Notes from MHRA MRC NCRI Workshop on Regulatory Issues in PET Imaging

held MRC Head Office, London , on Friday 10th Sept 2010

Slides from the workshop have been circulated to attendees.

Welcome and introductions: Paul Matthews

- Brief history of the meeting: Three major areas for PET applications:
  a) PET for diagnostics
  b) PET as a tool for drug development
  c) PET for disease biology

- Stakeholder workshop in 2008: Four main outcomes:
  a) Shortage of capacity (especially trained radiochemists)
  b) Widespread difficulties in managing demands or uncertainty of regulatory requirements
  c) Inadequate access to GMP (Good manufacturing Practice) facilities
  d) Not realising potential for academic industry collaboration

- Stakeholder meeting 2009 including MHRA and MRC to try and create an open dialogue and identify points needing clarification; four main issues identified:
  a) Understanding which regulatory route a PET study should follow (when is a radiotracer an IMP?)
  b) The regulatory package required for novel radiotracers and opportunities for sharing information between sites supporting IMP
  c) Ensuring appropriate manufacturing standards and sites
  d) QP assurance competencies and training in relation to PET-IMPs

Objectives for this meeting:

a) Highlight resources available
b) Identify and address common areas of uncertainty in understanding of the regulatory environment for PET research
c) Consider creation of a small “Super user” group to liaise more closely with the MHRA and facilitate a better general understanding of regulatory processes
d) To consider creation of a NeuroPET Research Network to share “best practices” and encourage optimally efficient use of national resources

Session 1: Chair - Paul Matthews

A. General overview: the regulatory environment for PET radiochemistry and experimental medicine – Elaine Godfrey, MHRA

- Key questions before you start any interaction (the two questions do interact to some extent):
  a) **Is my study a clinical trial or not?**
  Definition of clinical trial: Human subjects (includes healthy patients and patients); discover or validate pharmacodynamic effects, adverse reactions or study absorption, distribution, metabolism & excretion (ADME) of a molelcule administered; trial should not be non-interventional. Clinical trials are intended to discover or evaluate approaches to screening, prevention, diagnosis, or treatment of a disease
  b) **Is the PET ligand an IMP or not?**
  Definition of medicinal product: any substance (or combination) administered with the intention of making a diagnosis or to restoring, correcting or modifying physiological functions in animals or humans, i.e., used as a medicine or to make a medical diagnosis.

  An Investigational Medicinal Product is an active substance or placebo in pharmaceutical form being tested or used as a reference in a clinical trial (including medicinal products being used in the context of a clinical for new indications or investigated in new forms as medicines).

  It was emphasised that the same molecule may be considered an IMP in the context of a clinical trial (e.g., if intended for a diagnostic use) or as a NIMP in a different context (e.g., to provide information regarding a physiological state).

- IMP vs. NIMP in PET: Big difference in terms of legislation:
  Within the context of an IMP trial, NMIPs may be used; the provisions of articles 9 (data requirement) and 13 (manufacturer's authorisation) of Directive 2001/20 do not apply to NIMPs BUT the provisions of article 3(c) do apply (physical products etc)

- Clinical Trials Directive key aims:
  a) Protection of trial participants
  b) Protection of trial data

- The application of GMP and GCP brings an obligation to the sponsor:
  a) Authorisation from the Competent Authority
  b) Positive opinion from a REC
  c) Other necessary approvals (e.g. ARSAC)
  d) Pharmacovigilance
  e) Conduct of the trial in compliance with GCP

  For Clinical Trials, a Clinical Trials Autherisation required and this has to be supported by an IMP dossier

- IMP a formally constituted dossier (see MHRA guidance) with an iinvestigator/s brochure required for each IMP;
- NIMP - a less formally defined "dossier" also should be provided outlining the similar evidence to the sponsor

- Where a clinical study does not come within the scope of the Clinical Trials Directive, no clinical trials application to the MHRA is required!

- Guidance available (though this may be difficult to find when not clear where to look for it); MHRA website has a section which covers PET in particular (http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/SpecialInterestGroups/PET/PETGeneralinformation/index.htm) Elaine Godfrey would be happy to update this section if input provided, however, resources are limited and so MHRA would be unable to develop new materials.

