Meeting report – Clinical Trial Advisory Group on Rules of engagement (CTAG3)

Participants: Listed in Annex 1 / Comments: Listed in Annex II

Background

EMA has committed to make available clinical trial data of drugs for which a licensing decision has been made. The purpose of this document, and the upcoming rounds of discussions, is to advise the EMA on the conditions and processes in place when an external party ('requester') wishes to gain access to and download clinical trial data.

Further aspects of EMA's proactive trial data publication policy will be addressed by other advisory groups. Ours is the third of five consultative groups related to the planned release of clinical trial data by EMA to third parties. The groups cover the following topics:

1. Protecting patient confidentiality
2. Clinical trials data formats
3. **Rules of engagement**
4. Good analysis practice
5. Legal aspects

Introductory note

This is a draft summary of the first virtual meeting of the advisory group on rules of engagement (CTAG3) that took place on Thursday 7 February 2013 (15.00-17.30 GMT). This summary of our discussion was made without individual attribution of opinions, however, you are reminded that any comments sent in writing shall be attributed and made public.

You are also reminded to send us your comments using the comment form attached and are advised that comments received in any other format cannot be accepted. Please send your comment forms only to: CTDatagroup3@ema.europa.eu. Should one form not give you enough space for your comments, please use a second copy of the form.

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

Draft – 11 February 2013 - Version 1.0

What steps will a requester have to go through before being able to download 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 aggregate data (e.g. lists of studies conducted, clinical study reports) and patient-level data (e.g. SAS files with line listings).

1. Aggregate data: 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.
2. Patient-level data: No agreement was reached. The following positions were discussed:
    a. These data should be freely accessible without the need for identification. Arguments in favour of this position include:
        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. 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 (*Note: reference is made to CTAG1, which is discussing standards for de-identification/anonymisation to ensure patient data protection*)
        iv. Other?
    b. These data should be freely accessible *only* after the identity of the requester has been verified. Arguments in favour of this position include:
        i. Patient-level data is too sensitive to allow anonymous requesters to access because the risk of retrospective patient identification is never zero.
        ii. There is a risk of illegitimate commercial use of patient-level data (please refer to point 3).
        iii. Other?

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 be moot if the identity of the requester cannot be/has not 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. However, even in such case the practical relevance of enforceability was called into question.

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 data requesters to tick a 'read and accepted' tick box is considered ineffectual.

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

There is agreement that it is useful to advise data requesters of existing standards and guidelines for secondary data analysis before accessing clinical trial data. It is emphasised that this advice should not and cannot impose any obligations on the requester. (*Note: Reference is made to the work of CTAG4).*

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

6. Should requesters be allowed to share accessed data?

There is agreement that this is a moot point in case identification of the requester is not verifiable.

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.

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.

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.

ANNEX I List of attendees

European Medicines Agency

Dr Hans-Georg Eichler	Topic leader CTAG3
Monika Benstetter	Moderator
Dr Francesco Pignatti	Topic leader CTAG1
Frank Petavy	Topic leader CTAG2
Jim Slattery	Topic leader CTAG4
Hanneke Parkinson and Inge D'Hoker	Support

Remote participation via Adobe Connect

Dr	Christiane	Abouzeid	Represented by Mats Ericsson - BioIndustry Association (BIA)
Dr	Virginia	Barbour	Public Library of Science (PLOS)
Dr	Thomas	Brill	ethris GmbH
Dr	Eric	Caplan	Biopractices, LLC
Mr	David	Carroll	PharmAware, Queen's University Belfast
Mr	Pierre	Chirac	Prescrire
Dr	Alexis	Clapin	a2m2
Dr	Frank	Degner	Boehringer Ingelheim GmbH
Dr	Susanna	Del Signore	Sanofi
Mr	Peter	Doshi	Johns Hopkins University
Mr	Sebastiao	Ferreira da Silva	European Association of Hospital Pharmacists
Ms	Christine	Fletcher	European Federation of Statisticians in the Pharmaceutical Industry(EFSPI)
Mrs	Sue	Forda	Lilly
Prof.	Tony	Fox	Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians UK
Dr	Andreas	Franken	AESGP
Mr	David	Gilbert	Freelance Consultant and part time NDA Regulatory Advisory Board
Mr	Peter C	Gøtzsche	Nordic Cochrane Centre
Prof.	David	Healy	Bangor University
Mr	François	Houÿez	European Organisation for Rare Diseases (Eurordis)
Mrs	Petra	Jochemsen	RIVM (National Institute for Public Health and the Environment)
Mrs	Merete	Joergensen	Novo Nordisk A/S
Dr	Anthony	Johnson	Medical Research Council Clinical Trials Unit
Dr	Thomas	Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG)
Dr	Karmela	Krleza-Jeric	Ottawa group (also University of Ottawa and CMJ)
Mrs	Julia	Lloyd-Parks	TranScrip Partners LLP
Prof.	Duncan	McHale	UCB Pharma Ltd
Dr	Donna	McVey	Norgine Limited
Prof.	Eugene	Milne	NHS North East
Dr	Suzanne	Mouton	MSC-medical
Prof.	Bernd	Mühlbauer	Standing Committee of European Doctors (CPME)
Mrs	Bharti	Navsariwala	Takeda
Dr	Borislava	Pavlova	Pharmig – Verband der pharmazeutischen Industrie Österreichs
Dr	Liz	Philpots	Association of Medical Research Charities (AMRC)
Ms	Fiona	Reekie	Biogen Idec Ltd
Dr	Alexander	Reiprich	Immunservice GmbH
Mr	Luis Carlos	Saiz Fernandez	Drug Prescribing Unit, Navarre Health Service
Ms	Mary Anissa	Sinnathamby	Parkinson's UK
Dr	Paul	Smith	Professional Regulatory Services Ltd
Ms	Helen	Spain	Vectura
Dr	Brigitte	Stemper	Bayer Pharma AG
Prof.	Lesley	Stewart	NIHR Centre for Reviews and Dissemination
Dr	Pamela	Tenaerts	Clinical Trials Transformation Initiative

