Advice to the European Medicines Agency on rules of engagement for accessing clinical trial data

Draft – ~~27 February~~05 March 2013 - Version ~~5~~6.0 ~~(versions 2.0 to 4.0 internal drafts)~~

Preliminary comment:

EMA should only disclose confidential commercial information from non-clinical and clinical study reports and patient level data when there is an overriding public interest reason for doing so, under conditions which serve that interest. The EMA should always consult with the marketing authorisation holder (MAH) prior to disclosure, to allow the MAH to take any necessary steps to protect against unfair competition and/ or prejudice to regulatory data protection, patent or other IP rights.

Although the situations would be rare (perhaps when working with a new therapeutic class or a rare disease) it is not impossible that eCTDs and CSRs would contain competitively valuable information. The sorts of information (with historical examples that are no longer competitively sensitive) are:

- Methods to pursue newly vaidated / devised endpoints that are persuasive to regulators:

  e.g., the suite of validated measurements for assessing the effects of migraine on the whole body in support of the first approval of the prototypical 5HT1B/1D agonist sumatriptan p.o. and s.c.

- Identification of investigators that recruit well, especially for rare diseases / difficult patient populations:

  e.g., those with sufficient patients to support a clinical trial in cluster headache as a new indication for s.c. sumatriptan

- A novel trial design, streamlining and making more economical the proof of efficacy for an acutely acting compound: e.g., Armitage (adaptive) design that was novel and supported the approval of i.v. dantrolene

Note from EMA: stakeholders are invited to present ~~at next CTAG3 meeting~~additional concrete (historic?) examples and case scenarios how confidential commercial information from CSRs could be used for unfair competition and/ or prejudice to regulatory data protection, patent or other IP rights and what 'necessary steps' might be required. (See also comment under section3)

What steps will a requester have to go through before being able to access clinical trial data from the EMA website? After accessing the dedicated domain of the EMA website:

1. Should requesters have to identify themselves?

It is useful to distinguish between access to (1) aggregate data (e.g. lists of studies conducted, ICH compliant clinical study reports including the study protocol, statistical analysis plan and other

appendices, but excluding patient level data) and (2) patient-level data (e.g. individual case record forms, SAS files with line listings).

1. Aggregate data: No agreement was reached. The following positions were discussed:

    a. There is no convincing rationale that identification of requesters could or should be required. Such data should be accessible freely (similar to EPAR information today). It is assumed that aggregate data contains no personal data.

    b. In the interest of transparency, requesters should be identified, logged and their identity made public, primarily to ensure patient confidentiality is not compromised and to avoid the misuse of patient level data by third parties with commercial interests that are not related to healthcare research. Requesters of clinical trial data should also have sufficient qualifications and experience for any subsequent analysis of data obtained from clinical trials, as aligned with ICH-E9 and 'statistical principles for clinical trials'. Also, in order for any analysis of data obtained from clinical trials, there should be a legitimate scientific question being proposed in order for the request for data access to be considered. Requesters should not only identify themselves, but they should also provide details of their qualifications and experience which supports they are sufficiently educated and trained to implement any subsequent analysis of the data being requested. This information should be made transparent by the requester at the time of seeking access to data.

NOTE from EMA: such proposals may not be compatible with the legal framework under which EMA operates as a public body; to be discussed at upcoming CTAG3 meeting

2. Patient-level data: No agreement was reached. The following positions were discussed:

    a. These data should be freely accessible <u>without</u> the need for identification. Arguments in favour of this position include (not in order of importance):

        i. Lowering the hurdle for patients who wish to access data related to their own disease;

        ii. Proper verification of identity of the requester is near-impossible;

        iii. If the data are used for illegal actions such as illegitimate commercial use, there are legal actions which can be taken against the firm/country benefiting from the illegal action. Thus, this point should not be an argument to force requester-identification. Furthermore, if someone wishes the data for illegal action, he will surely and easily use a wrong identification or could only ask others to also request data in order to increase the number of suspects;

        iv. Any patient-level data that EMA makes available will be de-identified/anonymised, therefore the risk of retro-active patient identification is considered acceptably low, and the patient data protection is not an issue (it is argued that there is even no need to distinguish between aggregate data and patient level data). Therefore, there is no need to verify the identity of the requester (*Note: reference is made to CTAG1, which is discussing standards for de-identification/anonymisation to ensure patient data protection*);

v. There are cases of harassment by pharmaceutical industry when a physician declared an adverse event to an agency (example: Dr Chiche in Marseilles about the Mediator story). If the name of the requesters is given to EMA, how will EMA make sure that the name of the requester will not be known by the Marketing Authorisation Holder? In case of harassment linked to a data request, what would be EMA's responsibility?

vi. The privacy of study participants is important and their privacy should be warranted. On the other hand, the privacy should also be warranted for study participants, patients or other (EU) citizens who like to access patient-level data for their own private use. Namely, publication of their name on the internet involves the risk of unintended use of the personal data of this person, especially if this information can be detected by search engines such as Google. For example, the information (name + type of medication) may be detected during a background search performed for a job application; the information can be used by insurance companies; or the information can be used for direct marketing for registered or falsified medicines, including spamming. This is an argument to carefully consider whether the benefits of publication of the names of private persons outweigh the risks of unintended use and breach of privacy of those who access data. Thus, benefits of publication of the names of those who access patient level data may not outweigh the risks, because publication of personal data in combination with (type of) medicines for which data have been accessed creates the possibility for unintended and undesirable use of personal data;

vii. As data would be anonymous there is no sensitive data. Retrospective patient identification cannot be prevented by verifying the identity of the requester, nor can any violator necessarily be identified through such knowledge as there will usually be no conclusive link between the violation and the requester. We should keep in mind article 6.1. b and c. in directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Pursuant to this article collection of data must be adequate, relevant and not excessive in relation to the purposes. Registering the requester is also processing of personal data and should only be done for legitimate reasons and should not be excessive in relation to the purpose.