- Questions:
  - (Franklin) Does the definition between clinical trial and study essentially depend on the aim of the study- i.e., study by clinicians to learn about patients' *prognosis* vs a fundamental research objective generally defines whether a study is a trial or not. In that case, the context of the tracer use is the key consideration
  - (Elaine) Correct. So, depending on intent, even if tracer is novel and first in man, MHRA may not require application for CTA
  - (Franklin) IMP: does it cover PET applications in general or is there a difference between clinical study and research study? → (Elaine Godfrey) Depends how it is defined; tracer for receptor occupancy: defined as medicinal product but not an investigational one
  - (Erik Arstad) Does a precursor of a compound being produced under GMP standards need to be GMP grade? → Yes; if the precursor is not GMP grade, then can't make a GMP-grade product. GMP provides a framework to ensure that a product is made to a specific quality

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B. GMP regulation and issues – Mark Whelan, Wolfson Medical Imaging Centre (WMIC), Manchester

- GMP approvals:

  a) No all-encompassing GMP 'approval'
  b) There are specific licences (with obligations)
  c) Licences: marketing authorisation (MA); specials; IMP
  d) Bottlenecks to obtaining a licence:
    - Validation (the scale of validation required is underestimated)
    - Quality Management System (QMS) (new systems are often untried at first inspection therefore no evidence of implementation exists)
    - The independence of Production, QC & CA in small organisations
    - Finding a QP (Manchester have elected to train someone with pharma background and train that person in PET to be a PET-qualified QP, rather

than specifying that someone already has PET expertise before training them to be a QP)

- GMP approval summary:
  a) There is no single path to demonstrating GMP compliance'- even holding a specific licence cannot be interpreted as evidence that all your practices are compliant; just means that regulators have – in one context- agreed that practices appeared appropriate and they have not found a reason not to give you a licence
  b) GMP is not 'best practice', but the *minimum* requirement
  c) The goal posts are continually moving (in US often use the term current GMP; cGMP) (ie what was compliant last inspection may not be compliant next inspection)
  For example endotoxin testing has gone from a protocol that takes several days to one that takes several hours over the last few years. With these advances, improved processes are expected.

- Implementation of GMP (generally the hardest bit):
  a) General
    - Understanding the manufacturing process is the first step to being in control
    - This typically includes characterisiation of processes, e.g., sources of variability)
    - A combination of the 'pure science', the equipment & operator make-up the production process and each one as well as its interaction with the others needs to be understood and monitored
    - Ensure you have appropriate and experienced staff performing roles in quality control (lots of academic centres struggle with this; advice: take a well trained person from pharma and train that person on PET)
    - Beware of contractors (at least make sure that you understand what the contractor is doing and how far it meets your needs.)
    - GMP="say what you will do, do what you have said and record that you did it"
  b) Validation
    - What needs validating? (facilities and equipment (production and QC), processes (i.e. manufacturing), test methods)
    - How far do I go? (how critical is the system? Existing guidance)
    - Again-beware of contractors!
    - Re-validation
  c) QMS (ensure systems are sufficient to cope with the volume of work you expect to reach)
    - Documentation (have a system (hierarchy); policies (few, brief and systematic); procedures (simple and instructional); records (streamlined and 'easy' to complete)
    - Failure investigation (deviations, OOS and CAPA (corrective actions preventing actions))
  d) Other systems
    - Testing and batch release
    - Change control (difficult in research setting)
    - Training (always onerous)

  - Self inspection (how effective are you?)
  - Good-Inwards (raw material testing?)
  - Storage (reference and retain samples?)
  - Planned Preventative Maintenance
  - Etc.

e) In need of further clarification:
  - Where should 'GMP' start (e.g., consider how it could include cyclotron stages)?
  - What is the Active Pharmaceutical Ingredient (API)?
  - How should impurity limits be determined?
  - What are appropriate labelling requirements?
  - Expiry period/ shelf-life/ stability
  - Reference and retain samples?

- Example of stability and expiry of radiotracers:
  - At Manchester, RT will not be administered outside three half-lives (not enough activity for a scan)
  - Chemical degradation is the greatest risk over this timespan, so Manchester performs stability checks over three half lives (ie checks radiolysis)
  - Can also test other parameters e.g. pH, colour etc

- The Risk based approach:

a) GMP part 1 Annex 20 – Quality Risk Management
  - Where used correctly it can lead to many of the answers to PET GMP compliance questions

b) The pit-falls
  - You cannot cover every possible eventuality
  - The accuracy of the risk assessment is dependent upon the knowledge of the assessment team
  - It should never be used to justify a pre-conceived idea
  - It takes a high degree of discipline to conduct a good risk assessment

c) Patient safety and PET
  - Sterility (cleanrooms/ isolators; environmental monitoring; chemistry rigs; operators (training, qualification); raw materials/ reagents; processing aids; filtration; QC testing)
  - Residual solvents (type of solvents used (process/ cleaning); addition of solvents to chemistry rig; purpose of the solvent in the process; chemistry rig cleaning; QC residual solvents testing)

