**Stakeholder Engagement Meeting**

**16 November 2017 – MHRA Offices, BPR**

Martin O'Kane provided an update to the Clinical Trials Regulations – see slides.

Stakeholders were invited to discuss three areas of the Clinical Trial Regulations that require national legislation; who can be an investigator (Article 49), who can take consent (Article 29) and requirements for assembly of IMP in hospitals and health centres (Article 61).

Stakeholders divided into three groups to discuss these issues and feedback to all attendees.

## Group 1 – Who can take consent?

The group agreed that they would not want to see more restrictive legislation, and want to keep the ability for nurses to take consent. In general, the group believed nurses were often far better placed to take the consent in terms of ability and time to fully discuss the options. It would significantly reduce the breadth of the trials if consent was restricted to physicians. For example, midwives that are permitted to prescribe the medication, should be able to answer consent queries without having to refer to a Doctor.

Access to a Doctor may be useful if specific questions are to be answered, but this this is not always necessary with an experienced nurse practitioner. Therefore, availability of a Doctor to answer questions depends on the type of research; timeliness of this availability was also unclear. Availability of Doctors is often an issue; legislation could force an inexperienced Doctor (in terms of training to do consent), rather than a much more experienced nurse practitioner, to have to take consent.

It was stressed that if the legislation was clearer in relation to nurses being able to take consent this would be helpful with less risk adaption needed

It was also proposed that some groups would feel comfortable with Pharmacists taking consent due to the level of detail that they have in relation to the trial. This should be done on risk based approach, as for example pharmacists may not be able to answer clinical questions in relation to the type of trial.

The issue of new role of Physician Assistants was raised – currently they are not registered healthcare professionals, but will be carrying out many traditional Doctor's duties, including consenting. In addition, Advanced Critical Care Practitioners are trained in e.g. prescribing (and are comparable to junior doctors in terms of experience). If the requirement for consenting was to be a registered health professional, this would create problems.

Suggested wording from the group was 'suitably qualified individual' rather than a registered heath professional. If the procedure was in a clinical professional's daily role then in theory they should be able to take consent. The group considered the patient perspective 'Does it feel right that this is the right person having the conversation with me?' i.e. that the research nurse is sufficiently trained in the area and has the time to have the discussion. This would extend to physiotherapists who may also be in a better position to explain the trial.

For advanced therapy trials, it was discussed whether it would be appropriate for the Sponsor to take consent. The group raised concerns about the conflict of interest. HRA confirmed that RECs are likely to have concerns around this

Summary:

- Wording needs to be precise but not prescriptive.
- A risk assessment is needed which is not just determined by IMP type.

- A specific list of professionals that can take consent would not be supported as this could be restrictive in future as new roles are developed.
- Suitably qualified individual (rather than registered individual) was put forward as an option for wording.
- Joint guidance on expectations of consent taking from HRA/ MHRA is critical Worked examples in guidance (MHRA/HRA) would also be really useful in support of the legislation

**Group 2 – Who can be a PI?**

The group discussed some current issues, i.e. what is the problem we are trying to fix? It was felt that Regulations are sometimes applied with caution therefore even though other non Doctors could currently be a PI this is rarely seen e.g. Nurse Consultants. In addition, some applications for funding expect CI/PIs to be physicians. Also, examples have been seen of when the legislation can be limiting unnecessarily, for example; a Paramedic with a Lead academic research role who is an expert in that area cannot currently be a PI, although they are best placed to lead that research.

There was much discussion over qualifications of a PI, what the requirements should be and who would decide this. The consensus was that a PI should be within a current role that involved experience of patient care. All agreed there should be pragmatism and risk adaption applied.

More assessment would be needed of the PI suitability for a trial. Who would do this was discussed at length; i.e. the responsibility for assessment of PI; Sponsor, employer, REC, MHRA during application. Most felt the responsibility should fall to employer for ensuring general competence but Sponsor for assessing and assigning on a trial by trial basis. REC would continue to approve through site assessments. There was discussion on training of PIs, pathways for enabling those interested to become a PI i.e. framework should be put in place for research engagement. Current GCP training is about the regulations but doesn't train individuals to be competent at managing and overseeing a trial.

There was much discussion over professional accountability and professional registration, i.e. should the list of who can be a PI only include professions which require a professional registration and CPD to ensure sanctions could be put in place if serious issues were seen. This would therefore exclude chiropractors for example and therefore could also be over restrictive. However, it was also discussed that employers should still be able to impose sanctions and under the Clinical Trials legislation MHRA could issue infringement notices, press charges etc if the breach warranted it.

All agreed a PI should only be working within the boundaries that they are already eligible to work within.

Summary

- The Regulation should be kept simple and flexible
- Current wording in article 49 was considered not far off what would be required, but should further clarify that a medical doctor must also have the necessary scientific knowledge.
- There must be detail in supporting guidance documentation
- Risk based approaches should be applied for acceptability of a PI
- Emphasis should be on being competence based

- It was felt that work would be needed on training processes and processes for assessment of who should be a PI on a trial; however, this applies to the implementation rather then what should be in the legislation.

**Group 3 Arrangements for Exemption of GMP for Hospital and Health Centres**

Pharmacy aseptic units are moving towards outsourcing models for reconstitution of IMPs, but are not really geared up for this to be performed outside of hospital / health centre environments. There was concern regarding the application to ATMPs and ATIMPs. It was asked if it would be beneficial to have a system where commercial sites involved in reconstitution activities should need to 'register' to perform these non-manufacturing activities.

