

EMA's 2013 policy on access to clinical-trial data: Transparency in the public health interest

Joint Submission of comments on 'Policy 0070 on publication and access to clinical-trial data (September 2013)

Comments from:

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Key aspects of our joint response

Despite efforts by the European Medicines Agency in its 2010 policy, there is still - at present - a lack of full public access to the body of available scientific evidence about the effects of medicines on human health. This prevents informed choice and leaves European citizens at greater risk for otherwise preventable harm.

We welcome the opportunity to contribute to the public consultation on the European Medicines Agency (EMA) draft policy on the publication and access to clinical-trial data aiming to improve the current situation (i).

“The proactive publication of data from clinical trials submitted in support of a marketing-authorisation application” proposed by the EMA represents a first and very welcomed step towards greater clinical data transparency. The annex I of the draft policy, detailing the elements relating to clinical trials contained in the common technical documents as well as their access status, indicates EMA’s commitment to proactively publish several elements from the clinical study reports (CSRs).

Nevertheless, staff resources at the EMA must be sufficient to avoid that the proactive publication of clinical study reports delays the publication of European public assessments reports (EPARs) or in the case of variations, the publication of assessment reports. Advances in transparency should be maintained and strengthened (publishing proactively and in a timely manner).

Classifying information into three categories (category 1 “may contain commercially confidential information (CCI)”; category 2 “Open access” for “data without protection of personal data (PPD) concerns”; and category 3 “controlled access” for “data with PPD concerns”) is a pragmatic approach. However, according to the current EU law (article 4.6 of Regulation No 1049/2001), any exception to disclosure should only involve the removal of specific elements of information within a document and never be applied to an entire section or certain types of documents. The “category” descriptions within the policy should therefore refer to “data” but not to “documents”.

In our response:

- We highlight that access to clinical data (efficacy and safety data) protects the public from preventable harm, and therefore call on the EMA to:
 - Retrospectively provide access to clinical-trial data to all drugs approved over the last 10 years (period 2004 to 2014) either centrally (at EMA), or via decentralised procedure or through mutual recognition (CMDh);
 - Encompass access to CT data in other EMA processes particularly into pharmacovigilance and safety issues. European public assessments reports (EPARs) should be immediately updated, particularly when a variation is prompted by a safety issue;
 - Encourage national Drug Regulatory Agencies to apply the best transparency practices, particularly when acting as rapporteur or reference member states.
- We call for a more stringent definition of “commercially confidential information”, to ensure that transparency remains the rule rather than the exception.
- We caution about the use of patient data protection as a pretext to prevent clinical data disclosure.

Comments on text

Line number(s)	Comment	Proposed changes, if any
Introduction and purpose	<p>Preamble: A consultation amidst a particularly sensitive context</p> <p>In May 2012, seizing the opportunity granted by the ongoing discussions on the European Commission's proposal for a new regulation on clinical trials, the European Parliament (ENVI Committee) made an effort to align the legislative proposal with the EMA's 2010 policy and published in its report that <i>"in general the data included in clinical-trial study reports should not be considered commercially confidential once a marketing authorisation has been granted or the decision-making process on an application for marketing authorisation has been completed (...)"</i>(2). In addition, the ENVI Committee supported EMA's commitment to transparency: <i>"the Agency continues to extend its transparency policy to proactive publication of clinical trial data for medicinal products once the decision-making process on an application for a Union-wide marketing authorisation has been completed. Those standards on transparency and access to documents should be upheld and reinforced"</i> (amendment 30 creating a new recital 20a).</p> <p>On 22 November 2012, building on its transparency efforts initiated in 2010, the EMA organized a workshop on clinical-trial data and transparency. Following that workshop, the Agency established advisory groups on different topics to inform the policy's development. These groups met between January and April 2013. Our organisations – the <i>International Society of Drug Bulletins (ISDB)</i>, the <i>Medicines in Health Forum (MiEF)</i>, and Health Action International (<i>HAI</i>) Europe – participated actively in this policy development process. Unfortunately, due to the large over-representation of the pharmaceutical industry, or third-parties working on its behalf - such as legal advisers - working group discussions mainly revolved around exceptions, rather than on the implementation of overarching principles to facilitate a policy of access to data, as foreseen by the Agency as early as 2010. The pharmaceutical industry has been fighting heavily against EMA's transparency commitments:</p> <ul style="list-style-type: none"> - In March 2013, two pharmaceutical companies, AbbVie and InterMune, supported by European and US pharmaceutical industries trade associations (EFPIA and PhRMA), brought cases against the EMA and its 2010 policy at the European Court of Justice. These court cases have led to a regression in EMA's disclosure practices (3,4); - In July 2013, EFPIA and PhRMA published their "joint principles for responsible clinical trial data" which are very insufficient (with no access to clinical study 	<p>The 24 June 2013 EMA press release mentions that the legislative proposal on the Regulation of Clinical Trials which is currently under discussion at the EU Parliament and Council and the court cases that are currently challenging the Agency's 2010 access to documents policy are likely to impact on this new draft policy.</p> <p>We encourage the European Medicines Agency to commit to the active implementation of its access to data policy in a way that ensures full access to clinical data, putting public health ahead of commercial interests. The EMA should strive towards this aim, rather than responding reactively or passively awaiting future developments.</p>

