Comments on 'Definition of Investigational Medicinal Products (IMPs) and use of Auxiliary Medicinal Products (AMPs)', from Hammersmith Medicines Research, a contract research organisation specialising in clinical pharmacology.

General comments

We recommend incorporation of advice, based on the MHRA's very useful guidance on IMP versus non-IMP designation (available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/343441/Mock_examples.pdf), to help sponsors determine whether substances administered in clinical trials are IMPs (eg comparator), AMPs (eg a licensed medicine used in an interaction study as a CYP3A4 substrate but which is not expected to be co-prescribed with the IMP), or non-AMPs (eg alcohol used in an interaction study).

It would be useful if the guidance referred to a definition of a medicinal product (presumably that in EU Directive 2001/83/EC).

Please clarify that products (such as alcohol used in an interaction study) that do not meet the definition of AMPs do not need an AMP dossier or to be made to GMP. However, they must be of suitable quality for use in the trial. It would be useful to echo the wording in the current Annex 13 to GMP, and say that the advice of a QP should be sought.

Specific comments

Lines102–109: this is unclear — the sentence is incomplete.

Line 142: please add a full stop after 'authorisation'

Line 172: this is unclear — the sentence is incomplete. Also, where should serious adverse events/reactions associated with an unauthorised AMP be reported? The sentence mentions an annual safety report of the 'relevant IMP' – what is the 'relevant IMP'?

Annex 1

The title is 'Types of AMPs', but the annex includes the challenge agent tyramine, which is not a medicinal product and therefore doesn't meet the definition of AMP – so the title of the annex is misleading.

More examples of non-AMPs, such as methacholine, used for bronchial challenge, and PET ligands, microdoses of which are used only to measure receptor occupancy, would be useful.

Section 1

Rescue medicines may also be used to treat a side effect of a trial procedure (eg beta-2 agonist given as needed after inhaled allergen challenge or spirometry).

Rescue medicines for an *emergency situation* should be available in all clinical pharmacology studies, not just first in man trials of biological products. So the example given is not useful. All early phase research units must have available at all times on the ward a wide range of licensed medicines for emergency situations, such as anaphylactic shock (we have about 15 different medicines on our emergency trolleys). It would be unnecessarily burdensome for investigators, sponsors and regulators to specify that SmPCs for all routinely stocked emergency medicines should be included in applications for authorisation. It would be helpful and proportionate if medicines routinely stocked to treat emergencies or common adverse events (eg paracetamol, antihistamine) were explicitly classed as non-AMPs.

Section 2

Please add, as examples of non-AMP 'challenge agents', PET ligands that are not used in medical practice for diagnosis. They are not medicinal products and are administered in very small doses only to measure receptor occupancy by IMPs.