4. Application of the transparency requirements – data and documents to be made public and timing of publication

4.3.6

Question 5

We support the proposal set out in 4.3.6 that the database should allow for public access to a sponsor contact point to enable enquiries regarding the scientific aspects of the trial. It is also important that the database makes publically available the contact details of the investigator site. Trial participants, carers and healthcare professionals should to be able to contact the investigator site to seek further information about the trial. Furthermore, this information can be used by portals such as CancerHelp UK trials database¹ and the UK Clinical Trials Gateway², to promote trial opportunities to potential participants. We would welcome clarification from the EMA as to how the investigator site will provide this contact point, we think it appropriate that this information is captured as part of the site information in the initial clinical trial application.

4.4.1

457-466

We welcome the definition of commercially confidential information (CCI) set out in 4.4.1.1. In particular, we think it is right that the consideration of what might be commercially confidential is based on the nature of the trial and status of the medicinal product being studied, rather than the nature of the sponsor organisation conducting the trial. Many academic and non-commercial sponsors will have similar commercial considerations to commercial sponsors. For example, Cancer Research UK’s Centre for Drug Development (CDD) is the largest specialist sponsor of oncology trials in the UK³. Although the CDD is a non-commercial sponsor, more than 50% of its trial arrangements are with industry partners who may, for example, be providing the drug for the trial free of charge or an intellectual property license to have the study drug made. The assessment and consideration of what might be commercially confidential for such trials should be made in the same way as for commercially sponsored trials.

471-479

We welcome the EMA’s recognition that sponsors may need to retain some confidentiality of research plans in order to sustain their ability to conduct original research, to maintain funding and publish that research, and to pursue their future research programme. It is important that these concepts are considered to represent legitimate economic interests and we therefore welcome the

¹ http://www.cancerresearchuk.org/about-cancer/trials/
² http://www.ukctg.nihr.ac.uk/default.aspx
³ http://www.cancerresearchuk.org/science/research/drug-development/scientists/
EMA’s proposal that they fulfill the definition of commercial confidentiality for the purpose of the Regulation.

485-490

It is important that the EMA has acknowledged that in, specific situations, overriding public interest would prevail over and above general transparency rules established for the database. As stated in lines 489-490, a decision making process will therefore need to be established outside of the database to invoke the use of overriding public interest. We seek clarification from the EMA over how this decision making process will be drawn up and who will be responsible for invoking the use of overriding public interest.

4.4.2

Question 6

We support proposal 1.3: that the concept of marketing authorisation (MA) should be applied once a MA has been issued, by at least one member state (MS), for a medicinal product using that active substance and for the indication and formulation/route of administration under study.

This proposal would ensure that a product with MA being tested outside of its indication will have any new confidentially commercial information protected, supporting the development and broaden of use of existing treatments.

We are not supportive of proposal 1.1 as we believe it has the potential to discourage the further investigation of products already marketed, in a new indication. Under this scenario we understand that future study and product related documents relating to investigation of the product, in a new indication, would be published at the time a decision on the trial is made or possibly deferred until publication of summary results if justified. This may discourage sponsors from considering an early licensing approach in small indications of unmet medical need, preferring instead to wait until an MA in a larger indication can be achieved in order to protect the study and product specific information.

We have similar concerns that proposal 1.2 has the potential to discourage the development of novel and/or innovative formulations for agents already marketed due to the requirement to publish study and product related documentation at the time a decision on the trial is made or possibly deferred until publication of summary results.

4.4.3

Question 7

We support that the IMPD-Q section on Investigational Medicinal Product (IMP) quality and the related lists of questions, response and assessment report sections should be considered to be commercially confidential and not be made public for any trial at any time.
As outlined in the text in this section the IMPD-Q section provides full and detailed manufacturing and quality information for the IMP, which may also often include other proprietary formulation and manufacturing information. We therefore agree that this section should remain confidential indefinitely.

