Summary of queries for PET

Frequently asked questions fall into 5 groups:

1. IMP or Not IMP uncertainty
2. Study design queries
3. Regulatory & Licensing queries
4. Preclinical data requirement queries
5. Manufacturing queries

These are addressed below.

IMP queries

The majority of the IMP concern what constitutes an IMP and might therefore require an IMP licence.

So a clear definition of what constitutes a licensed product, an IMP and a non IMP would resolve most of these queries. Some examples might also be useful.

Also some comments around what is within scope of the licensing requirements as opposed to what is in the scope of the Sponsor/Ethics responsibilities

1. What is the definition of an IMP?
2. What is the definition of a non- IMP?
3. What rules can I follow to determine whether or not the material is an IMP
4. What are the regulatory requirements for non-IMP studies, (Ethics/Sponsor responsibilities?)
5. Do we need to inform the MHRA of studies not involving an IMP? If so, how and what information?

Study design queries

There were a number of questions around types of studies and what aspects of intent make a radiotracer an IMP or not.

A clear statement around the differences between methodology studies and clinical trials should resolve most of these queries. Again some worked examples may be useful.

1. Where can I go regarding access to advice for study design and access to previous studies?
2. What additional requirements are there for First Time in Humans studies?
3. Does the study design determine whether the radiotracer is an IMP or not?

Regulatory & Licensing queries

The requirement for a licence is not clear to practitioners. Our understanding is that non-

IMP tracers manufactured for studies fall outside the scope of licensing requirements and therefore do not require an IMP or Specials licence, but are controlled by the Sponsor and Ethics committee. The MHRA could clarify this general issue.

What licensing options are appropriate for

1. Manufacture of a Non IMP for a Clinical PET study
2. Manufacture of an IMP for a Clinical PET study (where the IMP is a PET product)
3. A licensed product study (Where the licensed product has been manufactured as a PET product)
4. Commercial manufacture and supply/distribution of PET Radiotracers
5. Manufacture of PET radiotracer for diagnostic purposes (e.g. NHS)?

Preclinical toxicity data requirement queries

These questions are far-reaching and may need input beyond that the MHRA can provide.

1. Where can I find toxicity data for non IMP and IMP PET products?
2. Are there additional preclinical data requirements for FTIH studies?
3. Does microdosing relieve us of generating toxicity data required or reduce the amount required?
4. Do IMP studies require more toxicity data than non IMP studies?

Manufacturing queries

These are general GMP and manufacturing queries and show there is uncertainty about what standards apply. Some of these were very detailed. Some general examples may help to clarify the issues.

1. How can we demonstrate sterility assurance?
2. Can the same equipment be used to produce different tracers on the same day?
3. What approach should be taken regarding cleaning validation considering we are micro dosing?
4. How should we set a specification, for example for impurity levels?
5. Is specific activity considered a quality critical parameter?
6. Why does the precursor need to be GMP grade when it undergoes a number of reactions and purification steps to become the injectable entity?
7. Does a QP have to certify the **Precursor** for an IMP?
8. Do GMP requirements apply to the manufacture of a non IMP?
9. What class of facility is required for manufacture of sterile PET products?
10. What level of product process validation is required?