88 **ANNEX II Comments received on draft meeting report**

Line	Comment and Changes proposed	Name	Affiliation
1	While the pharmaceutical industry strongly supports enhanced transparency of clinical research information, this increased transparency must be balanced with the legally required protection of commercially confidential information, intellectual property and personal data, so that the innovative research and development of new medicines continues to be supported and incentivised. This requires three basic conditions to be met for both the proactive and reactive release of data: 1) adequate procedural guarantees, 2) a proper review of what data are commercially confidential and 3) there should be no disclosure before the marketing authorisation (MA) is granted. It is EFPIA's position, and a requirement of EU law, that the 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.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
1	A more general comment. The background talks about making information available once the licensing decision has been made. However a licensing decision might be granted following submission of additional information. It is therefore important to define when a licinsing decision is considered final. And maybe it could also be worth while considering the global perspective.	Merete Joergensen	Novo Nordisk A/S
4	data should not be downloaded but accessed in a protected environment. Proposed change (if any): …..access clinical data from the EMA…..	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
4	Are we clear about the precise definition of "clinical trial data"? Trials often access information from clinical notes and summarise it briefly, e.g. "normal EEG" "blood parameters all in normal range." Where is the division between the trial data and the clinical data that underpin it?	Anthony Johnson	UK Medical Research Council Clinical Trials Unit

6	EFSPI strongly support requesters are identified, primarily to ensure patient confidentiality is not compromised and to avoid the mis-use of patient level data by third parties with commercial interests that are not related to healthcare research. EFSPI propose that 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 aligned with ICH-E9, 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. Proposed change (if any): EFSPI seek confirmation that requesters should not only identify themselves, but they should 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. EFSPI request that this information should be made transparent by the requester at the time of seeking access to data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
6	In the spirit of transparency, EFPIA deems it necessary that requestors to access anonymised patient level data be required to identify themselves. The name and affiliation of the requester (or the person on behalf of which the request is being made) and their research team should be logged and made public. Requestors should be required to complete this self-identification before gaining access to patient-level data held by the EMA (or other EU National Competent Authority assuming this remains a joint EMA/HMA policy). Patient level data from clinical trials that are not already publicly available should only be provided for legitimate research purposes on a case-by-case basis, directed by a scientifically sound hypothesis and research analysis plan. The EMA's mission and legal role necessitates its active involvement in the assessment of data held by EMA which is to be made available and necessitates an effective oversight of the process. Finally, but of chief importance, the MAH should always be consulted before release of information or data with the opportunity to comment and seek redactions. Unless the requestors identify themselves, agreement to respect personal data protection and not to exploit the data for commercial purposes becomes meaningless. For aggregated information –such as core clinical study reports—this can be made available publicly provided any personally identifiable information is removed and the MAH has the opportunity to redact any CCI.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
7	As patient level data may only be made available to the public in an anonymised form there are no issues regarding personal data protection. Therefore, there is no need to distinguish between aggregate data and patient level data.	Sameer Kohli	Danish Health & Medicines Authority
7	The distinction between aggregate data and patient-level data is useful for the whole process. However, the interpretation of "aggregate data" may differ between different people. While I am aware that the definition of aggregate data is within the scope of CTAG2, not CTAG3, it might be useful to be a little more specific, also in CTAG3, to make sure that we are all talking about the same type of documents. Concerning "clinical study reports" (CSRs) I propose to add a few words to clarify that by aggregate data we mean full CSRs including the study protocol, the statistical analysis plan and other appendices, not only the core report. Proposed change (if any): (e.g. lists of studies conducted, full clinical study reports including all appendices and excluding patient level data)	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany

7	For the access, only different levels of data have been discussed but not a possible hierachy for the users with access to different types of data for different user groups. For the EMA pharmacovigilance database, such an access policy already exist. (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) Proposed change (if any): Discuss the option to install a similar access policy for different user groups like it exists already for the Eudravigilance data. 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.	Andreas Franken	AESGP
8	The three levels of data mentioned at the teleconfernce were lists of trials, summary of results of trials, and analysis datasets. It is important to identify what part of the clinical trial report can be accessed, as the full CTR do contain patient level data, and might also contain CCI which should both be redacted prior to public access. Even very limited data on an individual can lead to the identification of the person. In a small country like Denmark you can get a long way just from knowing the individulas date of birth. Please also consider aligning with the suggested Clinical Trials Regulation from the European Commision which for Rectical 52 reads: 'No personal data of data subjects participating in a clinical trial should be recorded in the database….'	Merete Joergensen	Novo Nordisk A/S
9	Unfortunately, we did not yet discuss in which form the content of the aggregated data is presented. The publication of aggregated data gives the EMA an excellent opportunity to provide a reliable and factual summary of the clinical studies (other than the study report or Module 2.5 Clinical Overview) to both the general public and professionals who like to have more information than is provided in the EPAR. Such a summary should contain enough data to limit the need to access patient-level data. For example, the summary should preferably contain information on specific subgroups as well as an explanation why SAE's are related or not in a for patients understandable language. The risk exists that if the EMA does not provide such summary or other presentation, that other organizations and groups will develop such summaries. The quality and focus of these summaries will strongly depend on the organization or group who develop those summaries (insurance company, vaccine critical group etcetera). Low quality summaries can negatively affect our tasks as national health institute and therefore I prefer a good quality summary or other presentation of aggregated data by the EMA. Proposed change (if any): I like to propose to discuss the presentation of the aggregated data in a future meeting (of one of the advisory groups).	Petra Jochemsen	RIVM