	<p>reports, demands for applications to be reviewed by a “scientific board” to be appointed by the company in question), and are unlikely to be implemented by their members.</p> <ul style="list-style-type: none"> - In addition, in July 2013, EFPIA and PhRMA have made concrete proposals for a lobbying strategy that entailed “mobilising patient groups to express concern about the risk to public health by non-scientific re-use of data”. (5) - In a recent intervention in August 2013, an Abbvie representative asserted that some adverse drug reaction data should be considered commercially confidential (6) <p>This public consultation provides another opportunity to reiterate the need for a policy of full transparency and access to clinical data – both data submitted during the marketing authorization procedure and once authorization has been granted – collated through post-marketing surveillance activities by regulatory agencies.</p>	
<p>Scope</p>	<p>1. Access to clinical data (efficacy and safety data) protects public health from preventable harm</p> <p>Public access to full clinical data, including raw data, is particularly important to protect public health as it allows for independent analysis, enhancing knowledge about the real effects of medicines and allowing comparative effectiveness reviews (7). For instance, the identification of cardiovascular risks associated with rosiglitazone (Avandia[®]) in 2007 relied mostly on unpublished data. (8) Similarly, published summary-level data, research abstracts and data submitted to the FDA were used to demonstrate an increased risk of heart attacks among rofecoxib (formerly Vioxx[®]) users.(9) In contrast, the manufacturer had re-classified fatal events in several peer-review publications. (10)</p> <p>This policy should further amplify the scope and spirit of the current policy on access to documents (Policy /0043) (11). In parallel to making all post-2014 clinical data available on the database, the EMA and the CMDh (Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human) must progressively publish all the clinical data they hold on medicines that are already on the market (12). This should be done in a timely manner. While this data is not published, access must be provided upon request in a timely manner (current regulations foresee a response timeline of 2 months for information requests and 15 days for documentation requests (with an extension possibility of another 15 days). Yet, these deadlines are often extended.</p>	<p>The scope of the proactive disclosure has to be broadened to include all clinical data held by the Agency and the CMDh on medicines which are already on the market. As a first step, to provide retrospective access to clinical-trial data part of the common technical documents provided to the EMA and the CMDh over the 10 last years (period 2004-2014).</p> <p>In order to increase the transparency of older drugs and improve patients’ safety, the harmonisation procedures coordinated by the EMA (CHMP) should be used to reassess thoroughly the harm-benefit balance (re-analysing all clinical trials results, publishing an assessment report, and publishing an harmonised package leaflet and harmonised summary of product characteristics (SPC)).</p> <p>Clarification is needed on the policy implementation and its consequences to national DRAs particularly for decentralised and mutual recognition procedures (e.g. as regards variations to extend therapeutics indications).</p>