b. These data should be freely accessible only after verification of the identity of the requester. Arguments in favour of this position include (not in order of importance):

i. Patient-level data is too sensitive to allow anonymous requesters to access because the risk of retrospective patient identification is never zero. The legal liability associated with the release of the patient data from a data privacy perspective needs to be considered. There is reference to the risk of retro-active patient identification being "acceptably low", yet that still presents a risk to patient identification. Legal accountability needs to be

addressed if a patient is in fact identified and this is used improperly against an individual patient;

ii. The level of de-identification required to render patient-level data suitable for open public access is likely to seriously compromise the utility of that data for the purpose of research in the interest of public health. Much of the value of analysis of patient-level data over aggregate data is the ability to link and take account of patient characteristics in analyses. For example, if age and gender were to be removed from the dataset, it would not be possible to investigate possible treatment interactions with these characteristics or with these in combination with other characteristics that remain in the dataset. If dates are removed this reduces scope for scrutiny and (unless replaced with a series of derived times from event to event) precludes time to event analyses. This would mean, for example, that survival analyses in cancer trials would not be possible. This is an important consideration for individual participant data systematic (IPD) reviews and meta-analyses. Re-consider whether tiered access is feasible. Open public access for all documentation including clinical study reports, results, and aggregate data. Access to IPD restricted to being for the purpose of research in the interest of public heath - as demonstrated by provision of a protocol or research plan, disclosure of investigator name and affiliation and declaration of any potential conflict of interest (preferably at the point of release of data, but delayed if necessary);

iii. Strict assurances about the specific use of personal data are given as part of the consent process to trial entry; they do not include release except under strict rules. Release of individual patient data, even anonymised, contravenes the information provided as part of the consent process, and thereby infringes human rights.

iv. There is a risk of illegitimate commercial use of patient-level data (please refer to **point 3**). To mitigate this risk the identity of the requester must be verified;

v. The identity of the requester should be available and public. It is widely accepted in science that people have to disclose their financial interest. This principle should be applied here as well;

vi. The objective is clearly to restore trust in the system, not to create an all-purpose research tool. Patient data is not to be diverted to research purposes for which it was never intended or to "data mining", be it academic or commercial. Such misuse could otherwise lead to false claims of efficacy and safety of medicines. The EMA has previously stated the objective is to "(...) enable the independent re-analysis of the evidence used by the Agency's committees to determine their benefits and risks and is expected to lead to public-health benefits." The access process should be developed with this public health principle in mind;

~~vi.~~vii. There is also a risk of other unintended consequences: Some requesters may present out-of-context results that would lead to false impressions of

drug safety issues and lead to unfounded health scares (e.g. http://www.biomedcentral.com/1471-2458/2/6)

c. For access, a hierarchy for different user groups should be foreseen with access to different types of data. For the EMA pharmacovigilance database, such an access policy already exists. (EMA/759287/2009 corr., EudraVigilance access policy for medicines for human use) This paper is adopted after consultation with the Patients' and Consumers' Working Party and consultation with the Health Care Professional Working Group. The paper defines 4 types of stakeholder groups:

- Medicines Regulatory Authorities, the European Commission and the Agency (hereafter referred to as Stakeholder Group I)
- Healthcare Professionals and the General Public (hereafter referred to as Stakeholder Group II)
- Marketing Authorisation Holders and Sponsors of Clinical Trials (hereafter referred to as Stakeholder Group III)
- Research Organisations (hereafter referred to as Stakeholder Group IV)

There is a need to modify the categories according to an optional user identification process, granting access to e.g. patient level after authorisation. This would also allow for the processes discussed under topics 3, 4 and 6, setting reminders or making registered users aware of possible consequences after misuse.

2. Should requesters be required to 'Agree' to respect personal data protection?

It is agreed that this point is only relevant for patient-level data.

It is agreed that any requirement for the requester to actively agree to respect personal data protection would depend on whether the identity of the requester can be/has been verified. (No agreement was reached on that point, see above)

If the identity of the requester has not been verified (two positions):

a) Without requester identification, such `agreement` to respect personal data protection is only for information, but cannot be legally binding. As far as CTAG1 rules for patient data anonymisation are applied and effective, respect of personal data protection mainly forbids linking the data obtained from EMA with other databases/information.

b) Even if the identity of a requester cannot be verified, a disclaimer about the need for personal data protection should be "read and accepted" by the requester.

If the identity of the requester has been verified:

Should it be/have been possible to verify the identity of the requester, and the requester actively agrees to respect personal data protection, any violation of this agreement should be legally enforceable.

Requesters have to be made aware of EU and local data protection regulations. Ticking a box implies a contractual relationship between the requester and the database owner/holder of the data. However, in that case both contractual parties need to be fully identifiable. A contractual but

not necessarily public "digital" agreement appears to be preferable compared to a purely anonymous process.

Details of a contractual agreement should clarify that if any individuals are provided access to clinical trial data, then the holders of the data cannot be held accountable in any way for what the requesters subsequently do with the data; any re-analysis of the data is at the responsibility of the requester. If subsequent issues are found with respect to an incorrect re-analysis, misuse of the data for purposes outside of the research proposal originally specified, or any potential fraudulent behaviour, the original owner of the source data cannot be held accountable in any way.

3. Should the requester be required to 'Agree' to refrain from unintended commercial uses of information retrieved?

There is general agreement that EMA's policy on Access to clinical trial data should further the interest of public health, but should not abet usage of data for unintended commercial uses (e.g. obtaining a marketing authorisation in a third, non-EU, jurisdiction). EMA's policy should attempt to mitigate this risk without compromising transparency. The option of requiring anonymous data requesters to tick a 'read and accepted' tick box is considered ineffectual.

No agreement was reached on the following point (two positions):

a) The requester should be required to sign a legally binding agreement affirming that the information and data will only be used for the agreed public health research purpose and not for any commercial use. Requests for patient level data from requesters to the EMA must be handled on a case-by-case basis, and follow consistent criteria to establish if and how the information provided will be used for valid scientific purposes and to benefit patients.

b) It is unclear which situations we are talking about and "unintended commercial uses" may be used as a "killer argument". For example, if industry fears that one cannot exclude that a full CSR may be used for obtaining a marketing authorisation in a non-EU jurisdiction, this may prevent full transparency. Some real-life examples of "unintended commercial uses" should be given during the next CTAG3 session.