9	The distinction between aggregate data and anonymised patient level data is useful and should help to focus the debate on creating adequate safeguards for the access to the latter. Nonetheless, it has to be recognised that aggregate data may contain personal data and commercially confidential information that first has to be removed.	Mats Ericson for Christiane Abouzeid	BIA
9	EFSPI disagrees that the identification of requesters of aggregate data is not required. As noted in the comment above for line 6, in order to ensure good scientific practice and in the interest of public health, anyone wishing to analyse aggregate data should be sufficiently qualified and trained otherwise the requester is not sufficiently able to implement legitimate scientific research. Given statisticians who are involved in the design and analysis of clinical trials must be appropriately qualified and trained as per ICH-E9, surely these minimum standards should be expected of any requester wanting to acces clinical trial data. The way in which aggregate data is to be made available should be described in more detail. For example, would a clinical study report synopsis be sufficient to be released once access is granted rather than a full clinical study report, as the synopsis is more likely not to contain any patient level information compared to a full clinical study report? Or could the clinical study report synopses be made available earlier than full clinical study reports whilst the latter have patient level data removed? Proposed change (if any): EFSPI requests that minimum criteria should be defined for requesters concerning the training and education that should be met in order to be granted access to clinical trial data. EFSPI requests that further information is made available regarding how aggregate data is to be made available once access is granted.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
11	Aggregate data such as clinical study reports may also contain commercially confidential information. Proposed change (if any): "Is is assumed that any personal data or commercially confidential information has been removed before access is granted".	Mats Ericson for Christiane Abouzeid	BIA
11	"Aggregated data" i.e. clinical trial reports do contain "key-coded" patient-level data in the tables, in the narratives and in the annexes . Proposed change (if any): It is assumed that aggregate data contains no personal data" to be changed to "Where aggregated data is provided in documents such as core clinical study reports non-anonymised patient level data must be redacted" .	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)

12	Our assumption is that access will provided to a secure data environment and the requester therefore has to identify himself/herself and with the institution. Certain conditions need to apply (agreement to respect personal data, refrain from commercial use, an analysis plan defining hypotheses to be tested, analyses to be conducted etc). Setting conditions will of course only be possible if the requester can be identified. The advisory may need to consider ways of veryfying the identify of the requester. It is important to set the expectations straight for all stakeholders from the beginning. The objective is clearly to reinstore 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 prevously 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.	Mats Ericson for Christiane Abouzeid	BIA
12	EFSPI strongly supports patient level data is only made accessible to requesters who have been confirmed as legitimate researchers who can demonstrate they have the appropriate qualifications and training to conduct scientifically sound research in pursuit of furthering publich health. Proposed change (if any): EFSPI requests further details are noted about how patient level data is made available. There are two primary approaches that maximise patient confidentiality - 1) requesters access patient level data on EMA servers and analyse the data on the server and can only download summary statistics, or 2) restricted versions of patient level data sets (e.g. stripped down versions of SDTMs and ADaMs) are made available where specific variables that could compromise patient confidentiality are removed	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
13	I support position 2a.	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany
13	The arguments for the requestor not being identified are not compelling. Where patients and researchers have the research background and statistical expertise needed to effectively navigate, understand and utilise the patient level data it seems reasonable that they should be identified (see also recommendation from Good analysis Practice group line 97). While "proper" verification is difficult--public disclosure ensures there is public scrutiny of requestors. It is well recognised that anonymisation of data is not sufficient to protect the privacy and confidentiality of research participants. These data can be combined with other data in the public domain to readily identify individuals.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
15	This comes at the expense of any casual browser also being able to access this data. We do not know how potential trial participants would trade these, or the impact on future trials.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York

15	As was also mentioned at the 22 November meeting in London, what is needed is knowledge, i.e. results of the trials. It is highly unlikely that patients will be able to navigate patient level data and reach any meaningful – and correct - conclusions. Navigating patient level data requires significant resources in terms of technology and statistical skills which make this option irrelevant for most people and organisations. In fact opening up for patient level data for un-checked layman analyses and interpretation may cause unnecessary worries and confusion for patients possibly resulting in incompliance and other negative effects on public health. Reference is made to the EudarCT version 9 where aggregated results data are soon to become available to the public.	Merete Joergensen	Novo Nordisk A/S
17	It would be serious scientific misconduct to give false information and if revealed should have serious consequences.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York
17	EFPIA would query this as currently the EMA is able to identify the party requesting MA dossier data under the Transparency Regulation and often provides this information to the MAH. Evidence should be provided about the true challenges involved in identifiying the requester	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
17	Even if it not possible to 100% verify the requester's identity there are ways to ensure the that the submitted identity is likely to be correct.	Merete Joergensen	Novo Nordisk A/S
18	agreed	Sameer Kohli	Danish Health & Medicines Authority
18	Summary of the discussion of CTAG1 should be given to other groups.	Alexis Clapin	
18	Without other information, re-identification of patients from the raw data of a clinical trials is seems to be quite impossible if obvious identifiers are excluded. Are they cases where patients could be re-identified without other information? If yes, what kind of identifier allowed re-identifying?	Alexis Clapin	
18	Name of requester should not be requested to get the data but a full information set should be given to inform the requester on the various points listed by the CT3AG and CT4AG	Alexis Clapin	