Comments were made that it would be good to have better/more guidance on when the Regulation 37 exemption can be applied. Note – an NHS guidance document relating to where reconstitution and/or assembly activities may be performed under the exemption or requires an MIA(IMP) is in final draft stages and MHRA GCP, GMP and CTU representatives have been involved with the review.

The principle of allowing commercial Phase I units to perform assembly under the exemption was discussed (*Note – there were no attendees from these types of organisation at the StEM*) and the general feeling was that if the exemption applies in hospitals then why not also allow commercial Phase I units this flexibility, depending on how the oversight and standards are applied? This discussion extended to institutions such as care homes and palliative care settings which may be involved in trials.

For exempt activities under the CTR, it was felt to be Important that GMP standards are maintained. The group suggested that principles of EU GMP should be followed supported by PICS guidance. There was concern relating to dilution of EU GMP. It was considered Important that labelling continues to be supported by the exemption in the CTR.

There is a difference in how a product may be handled in relation to whether it is manipulated by pharmacy or via a nurse on the ward. The sponsor should be aware of how the product will be handled and by extension should describe what the GMP expectations are in relation to the administration process. This may differ dependent on whether the IMP for immediate administration or being stored prior to giving to the patient.

Summary

- There is a need for further clear guidance on what is allowed by the section 37 exemption / reconstitution/activities defined in Article 61(5).
- Risk adaptive controls should be explored
- Assembly does not cover just injectables – need to consider other formulation types
- Principles of EU GMP supported by PICS guidance recommended as a standard for national legislation
- Assuming assembly activities were under the supervision of a pharmacist that the exemption should include phase I units
- Existing regional QA audits used for section 10 work could continue in collaboration with MHRA to ensure proportionate approach to GMP inspections
- Perceived low impact of implementation of article 61(5)

## Appendix 1 – List of Attendees

| Organisation | Name | Group |
|---|---|---|
| MHRA - GCP Inspectorate | Gail Francis | All |
| MHRA - Clinical Trials Unit | Martin O'Kane | All |
| Association of the British Pharmaceutical Industry (ABPI) | Sheuli Porkess | 1 - Consent |
| Academy of Medical Sciences (AMS) | Peter Brocklehurst | 1 - Consent |
| Association of Clinical Research Organisations (ACRO) | Derek Johnston | 1 - Consent |
| Cancer Research UK (CRUK) | Sue Waller | 1 - Consent |
| European Forum for Good Clinical Practice (EFGCP) | Paul Strickland | 1 - Consent |
| Health Research Authority (HRA) | Clive Collett | 1 - Consent |
| Human Tissue Authority (HTA) | Dr Amy Thomas | 1 - Consent |
| Royal College of Anaesthetists | Rupert Pearse | 1 - Consent |
| Royal College of Obstetricians and Gynaecologists | Edward Morris | 1 - Consent |
| Chief Scientists Office Scotland | Joanne Rodger | 1 - Consent |
| Scottish Government | Dr Caroline Watson | 1 - Consent |
| UK Clinical Research Network (UK CRN) | Gill Eddison (nee Booth) | 1 - Consent |
| Wales - Health and Care Research | Lynette Lane | 1 - Consent |
| Clinical and Contract Research Association (CCRA) | Professor Atholl Johnston | 1 - Consent |
| Health Sciences Records and Archives Association (previously SAG) | Sarah Howard | 1 - Consent |
| MHRA – GCP Inspectorate | Jennifer Martin | 1 - Consent |
| MHRA – GCP Inspectorate | Paula Walker | 1 - Consent |
| NHS England | Angela Manning | 2 - Investigator |
| Royal College of Physicians | Dr Marc George | 2 - Investigator |
| NHS Research Scotland | Charles Weller | 2 - Investigator |
| UK BioIndustry Association (UK BIA) | Esteban Herrero-Martinez | 2 - Investigator |
| Welsh Ambulance Service | Nigel Rees | 2 - Investigator |
| Association of UK University Hospitals | Heather House | 2 - Investigator |
| NIHR Clinical Research Network (NIHR CRN) | Anthea Mould | 2 - Investigator |
| R&D Forum | Kate Greenwood | 2 - Investigator |
| Association for Human Pharmacology in the Pharmaceutical Industry (AHPPI) and British Pharmacological Society | Mike Hammond | 2 - Investigator |
| Institute of Clinical Research (ICR) | Dr Alison Messom | 2 - Investigator |
| Royal College of Nursing | Rachel Taylor | 2 - Investigator |
| Research Quality Assurance (RQA) | Barney Horne | 2 - Investigator |
| MHRA – GCP Inspectorate | Balall Naeem | 2 - Investigator |
| MHRA – GCP Inspectorate | Hayley Dixey | 2 - Investigator |
| North East and North Cumbria Regional QA Specialist Pharmacist | Anne Black | 3 - GMP Exemption |
| National Pharmacy Clinical Trials Advisory Group (NPCTAG) | Mandy Wan | 3 - GMP Exemption |
| Public Health England | Elizabeth Coates | 3 - GMP Exemption |
| Scottish Government | Dr Elizabeth Douglas | 3 - GMP Exemption |
| The Organisation for Professionals in Regulatory Affairs (TOPRA) | Jenny Lamport | 3 - GMP Exemption |
| Torbay & South Devon NHS Foundation Trust | Mark Santillo | 3 - GMP Exemption |
| UK Radiopharmacy Group | Jilly Croasdale | 3 - GMP Exemption |
| MHRA – GCP Inspectorate | Jason Wakelin-Smith | 3 - GMP Exemption |
| MHRA – GMDP Inspectorate | Alan Moon | 3 - GMP Exemption |
| MHRA – Clinical Trials Unit | Graham McNaughton | 3 - GMP Exemption |