4. Should the requester be made aware of quality standards for additional / secondary analyses?

No agreement was reached on this point (two positions):

a) It is emphasised that advising requesters of quality standards for additional secondary analyses should not and cannot impose any obligations on the requester. (*Note: Reference is made to the work of CTAG4).*

   The use of such advice is questioned. This may discourage non-professional users from downloading and using such data. There is no benefit from such advice but it may mean a subjective additional hurdle to lay groups/patients.

b) The requester should be advised of quality standards for additional secondary analyses. The same standards must be applied equally to the requester as would be applied to the MAH. It is emphasised that such advice should imply clear obligations on the requester.

5. Should the requester have to declare whether they wish to upload a protocol / analysis plan?

There is agreement that good scientific practise requires those who wish to engage in secondary data analysis to complete and submit a study protocol before accessing the data. Therefore, the opportunity (but not obligation) to upload a protocol on an EMA managed repository is welcomed. There was no consensus as to the time of publication of such uploaded protocols. Options discussed were:

a) Immediately after uploading the protocol

b) After a fixed time span (e.g. 1 month, 1 year?)

c) Around the time of publication of the results of secondary analysis

d) Timing of publication decided by requester

Several comments/views along the following lines were expressed:

A requester should have to submit a protocol or analysis plan before being granted access to the data as this enables full transparency of the purpose and intention for requesting access to the data and this helps to minimise any misuse by third parties. In order to ensure there is a legitimate research question(s) being proposed, pre-specifying the clinical hypotheses to be investigated ensures the scientific credibility of the research to be undertaken.

Provision of a protocol demonstrating good research methods, fair use of data and the purpose to which it will be put seems an entirely reasonable exchange for access to data. There seems to be a danger of introducing double standards with requirement for access to clinical trial protocols and clinical trial data, but not to protocols for subsequent use. For IPD, make provision of a protocol (with delayed public access if necessary) a prerequisite for access to or release of data. A link to a formally published protocol would be acceptable.

Therefore the protocol must be reviewed before the patient level data is provided.

NOTE from EMA: such proposals may not be compatible with the legal framework under which EMA operates as a public body; to be discussed at upcoming CTAG3 meeting

6. Should requesters be allowed to share accessed data?

It was agreed that this ~~is a moot point~~would become uncontrollable in case identification of the requester is not verifiable.

No agreement was reached on the following point of sharing data (two positions):

a) Should it be/have been possible to verify the identity of the requester, EMA may consider restricting data sharing. However, in such case any third party would have to be given access to the same data as the first requester directly from the EMA.

b) Requesters should not be allowed to share accessed data because that way the validity of the dataset cannot be controlled. Requesters should need to explicitly confirm that they will not forward the downloaded original dataset to third parties. It is acknowledged that others must be able to repeat research findings; that is a basic principle of research. However, such groups would then have to identify themselves separately before accessing the same data.

7. How should EMA's policy be rolled out (timelines)?

There was brief discussion as to whether the policy should be rolled out in a staggered way, starting with high-level (aggregated) data, followed by more granular (patient-level) data sets. No conclusion was reached (three positions).

a) If the name of the requester is not needed for aggregated data, then most points do not need further discussion. A staggered roll-out should not delay implementation of the rules to make data publicly available.

   There is no obvious benefit and no reason to use a staggered way other than limited capacity. Hence, there is no reason to postpone access to patient-level data

b) A staggered roll-out would be preferable as there are already many challenges to opening up access to aggregated data which need to be solved. Aligning with the roll-out of the EudraCT version 9 and access to results for many clinical trials could be an important step forward.

c) A staggered approach would be pragmatic and could achieve much almost immediately. There are many issues around the release of IPD, particularly around open public access versus some model of conditional access. If this could be set aside for now with focus on release of aggregate data and results of all statistical analyses as set out in the trial protocol, rapid progress could be made. Access to IPD could follow after sufficient time for discussion and enquiry. For example, potential impact of public release of IPD on participant consent needs to be investigated. Therefore, separate the issues of (1) release and access to trial information, results and aggregate data from (2) release and access to IPD, and move ahead immediately with 1. Do not delay implementation of 1 while 2 is addressed (it is much more complex and requires careful consideration). Extend the time period to allow proper consideration and investigation of issues pertaining to 2.

8. Should requesters be encouraged to provide feedback?

There is agreement that users of data should be encouraged to link back the results of their analyses to the accessed data in order to ensure two-way transparency.

While a link back of results of individual analyses is desirable, it should be located on a separate database in order to not increase subjective hurdles to lay people. This database should/could be linked to the database of analysis plans/protocols.

It may also be useful to add a user/log-in concept to the repository to allow requesters to build project websites. These project websites would give requesters the opportunity to publish timelines, the protocol and the results of their project (or links to such documents).

Several comments/views along the following lines were expressed:

- Just encouraging requesters to link their analyses back to the data accessed is not sufficient. Further discussion is needed on how any resulting publications arising from secondary analyses are linked back to data access requests. Principles should be included on minimal expectations of requesters and what should be fed back having been granted access to data. For example, should the requester have to summarise their key findings of their analyses as a minimum?

- On the assumption that access to anonymised patient level data is granted for a defined research project, access to a secure area should be granted for a defined duration (the duration necessary to complete the project). An open-ended access (beyond the research project) would undermine the benefits of identification and declaration of research purposes. NOTE from EMA: such proposals may not be compatible with the legal framework under which EMA operates as a public body; to be discussed at upcoming CTAG3 meeting

- Requesters should be given a time frame within which they are obliged to publish/make public any outcomes and conclusions resulting from their analyses.