18	The level of de-identification required to render IPD 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 IPD 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 inividual participant data systematic (IPD) reviews and meta-analyses. Proposed change (if any): 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).	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York
18	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 there 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. Proposed change (if any): Even if any patient-level data that EMA makes available will be anonymised, the risk of retro-active patient identification is not zero, the patient data protection rules do apply.(Note: reference is made to CTAG1, which is discussing standards for anonymisation to ensure patient data protection)	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
18	Even if the risk of retro-active patient identification is considered acceptably low now, data mining technology develops fast. Moreover, for rare diseases retro-active patient identification is possible even with anonymised data.	Merete Joergensen	Novo Nordisk A/S
20	I disagree as the majority of patients entered in trials will be able to identify themselves as will members of their families - the risk is not "acceptably low."	Anthony Johnson	UK Medical Research Council Clinical Trials Unit
24	There are cases of harassments 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 MAH? In case of harassment linked to data request, what would be EMA responsibility ?	Alexis Clapin	

24	I agree that the privacy of study participants is important and that their privacy should be warranted as good as possible. On the other hand, I like to point out that 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, as previously proposed, involves the risk of unintended use of the personal data of this person, especially if this information can be detected by search engines 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 unintended use is an argument to carefully consider whether the benefits of publication of the names of private persons outweighs the risks of unintended use and breach of privacy of those who access data. Proposed change (if any): 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 that have been opened creates the possibility for unintended and undesirable use of personal data.	Petra Jochemsen	RIVM
25	EFSPI acknowledges there are a number of databases that exist which allow for secondary analyses to be conducted. One such example is CPRD (Clinical Practice Research Database) in the UK. There may be some useful best practices that could be considered to put in place relating to the EMA Transparency initiative relating to checking the validity of requesters, confirming the legitimacy of the research being planned, and processes to control the access to data. Proposed change (if any): EFSPI suggest noting other database systems exist that enable secondary analyses to be conducted. The way in which these systems have been set up should be explored to see if any best practices relating to protecting patient confidentiality and ensuring legitimate clinical research is conducted can be considered for the EMA transparency initiative.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
25	The identity of the requester should be available and public. It is widely accepted in science that people have to disclosë their financial interest. Why should this principle not be applied here as well?	Merete Joergensen	Novo Nordisk A/S
26	identity of the requester has been verified' - is this really necessary/possible (technically & within EMA staff resources)? Would it not be enough to ask for requesters to provide information, without a verification step? This would allow transparency without preventing the public from accessing the data.	Liz Philpots	Association of Medical Research Charities
27	As data would be anonymous there is no sensitive data. Retrospective patient identification cannot be hindered through the knowledge of 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.	Sameer Kohli	Danish Health & Medicines Authority
27	Even if the requester gives his name, it will not solve the problem of publication or use of re-identified patients data. If 10 people, giving their names are getting the data, how will you know who is responsible for patient re-identification if patients characteristics are published anonymously.	Alexis Clapin	

27	risk is zero even for rare disease if anomysed and city not mentioned	Pierre Chirac	Prescrire
29	If the data are used for illegal actions such as illegitimate commercial use, there are legal actions which can be done 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 some other people to request data in order to increase the number of suspects !	Alexis Clapin	
31	In order to allow for investigation of potential illegitimate use of patient level data it is required to know who has downloaded the data and what the intended use/ purpose/ scope is. Known illegitimate use of data from this repository may lead to denial of future access of this requestor (being fully aware that enforcability may be challenging). The intended use could be classified by items like regulator/ manufacturer/ payer/ patient/ other. Proposed change (if any): add: In order to allow for investigation of potential illegitimate use of patient level data it is required to know the identity of the entity/ person who has downloaded the data and to classify the intended use of the data.	Alexander Reiprich	Immunservice GmbH
31	An additional advantage for the need to identity to be required. Proposed change (if any): Clinical trial data sets are large and complicated. Multiple, parallel attempts to download data will likely be impossible (the system will crash repeatedly) and requesters may need IT support to help them obtain the data they want. This cannot be provided anonymously.	Donna McVey	Norgine Limited
31	Additoinal point #1. Proposed change (if any): Collecting infomraiton on who has requested data will allow EMA & wider population to see what appetitie there is for making data available - is it worth doing it?	Liz Philpots	Association of Medical Research Charities
31	Additional point #2. Proposed change (if any): Group 4 (good analysis practice - line 97-100) have requested that requesters provide names and organisations in the interest of transparency	Liz Philpots	Association of Medical Research Charities
31	Proposed change (if any): b.iii There is a risk that patient level data is diverted to unrelated research purposes. b.iv There is a risk of 'data mining' by unidentified individuals (not based on a sound scientific hypothesis and analysis plan) that may lead to claims unsupported by evidnece and the detriment of patients' and public health. b. v there is an additional risk of "discrimination" for certain groups of patients (identified by CTAG1)	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
31	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.	Anthony Johnson	UK Medical Research Council Clinical Trials Unit
31	Reports as well as Patients level data might further include Commpany Confidential Information, in which case the identity of the requester is crtical to be able to assess whether an overriding public interest exists in disclosing such data (the Transparency Regulation provides for a 2 steps assessment, CCI cannot be upfront disclosed, unless there exists an overriding public interest)	Merete Joergensen	Novo Nordisk A/S