- At the Manchester WMIC: Risk assessment uses a matrix system – degree of severity vs degree of likelihood. Low risk acceptable; medium risk should be resolved ASAP; high risk unacceptable. In risk assessment, WMIC do assessment before and after risk controls are applied. This helps to determine whether risk is being controlled or not. However, the risk management approach needs to be tailored to the site and its needs. Different dimensions (e.g., risk to subjects, compliance risk, time risk) of risk management also may be useful to consider in developing the optimal approach.

- Questions:
  - (Franklin) Where does GMP stop? Do we differentiate in making the PET tracer one dose vs. thousands of doses in terms of risk? → (Ian Thrussell) You should be thinking, “where does GMP start!” Do you consider the risk of controls from the perspective of the community as a whole or from the perspective of the individual receiving the product? This will drive you to different positions; risk assessment the most important thing to do because you have to understand the process. Without the knowledge of inputs and outputs you cannot do a good risk assessment. Risk assessment actually enables you to concentrate your efforts on what really matters. Doing good risk assessment will drive you to the things that are important--- if you can show that certain things are not important in terms of risk assessment, that allows you to focus on those that are.
  - → (Ian Thrussell) Need to know/develop evidence to demonstrate that you are making a sterile product. Be careful not to overinterpret what a test is telling you and remember that one test won’t tell you about the future.
  - GMP allows for alternative approaches to demonstrate quality of the product- find the approach best suited to your site.
  - (Eric) Patient and community perspective in terms of working safely; Mark to elaborate on matrix for patient safety with an example
  - → (Ian Thrussell) Another matrix could be of point of view of the study (study to be confounded in some way etc.) showing “if certain things go wrong within the study, what happens to patient recruitment etc”
  - (Ian Thrussell): Risk assessment with using numbers: problem is that people put too much into the numbers matrix; purpose of risk assessment is all about working through the process and reducing risk; overall risk is so complicated, you have to break it down into sub-risks. Aim is to create a priority list to reduce risks.

Session 2: Chair - Fiona Gilbert

C. Terminology and design of studies with a view to finding the optimal regulatory context: Overview – Roy Baxendale, GSK

- Where does PET fit into the regulatory process?
  a) Clinical PET products
  b) PET in research
  c) Clinical trial application processes
  d) Pre-clinical applications

- Pet in pharmaceutical development: PET fits in early process development, output: clinical PET products like FDG; internal use in facility: 'specials licence' required; commercial selling of PET tracers requires product and manufacturing authorisations

- PET in research:
  a) PET tracers are not therapeutic agents
  b) PET tracers used as end point assessment tools (imaging agents) and defined as NIMP
  c) Micro-dosing
     - PET tracer <1/100NOEL
     - Impurities << threshold of toxicological concern
  d) Scale of studies (very specific and focused)
     - Specific study design
     - Small number of subjects

- Three considerations that will help to generate a successful study:
  a) Good science
  b) Legal/ technical knowledge (about terminology and understanding)
  c) Process understanding (preparing for an application to winding up the study)

- The study aims will influence the design of your PET centre (whether IMP or non-IMP studies to be performed)
- The MHRA clinical trials helpline can help you decide whether a study is likely to be a clinical trial or not

- Algorithm/ Decision tree:
  a) Intent of study (MHRA algorithm; widely published, but lots of people have issues with interpretation)
     - First question: Is a CTA required (call the clinical trials help line!)
     - Found generally confusing: PET products not a medicinal product in 99.9% of cases BUT it is an active substance in a pharmaceutical form (A.3). Column C in MHRA figure is key to deciding whether a study requires CTA or not.

  The Belgians are trying to interpret the EMEA directive on PET studies so that early phase clinical trials have a lower level of regulation. It is possible

to do this in Belgium because exploratory clinical trials can only be performed at a few PET centres and these have good communications with their regulatory body.

- CTA or not CTA: Exploratory clinical studies are those intended to be conducted early in phase I, involve limited human exposure, have no therapeutic or diagnostic intent, and are not intended to examine maximum tolerated dose. They can be used to investigate a variety of parameters such as pharmacokinetics, pharmacodynamics and other biomarkers, which could include PET receptor binding and displacement
- Clinical trial application process: MHRA guarantees to provide an initial response within 14 days (phase I)/ 30 days of date of receipt of valid application (see below); final response usually within a total of 60 days from receipt of initial application (it should not be 60 days because it causes substantial delays!)