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Line	Comment and Changes proposed	Name	Affiliation
6	Lines 6-8. The first sentence of the preliminary comment discusses whether EMA should disclose confidential commercial information. I do not understand the relevance to CTAG3. This seems more of an issue for CTAG2. Proposed change (if any): Remove sentence from document.	Peter Doshi	Johns Hopkins
8	Delete would make access nearly impossible, or you inform and the answer has to be in 2 working days...which also would not make sense. Proposed change (if any): "The EMA should always consult..."	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
8	EMA consultations to MAH shouldn't imply long delays in releasing data.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
8	Lines 8-11. The comment that "EMA should always consult with the marketing authorisation holder (MAH) prior to disclosure" may introduce delays that detract from the concept of "proactive" dislcosure. Whether not a particular material can be disclosed, and under what terms, should be decided prior to readying materials for disclosure, and is probably more appropriate for CTAG2. Proposed change (if any): Remove sentence from document as this seems to be an issue of what can be disclosured (CTAG2) rather than the rules of engagement.	Peter Doshi	Johns Hopkins
12	CTD and CSR will be available once the product has been approved. At this time, the good results for the product will quite surely be published soon. Furthermore, if the new method, endpoint... is an argument for the approval, it should be made publicly available in the EPAR and properly described in any guideline applying to the evaluation of products in the indication.	Alexis Clapin	a2m2
12	Even if a competitively valuable information was found interesting not to release (concrete cases must be listed), open access should be restricted ONLY for this sensitive part of the CSR.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service

12	I do not personally believe that these examples should nowadays be legitimate examples of commercial sensitivity. At the time these drugs were being developed, they may have been thought to be legitimate examples simply because of the way drug development was done then. But a major point of this whole debate is that we're meant to be moving on to a new way of acting for the public good. Today I would regard them as being examples that overall make clinical development more efficient and as such should be shared. Any alleged commercial sensitivity resides therefore in the effect of EMA's intent to release clinical trial data on products that rely on data protection laws to prevent generic competition in other territories. Companies have fairly been asked repeatedly, to cite historical product examples where, had EMA done so, these consequences could have had a high risk of occurring. The EMA also asked about the degree to which there is industry "buy-in" for the move towards greater transparency around clinical data release. As we all know this topic is complex, with many diverse beliefs and prejudices exhibited by participants in the debate. Confusion and differences of opinion can arise simply by the inclusion or exclusion of a single word in a sentence! From an industry perspective, there is a vastly heterogeneous make up, coupled with years and years of historical operation on a largely closed basis to contend with. This predicates that some will "get" the point of greater openness far quicker than others. It's therefore imperative that in order to get the most accurate answer to your question, it is phrased in as precise and detailed a way as possible, and that all companies hear the same question. Please can EMA articulate the desired question in this way and I'm sure all industry reps on the group would be happy to do their best to provide a granular answer.	Mark Edwards	R&D Director, EMIG
12	Lines 12-25. Most of this section is not applicable to CTAG3. But the materials is useful in that it lists the types of information that may be perceived as being "competitively sensitive". Third-party requestors may need some of these to carry out proper re-analysis and verification of results, such as trial protocols, but may not necessarily need all of them (e.g. identification of investigators that recruit well). Proposed change (if any): If this section will remain in this document even though it seems more of a CTAG2 issue, a comment should be added that certain elements may contain valuable information that is nonetheless necessary to share to enable third-party re-analysis, while other elements may not fall into this category.	Peter Doshi	Johns Hopkins
12	This paragraph introduces some examples for confidential commercial information (CCI). However, the term CCI is not used in this paragraph. Instead, the term „competitively valuable information“ is used. I do not agree with the implicit statement, that every competitively valuable information is confidential commercial information. For example, a negative study result is obviously a competitevely valuable information, but this should not make it confidential commercial information. I propose to add that study methods and study results are never confidential commercial information. Proposed change (if any): change line 13/14 to "…would contain confidential commercial information (CCI). However, neither study results nor study methods are CCI. The sorts…"	Thomas Kaiser	IQWiG

13	The text could be enhanced, without altering the meaning, as follows: Proposed change (if any): Suggest changing the wording from "....it is not impossible that eCTDs and CSRs...." to "...it is possible that eCTDs and CSRs...."	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
16	This example is about study methods. Study methods should never be CCI. The information is essential for the interpretation of the study results and should be available for the public. EMA's policy will ensure that this will be done only after a decision about marketing authorisation has been made. Proposed change (if any): delete lines 16-18	Thomas Kaiser	IQWiG
17	EFPIA deems that reference to a specific product is not obligatory to the statement at hand and is not consistent with the high level approach used throughout the document. Proposed change (if any): Remove lines 17-18	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
19	Information on good investigators in CTD and CRS will be also for most of it available in the publications. In CTD and CRS, this information will be available at least two years after the end of the study. Trialists will be the main key opinion leaders and be wellknown from competitors. The competitors will probably not wait for this information to start their trials and will easily know who is a specialist of the disease when they start the development of the product (everyday job in the pharmaceutical industry = find good friends and prescription sources !). Furthermore, in case of rare diseases, competitors will also have to evaluate is the good recruiters have dried up their pool of naive patients or not. To conclude, the information is not such a "scoop" and remains to be checked by competitors.	Alexis Clapin	a2m2
19	This is not a good example: Identification of investigators should always be public in order to make clear conflicts of interest between MAH and professionals.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
21	EFPIA deems that reference to a specific product is not obligatory to the statement at hand and is not consistent with the high level approach used throughout the document. Proposed change (if any): Remove lines 21-22	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
23	See line 12 : if the new method provides regulators with an argument to approve the product, it should be made public. Could we have some more information about this case as Armitage publications on sequential trials seems to have occured prior to dantrolene approval.	Alexis Clapin	a2m2
23	This example is also about study methods (see previous comment). Proposed change (if any): delete lines 23-25	Thomas Kaiser	IQWiG

26	CSRs may contain information on bio-analytical product-characterization methods which are the intellectual property of the MAH - public disclosure could be an infringement of the MAH's IP rights. Furthermore, the use of some specific analytical tests described in the CSR can provide information indicative of the active product substance/molecule that can therefore be identified and used by competitor companies (e.g. tests on molecule-specific epitopes providing information allowing identification of the commercial confidential molecule). Proposed change (if any): - Analytical tests described in the CSR can provide information indicative of the active product substance/molecule that can therefore be identified and used by competitors (e.g. tests on molecule-specific epitopes providing information allowing identification of the commercial confidential molecule)	Borislava Pavlova	Pharmig
26	If new concrete examples are given, the opportunity to discuss them should be given to the group	Alexis Clapin	a2m2
26	Since this is a new policy by EMA, there hasn't yet been a long enough time period for the harms and risks that industry has identified to actually run their full course. The EMA has only relatively recently started disclosing data in response to third party requests and we anticipate, unfortunately, that the significant concerns that industry has raised will in fact become a reality. Details regarding the IP risks that we are most concerned about - to commercial interests, regulatory data protection, patents and other IP rights - are described in our EFPIA Legal Aspects paper recently submitted to the Agency. Of particular concern with the proposed proactive broad disclosure of clinical trial data is the potential for inappropriate use of such data by third parties either to circumvent existing regulatory data protection (RDP) rules, or take advantage of the absence of such rules in the many countries which do not have robust systems of RDP equivalent to that in the EU. For instance, data exclusivity in Australia, China and Mexico is directly undermined by publication of the relevant data, anywhere in the world. We believe that the significance of the case scenarios described above validate our previously articulated concerns regarding the release of clinical trial data and to assert that the MAH should be consulted prior to the release of any of its information.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)

