AHPPI

Association for Human Pharmacology in the Pharmaceutical Industry

Annual Meeting 2022

The current state of investigator training in the UK

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Faculty of Pharmaceutical Medicine

Stakeholder Workshop Early Phase Principal Investigators Capabilities

Starting point:

Tegenero incident 2006

Duff report with recommendations regarding early phase Principal Investigators' (PI) and clinical trials units' capabilities

MHRA Phase 1 Accreditation scheme 2008

PI accreditation either by Diploma in Human Pharmacology (King's) or by exemption for PIs with extensive experience

(Exemptions granted by Faculty of Pharmaceutical Medicine)

Overarching aims of PI training and certification

Step 1:

Make physicians' training and capability assessments in early phase clinical trials **relevant**

Step 2:

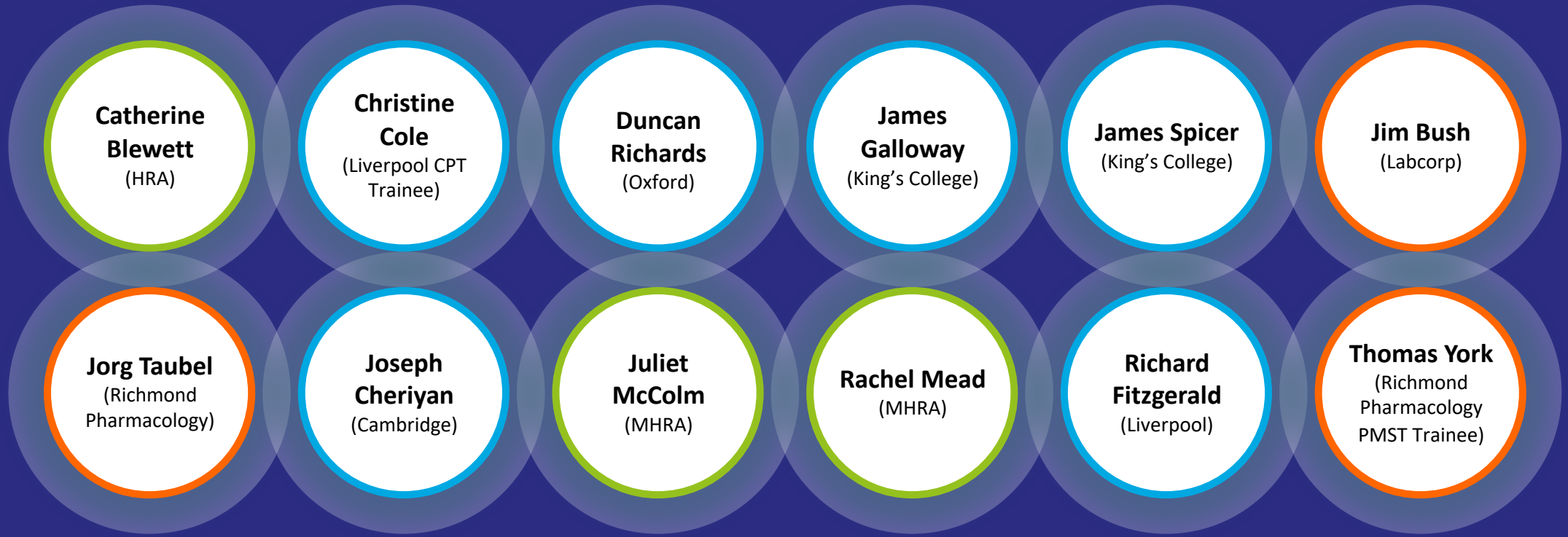
Make them **accessible**

Step 3:

Make them **attractive** and provide **certification**

Stakeholder Workshop Early Phase Principal Investigators Core Capabilities

Stakeholder group participants



& FPM Training and Education Team representatives

Step 1

Make physicians' training and capability assessments in early phase clinical trials relevant:

To make training and assessments **relevant** we need to ensure that it matches the work PIs for these trials do:

- Shift from traditional clinical pharmacology to applied human pharmacology with a different skill set for PI
- Scope of work and relevant capabilities of early phase PI vary depending on their background and workplace
- Emphasis on medical oversight and focus on clinical risk management
- Curriculum should include innovative study designs, advanced therapies, healthy volunteer and patient populations

The stakeholder group's task was to work out the common areas of core knowledge, competence, and behaviours (capabilities) an early Phase PI needs to have, irrespective of their scope of work

Outcome Step 1:

Core Capabilities Overview

A: OVERARCHING THEMES	
A1	Continuously assessing whether a trial has a reasonable chance of success
A2	Risk management encompassing all stages of a trial
A3	Medical Oversight of regulatory, operational, and quality aspects
A4	Medical Oversight of data management and statistical analysis
A5	Learning and Development (PI's own speciality training or revalidation; training of others)

B: TRIAL JOURNEY	
B1	Review potential new trial and whether it can be conducted in the PI's environment
B2	Trial Design/Trial Protocol
B3	Regulatory/Authorisations
B4	Safety monitoring during a trial
B5	Data analysis and reporting
B6	Publishing and transparency

CAPABILITY LEVELS DESCRIPTORS	
Level 1:	Entrusted to observe only
Level 2:	Entrusted to act with direct supervision: Has applied knowledge and understanding of skills required for capabilities and is able to act with them in practice under continuing supervision
Level 3:	Entrusted to act with indirect supervision: Applies knowledge and skills capably to undertake tasks and activities whilst remaining under continual supervision
Level 4:	Entrusted to act unsupervised

Example Overarching Themes:

Medical Oversight of Regulatory, Operational and Quality aspects

Essential Capabilities	Detail	Capability levels (examples)	Mapping to CPT/PMST and other specialty training curricula
1. REGULATORY			
Full awareness and acceptance of all applicable law, regulation, and guidelines	Sustainable plan to stay up-to-date		
	Continuous professional development knowing the law		
	Apply proactively		
	Justify when deviating		
	Not re-inventing the wheel		
2. OPERATIONS			
Good understanding of operational aspects	How a trials fits into location, healthcare environment	"Level 3: PI uses a facility for a trial and assesses it as reasonable and complete Level 4: PI is in charge of facility; its set-up, maintenance and decides whether trial specific adaptations to the facility's standard procedures can be made."	
Capable of assessing, using or building an infrastructure to fulfil PI duties		At all levels, the team capability must cater for the potential worst case scenario	
Capable of building a team that comprises all the skills one might need	Minimum safety standard needs to be able to deal with all potential risks of a trial/trials that are performed in the environment		
Capable of setting minimum safety standard that is acceptable for the environment			
Capable of using, developing, maintaining and improving standard operating procedures (SOPs) for the environment		Level of capability reflects the levels of innovation and leadership in this area	
3. QUALITY			
Capable of assessing, using or building a quality system to fulfil PI duties		Level 3: use for a trial, assessment as reasonable and complete Level 4: PI is in charge of a facility and uses, assesses and builds an overarching quality system for a facility	
Capable of appropriate issue reporting and of implementing appropriate corrective and preventative actions			
MHRA Phase 1 accreditation (where applicable)		Level 3: awareness and compliance Level 4: Key personal on licence, in charge of overall facility accreditation and ongoing maintenance and development	

Outcome Step 1:

Example Trial Journey: Safety Monitoring during a trial

Essential Capabilities	Detail	Capability levels (examples)	Mapping to CPT/PMST and other specialty training curricula
Selection of participants for whom the trial is safe	Balancing diversity of the target patient population and safety of individual participants		
Specific monitoring based on potential adverse reactions that are anticipated or expected	Identify potential risks prior to trial start and check compliance with all medical risk management processes		
Ensure facility is set up to deal with all potential adverse reactions	See A2		
	If necessary, make appropriate arrangements with other external experts or hospitals		
Ensuring data validity	See A4		
	100% QC of essential data for decision making		
Ensuring all safety data is easily and promptly accessible to PI's medical team	Practically feasible, timely, complete and accurate review of all relevant safety data		
	Ensuring all safety data is visualised in a way that makes the data easily accessible and understandable within their context		
Regular meetings/handover with members of PI's medical team	E.g. daily "ward-rounds"		
Communication with sponsor and other senior stakeholders as pre-agreed	Agreement on communication plan with senior stakeholders (such as Co-investigators for multi-centre trials and other clinical experts as well as senior sponsor stakeholders)		
	To have adequate reporting, discussion and decision making		
Expedited safety reporting to sponsor and Competent Authority where applicable: SAE and SUSAR reporting	In accordance with regulations and PV standards of the environment		
Non-expedited safety reporting	In accordance with defined communication and PV plans		
	Case reports		
	Interim safety reports		
Unblinding	Capable of managing emergency and non-emergency unblinding procedures		
Presentation and analysis of relevant safety, PK and PD data at appropriate intervals for decision making	Reviewing of interim safety, PK and PD reports		
	Predictions for upcoming trial periods and parts (in collaboration with other experts, such as pharmacokineticists)		
	Ensuring that predictions are within protocol defined limits;		
	Leading SRC/DSMB meetings for the PI's team		
Ensuring appropriate follow up of participants	Especially in case of adverse reactions and for long-term trials		
Decision making	In compliance with protocol rules and best medical practice;		
	Appropriate documentation for audit trail		
Competent interaction with pharmacy to ensure safe and correct IMP administration	Capable of addressing competently pharmacy topics such as: Blinding		
	Administration site/nature Site reactions and their assessment		
	Systemic reactions		
	Evidence of correct administration		

Thoughts from stakeholder group:

MHRA accredited academic units:

- PIs often trained in their medical specialties
- clinical trial training informal, beyond curriculum of their specialty
- National curriculum thin on early phase trials, even in oncology
- training supervision by senior PI is possible for two to three projects up to level 1 or 2 capability then senior oversight is no longer feasible

Most NHS early Phase PI operate outside accreditation umbrella, there is no oversight

How to deal with safety concerns?

No certification

This is a large group of current and potential PIs we could engage with an offer of flexible assessment and certification for their scope of work.

Future step 2:

To make physician's training and capability assessments in early phase clinical trials accessible:

- Core capabilities should **assume significant emphasis on collaboration with other experts, so that PIs can operate within their limits of competence and fill gaps through collaboration.**

  This will **lower barriers to entry** and should encourage a wider group of clinicians to seek training and accreditation.

- **Accessibility** can also be achieved by **using training and assessment systems and processes that can be used within current appraisal systems (revalidation, ARCP) that comply with GMC processes.**

- Putting together an **expert group of appraisers/ educational supervisors** (this could include MHRA representatives in addition to current FIH PIs), who will appraise the PI part of doctors' annual appraisal portfolios. The expert appraisers will then certify a doctor's competence to be a PI within their current scope of work on an annual basis.

- **Learning management system** including e-portfolio.

Future step 3

To provide certification:

It is important to provide certification for early phase clinical trial capabilities for two reasons:

To acknowledge achievement
and to **inspire confidence and trust** by patients, regulators, collaborators, and sponsors.

Two potential pathways:

Flexible for any current or potential PI who wants to certify and expand their capabilities and their scope of work

FPM Postnominal

Formal GMC credential

Level 1 and 2 capabilities could be overseen by ARCP and revalidation process in the workplace

Level 3 and 4 capabilities could be overseen by MHRA accreditation process and expert appraisers either available in the workplace, or provided by FPM

re-certification on an ongoing basis

in line with revalidation/specialty training requirements.

Support needed from many parties (Royal Colleges, GMC, FPM, MHRA, HRA, BPS, trainees, trainers, educational supervisors, appraisers, experts