32	The description should be very precise on what is "respect of personnal data protection" . Without requester identification, it should of course only be an information for the requester on what can be done and what should not be done. As far as CT1AG rules for patient data anonymisation are applied and effective, respect of personnal data protection mainly forbids gathering the data obtained from EMA with other databases/information.	Alexis Clapin	
32	Requesters have to be made aware of EU and local data protection regulations. Ticking a box implies a contractual relationship between the requestor and the database owner. However, in that case both contractual parties need to be fully identifyable. So the question has to be addressed, whether or not a contractual relationship is a prerequisite for data access. A contractual but not necessarily public "digital" agreement appears to be preferable compared to a purely anonymous process.	Alexander Reiprich	Immunservice GmbH
32	EFSPI support requesters agree to personal data protection by entering a legal contract when they are granted access to the data. Details should clarify that if any individuals are provided access to clinical trial data, then the owners of the data cannot be held accountable in any way for what the requesters subsequently do with the data. EFSPI support any measures that ensure legitimate research is planned and subsequently conducted for furthing public health and measures minimising and preventing illegitimate research are carefully considered. Proposed change (if any): EFSPI requests it is noted that once access to data has been granted, that 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, mis-use 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. EFSPI requests the EMA considers measures that could be employed that enable legitimate research to be performed and prevent illegitimate research and mis-use of clinical trial data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
32	Following the comment above (on 31), only under a requirement for the requestor to identify themselves will it be possible for the requestor to also agree to respect personal data protection. The provision of data must be done in ways that minimise risks to research participants' privacy, the risk of false claims (efficacy and safety) being based on poor science and and to commercial confidentiality. Research use must align with permission provided by research participants through the informed consent obtained in the original clinical studies. Secondary use for novel/secondary research may not be within the scope of the original informed consent. Since data sharing will be linked to the submission of a prospective analysis plan (as described in the comment for line 6) and data will be stored on the Agencies database rather than transferred, requestors should also commit not to share the data or information received any further with other third parties.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
33	It should not be possible to access patient level data via a public EMA website, which could lead to risk of infringing personell data protection laws. It can not be expected that the public will be aware of the laws related to personell data protection globally. Normally it is the organisation publishing the information, which carries the responsibility.	Merete Joergensen	Novo Nordisk A/S
35	I agree with this position. However, I propose to add a disclaimer about the need for personal data protection even if the identity of a requester cannot be verified. Proposed change (if any): … not been verified. Nevertheless, a disclaimer about the need for personal data protection should be "read and accepted" by the requester.	Thomas Kaiser	Institute for Quality and Efficiency in Health Care

			(IQWiG), Germany
36	Violation of data protection laws will be punishable through the data protection rules regardless of whether the requester agrees to respect the rules.	Sameer Kohli	Danish Health & Medicines Authority
40	See comment for line 29: If the data are used for illegal actions such as illegitimate commercial use, there are legal actions which can be done 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 some other people to request data in order to increase the number of suspects !	Alexis Clapin	
40	Requesters have to be made aware of the need to refrain from unintended commercial use of the data. Ticking a box implies a contractual relation between the requestor and the database owner. However, then both contractual parties need to be fully identifyable. So the question has to be addressed, whether a contractual agreement should be implemented or not.	Alexander Reiprich	Immunservice GmbH
40	The requester should agree not to use the anonymised patient data for commercial purposes. Also, as long as the data can not be downloaded, certain forms of commercial misuse will be rendered more difficult (e.g. inclusion of data in non-EU filings).	Mats Ericson for Christiane Abouzeid	BIA
40	As noted in line 32, there should be a legal framework that prevents the use of unintended commercial use of the data. Proposed change (if any): EFSPI requests a reference is made to the legal advisory group to ensure this aspect is covered in their discussions	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
40	As stated in the comment for line 1, while the pharmaceutical industry strongly supports enhanced transparency of clinical research information, this increased transparency must be balanced with the legally required protection of commercially confidential information, intellectual property and personal data, so that the innovative research and development of new medicines continues to be supported and incentivised. The requestor 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. In order to ensure the innovative ability of the industry, no data should be released until after authorisation of the product and, as applicable, publication of relevant individual studies in the scientific literature (or after it has been confirmed by the sponsor that where it has not been possible to publish a study). Requests for patient level data from requestors 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.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
45	this risk is not different from the risk of seing agregrate results being used for unintended commercial uses	Pierre Chirac	Prescrire