37	and tefering to all other lines containing the phrase "No agreement was reached". I find it extremely unsatisfying, that this advisory group appears not to be able to come to reasonable compromises on the key questions. I have to apologize for not participating at the last meeting - I was caught by the really serious flu crossing through Germany these days. So I cannot comment on details of the discussion which resulted in the actual draft Advice. However, after the first meeting, I was quite expectant that the group was on its way to find compromises on most of the topics discussed, even if not on all. In the present form the advice is not of any help for administrative persons involved in this process not to mention the politicians who will have to decide at the very end. In easy words, the the present draft Advice reads as "on the one hand, industry wants to construct as many hurdles to impede transparency, while, on the other hand, non-profit biomedical research wants so much access to as many data as possible". Who'd have thunk? Proposed change (if any): So I urgently plead for another meeting with the clear aim to formulate reasonable compromises in as many topics as possible. Please do not forget that, to create or increase transparency is the clear mission for this legislative process. And, its politics! Neither "I want to know all details" nor "the rules impede data access as much as possible" will stand at the end. So let us help with reasonable compromises!	Bernd Mühlbauer	Standing Committee of European Doctors (CPME)
40	It is inaccurate to presume that aggregate data does not contain personal data. The core clinical study report contains mainly aggregated data but there is personal data in the core report that would need to be redacted. This can be made available publicly provided any personally identifiable information is removed and the MAH is consulted before release with the opportunity to redact.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
41	delete version b.	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
41	Identification of requestors. Proposed change (if any): We do agree that requestors should be identified. We don't agree it's impossible to do so accurately - you could perhaps use an ORCID ID to identify requestors	Virginia Barbour	PLoS
44	Lines 44-53. The suggestion that "requestors of clinical trial data should also have sufficient qualifications and experience for any subsequent analysis of data…" is neither practical nor desirable for either aggregate data or patient-level data. It would entail subjective and arbitrary judgements about what qualifications and experience are "sufficient". Proposed change (if any): Please clarify whether the "NOTE from EMA" (lines 54-55) refer to Lines 44-53 or both sections 1a and 1b.	Peter Doshi	Johns Hopkins

44	The comments from lines 44-53 were made with reference to access to patient level data and not aggregate data. Proposed change (if any): Please could these comments be moved to the end of line 143	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
48	The aim of transparency shouldn't be only to allow a potential reanalysis. For example, drug independent bulletins need full information of clinical trials not for research purposes but for education purposes in health areas. A watchdog activity is high useful to citizens and also for drug regulatory bodies. So in many cases there won't be a "legitimate scientific question" to be considered. Transparency goes beyond reanalysis purposes.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
49	In fact the proposed text asks requesters to publicly share their personal details, education and training before getting access even to aggregate data. However, this requirement would violate data protection regulations and induce a hurdle for non professional user groups (see lines 83-112).	Robert Alexander Reiprich	Immunservice GmbH
51	Scientific community will give or not their support to these analysis based on its scientific value.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
54	EFPIA would appreciate the EMA referencing which legal framework precludes identification of the requestor(s).	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
54	Information on the legal framework should be given to the participants. If this legal framework does not allow selection of the requester or consider that document held by EMA are to be made publicly available, most of our discussion is useless. Could we have this information prior to any further meeting ?	Alexis Clapin	a2m2

56	According to CHMP/EWP/2998/03 - Note for guidance on the inclusion of appendices to clinical study reports in marketing authorization applications, the Clinical Study Report Appendices are not required to contain source files/datasets. For the CSR Appendices 16.2 Patient Data Listings, only protocol deviations and adverse events listings are required. Therefore, CSRs and CTDs submitted to European competent authorities and EMA do not even contain "individual case report forms, SAS files with line listings etc". Thus, as these patient-level data are not included in CSRs or submission dossiers, they cannot be made accessible from the EMA website. Retrospective inclusion of patient-level raw data (e.g. annotated CRFs, SAS (.xpt) files, DDTs etc) for the purpose of additional secondary analyses would also not be feasible because of incompatibility with former standards (e.g. no CDISC conformity). Proposed change (if any): To allow for public access to patient-level data in the future, they would have to be a mandatory part of the clinical submission documents, and reflected in the relevant CHMP guideline documents such as CHMP/EWP/2998/03. Furthermore, the potential use of patient-level data outside of the clinical study scope should be covered in the study informed consent form such that the subject agrees to the future "secondary use" of patient-level data outside of the study scope.	Borislava Pavlova	Pharmig
57	delete a; b. or c. are possible to ascertain the scope stated in paragraph 1	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
59	How does providing data access to patients relate back to the original intent for the initiative which is '…to enable independent re-analysis of the benefits and risks'? As noted in lines 44-53, to analyse clinical trial data requires individuals to have specifics qualifications and expertise. Proposed change (if any): Clarify how providing patients access to data relating to their own disease is aligned with the remit of access to data which is being able to independantly re-analyse the benefit-risks. Anyone wishing to re-analyse data should have minimal qualifications and expertise and we should not be suggesting individuals who are not equipped with the relevant skills should attempt to re-analyse data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
59	Patients can already access their medical information from the trial investigator.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)