We also agree that any related lists of questions, responses and assessment reports should remain confidential for the reasons outlined above.

Question 8

As outlined in response to question 6, we think that the concept of MA should be applied once a MA has been issued, by at least one MS, for a medicinal product using that active substance and for the indication and formulation/route of administration under study.

Using this concept of a MA, we do not think that confidentiality could be justified on the grounds of protecting CCI for trials conducted solely on products with a MA and would therefore disagree with the proposal outlined in paragraph 5 (lines 648-651). We believe that the study and product specific documents from phase IV and low-intervention trials should be made public at the time of the decision on that trial. In such case, sponsors should not have the right to defer the publication of study specific and product specific documents.

We are concerned that the current text of the addendum does not outline when study and product specific information from a trial with two or more IMPs, and where one or more IMP does not have a MA, should be made publically available. A significant number of early phase trials sponsored through the CRUK’s CDD or coordinated through the charity’s Combinations Alliance initiative (see case study below) involve the investigation of a novel IMP given in combination with another novel IMP, chemotherapy (IMPs with a MA often used within their licensed indication) and or radiotherapy. For the purpose of implementing the transparency provisions of the Regulation, we consider that such trials should be treated as clinical trials on products without a MA and should not be required to make study and product specific documents publically available at the time of the decision on that trial (see response to Question 10 for further information).

CR-UK Combinations Alliance Case Study

Established in 2010, the Combinations Alliance is a joint initiative between CRUK’s Centre for Drug Development, the ECMC network and industry. It plays a significant role in the fight against cancer by increasing the number of early phase clinical trials investigating novel drugs in combination with other novel drugs, chemotherapy and or radiotherapy among people in the UK with cancer. The Combinations Alliance initiative is built on partnerships with pharmaceutical companies, to gain access to their portfolio of investigational oncology agents which can then be investigated in academic sponsored (NHS Trust or University) trials in combination with other agents, many of which may already be licensed and standard of care for patients.

The Alliance is unique and is proving to be an attractive model for industry and the ECMC network. It provides companies with an opportunity to explore the potential of their drugs in patient
populations and in combinations they may not otherwise explore. In time, this could provide key evidence that could substantially expand the number of patients who may benefit from the novel agents. Patients also benefit through the Alliance as they get access to treatments that may not otherwise be available in a clinical trial in the UK.

**Question 9**

It is important that study specific and product specific information is published and made available at the earliest opportunity, whilst acknowledging that it is also important to protect commercially confidential information.

**Proposal 1**

We disagree with this proposal as it does not allow for any confidentiality of study and product specific information that should be justified for phase I, II and III trials on the grounds of protecting CCI through Article 81(4)(b) when applying the concept of MA (assuming the EMA adopts proposal 1.3 of 4.4.2, which we have previously outlined our support for).

**Proposal 2**

We disagree with this proposal as we consider that for phase III studies, there would be overriding public interest to make the study specific information publically accessible at the time the summary of trials results is loaded into the database.

**Proposal 3**

We support the principle behind proposal three, which takes a differential approach to the timing of the publication of study specific and product specific documents depending on the stage of product development. However, our support for this proposal should be considered alongside our support for proposal 1.3 (see answer to question 6 above) and our recommendations to amend 6.5 (see answer to question 10 below).

It is right that this addendum acknowledges the higher degree of commercial confidentiality associated with products being tested in phase I and II trials, over products in phase III trials, by setting out conditions that allow for study specific information to be made publically available at a slightly earlier stage for phase III trials. Furthermore, we agree that the case for overriding public interest is likely to be stronger for phase III trials where there is wider availability of the active substance and its use is in larger subject populations for therapeutic purposes. It is therefore right that the study specific information from these trials is made publically available at the same time as the summary of trial results, if not earlier.

We therefore recommend that:

- For phase III trials, the study specific information should be made public at the time the summary of trial results is loaded into the database or earlier.
• The study specific and product specific information for Phase I and II trials, and the product specific information for Phase III trials, should only be made available when the earlier of the conditions set out in 6.5 are met (assuming our recommendations to amend 6.5 are adopted).

