hands of competitors. Therefore, the **consultation of the MAH before disclosure must remain mandatory** not only where third parties request access to this information but also where the information is proactively disclosed by the Agency. **<u>Principles for Responsible Clinical Trial Data Sharing</u>** Biopharmaceutical companies already publish their clinical research, collaborate with academic researchers, and share clinical trial information on public web sites at the time of patient recruitment, after marketing authorisation, and when investigational research programs have been discontinued. Building on those continuing efforts, **EFPIA and PhRMA have**	

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		recently adopted Principles for Responsible Clinical Trial Data Sharing. These set out industry's commitments to: (i) enhance data sharing with researchers; (ii) enhance public access to clinical study information; (iii) share results with patients who participate in clinical trials; (iv) certify procedures for sharing clinical trial information; and (v) reaffirm commitments to publish clinical trial results. We request that the EMA take into account the Principles for Responsible Clinical Trial Data Sharing adopted by EFPIA and PhRMA and assess the added value of its draft Policy against these broad ranging commitments. These Joint Principles **represent the consensus views of a large part of the world-wide biopharmaceutical industry**, which commits to data sharing of study level and patient level data, and protocol information with researchers, to enhance public access to clinical study information. Following approval of a new medicine or new indication for an approved medicine in the US and EU, biopharmaceutical companies will make publicly available, at a minimum, the synopses of clinical study reports (CSRs) for clinical trials in patients submitted to the Food and Drug Administration (FDA), European Medicines Agency (EMA), or national competent authorities of EU Member States', and to share results with patients who participate in clinical trials. The EFPIA/PhRMA principles include responsible controls on disclosure in order to ensure that clinical trial information released is used to conduct quality research, respecting patient privacy, and is not used inappropriately for competitive commercial purposes. **Release of clinical trial information under these principles will therefore be assured of serving the public health interest, while at the same time protecting personal data and CCI**.	