62	If a competitor (i.e., requestor) obtains a data package from the EMA under its disclosure policy, which is lawful, then submits it in support of an application for a copy product, in an ex-EU country where (unlike the EU) such an application is sufficient and lawful, then no legal action would lie against either the applicant or the ex-EU regulatory authority. The applicant would simply be taking advantage of (i) the data made available by the EMA, coupled with (ii) the absence of regulatory data protection (RDP), or the existence of less sophisticated or strict RDP in such an ex EU country, and the innovator/EU MAH would have no legal recourse. (This may be different if the competitor sought to make such an application in the EU, where the EC has taken the position that would be unlawful under EU law, and the MAH may pursue legal action in that context.) Proposed change (if any): Please add in after: 'If the data are used for illegal actions such as illegitimate commercial use, there are legal actions which can be taken against the firm/country benefiting from the illegal action…. 'Industry contends that if data are obtained from EMA under its disclosure policy and used lawfully in a third country then the EU MAH would have no legal redress'	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
62	If a requestor uses data for an illegitimate use, is the EMA liable for failing to protect patient confidentiality? There is no secure path forward when granting control to anyone to secure patient confidentiality. Industry can do certain measures to ensure that data confidentiality is given within a dataset. But there is no measure available to secure this when a requester has access to the clinical trial data for the purpose to re-analyse it, as they would then have the potential to merge the clinical trial data with other available data. The only way to secure patient confidentiality is to have a step that checks the request for access is scientific (good intent) and clear rules noting that data can not be further disseminated. If the rules require the uploading of a protocol or analysis plan then this using a restrictive access approach increases the protection against unintended use of the data. Proposed change (if any): Liability and violations to patient confidentality is a huge issue that could be further discussed. The policy will need to clarify who is liable for any illegitimate use of data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
85	It should be recognised that clinical trial participants are providing sensitive health information while those who are accessing anonymised data would not be required to provide sensitive health information. For example they would be required to provide their name, address and research institution.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
98	It is difficult to understand why the name of a researcher who accessed data for a particular disease would result in insurance or any other consequence. Merely accessing the data does not indicate or suggest that the individual has that disease or condition. In addition if an email address is not made public (and there is no reason to do so) there is little or no risk of spamming.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)

101	We counter that it is possible (and will be even easier in the future) to combine anonymised data sets with other data that is readily available publically to identify individuals. This is important for privacy particularly as the data contains health information that can be sensitive and assumed to be private by the clinical trial participant. For example please see : http://online.wsj.com/article/SB10001424127887323783704578247842499724794.html and the original article 'Identifying Personal Genomes by Surname Inference. Melissa Gymrek et al. Science 339:321, 2013'.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
105	I believe EU Directives specify a minimum standard to be adopted by Member States but that Data Protection Acts in individual Member States may be more restrictive. Proposed change (if any): Line 107 add after 1995, ", as well as relevant clauses in Data Protection Acts enacted within individual Member States,"	Anthony Johnson	UK Medical Research Council Clinical Trials Unit
110	We do not believe that registering a name and address (research institution) would be excessive. This would be related to the purpose of further research.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
113	Most of the arguments to make data available only after verification of the identity of the requester are considering that the requester will in the future have illegal or unfair misconduct. It looks like "minority report" movie. The rules on engagement should mention for information what should be or should not be done by the requester and any legal issue should be done once the requester has acted in an improper way. Information on these improper ways could be given (I would thus insist on : no anonymous publishing, possible discussion of the data). The rules of engagement should not include any pre-selection or pre-identification and publication of the requester name for another simple reason: a patient can ask for the data about a product he has to take for his/her disease. Furthermore, if specific qualifications are requested, you will easily know who are the requesters with a personnal interest in the product (those without clear qualifications).	Alexis Clapin	a2m2
113	Same comment as above (line 41) We do agree that requestors should be identified. We don't agree it's impossible to do so accurately - you could perhaps use an ORCID ID to identify requestors	Virginia Barbour	PLoS
117	It is needed to identify those specific trials where it is possible such a patient identification and provide alternatives in these cases to harmonize patient and health professional rights.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service

120	There is always some risk that even anonymised clinical study data may allow identification of the patients indirectly by a combination of potential flags (e.g. birthday, study center, city, etc). Especially subjects suffering from rare diseases in closed communities can be identified easily. However, if these indirect identifiers have to be eliminated to prevent any potential identification, then the utility of the data will be seriously compromised for the purpose of research – as described in 2bii. Proposed change (if any): Access to data on clinical studies conducted in patients with rare diseases should be restricted and treated under different provisions, such as mandatory registration and identity verification of the requestor, and contractual agreements covering the consequences of misuse and/or inadvertent identification.	Borislava Pavlova	Pharmig
139	If access to IPD would be restricted to being for the purpose of research in the interest of public health, then of course it has to be made clear, what the specific terms and conditions to be met are and who would make the decision whether or not these conditions are met by a specific requestor.	Robert Alexander Reiprich	Immunservice GmbH

139	Should access to patient level data also be categorised to whether a requestor wants to "independantly re-analyse data" or they wish to "use the data in secondary analyses to address new clinical questions"? Should the level of access determine the level of governance? For example open access could be granted for aggregate annonymised data and restricted access for patient level data where access is controlled by EMA? When a requestor attempts to independantly re-analyse clinical trial data, it will be extremely difficult to obtain results that completely match due to the complex data structures, missing variables due to providing annonymised data sets, and no access to the computer software/code used to generate the analyses. Requesters could also fail to match results because of conducting an incorrect analysis due to a misunderstanding of the data structures. If a requestor independantly re-analyses data and their results do not enable the same conclusions to be drawn about the data, who is the 'arbitrator' in such situations? Should publication of any re-analysis only be allowed following a dialogue between the requester and the owner of the data to confirm the validity of the re-analysis? Regarding secondary analyses of data, requestors may attempt to generate additional analyses on the data which may be inappropriate. This may be due to the data being collected specifically to address the original clinical hypotheses stated in the clinical trial, and other clinical questions may not be able to be addressed based on how the data was collected. Before generating additional new analyses of the data, it would be useful for the requester to verify results from the original analyses to confirm the requester has understood the data structures sufficiently - it may not be feasible for the requester to match exactly the results by the sponsor due to annonymising the datasets, but the results should be close enough that the conclusions drawn are similar to those made by the sponsor. If inappropriate secondary analyses are conducted to address new clinical questions that the original data are not able to address, who would be the 'arbitrator' in such situations? Again, a dialogue between the requester and the owner of the data would enable both parties to agree under what situations new analyses would be supported and which ones would not be supported by the available data. Proposed change (if any): Consider differentiating between requests for data to "independantly re-analyse trial data" and requests for data to be used in "secondary analysis to address new clinical questions" and how this could determine the level of data access required. Some of the issues noted above could be included to explain different scenarios. The complexity of taking patient level data and all the associated meta-data should be noted, and this complexity could lead to incorrect analyses being generated unless appropriate checks are put in place to deal with such situations	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
144	Lines 144-148. The comment that "release of individual patient data, even anonymised … infringes human rights" needs substantiation. Proposed change (if any): The party that introduced this paragraph should be asked to substantiate the claim.	Peter Doshi	Johns Hopkins