	<p>All information made available online should be in a legible, easily usable and searchable format, so that users can retrieve it easily using key words.</p> <p>To a large extent the EMA’s activities and decision-making rely on the opinion of experts from different member states. Any divergences in the application of access to data policies should be avoided, and an alignment should take place among regulatory agencies in the EU. The priority for any medicines’ regulatory agency shall be to ensure the highest standards of medicines quality, efficacy and safety. Harmonisation of procedures amongst the EMA and national medicines agencies should apply the highest existing standard. The convergence of transparency and access to data policies must also be applied according to this principle. The best existing standards should be used as a point of reference.</p> <p>The EMA’s policy on access to data should also go beyond its current scope, and not just apply for approval of centrally approved medicines but also for other decision making process such as variations, referrals and work-sharing procedures (such as the PSUR centralised analyses)</p> <p>Moreover, the CMDh should also proactively publish data from clinical trials submitted in support of a marketing-authorisation application through the decentralised or the mutual recognition procedure.</p>	<p>Encompass access to CT data in other EMA processes, particularly in the pharmacovigilance field: add variations, referrals and pharmacovigilance data disclosure (PSURs, PSURs assessment reports, consumption data) as components of the policy (category 2 “Open access” with proactive publication).</p> <p>Moreover, the Agency’s ‘Eudravigilance access policy for medicines for human use’ (EMA/759287/2009 corr.) should be revised to include individual detailed anonymised case reports (ICRs). Detailed ICRs are needed to be able to analyse and interpret accurately the data. Eudravigilance is a centralised ‘mega-database’ where suspected adverse drug reactions (ADRs) are coded using ICH terminology (MedRA dictionary). In practice, spontaneous reports can be stripped of clinical significance, by reducing the available information by coding, resulting in the significance of the data being minimised. (13) (14)</p>
<p>Introduction and purpose Line 35 Lines 113 to 115</p>	<p>2. The EU Legislative framework governing access to documents also applies to the EMA</p> <p>The European Medicines Agency transparency requirements are defined in the European (freedom of information) Regulation (Regulation (EC) 1049/2001) adopted in 2001 (15); as well as in the medicines legislative framework (Directive 2001/83/EC as consolidated by Directive 2004/27/EC (16) and consolidated Regulation (EC) 726/2004/EC) and in Article 15 of the Treaty on the Functioning of the EU, as well as in the Charter of Fundamental Rights of the European Union (article 11).(17)</p> <p>In particular, European citizens are entitled to access any documents produced or received by European institutions, especially where an overriding public interest is at stake (article 2.3 of EC Regulation 1049/2001).</p> <p>We therefore welcome the mention that <i>“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 (...)”</i> (lines 113 to 115).</p>	<p>Align the EMA’s policy to the legislative framework and transparency requirements i.e. to Regulation (EC) 1049/2001 and, article 11 of the Charter of Fundamental Rights of the European Union and Article 15 of the Treaty on the Functioning of the EU(e.g. before the paragraph on “protection of personal data” at line 35 <i>“Protection of citizens right to freedom of information”</i> (NEW)).</p>

	<p>Since "<i>all rules concerning access to documents of the institutions should be in conformity with this Regulation[EC N°1049/2001]</i>" (Article 12 of the recital), any guidance document adopted by the EMA and/or national regulatory agencies concerning disclosure of information must abide by current regulations on access to documents.</p>	
	<p>3. Clinical data belongs to the public, not to pharmaceutical companies</p> <p>The clinical data held by medicines regulatory authorities is related mainly to clinical trials conducted under the auspices of the Declaration of Helsinki. The Declaration of Helsinki explicitly refers to the ethical obligation to disclose the results from research and insists on the completeness and accuracy of the reports (articles 30 and 33). (18)</p> <p>In fact, patients accept to put themselves at risk, taking part in clinical trials, notably in the hope that their participation will benefit society through the advancement of science. The WHO Informed Consent Form Template for Clinical Studies clearly divides benefits into: "benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question." (19)</p> <p>Yet science is hampered when data from these studies are never made public, which is often the case especially when their results do not favour the sponsor's product- "publication bias" . Since publication bias and the selective reporting of positive study results are widespread practices in biomedical research, (20) failure to make all the data available greatly diminishes the social value of research. Moreover, industry-funded research often benefits from publicly funded research bodies (access to investigators and research teams at publicly research sites; public funding for basic research through EU grants and member state funding, etc.). It is therefore more than reasonable to expect that all data from biomedical research is made publicly available.</p> <p>Granting public access to detailed clinical data, including raw data, is crucial to minimise dangerous practices of reporting bias, which overrate the benefits of a drug while underestimating its harm. (21)</p>	<p>Emphasize in the policy that clinical data is scientific data of an overriding public interest and therefore public good (and adapt CCI definition – read below).</p>

