Medicines & Healthcare products Regulatory Agency

Inclusion and exclusion criteria
At least one of the following inclusion criteria
Condition A: all of the following are true: • all investigational medicinal products (IMPs) are authorised for use in the UK • all IMPs are used (a) according to that authorisation or (b) outside of the licensed indication, provided that this use is established practice and supported by sufficient published evidence and/or guidelines • all IMPs are unmodified
Condition B: a previous clinical trial of each IMP (including placebos) has been approved in the UK within the last 2 years where the IMP was investigated at the same (or a higher) dose, the same (or higher) dosing frequency, the same (or longer) duration and utilising the same route of administration, for the same indication, and utilising the same manufacturing process and controls for the drug substance and product. Note that 'same indication' refers to the same target disease (not a subset or subtype), of the same severity, in the same age group and, if relevant, in the same drug combination or line of treatment. For trials conducted in healthy volunteers, this should be the intended indication for the IMP
Condition C: the trial has been assessed and approved in the USA (and it has been 30 days since the investigational new drug (IND) application or amendment to the IND was submitted with no notification of a clinical hold), EU, or an EEA state. The new UK application should be based on the same versions of the protocol and Investigator's Brochure (IB) and, for EU or EEA approvals, the same version of the IMP dossier. For trials approved in the USA only, the IMP dossier submitted in the new application should document the same IMP manufacturing process and controls
None of the following exclusion criteria
The sponsor is aware, having made reasonable enquiries, of ongoing significant safety concerns with the IMP(s), including: • any post-marketing regulatory restrictions • any other trials on temporary halt or clinical hold • any other trials with unresolved urgent safety measures

- pivotal non-clinical toxicology studies have not been conducted in an Organisation for Economic Co-operation and Development (OECD) Mutual Acceptance of Data member country
- ongoing serious breaches of GxP by the sponsor
- any known or suspected impurity related concerns in healthy volunteer trials, including from nitrosamine impurities
- the IMP's initial first-in-human trial has not been completed or the data derived from it has not been fully assessed and approved in the UK, USA, EU or an EEA state as part of an application for approval of a trial that was conducted subsequently to the first-in-human study
- the IMP is being given at a dose or level of systemic exposure that exceeds what has previously been tested in humans, including where changes to the IMP formulation result in an increase of the IMP systemic exposure that may exceed the C_{max} or AUC previously observed in humans at the dose levels tested in previous studies
- the trial population of the IMP's initial first-in-human trial is not adequately generalisable to the proposed population and a bridging study is required (e.g. when the ethnic group in the first-in-human trial is not representative of the UK population)

The trial population includes participants who are any of the following:

- under 18 years of age
- pregnant
- breastfeeding

Any IMP(s) used in the clinical trial are first-in-human

The clinical trial involves an advanced therapy medicinal product, as defined in the Human Medicines Regulations 2012