Definition of Investigational Medicinal Products (IMPs) and use of Auxiliary Medicinal Products (AMPs) – August 2016

Joint response from Cancer Research UK and the British Heart Foundation

It is vital that the rules and regulations for clinical research always support patient safety, address ethical concerns and ensure scientific validity. However, unnecessary or inflexible regulations create significant extra costs in running clinical research for funders. We therefore welcome the opportunity to respond to this consultation on what we perceive to be an issue of vital importance.

In particular, the guidance provides welcome clarification of what constitutes a background medication. Under the current directive, chemotherapy drugs used as part of a background treatment in clinical trials are considered IMPs. These drugs are therefore subject to IMP pharmacovigilance requirements, even though they are not under investigation, and despite being standard of care. Adherence to pharmacovigilance requirements for these drugs is therefore an undue regulatory burden and an unnecessary drain on resources. For charities with limited budgets, the extra costs of complying with excessive regulation means that the total amount of money that can be spent on clinical research is reduced.

General comments:
The language used in the guidance is at times too similar to the legal writing style used in the Regulation and is difficult to understand. Since this guidance document is designed to make the Regulation easier to understand, and ensure consistent interpretation by different member states, it would benefit from use of some of the principles described in the 'Summary of clinical trial results for laypersons' guidance.

Comments relating to specific lines:

Lines 43-45
This language is difficult to interpret and should be clarified.

Lines 87-95
The guidance should clarify, perhaps using examples, what justifications for using unauthorised AMPs are acceptable.

Lines 102-109
The paragraph appears to be incomplete – are some sentences missing from the end?

Section 3.2
The guidance provided under Section 3.2 (Requirements for AMPs) lacks clarity.

- In particular it is unclear whether the entire section describes non-authorised AMPs or just the first paragraph.
- If the final paragraph applies to unauthorised AMPs only, in line with Regulation 536/2014 (article 51), it should be clearly stated.

Line 117-118
The guidance should clarify, using examples, what justifications for deviation would be acceptable?

Lines 129-134
Paragraph 46 of the Regulation requires traceability only of unauthorised AMPs. Therefore it is unclear why full traceability of AMPs is required here. If AMPs are used in standard care, the hospital will supply them from their own stock, and it is our understanding that normal pharmacy documentation should suffice. These products are not under investigation, and their characteristics are known. Therefore they shouldn't be subject to the same requirement for traceability as IMPs.

Line 134
The guidance should clarify how 'where necessary' is defined.
The guidance needs to make provision for unusual circumstances such as rescue medications. Rescue medications could be an over the counter product brought by the patient in a chemist. The information regarding the active ingredients of the IMPs would be listed on the patient card and therefore allow identification of what rescue medicine is required. A pragmatic solution for documentation in similar situations is required.

Lines 140-142
The guidance states that "As a general rule, the documentation requirements in the application dossier for IMPs also apply to AMPs irrespective their marketing authorisation". We feel that the statement is misleading, since according to Regulation 536/2014 Annex I, no documentation is required to be submitted for authorised AMPs.

Line 154
We suggest that 'Medicinal Product' is replaced by 'AMP' for consistency and clarity

Line 182
Requires start of a new paragraph.

Lines 200-201
AMPs are not always used in accordance with their marketing authorisation (MA) and this flexibility needs to be maintained.

Line 219: Feedback request to elaborate further on early escape procedures
We have an example of a clinical trial with a highly innovative design. A licensed product (rituximab) will be used as a rescue medication in the case of significant toxicity.

The virus that the cells are transfected with results in expression of a specific marker (CD20) on the transfected, expanded T cell population. In the event that we see significant toxicity from T-cell expansion, we can administer rituximab as a rescue medication. Rituximab targets CD20 and will neutralise/destroy the expanded T cell population produced as result of the IMP administration. The AMP may never be used, but if it is then it will be outside of the conditions of its marketing authorisation.

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Cancer Research UK

Cancer Research UK's vision is to bring forward the day when all cancers are cured. Over the last 40 years, cancer survival rates in the UK have doubled. In the 1970s just a quarter of people survived. Today that figure is half. Our ambition is to accelerate progress and see three-quarters of patients surviving the disease within the next 20 years.

Every year more than 25,000 people take part in one or more of over 250 clinical trials supported by the charity. In 2015/16, Cancer Research UK spent spent £432 million on research across the UK, including our £28 million contribution to the Frances Crick Institute. CRUK directly funds over 200 clinical trials. More than a quarter (28%) of these trials involve at least one other EU country. One in three (33%) of CRUK-supported clinical trials have involvement from countries outside of the UK.

British Heart Foundation

The BHF is the UK'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. Thanks to modern treatments built on our research, huge progress has been made in saving lives. Most babies born today with heart defects survive and seven out of ten people survive a heart attack. However, heart and circulatory disease still kills one in four people and affects 7 million people in the UK, so there is so much more to do.

The BHF is the largest independent funder of cardiovascular research and the third largest charitable funder of medical research in the UK. Each year, thanks to the generosity of our supporters, we are able to fund around £100 million of new research across the UK, in all four nations. Our funding portfolio extends from laboratory science to clinical trials and population studies. We fund people from PhDs to professors as well as investing in large programme and project grants.