152	Although the identity of the requester indeed should be known to the database owner, it is not conclusive to request publication of these names and addresses. Also, it is not clear, why requestors should make public their financial interest when requesting data access.	Robert Alexander Reiprich	Immunservice GmbH
152	Financial interest should be disclosed when the reanalysis is published, not before be granted for access to data.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
155	Lines 155-163. The objective of the system is defined too narrowly. The paragraph currently states that the "objective is clearly to restore trust int eh sytem, not to create an all-purpose research tool." European regulators clearly have articulated a vision that goes beyond simple re-analysis or incorporation of results into meta-analysis, but includes using old data for new purposes. Eichler H-G, Abadie E, Breckenridge A, Leufkens H, Rasi G (2012) Open Clinical Trial Data for All? A View from Regulators. PLoS Med 9(4): e1001202. doi:10.1371/journal.pmed.1001202. Proposed change (if any): This paragraph should be removed or corrected to be made accurate, as the present language seems to mischaracterize the objectives of the EMA's planned prospective data release system.	Peter Doshi	Johns Hopkins
159	To address the objective of "independent re-analysis" of clinical trial data, have the EMA considered following the approach used by the US regulators, FDA, where the regulators re-analyse the patient-level data themselves and the patient level data remains confidential to the regulators? This would remove the need for open access to patient level data and permit open access to aggregate annonymised data. Proposed change (if any): Note whether it would be feasible for the EMA to re-analyse patient-level trial data to address the "independent re-analysis" of trial data. If this approach was possible, this could lead to granting open access to aggregate annonymised data, and EMA and other nominated stakeholders considered "independent" to access to patient level data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
164	It is not clear, how identification of the requestor would prevent from presenting out-of-context results. If drug safety issues are being brought up by such out of context publications, then of course this can be corrected by giving a full perspective and the right context.	Robert Alexander Reiprich	Immunservice GmbH
164	Sometimes it's in fact the opposite. Some requesters use data from drug regulatory agencies to minimize unfounded health scares with potential harms in other senses: for example, the PPI-Clopidogrel interaction case http://www.nature.com/ajg/journal/v106/n7/full/ajg2011126a.html	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
164	The consequences of out-of-context results which generate unfounded health scares is a huge issue for public health. A patient or individual may not care nor fully understand the background of the person generating the out-of-context results. But the damage to healthcare will be long-term and will impact all concerned, regulators, Industry and researchers in publich health. Proposed change (if any): This risk is of high importance to the ultimate decision of whether patient level data should have open access and the long term consequences should be discussed.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)

167	If an individual criticises a publication in a peer-reviewed journal, I believe they should either reference a relevant peer-reviewed article or letter, or present their case in writing. Proposed change (if any): Delete reference to specific example	Paula Williamson	University of Liverpool
168	The hierarchy of user groups is an important consideration, and one that has not been discussed in terms of level of access. For example, stakeholder group 1 should have access to all data whereas the other stakeholders should have different levels of access. Proposed change (if any): Further discuss and note how the hierarchy of user groups could be used to define levels of access for each user group	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
176	If hierarchy for different user groups were finally considered, healthcare professionals should have access to the higher possible level of information.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
186	See comment under line 40 : It is inaccurate to presume that aggregate data does not contain personal data. The core clinical study report contains mainly aggregated data but there is personal data in the core report that would need to be redacted. This can be made available publicly provided any personally identifiable information is removed and the MAH is consulted before release with the opportunity to redact.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
199	delete, legal questions - who should monitor or verify a violation? Thats not an obligation of EMA. Proposed change (if any): ".. any violation of this agreement should be legally enforceable"	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
209	It should be noted that there would be consequences to individuals who mis-use data. Proposed change (if any): Note the legal framework will cover the consequences for individuals who mis-use data and note what these could entail	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)

212	Point 3a. The relationship between knowledge and profit-making is too complex to have it be contractually bound during the data release process. For example, a requestor may conduct an network meta-analysis of drug A, drug B, and drug C, following access to data. That analysis may show drug A to be safer than drug B in a certain population. This may result in a change in prescribing patterns, which has commercial impact. At the same time, this has a clear public health impact, as the new knowledge led to changes in behavior. Thus there is no simple distinction between using data for public health research and commercial use. There are distinctions, I agree, but they are not simple, so the suggestion of a legally binding agreement regarding this seems the wrong way to deal with the concern. I would instead propose that EMA and other regulators think about how they will make decisions in future scenarios where, for example, they receive a marketing authorization application that includes data, or has benefitted from access to data, that was released under EMA's documents release policies. Proposed change (if any): If this section is retained, the party suggesting a legally binding contract requiring the requestor to guarantee to use the data for public health purposes and not commercial purposes, should be clarified as to how commercial purposes and public health purposes will be defined and disentangled in practice.	Peter Doshi	Johns Hopkins
229	See above comments under Line no. 26. Since this is a new policy by EMA, there hasn't yet been a long enough time period for the harms and risks that industry has identified to actually run their full course. The EMA has only relatively recently started disclosing data in response to third party requests and we anticipate, unfortunately, that the significant concerns that industry has raised will in fact become a reality. Details regarding the IP risks that we are most concerned about - to commercial interests, regulatory data protection, patents and other IP rights - are described in our EFPIA Legal Aspects paper recently submitted to the Agency. Of particular concern with the proposed proactive broad disclosure of clinical trial data is the potential for inappropriate use of such data by third parties either to circumvent existing regulatory data protection (RDP) rules, or take advantage of the absence of such rules in the many countries which do not have robust systems of RDP equivalent to that in the EU. For instance, data exclusivity in Australia, China and Mexico is directly undermined by publication of the relevant data, anywhere in the world. We believe that the significance of the case scenarios described above validate our previously articulated concerns regarding the release of clinical trial data and to assert that the MAH should be consulted prior to the release of any of its information.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
231	advice (as link) may be offered but cannot impose an obligation on the requester	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
234	I support this idea. It would be appropriate to ask EMA to amply communicate their own quality standards when a public statement is issued.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health