Definitions

CCI

Line 49

Lines 109-115

4. A precise and narrow definition of commercial confidentiality is needed

The policy mentions that *"In general, however, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI."* (line 49). We welcome this statement, which should also be added to the definition of commercially confidential information in order for the **EMA to fully comply with the Regulation on access to documents and the TFEU, which identifies the "protection of health and life of humans" as an overriding public interest.** (22)

Under Regulation No 1049/2001 on access to documents, **confidentiality is an exception:** *"In principle, all documents of the institutions should be accessible to the public. However, certain public and private interests should be protected by way of exceptions"* (Regulation 1049/2001, recital 11).

In general, **EMA's** default position must be that information is not commercially confidential and companies should have to prove otherwise.

A redefinition and narrowing of the notion of commercially confidential information (line 109) is essential to prevent the EMA from relying solely on the self-classification by the company of the information that may undermine the company's economic interest or competitive position (read right column).

Companies must be required to provide detailed information that shows that the release of information that they claim to be commercially confidential would truly harm their interests and that non-disclosure would not be detrimental to public health.

In light of the objectives pursued in Regulation No 1049/2001 (article 4(2)), CCI can be overturned whenever **there is an "overriding public interest in disclosure"**.

All data with a bearing on human health, notably clinical data, should be excluded from the definition of **"commercial confidentiality"**. This includes pre-clinical laboratory and animal data, pre-market clinical trial data, and post-market safety and effectiveness data, as well as the sales volume (needed to assess exposure levels in adverse drug reactions). An assessment from the European Ombudsman concerning a complaint lodged against the EMA for its refusal to disclose clinical trial data found that neither trial protocols nor clinical study reports contained CCI. (23) The same conclusion applies to another assessment concerning the disclosure of ADR reports. (24)

Redefine CCI as follow:

"(...) CCI shall mean *any* information that is not in the public domain or publicly available and where disclosure *may* is duly justified to undermine the legitimate economic interest of the *owner of the information* clinical trial sponsor during a period of time that should be specified to the requesting person. In general, CT data cannot be considered CCI; the interests of public health outweigh considerations of CCI. If only parts of a requested document contain CCI, the remaining parts of the document shall be released."

In addition, **any exception to disclosure rules should only involve the removal of specific elements of information within a document and never be applied to an entire section or certain types of documents.** As clearly stated in article 4.6 in Regulation No 1049/2001: "If only parts of the requested document are covered by any of the exceptions, the remaining parts of the document shall be released."

The Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals adopted in 18 December 2006, establishes in its article 118.2 a list of items deemed to undermine the protection of the commercial interests.²⁵ Nevertheless, should urgent action be needed to protect human health, safety and the environment, the Agency may disclose the information referred to in this paragraph.

The European Medicines Agency could envisage applying a similar positive listing, in which details of the manufacturing or the finishing process, links between a manufacturer or importer and raw material providers or distributors would be considered to be commercially confidential information.

Definitions

Personal data
Lines 36 and 102

5. Patient confidentiality should not be used as a pretext to prevent clinical data disclosure

The protection of personal data in the EU is safeguarded by Regulation (EC) 45/2001 (26) with regard to the processing of personal data by the Community institutions and by national data protection laws implementing Directive 95/46/EC. (27) EU regulations establish that clinical trial data submitted to regulatory authorities has to be anonymised. According to good clinical practice, codes are used to protect patients' identity. (28)

A recent study published in *BMJ Open* confirms that clinical study reports contain only anonymised individual data achieved by means of identification numbers and that patient confidentiality is safeguarded when this information is disclosed. (29) This is in line with previous findings from the European Ombudsman. (30) These findings show that applied de-identification methods uphold the protection of participants' data – as the EMA notes in lines 38-39 of this proposal - *"there are established ways and means to anonymise data and protect patients from retroactive identification"*.