45	While I support the position that "unintended commercial uses" should be avoided, it is unclear to me which situations we are talking about and I am afraid that "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. I therefore propose that EMA gives some real-life examples of "unintended commercial uses" during the next CTAG3 session.	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany
46	agreed	Sameer Kohli	Danish Health & Medicines Authority
46	Agree that tick box is ineffectual. Not required for access to results or aggregate data but for IPD a more formal requirement would seem appropriate.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York
47	What is the use of this advice? This may discourage non professional users from downloading and using such data. I cannot see any benefit from such statement but it may mean a subjective additional hurdle to lay groups/ patients.	Alexander Reiprich	Immunservice GmbH
47	The requester should submit an analysis plan upfront (see comment Line 12).	Mats Ericson for Christiane Abouzeid	BIA
47	The requester should be made aware of quality standards for additional secondary analyses. Also, EFPIA believes that there should be periodic assessment timeframes and methods established in which the EMA (or its agent) would assess the public health impact (both positives and negatives) as well as the resource expenditures by EMA and industry to implement this transparency initiative. In terms of potential, undesirable public health impacts, even when the results are based on good science, poorly communicated results can lead to unintended consequences. This is another important consideration for assessing the comprehensive potential consequences to patients and their medical care.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
49	agreed	Sameer Kohli	Danish Health & Medicines Authority
50	Primary as well as secondary analyses must follow generally accepted quality standards. However as the primary results are available at the time of these secondary analyses, these secondary results can only from a statistically scientific point of view be considered hyphothesis generating by nature. Further considerations are needed to see how best to avoid incorrect and incomplete analyses that might cause unnecessary worry among patients and harm to public health.	Merete Joergensen	Novo Nordisk A/S
51	The same standards must be applied equally to the requestor as would be applied to the MAH. There cannot be justification of poorly conducted scientific analysis. It would appear from this statement that any analysis may be conducted across all clinical data without pre-defined or disclosed data handling or analysis plans, we do not see how this would further collaborative scientific research in the area of public health. Proposed change (if any): It is emphasised that this advice should imply clear obligations on behalf of the requester.	Susan Forda	European Federation of Pharmaceutical Industries and Associations

			(EFPIA)
53	As far as it is not mandatory to upload a protocol to get the data, it should be considered as a way to improve research quality and built in order to have as many uploads as possible. To reach this aim, the requester should have the hand on when the protocol should be made public.	Alexis Clapin	
53	This database may not be the appropriate instrument to publish protocols/ analysis plans. A database for protocols/ analysis plans should be separate from the clinical database in order to decrease subjective hurdles to lay groups/ patients accessing the database. If such a separate database is implemented, the uploader should be able to access and change the protocol/ analysis plan at any time, changes have to be traceable. This database should also include the possibility to upload and publish the results of individual analyses.	Alexander Reiprich	Immunservice GmbH
53	EFSPI strongly support 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 mis-use 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. EFSPI support a staggered approach such that at minimum a protocol is defined up front specifying the clinical hypotheses to be investigated, and an analysis plan is provided at a later date for full transparency once access to the data has been allowed and the data structures are understood. The requester should at a minimum demonstrate that the statistical analysis plan was finalised before the statistical analyses were conducted. This is aligned with ICH E9 and good statistical principles relating to clinical trials. Proposed change (if any): EFSPI requests that it is noted there is a mixed view on this aspect, and there is not agreement that uploading a protocol or analysis plan is optional. EFSPI requests EMA considers uploading a protocol or analysis plan should be mandatory in order to verify that the proposed clinical research is legitimate.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
53	The requestor should be required to submit a research proposal including: a description of the data being requested; the rationale for the proposed research; the analysis plan (including the strengths and limitations); the publication and posting plan; any conflicts of interest and their management; and research funding	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
55	open access to raw data does not mean only for purpose of secondary data analysis ; so this point is meaningless	Pierre Chirac	Prescrire

55	In any good science it is well accepted that a protocol is provided. In an environment with multiple secondary analyses it is important to ensure that both positive as well as negative results are made public, to limit the options of publication bias. Trials are today being registered to ensure a publication can be compared to the originally planned analyses. Further the results summaries available at clinicaltrials.gov and soon to come for the European Clinical Trials Registry makes it possible to ensure that results are also made publicly available for EU trials. Now it is important to ensure that also secondary analyses positive as well as negative are published to limit the potential publication bias.	Merete Joergensen	Novo Nordisk A/S
57	agreed	Sameer Kohli	Danish Health & Medicines Authority
57	With repect to access to IPD: As a researcher (who has spent her career carrying out IPD meta-analyses) 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. Proposed change (if any): 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.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York
57	Some organisations (including Cochrane and IQWiG) already publish the protocols of systematic reviews on their websites. It should also be an option to simply upload a link to these protocols. Proposed change (if any): …to upload a protocol or a link to a protocol on an EMA ….	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany
57	Proposed change (if any): If there is agreement that good scientific practice requires a study protocol there should be an obligation to upload OR complete an on-line form so "required" information is supplied. Further, it is not sufficient just to upload a protocol - it could be poor science and result in public health issues if a false claim (efficacy or safety) is made on the basis of the research. Therefore the protocol must be reviewed before the patient level data is provided.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
58	For clinical trials, the use of public registers for the publication of study protocols before starting a clinical trial is mandatory. No medical journal rejects a publication of clinical trial results after the protocol was made public available before. I can see no reason, why the access to a protocol for a data analyses of already public available data should be delayed. There is a need for equal treatment of clinical trial sponsors and researchers using the published data.	Andreas Franken	AESGP
60	Immediately is preferable. If delay is sought, the reason should be supplied and attached to the protocol.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York