Consideration should be given to how this approach will affect Phase IV and low interventional trials as the issue of research confidentiality would still apply to these trials.

Proposal 4

We disagree with this proposal. Although we agree with the principle of taking a differential approach to the timing of the publication of documents depending on the stage of product development, we are concerned over how the stage of product development would be established, particularly in the oncology setting. This proposal would require sponsors to declare the therapeutic or prophylactic intent of the trial. Given the automated nature of applying the transparency rules through the database, the extent to which this declaration could be certified would be limited. Furthermore, we have concerns that the therapeutic or prophylactic intent does not always reflect the stage of product development.

Question 10

Assuming that the concept of MA is defined as set out in proposal 1.3, we support 6.5.1. 6.5.1 sets out that where the granting, refusal, or withdrawal of the MA application has triggered the publication of the clinical study report (CSR), the publication of the CSR should trigger the publication of study and product specific information for that trial, which has been kept confidential under Article 81(4)(b).

It is important that in this addendum, the EMA recognises that many trials involve multiple IMPs (see case study on CRUK’s Combinations Alliance initiative outlined in the text of our response to question 8). The EMA should therefore amend the text to clarify that where a trial involves multiple IMPs, it would be necessary for all IMPs included in that trial to have been granted or refused an MA, or had an MA application withdrawn, in order to trigger the publication of the CSR and therefore then publication of study and product specific information.

It is right that the EMA has considered that an alternative trigger is necessary for the publication of study and product specific information for trials where a MA application may never be submitted. As acknowledged by the EMA, many clinical trials are carried out on non-authorised medicines, which are never used later in support of a MA application as the development of that medicine may be discontinued or the trial may not have been conducted in preparation for a MA, but as basic research. It is still important that the study and product information from these trials is made publically available, but the timing of this publication needs to be carefully considered.

The proposed trigger outlined in 6.5.2 is necessary in addition to 6.5.1 to ensure that data is published even if a marketing authorisation is never filed, which we support. We would ask the EMA to clarify the rationale behind the timeframe outlined in the proposal. We are unclear as to why the EMA has specified that the trigger of publication should be nine years after the date of the first
summary of results of the trial are published. The EMA states that this is a ‘reasonable period after the trial has been completed’ (line 719), but does provide any evidence to support this presumption, except to say that it corresponds, but is not actually linked to, the data protection period provided for in the EU.

5. Proposed addendum to the ‘functional specifications for the EU portal and EU database to be audited’.

We are broadly supportive of the proposed addendum to the functional specifications. We agree with the EMAs approach to ensure the publication of clinical trial information occurs by an automated process based on predefined rules to be agreed through this consultation. We are also supportive of the manual override option, but would welcome clarification from the EMA over who would be responsible for this manual override and the decision making process for initiating this.

Although we understand that the additional questions to be included in the application form will need to be adjusted based on the final outcome of this consultation, we do not consider that question 5 or 6 would be necessary in any instance. The suggestion by the EMA to include these is at odds with its proposal set out in 4.4.1.1, which considers the nature of the sponsor organisation to be immaterial when considering what might be commercially confidential.

About

Cancer Research UK
Cancer Research UK is the world’s largest independent cancer charity dedicated to saving lives through research. We support research into all aspects of cancer through the work of over 4,000 scientists, doctors and nurses. In 2013/14, we spent £386 million on research in institutes, hospitals and universities across the UK – including the £35 million contribution we made to the Francis Crick Institute.

British Heart Foundation
The British Heart Foundation (BHF) is the nation’s leading heart charity. We are working to achieve our vision of a world in which people do not die prematurely or suffer from cardiovascular disease. In the fight for every heartbeat we fund ground breaking medical research, provide support and care to people living with cardiovascular disease and advocate for change.