Rephrase policy to mitigate "myths" on patient confidentiality (line 36).
Restrict the definition of "personal data" by replacing "one or more factors" by "several" and precise that "a mere hypothetical possibility to single out the individual is not enough to consider the person as identifiable".

	<p>In order to allow for re-analysis, anonymisation methods have to be applied in ways that protect patients' confidentiality while the robustness of the data is preserved. In very specific cases (rare diseases), when, after all available means, re-identification is possible, additional measures should be implemented to prevent this from occurring. Taking into account that rare diseases are often under-researched, it is all the more important to make sure that available scientific data is shared. (31)</p> <p>A mere hypothetical scenario cannot be invoked against the disclosure of anonymised patient-level data. "Unlikely to happen" events need to take into consideration the current situation, where millions of otherwise avoidable adverse drug reactions are taking place because anonymised data is not disclosed.(32)</p> <p>As noted by the EMA, established ways to anonymise participant-level data safeguard patient confidentiality (lines 38-39). In spite of this statement, the EMA goes on by referring to concerns based on hypothetical scenarios. It is important to note that the Data Protection Working Party in its Opinion 4/2007 established that: <i>"(...) a mere hypothetical possibility to single out the individual is not enough to consider the person as "identifiable". If, taking into account "all the means likely reasonably to be used by the controller or any other person", that possibility does not exist or is negligible, the person should not be considered as "identifiable", and the information would not be considered as "personal data" (...)</i>.</p>	
<p>Introduction and purpose Line 57</p>	<p>6. Claims of data misuse and misinterpretation are unfounded</p> <p>Claims that the disclosure of clinical trial data would lead to the misinterpretation of data and to the dissemination of skewed information that would scare the public reflect outdated paternalism and are not evidence-based.</p> <p>Again, proportionality in ethics has to be taken into account. There is overwhelming evidence of drug-induced harm being routinely hidden by pharmaceutical companies to the detriment of public health, while there is no example of misinterpretation of data and misuse from the last 2.5 years during which the European Medicines Agency released clinical data on request. There is no evidence of data manipulation from data sharing/open data.</p> <p>On the contrary, if data are publicly available, full scientific evaluation of any analysis is possible, and the reasons for differences between a primary and secondary analysis can be discussed openly. Open science stimulates advances in methods. Everyone is better protected against data manipulation when a climate of openness prevails.</p>	<p>Rephrase paragraph (line 57) to bear into account the proactive role of the EMA and the need to ensure robust evaluation procedures.</p>

	<p>The publication of individual-patient data has become a reality. Some authors want to promote transparency and opt to publish the individual-patient raw data along with the scientific article. This is done currently done on a voluntary basis but should ultimately apply to all clinical trials. (33)</p> <p>Rather than “addressing the consequences of inappropriate secondary data analysis” (as referred in line 57), the Agency should protect public health by making sure that new medicines being authorized into the European market have an added therapeutic value, when compared to the existing drugs, either in terms of efficacy, safety or convenience. Decisions of the EMA should be based on evidence, guided by science, in the absence of conflicts of interest, so that medicines can be adequately evaluated, and benefit public health. Access to the full evidence on which EMA decisions are based, and to the rationale that has lead to those decisions is vital.</p> <p>According to Prescrire’s analysis, the majority of new medicines (52%) entering the EU market over the last 10 years were nothing new (copies) which did not respond to unmet clinical needs. Another sixteen percent were considered unacceptable and brought nothing else but disadvantages. (34)</p>	
	<p>7. Following up the policy’s implementation and tracking progress We would strongly encourage the EMA to:</p> <ul style="list-style-type: none"> • Publish on an annual basis a report describing <ul style="list-style-type: none"> - access to clinical data requests - quantitatively and qualitatively (type of documents requested); as well as - the Agency responses to those requests, including difficulties faced; - overall rate of acceptance and refusal of access to document requests (including for those in controlled access by type of document and requesting entity – competitor company, academia/researchers, healthcare professionals, citizens) - quantitatively (numbers) and qualitatively (document types) the information deemed CCI; - the data proactively shared online by the Agency during that given year; - a list of the documents being withheld, including an abridged summary of their contents, when information is not being disclosed by the EMA . 	<p>To be added to the policy.</p>

While the disclosure of clinical trial data should be an obligation for all marketing authorisation holders, we would encourage the EMA to develop an incentive strategy and establish a Transparency Recognition system, which acknowledges the most proactive and transparent pharmaceutical companies, and highlights others with persistent shortcomings in disclosure (that unduly classify documents as CCI in order to prevent access).