Protocol is to first of all ask for a Eudra number for study. Then submit request for authorisation. MHRA will usually respond within about 30 days Also need to be talking to ethics committee as need CTA in data package

- Main problems with validity encountered by MHRA when investigators submit a Clinical Trial Application:
  - Failure to supply an XML file of the completed clinical trial application form
  - Failure to complete section C1 of the clinical trial application form or section D1 of the notification of amendment form (contact name and details)
  - Failure to supply a letter of authorisation from the sponsor
  - Failure to provide PDF documents for the protocol, investigator's brochure, investigational medicinal product dossier (MPD) and summary of product characteristics (SPC) where appropriate (that have undergone optical character recognition (OCR)
  - Discs are password-protected and cannot be read

- Key documents to include:
  a) Covering letter
  b) Application form [IRAS]
  c) EudraCT XML file
  d) Protocol
  e) Investigator's Brochure (IB)
  f) IMP dossier/ SMpC*
  g) Manufacturer's authorisations* (problem with multi-centre trials)
  h) QP declaration*
  i) Examples of labelling (on product)
  * As applicable

- Pre-clinical requirements: toxicology work to GLP (regulatory standard); GLP can get very expensive; one must be part of the programme and monitored to be allowed to do GLP trials; a max dose of 1000-fold the clinical dose on a mg/kg basis for iv and mg/m^2 for oral administration should be used; greater activity of lower concentrations as a trend in pharma

- GMP requirements:
  a) Drug substance: general information; manufacture; characterisation; control; reference standards; container closure; stability
  b) IMP: composition; development; manufacture; control of excipients (carriers that should be pharmacologically inactive); control of IMP; reference standards; container closure; stability
- Do not need to hold IMP manufacturers authorisation in all situations. Manufacturing or assembly of a product needs to be to standard for product that has authorisation for production.

- Issues:
  a) NIMP guidance proposals – QP requirements
  b) Exploratory Clinical Trials guidance (phase 0)
  c) Consistency vs. regulatory development
  d) Risk based inspection programme

D. Case studies – Erik Arstad, UCL

- GMP interpretation appears to be much stricter in UK than Europe
- PET tracers are generally seen as NIMPs unless used as diagnostics

- Whether a PET product is seen as 'active substances in a pharmaceutical form' decides on IMP or NIMP

- Key points for early phase clinical PET studies:
  a) First in man studies a major bottleneck for development of tracers for clinical use
  b) Increasing regulatory hurdles are perceived by many in the research community to pose a risk to PET research by adding to the cost and technical challenges

  - A simplified PET tracer classification/ interpretation could be adopted, e.g., PET tracers at microgram doses are NIMP, unless the clinical study is intended to underpin licensing applications for diagnostic or therapeutic use

- Proposed solutions:
  a) Develop a separate MHRA CTA algorithm for PET tracers
  b) An algorithm for PET 'Specials Licence' would also be helpful (e.g. case study A)

  - (Elaine Godfrey): the MHRA algorithm is not an MHRA one but a European document accessible through the MHRA website

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D. Case studies – Franklin Aigbirhio, Cambridge

- Generally in agreement with case C & D

→ Case C: Study a) could be an IMP; framing/ wording the question is the key

- Case E: Grey area
  → a) IMP? Interpretation on one way or another (radiotracer to be used for binding potential (IMP) OR correlation with binding potential (NIMP))

- No agreement with case G
  → Question which is asked is: can PET tracer been used to detect a malignancy; therefore it should be IMP

Panel Discussion

- Aim: to make language and accessibility more easy; suitability for users
  - (Erik Arstad) Can MHRA make room for flexibility of interpretation of regulations
  - (Elaine Godfrey) Problem is interpretation; legislation and guidance is written from people with a legislative background; the misunderstanding probably comes from the regulatory language used coupled with the scientific complexity of the studies. Easy to understand scientific language is very important for the MHRA to understand what issues are involved in a study
  - in volume 10 of rules governing medical products in the EU there will be further clarification around PET. However, volume 10 will not discuss the Special's licence as this is UK-specific;