60	Protocol or at least a summary should be made public immediately (or even before) the analysis is conducted (in similar way to clinical trial protocols being registered). This is to ensure that all relevant stakeholder are transparently aware of the ongoing secondary analyses and that researchers do not change endpoints and methods to get pre-determined results or not publically disclose parts of their research	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
61	Lodging protocols upfront, provides some safeguard against bias and 'data fishing'. It also helps prevent unintended duplication of research. Proposed change (if any): If requested, delay for requested period of up to 6 months or 1 year with default publication at that point.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York
63	I support option 5d.	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany
64	Even if the name of the requester is not mandatory to get the data, rules of engagement could include some points on the publication of data as advice to the requester: 1) data obtained from EMA should not be linked on a patient basis to any other database, 2) anonymous publication of data received by EMA should be discouraged, 3) Publication of results from data obtained from EMA should always be made in a way allowing discussions about the results. Possibility (or advice) to publish raw data by the requester with his/her publication should also depend on the delay needed to get the data from EMA. A one month delay would limit the possibility to have a reactive action in case of disagreement.If data can be immediately downloaded from an EMA website, possibility to publish the raw data by the requester is useless. Of course, if the name of the requester is not requested, the requester should have the right to publish the raw data with his/her publication.	Alexis Clapin	
64	Requesters should not be allowed to share accessed data because that way the validity of the dataset cannot be controlled. Requesters should need to explicitely confirm that they will not forward the downloaded original dataset to third partys.	Alexander Reiprich	Immunservice GmbH
64	BIA is of the opinion that downloading of anonymised patient level data and sharing with other groups should not be permitted. It is acknowledged that others must be able to repeat research findings, that is a basic principle of research. However, it is our view that such groups would then have identify themselves separately before accessing the same data.	Mats Ericson for Christiane Abouzeid	BIA
64	EFSPI support that sharing of data by the requesters to other parties is not allowed and this aspect is governed by the legal framework. Sharing of data will increase the chance of mis-use of data and increase the potential for patient confidentiality to be compromised. Proposed change (if any): FSPI requests the sharing of data is considered in the legal advisory group and appropriate references are included relating to rules of engagement that do not permit the sharing of data.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)

64	EFPIA's position is that in order to help ensure that data are only used for the agreed purpose and to help protect the privacy and confidentiality of research participants, access should be provided in a secure internet environment with controls in place to prevent the data and documents from being downloaded or distributed beyond the scope of the approved use of the data.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
64	Again as above to ensure the integrity of secondary analyses and ensure analyses are within the scope of Ethics approvals for the use of the collected data, datasharing beyond what has been agreed to should not take place.	Merete Joergensen	Novo Nordisk A/S
65	not agreed; see comment related to line 17.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
66	I agree on this point of view. But the group should discuss the implication of copyright, that the user of the data quotes correctly and indicates the source of the data and the data owner. Proposed change (if any): Add tick box for "Good Quotation practice"	Andreas Franken	AESGP
67	agreed	Sameer Kohli	Danish Health & Medicines Authority
69	If the name of the requester is not needed for aggregated data as agreed line 10, then most points do not need further discussion. A staggered way should not increase the delay for implementation of the rules to make data publicly available.	Alexis Clapin	
69	There is no obvious benefit and no reason to use a staggered way other than limited capacity.	Alexander Reiprich	Immunservice GmbH
69	A progressive roll-out is more likely to be succesful and is strongly encouraged. An obvious question is how data for existing products will be managed. It is acknowledged that aggregate data for existing products may be made available but the EMA does on the other hand not hold patient level data for these products. We therefore suggest that access to anonymised patient level data apply to products approved after implementation start date only.	Mats Ericson for Christiane Abouzeid	BIA

69	EFSPI support a staggered approach to rolling out the final process. Further details need to be considered about what is in scope in the roll out. For example, will the final process be rolled out to all clinical trials that are included in an EMA submission where the EU commission provides a final outcome on or after 1st Jan 2014? Will the initial process be forward looking initially, and once that process is established and stable, a second tier may consider data access for previous EU commission outcomes made before 1st Jan 2014? Proposed change (if any): EFSPI requests that what is to be in scope as of 1st Jan 2014 should be clearly defined, and more details of what data is to be made available as of 1st Jan 2014 relative to the timing of existing or new marketing authorisations yet to receive an EU commission decision, and a process defined for retrospective EU commission decisions made before 1st Jan 2014.	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
69	EFPIA notes that there are several critical timing aspects for release of information. Firstly, no data should be released during the MA procedure, so as to maintain the independence of that procedure and not to undermine the outcome of the ongoing investigation as provided for under Article 4(2) of the Transparency Regulation (EC) No. 1049/2001. Furthermore, no data should be released before actual grant of the MA for which the data were submitted, to reduce the risk of disclosure of information by the EMA that could constitute prior art and prevent the MAH from applying for a patent. Also, as expansion of the EMA's transparency processes are considered, any new processes should only be applicable to marketing authorisation application (MAA) content for medicines authorised after the final new policy becomes effective since previous MAA content was submitted entirely in the absence of EMA's proactive trial data publication policy. Finally, from the policy roll out timing perspective, it is essential that resource constraints for the EMA as well as the MAH be appropriately considered and conserved.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
69	A staggered process would be preferable as there are already many challenges to opening up for access to aggregated data which need to be solved. Aligning with the role out of the EudraCT version 9 and access to results for many clinical trials could be an important step forward.	Merete Joergensen	Novo Nordisk A/S
69	For possible timelines, I refer to my comment above on line 7. For the EMA project of granting access to EV data, an additional explanatory note with a roadmap was published (EMA/529383/2011). This roadmap builds on a stepwise access by user groups.	Andreas Franken	AESGP
70	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 trila 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 policy on participant consent needs to be investigated. Proposed change (if any): Separate the issues of (1) release and access to trial information, results and aggregate data from (2) release and access to IPD. 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 time period to allow proper consideration and investigation of issues pertaining to 2.	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York