Other specific comments on text

Line number(s) (e.g. 20-23)	Comment	Proposed changes, if any (If changes to the wording are suggested, they should be highlighted using 'track changes')
Use of patient data within the boundaries of patients' informed consent 47 and 192	<p>It is not clear what the Agency means by mentioning: "any other use of patient data oversteps the boundaries of patients' informed consent". What are the other uses beyond public scrutiny and secondary analysis that would not be contemplated?</p> <p>Sometimes patients' informed consent procedures are not concrete enough in delimiting those boundaries. Moreover, pharmaceutical companies could add restrictive statements in the informed consent forms to avoid secondary analysis of CTs.</p> <p>A reference should be made to the Helsinki Declaration.</p>	<p>Line 47: Provide list of other uses. Clarification is needed.</p> <p>Line 192: Add reference to the Helsinki Declaration.</p>
CCI definition: Trade secrets 112	<p>According to the European Ombudsman (decision 2560/2007/BEH) neither study protocols nor clinical study reports can be classified as trade secrets and/or commercial confidences. A medicine's qualitative and quantitative composition cannot be considered a trade secret (this principle should apply to excipients). Back in 1926 in France, medicines were granted the status of industrial pharmaceutical products only if their chemical components were included in the label. Further clarification is needed on what the Agency would consider to be a "formula".</p>	<p>Clarification is needed, rewording.</p>
Access to information classified as category 1 133	<p>"If a document is deemed to contain CCI, it will not be made available under the policy."</p> <p>According to the current regulation, any exception to disclosure should only involve the removal of specific elements of information within a document (for example when individual privacy protection is required) and never be applied to an entire section or certain types of documents.</p> <p>As clearly stated in article 4.6 in Regulation No 1049/2001: "<i>If only parts of the requested document are covered by any of the exceptions, the remaining parts of the document shall be released.</i>"</p>	<p>Clarification is needed, rewording as follows: "If a document an information is deemed to contain CCI, it will not be made available under the policy."</p>
Category 2 150	<p>It is important that proactive access to clinical trial data and related documents does not impair the timely access to the European Public Assessment Reports and their updates. All disclosed data needs to be easily accessible by the general public.</p>	
Category 3 161	<p>The proactive publication of duly anonymised raw data following established anonymisation methods must be the rule, as it does not compromise patient confidentiality.</p>	<p>Not consistent with EMA's statement in lines 38-39</p>

Category 3 179	How will the EMA verify the identity of the requester? Which means will be used?	Clarification is needed.
Category 3 184	Public scrutiny should be added to the list.	Add public scrutiny.
Category 3 198	"...have obtained ethics-committee approval, as appropriate". This requires further clarification, since it not clear whether the appropriateness will be deemed necessary by the EMA or by the requester.	Clarification needed.
Category 3 "destroy CT data accessed" 205	This sentence should be deleted. There is no rationale in asking for the accessed CT data to be destroyed. First, because duly anonymised raw data does not jeopardise patients' confidentiality. Second, requesters are committed to act in good conduct, following the provisions set up by the EMA (lines 182-204) Third, it is against good scientific practice to destroy the material on which assumptions are based. In addition, these data might still be relevant for research purposes long after they have been released (follow up studies, etc.).	Delete sentence.
4.2. Data standards 242	Delete "wherever possible". The use of this terminology opens the door to interpretation and can be abused.	Delete "wherever possible".
Making available of category 3 ("C" data) 256	According to EU regulations, data submitted to regulatory authorities for marketing authorisation is submitted in non-identifiable form. Currently applied anonymisation methods safeguard patient confidentiality. Only in very specific cases (e.g., rare diseases) additional measures might be required to prevent re-identification. Nevertheless, this might only be necessary in very limited cases.	There is a problem with the whole paragraph, as it refers to an administrative burden that in general does not exist.
Annex 1 5.3.1 Reports of Biopharmaceutic Studies 5.3.2 Reports of Studies pertinent to pharmacokinetics using human biomaterials	There is no public health rationale in withholding this information. At best, 5.3.1.4. "Reports of bioanalytical and analytical methods for Human studies" could be considered "may contain commercially confidential information". All the other points are very relevant to the protection of public health (information on bioavailability, biokinetics, drug interactions, etc.) and as such, there is an overriding public interest in disclosure. The EMA has to comply with Regulation 1049/2001 on access to documents and apply the exception of commercial confidentiality restrictively. The access to documents request by one of the ISDB members when conducting a study on the interaction of Clopidogrel and proton-pump inhibitors is a good example. This request resulted in a complaint to the EU Ombudsman and eventually all the documents received from the EMA after the complaint contained no commercially confidential information.	Replace CCI by O.
Annex 2	Provided that the data is duly anonymised, there is no rationale to justify not	Replace C by O.