    Action 1: Elaine to share volume 10 with PET community when published
  - (Ian Thrussell): It does not matter what licence it is, the product has to be done to high quality standards. Need everyone to communicate in the same language. Education is important.
  - (Andy Scarsbrook): Several ligands are in regular use in other countries; However, the regulatory hurdles for a new tracer in the UK (e.g. F-Choline) are huge, restricting the use of these tracers for research in the UK; difficult to understand the rationale behind the hurdles
  - (Elaine Godfrey) Manpower limitation is probably a major issue, as well as understanding the steps involved. We should produce a worked example and disseminate it through website; collaboration between MHRA and PET community; MHRA, Erigal and academic person willing to produce open (i.e. publically available on website) documentation on F-Choline production and make it freely available/ accessible. However, MHRA not willing to do this if the intent is to apply for a commercial licence for this tracer.
  - **Action 2: Work with Elaine Godfrey to develop an illustrated IMP dossier to be made publicly available and used by the community -tapping into Cambridge experience (Franklin Aigbirhio)**
  - (Eric, Paul): It is all about how you frame the intent of using F-choline in the trial, i.e. how the tracer is used. For example, GSK applied for two independent studies involving an apoptosis tracer. In the first one the tracer was a NIMP, as the tracer was used as an endpoint assessment

tool. In the second study it was an IMP, as it was used to investigate the relationship between clinical outcome and apoptosis

- (Ian Thrussell): Limited number of tracers in use; Could a dossier not be prepared for for each tracer? Does it not make sense to cooperate and put together a dossier for the PET community? At least concerning the manufacturing control and tracer production you could prepare a shared dossier
- (Franklin): We are trying to create a common document (even if equipment and technology may be different from site to site) for the community. Radiotracer group could use this document as a template to try and achieve something along these lines
- (Ian Thrussell): Think about the total cost of doing this; it might be cheaper to throw away your equipment and buy something other people have used rather than fighting with everything alone and not making use of existing strategies etc.
- (Erik Arstad): It is all about funding – equipment is not that easy to obtain. Also some equipment is better in some roles than others
- (John Clark): Focus should be on doing the same chemistry and same QC, don't need the same equipment to do this
- Elaine Godfrey) – Agree it is not necessary for everyone to have the same equipment to do this
- (John Clark) – Should import data (e.g. toxicology data) from overseas where possible (e.g. FLT study in USA)
- (Elaine Godfrey): Dossier can be used to share the data. If you can get hold of others people's data, do it; from MHRA perspective it is not necessary to reinvent the wheel; difficulty sometimes is the amount of commercial confidence, i.e. you may come to me and share things with me but I might not be able to share other people's information with you
- (Catherine): Is there an equivalent on the neuroscience side with respect to the preparing a comparable dossier for that to be developed for F-Choline?
- (Tony Gee): Not necessary to have a worked example for both oncology and neuroscience. One is sufficient. The idea of a dossier appears to be worrying a lot of people. What is the expectation around the dossier? Maybe it just needs to be concise, does not necessarily have to be a huge document. Guidelines for creating a dossier would be useful
- (Eric): Type and level of information is the important bit; that can be sorted with a will behind it
- (MHRA) – For a dossier you need to pull clinical and non-clinical data together
- (Roy): How long did it take to put a dossier together? → 2-2.5 months for one person, 50% of time (i.e. 3-4 weeks in total); however, this is only the last bit of a very time consuming process. The person involved was also setting up the process at the same time and distilling information from this to put into the dossier. In addition, regulatory help/advice was available from within the company
- (Ian): The biggest problem is that most people don't know how to do this. Need a guidance plan

- (Marie-Clare Pickard) It is worth looking outside your own discipline, there might be people who might be able to help with your application, maybe not the very detailed bits but they may have a lot of advice. Transferable skills/information can be very useful
- (Elaine Godfrey) Important thing that we need to capitalize on the will that is expressed and build on this to make things easier for everyone; need to know

  a) Does that work for you?

  b) Are there other practical things that we can do (if resources available)?

  Idea of 'Super user' group is good, and this should work well in small community; Happy to help with preparation of dossier; also if other study examples are required, am happy to add them to the existing ones (note: the MHRA examples were developed and more examples added for the present meeting)
- (Ian Thrussell): Most chemistry facilities have some sort of licence; there is obviously some concern about what to do to validate GMP facilities etc; collectively you have the ability to put together generic risk assessments for different tracers/processes; if risk assessment process is good at centre, inspectors will be happier, the inspection process will be easier and money will be spend on keys parts of the process. Once you have got one risk assessment it will be much easier to do the next one because you have some kind of model to use
- (Fiona) – Availability of QP's is still an issue
- (Bev Ellis) – Working group set up to address this. Summary points were published as an editorial in Nuc Med Comm.