			Service
237	Why would non-professional users be given access to data if they are not able to fulfil the purpose of being requested access - which is to either independantly re-analyse trial data or to conduct secondary analyses? Proposed change (if any): Confirm why would patients be given access to clinical data if they are not a professional user of the data	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
243	Protocols. Proposed change (if any): Agree that requiring a protocol is advisable and should be given a unique identifier, which is also quoted in each publication that arises from the analyses	Virginia Barbour	PLoS
245	EFSPI wishes to highlight again they feel strongly that the uploading of a study protocol or statistical analysis plan should be mandatory before access to patient level data is granted. This enables the scientific integrity of the analysis to be demonstrated before data access. It also enables the requester to demonstate they have a valid research intent for asking for access to data. Different processes could be described depending onwhether the request for access is to independantly re-analyse trial data versus conducting secondary analyses. For the former, as an example, encouraging the requestor shares their protocol or analysis plan with the originator could help to avoid any incorrect analyses being pursued due to lack of understanding of the data structures. For the latter, as an example the existing scientific standards for conducting secondary research could be referenced. Proposed change (if any): Please note there is at least 2 opinions/views on topic 5 and EFSPI strongly recommends the mandatory upload of a protocol or statistical analysi plan before access to data is granted. The process to be followed could be tailored to the remit for the request for access to data - independent re-analysis versus secondary analyses of existing data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
246	a study protocol is good scientific practice so there should be an obligation for havibng a protocol as upload or as link to a" trial register" A review of the protocol should be provided by the requester (ethics commitee)	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungstr äger
250	The requester should not be allowed to share access data with any unidentified partner. If a collaboration between 2 requesters is necessary(i.e. Academia + industry or data management company), EMA should be informed and give approval. This can be anticipated in the analysis plan.	Didier Jacqmin	Chairman SPO EAU
257	The protocol or analysis plan submission previous to access won't avoid misuse of data. In fact, at this moment we have access to EPAR data and it is possible to misinform about this source of data.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
266	EFPIA would appreciate the EMA referencing which legal framework precludes the Agency, or its appointed delegate, from reviewing a scientific research protocol based on its merits before granting access to anonymised patient data with the objective of preventing erroneous analyses that could	Susan Forda	European Federation of Pharmaceutical Industries and

	negatively impact public health.		Associations (EFPIA)
269	Asepcts relating to the security of data given to requesters should be covered in topic 6. Requestors will be responsible for the secruity of the data they gain access to. Without this accountability, the sharing of data could quickly become widespread and there are mechanisms that can be referenced in the policy to minimise and control data sharing - for example this can be avoided in requesters have restricted access to data sets in a controlled system. Proposed change (if any): Discuss and highlight issues around maintaining the security of data once it is granted to requesters and how this will be considered in the draft EMA policy	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
276	preferable version b. Proposed change (if any): delet version a	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
276	The validity of the dataset cannot be controlled in any way, everybody can alter the original dataset once is released by the drug agency. So I don't well understand the ban of sharing data, it is obviously useless.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
284	Aggregated data, after consultation with the MAH for removal of CCI and PPD, is more likely to have value to a wider audience and therefore should be of initial focus.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
286	Feedback should be encouraged to allow EMA to get more information on the conclusions possible to improve its knowledge.	Didier Jacqmin	Chairman SPO EAU
291	A staggered roll-out should be done by running several pilots to evaluate potential issues. As greater transparency creates the potential for new challenges (e.g. secondary & meta-analyses with new “findings”, contradictions to EMA assessments & other publications, data dumping etc.), this will permit the revelation of limitations based on real and not on historical examples. Proposed change (if any): A staggered roll-out should be done by running several pilots to evaluate potential issues.	Borislava Pavlova	Pharmig
293	EudraCT V9 is currently being built to allow the publication of clinical study results in the EU- Clinical Trials Register. Therefore, the release and access to trial information, results and aggregate data from the EMA website will become obsolete.	Borislava Pavlova	Pharmig
295	preferable version c but only if the the delay of the access to IPD is only delayed a short time - one year	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger

307	This is a very important issue. EMA should be committed to comment / answer in some way whatever new evidence brought up by requesters after its analysis.	Luis Carlos Saiz	Drug Prescribing Unit, Navarre Health Service
311	As protocols have to submitted/linked a obligation of publishing results is a logical consequence. But publishing has to be accepted not only by articles in journals but also as other documents with open access from the interent.	Gottfried Endel	Hauptverband der Österreichischen Sozialversicherungsträger
326	EFPIA would appreciate the EMA referencing the legal framework of relevance.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
328	I disagree with the idea of a time frame within which requetors are obliged to publish/make public the results of their analysis. There should be no such requirement. However in this vein of following-up on requests, if the EMA is constructing a database that will showcase the requests that have come in, also indicating which parties accessed what data, it would be nice to also include space for requestors to not only say what outcomes have resulted from their analysis (e.g. publications) but also encourage requestors who did not publish any resulting analyses to explain the reasons for no publication. Proposed change (if any): Include above suggestion.	Peter Doshi	Johns Hopkins
328	If the requester is a patient, he might not publish any information. Why couldn't be allowed some kind of publication bias for the requesters ? Such a bias exists for other researches. Should it be published on some kind of EMA website or in a peer-reviewed journal?	Alexis Clapin	a2m2
328	What if there are no specific outcomes and conclusions? What if the timeline would not be met? Would there be any action taken against the requestor? How would that be legally based?	Robert Alexander Reiprich	Immunservice GmbH
329	With respect to dissemination of results. Proposed change (if any): Requestors should be required to make publications derived from this work open access either via a journal or via deposition in a publicly avilable repository within 12 months of the completion of the work and a copy of the work supplied to EMA	Virginia Barbour	PLoS

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