European Medicines Agency: draft policy on publication and access to clinical trial data
September 2013

Joint response from the Academy of Medical Sciences, the Association of Medical Research Charities, Cancer Research UK, the Medical Research Council, Parkinson’s UK, and the Wellcome Trust

Key points:

- We welcome the European Medicines Agency’s plans to increase transparency and publish clinical trial data; however, we have serious concerns over the lack of a well-defined review process for requests relating to data in Category 3.
- We support a controlled access mechanism for patient-level Category 3 data, and believe that the EMA or an independent panel should judge the competence of requesters to analyse the data and review the proposed statistical analysis plan.

We welcome the European Medicines Agency’s plans to increase transparency and publish appropriately safeguarded clinical trial data. We agree that the sharing of clinical trial data for secondary analyses has great potential to be translated into significant benefits to public health.

However, we have serious concerns relating to the sharing of patient-level Category 3 data, specifically the lack of a well-defined review process for requests for access to data in this category. We believe it is vitally important to put appropriate mechanisms in place to prevent inadvertent or inappropriate disclosure, to protect patient confidentiality, and to ensure the scientific and analytical robustness of the proposed data use. While the principles and intentions of the draft policy are sound, we are concerned that the lack of such a review mechanism will jeopardise its effective implementation.

We consider it to be crucial to establish appropriate mechanisms to mitigate the following concerns:

- We would be concerned about the security of Category 3 data that leaves the EMA in a potentially identifiable format. To prevent inadvertent and inappropriate disclosures it would be responsible to verify the requesters’ data-handling competence and require that requestors provide a plan of how they will store data securely.
- Similarly, potential harm could result from wrongful secondary interpretation of clinical trial data. Whilst we agree that greater openness could put clinical trial data under productive scrutiny, the consequences of secondary analyses that wrongfully contradict the published findings could be severe, and are certainly not in the interest of public health.
- Finally, requestors of Category 3 data cannot necessarily be expected to understand the nature of the consent obtained for the original clinical trial, especially in cases where patients have been recruited from a number of different settings.
We therefore support a controlled access mechanism with an appropriate review process, in line with existing data access committees that oversee data requests to, for example, genomics studies, and in line with the mechanisms in use by other organisations. As part of this review process, we believe that the EMA or an independent panel should judge the competence of data requesters to analyse the data and review the proposed statistical analysis plan in order to prevent the data from being misinterpreted or inappropriately analysed, as well as ensuring that data access requests fall within the boundaries of the original informed consent. While the EMA’s proposed data sharing agreement requires the requester to guarantee that their analysis is ‘in the interest of public health’, we argue that requesters themselves cannot objectively make this assessment, and hence that there is a need for a review process that provides the safeguards set out above. We recognise that this will have resource implications, and that further work will be needed to explore the detail of potential mechanisms and ensure appropriate oversight, such as through a ‘safe haven’ or ‘honest broker’ model – but such issues should not preclude the broader considerations set out above.

Appropriate access to clinical trial data will be an invaluable resource for biomedical research, but public acceptability and trust are essential to its success. To enhance the integrity and ultimate benefit of research, controlled access to patient level data should ensure that access only follows after appropriate independent review of the proposal.

More detailed line-by-line comments on the draft policy are set out in Annex A.
Annex A: detailed comments on draft policy text

<table>
<thead>
<tr>
<th>Line number(s)</th>
<th>Comment</th>
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<tbody>
<tr>
<td>44-48</td>
<td>Broad consent for data sharing should be encouraged in order to ensure that data are used to their full potential. Some guidance from the EMA, drawing on existing guidelines, on the wording of such consent for future trials (subject to ethical review) would be helpful.</td>
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<tr>
<td>57-61 &amp; 216-218</td>
<td>We are concerned that the EMA will not assess the methodological robustness of the requester’s proposed secondary analysis, or the requester’s competence to analyse the data. We support an appropriate review mechanism that would make such assessments, as described in the main body of the response, above.</td>
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<td>109-115 &amp; 129-132</td>
<td>It would be helpful to have greater clarity on who can decide whether information is classified as CCI.</td>
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<td>143, 165, 172-175 &amp; 278-281</td>
<td>We would appreciate further clarity on whose responsibility it will be to carry out adequate de-identification of data, and to verify that de-identification has been carried out to an appropriate standard.</td>
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<td>149</td>
<td>We are concerned regarding the statement that personal data of CT personnel is not regarded as confidential. Although we agree the names of the investigators and institutions should be in the public domain, we do not think that contact details or the names of all CT personnel should be available.</td>
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<td>181</td>
<td>It is not clear how such a data sharing agreement would be enforced, or what the EMA would do if the requester fails to adhere to it.</td>
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<td>183 &amp; 198</td>
<td>We would welcome further clarity as to who will decide that research is in the interest of public health, and who will define what is appropriate in terms of ethics committee submission.</td>
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<td>191-192</td>
<td>The EMA should take account of the possibility that an ethics committee could approve the secondary use of data that is outside the scope of the original consent (as is currently possible under the laws of many member states).</td>
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<td>244-247</td>
<td>We are concerned over the requirements with regard to data formats for raw datasets, as CDISC format is not yet a universal format for data sharing outside of the pharmaceutical industry. Datasets from outside the sector will not necessarily be CDISC compliant, and many academic organisations and patient groups would not be able to use the format.</td>
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Contact:
Will Greenacre, Policy Officer, The Wellcome Trust
+44 (0)20 7611 8490 / w.greenacre@wellcome.ac.uk

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