Action 3: Beverley Ellis to circulate NMC editorial

- (Tony Gee) – A PET chemistry discussion forum has been set up

Action 4: Tony Gee to provide MRC with joining details of this forum

- (Ian Thrussell) – All hospitals have own protocols for Lab inspections and don't seem to learn from other sites. Very inefficient.
- (John Clark) – Yes, and several PET groups are often trying to solve the same problems. Similar issues there
- (?)- Is a new PET group required? Should this be multi-area (Oncology, neurology & cardiology?) people felt one group would cover all areas as the PET community is relatively small and groups can cover more than one scientific area.
- (Franklin) – I am happy to act as the link person for PET superusers group (Note: Franklin and Elaine will meet or communicate by phone to agree how to set up this group of Superusers. Franklin invited Elaine to the radiochemistry meeting taking place in Cambridge on 22nd Oct 2010.

Action 5: Franklin Aigbhirio and Elaine Godfrey to take forward ideas for a Superusers group of a few key individuals with or who could develop specialist expertise, so that they could interact with both the MHRA and PET scientists to help clarify regulatory issues.

Summary and review of meeting objectives by Fiona Gilbert

- Resources available:
  a) Supporting resources on regulatory issues form this meeting will be available on MHRA, MRC and PRN website
  b) Publication of workshop material to widely disseminate information to the community and highlight some additional info
  c) All: Please disseminate material from this meeting to your local research community

- Identify and address common areas of uncertainty in understanding of the regulatory environment for PET research
  b) Shortage of QP still a problem
  c) Setting up a GMP facility is huge amount of work
  d) Are there common practices that could be adopted by UK sites (e.g. flowcharts, templates for documentation)?
  e) Share failures and corrective actions?
  f) Where should GMP start, what is the API, how should impurity limits be determined, labelling requirements, shelf-life/ stability, reference and retain samples
  g) Good effective risk assessment is essential – Mark Whelan was asked by FG if he would be willing to produce Risk Assessment templates for sharing and perhaps run a risk assessment workshop.
  h) Active risk management programme to reduce risk
  i) Share good practice from inspections
  j) To CTA or not to CTA? If in doubt about whether something is a clinical trials phone CT helpline!! Email a draft protocol to clintrialhelpline@mhra.gsi.gov.uk for comment.

  - (Fiona) Communal sharing important!

- Creation of a small "Super user" group to liaise more closely with the MHRA and facilitate a better general understanding of regulatory processes
  a) 'Super users' to be led by Franklin will liaise with MHRA to facilitate communication with research community
  b) These individuals will support and provide additional resource for the research community on regulatory issues

- To consider creation of a NeuroPET Research Network to share "best practices" and encourage optimally efficient use of national resources
  a) General willingness for a NeuroPET research Network
  b) Ideally to be supported by MRC
  c) Similar template to NCRI PRN but in a leaner format
  d) Small working party to produce business case – chair to be appointed following this meeting

  - (Jonathan Owen): This is basically a step back from how we started in Scotland; there should be an interaction between groups; focus of the group should maybe be slightly different; not only Neuroscience

- (Catherine): Group focus could be reconsidered at the meeting on 5th October.

Next steps

- **Meeting at MRC to agree and prioritise actions on 5th October 2010**
- **MRC to circulate slides from the meeting together with a summary of this meeting**
- **Work with MHRA to make further revisions to website to improve accessibility of regulatory information**
- **Roy Baxendale is currently establishing a model QMS for academic institutions that could usefully be shared in due course**
- **Mark Whelan will consider if he would be able to provide a risk assessment template(s) for community use and provide advice in a workshop**
- **All: Feedback from this meeting to Catherine Moody at MRC by email.**

Specific actions

Action 1: Elaine to share volume 10 with PET community when published

Action 2: George Duffy (Erigal) to work with Elaine Godfrey to develop a dossier for F-Choline that could be used by the community, tapping into Cambridge (Franklin Aigbirhio) and other? academic experience

Action 3: Beverley Ellis to provide MRC with copy or link to editorial published in NMC

Action 4: Tony Gee to provide MRC with the link and joining details for web based PET discussion forum

Action 5: Franklin Aigbhirio and Elaine Godfrey to take forward ideas for a Superusers group of a few key individuals who would interact with both the MHRA and PET scientists to help clarify regulatory issues.

September 2010