71	In the light of problems with patient-level data, I support the idea that the policy should be implemented in 2 steps (step 1: aggregate data, i.e. study lists and full CSRs / step 2: patient-level data). This will ensure that full CSRs are published immediately after market authorisation from the beginning (i.e. January 2014), and this would be a major step forward in transparency.	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany
71	This should be further discussed at the next meeting of this group.	Susan Forda	European Federation of Pharmaceutical Industries and Associations (EFPIA)
72	there is no reason to postpon access to patient-level data	Pierre Chirac	Prescrire
73	why not, if it is only an encouragement. How would it be organised?	Alexis Clapin	
73	Similar to the proposed upload of analyis plans/ protocols, a link back of results of individual analyses is desirable but 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.	Alexander Reiprich	Immunservice GmbH
73	It may 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).	Thomas Kaiser	Institute for Quality and Efficiency in Health Care (IQWiG), Germany
73	EFSPI support full transparency from a requester asking for data with a pre-defined protocol or analysis plan through to subsequent publications. Just encouraging requesters to link their analyses back to the data accessed is not sufficient. Proposed change (if any): EFSPI requests it is noted that 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?	Christine Fletcher	EFSPI (European Federation of Statisticians in the Pharmaceutical Industry)
73	Feedback is essential for sponsors and marketing authorisation holders. This might be important knowledge for the ongoing drug development process or the marketed drug in the light of patient protection. If necessary the revocation of an active substance (IMP or marketed drug) should not be delayed by waiting for a publication or the MAH be informed indirectly by the competent authority. Proposed change (if any): Add equal treatment for the results of additional data analysis to be made public available. Discuss possible impact on patient information (those who use the register) in the light of puzzlement by differing results.	Andreas Franken	AESGP
76	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.	Mats Ericson for Christiane Abouzeid	BIA

	Not noted, but on the call there was some discussion about whether data should be available for download or only for manipulation on the site. Facilitation of IPD systematic reviews and meta-analyses would require that trial IPD on the EMA site can be downloaded and analysed in the same model as trial IPD from elsewhere..	Lesley Stewart	NIHR Centre for Reviews and Dissemination, University of York
?	It is difficult and artificial to consider this very complex issue as 5 discrete working groups. These are silos and siloed thinking and action is what we all suffer from. Yet, all the working groups inter-link. How are the outputs from the 5 groups going to be analysed holistically, such that the final output makes sense to all stakeholders?	Mark Edwards	R&D Director, EMIG
?	I support fully the intent to release clinical research data, but a clear distinction needs to be drawn between "results" and "data". The former should be freely available. The latter however, should follow a formal application and peer-review process moderated by a suitable gate-keeper. Following a full regulatory review of a total clinical database to assess benefit/risk, maintenance of data and its analytical intregrity is surely key to all? Who wants another MMR debacle?	Mark Edwards	R&D Director, EMIG
?	The principle for this type of "request and review" established by GSK should be supported fully and adopted centrally by the EMA, or its designate. Central management is needed because small companies in particular (i.e. the type of company that the EC is so keen to see grow) don't have the resources to manage or fund their own peer-review processes. So, who is going to manage and fund this critical process?	Mark Edwards	R&D Director, EMIG
?	Requesters must surely be verifiable, and submit full prospective protocols and analysis plans. That is just good practice. However, the EMA needs to recognise that once released, it has no "real world" control whatsover on what happens subsequently to the data, unless some form of legally-binding agreement is put in place between the EMA and the requester, that "the data is for the requester's own use and no one else".	Mark Edwards	R&D Director, EMIG
?	I hope that data protection concerns are being dealt with elsewhere, but they are legitimate concerns for companies where their products rely on this instead of patent cover. This is an important reason to look at this whole issue holistically, where the outcome must support greater transparency, yet be fair to the inventors, as well as their legitimate competition. Done without due consideration for these aspects, the worst outcomes could be scenarios that put EU patients at the back of the queue for certain new medicines, or potentially not have access to them at all.	Mark Edwards	R&D Director, EMIG
?	Generally, there was no dicussion at all whether, besides from protecting patient identity, other personal identity requires to be protected as well. This includes for instance names of health care provider institutions and individual health care workers. Information from this data repository could be easily linked to clinical trial databases etc., thus allowing backtracking of hospitals and investigators involved in the generation of this data. This may also enable identification of individual patients at these insitutions. Although this issue is not in the focus of this advisory group, clearly all statements regarding the protection of patient identity in the summary should be replaced/ extended by statements including any personal or even institutional identity data. Proposed change (if any): Add adequate comments in lines 18-23, 27-30 and 33 and where applicable	Alexander Reiprich	Immunservice GmbH

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