16.2 Patient Data Listings	making that information publicly accessible.	
Annex 2 16.3 Case Report Forms	Provided that the data is duly anonymised, there is no rationale to justify not making this information publicly accessible.	Replace C by O.
Annex 2 16.4 Case Report Forms	Provided that the data is duly anonymised, there is no rationale to justify not making this information publicly accessible.	Replace C by O.
Annex VI Listing of Patients and Observations excluded from Efficacy Analysis	Provided that the data is duly anonymised, there is no rationale to justify not making this information should publicly accessible.	Replace C by O.

References and notes:

¹- European Medicines Agency. *Publication and access to clinical-trial data. Draft for public consultation*. Policy/0070. Released 24 June 2013. Accessed on 1 August at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf

²- European Parliament ENVI Committee "Report on the proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (COM(2012)0369 – C7-0194/2012 – 2012/0192(COD)). 10 June 2013. Accessed on 7 August 2013 at: <http://www.europarl.europa.eu/sides/getDoc.do?type=REPORT&mode=XML&reference=A7-2013-208&language=EN>

³- Dyer C "European drug agency's attempts to improve transparency stalled by legal action from two US drug companies" *BMJ* 2013; 346:f3588.

⁴- Prescrire Editorial Staff "The European Medicines Agency refusing access to administrative documents: Prescrire denounces an unacceptable retrogression" Letter to the Director of the European Medicines Agency ; June 2013. english.prescrire.org/en/79/207/46302/2781/2506/SubReportDetails.aspx

⁵- Sample I "Big pharma mobilising patients in battle over drugs trials data - Leaked memo from industry bodies reveals strategy to combat calls by regulators to force companies to publish results" *The Guardian*, Sunday 21 July 2013.

⁶- Hawkes N "Industry and Drug regulators disagree on which data should remain confidential" *BMJ* 2013 ; 347: f5390.

⁷- Tucker M "How should clinical trial data be shared?" *BMJ* 2013; 347 doi: <http://dx.doi.org/10.1136/bmj.f4465>

⁸- Nissen SE et coll "Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes". *NEJM* 2007; 356: 2457-71.

⁹- Jüni P et al "Risk of cardiovascular events and rofecoxib: cumulative meta-analysis" *Lancet* 2004; 364 : 2021-2029.

¹⁰- Egilman DS, Presler AH "Missing Safety Data and Merck-y Ethics in the ADVANTAGE trial" *Ann Int Med*. 3 Aug 2005.

¹¹- European Medicines Agency "European Medicines Agency Policy on access to documents (related to medicinal products for human and veterinary use) Policy /0043 of 30 November 2010. Accessed on 7 August 2013 at: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2010/11/WC500099473.pdf

¹²- "All trials Campaign: All Trials Registered | All Results Reported" <http://www.alltrials.net/>

¹³- Prescrire Editorial Staff "Patient reporting improves pharmacovigilance" *Prescrire International* 2008 ; 17 (98) : 241-242.

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- ¹⁴ - ISDB & MIEF *"Pharmacovigilance in Europe: the European Commission's proposals endanger the population"* Joint analysis; October 2009.
- ¹⁵ - Article 73 of Regulation (EC) 726/2004 foresees that Regulation (EC) 1049/2001 applies to EMEA.
- ¹⁶ - "Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use" Consolidated version dated 30 December 2009.
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