

Certification: A smart move for investigators

Why are so few physicians undertaking programmes to certify them as investigators? As a certified investigator himself, **Dr Charles Pierce** explains that not only is it the right thing for them to do, it is the smart thing to do – and, with many programmes on offer, now is the right time for them to take the plunge

Are physicians inherently qualified to undertake clinical research? Some people, mainly physicians, argue that by the very nature of their education and training, they are also qualified to perform and direct research on diseases and the treatment of diseases of their patients. They say the doctor-patient relationship and the care that doctors bestow on their patients are enough to ensure that physicians know what they are doing and that their patients are protected from any harm during a study.

This argument clearly does not hold water, as has been shown by the closure of several academic research programmes by the US federal government following a number of highly publicised deaths during clinical trials. In response to this situation, Greg Koski, the former director of the US Office of Human Research Protections (OHRP), has said ‘the single most important step we could [take] to improve clinical trials... is to make sure that those doing the research are qualified to do it’.

In fact, when principal investigators (PIs) sign the form 1572 (Statement of the Investigator), they are certifying that they are qualified to conduct, and be fully responsible for, all aspects of the clinical trial in question. Interestingly, clinical research is the only specialty that physicians do not have to prove, by examination, that they are qualified to undertake before they practise it. At this time there is no standard method of assessing whether the person who signs form 1572 is actually qualified. A certification process may be of value in this regard.

Apart from the obligations of form 1572, there are several other compelling reasons why investigators need to learn the ever-growing rules and regulations of the drug and device development process. Keep in

mind that this process is big business, with literally billions of dollars at stake. Financial considerations, result expectations, and the opportunity to publish can all influence an investigator’s behaviour, so an understanding of the regulations that govern conflicts of interest would aid investigators to understand and manage conflicts, whether perceived or real.

Another complicating conflict of commitment is when doctors perform research on their own patients, for whom they are already obliged to provide care. The relationship between doctor and patient may create

a conflict in the consent process, because research and patient care are altogether different. Some believe it is ethically questionable for physicians to consent their own patients. An increasing number of institutional review boards actually forbid the practice, although this remains somewhat controversial as there are some compelling arguments in favour of PIs enrolling their own

patients. All these external factors and ethical dilemmas have taken a toll and jeopardised public trust in the clinical research process.

If one looks at the number of FDA audits and actionable deficiencies it is clear that investigators must do better. A visit from a regulatory auditor can cause great anxiety. Nothing points out how little an investigator knows about the process or operation of his or her own study as when he or she is faced with an exacting inspector asking tough questions. This auditor will expect honest answers, answers that the investigator should know. Alarming, investigators rarely do know what they are responsible for knowing! The learning process and certification of investigators could easily correct the deficiencies commonly found.

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Responsibilities of the PI

What is the PI actually responsible for? The answer is one word: everything. The PI’s remit covers for all aspects of the study, from the protocol to the final report. This includes, of course, the fundamental safety and well-being of the study participants. PIs are also responsible for the actions of every person on their staff who interacts with any study participant, no matter how briefly. Furthermore, PIs are responsible not only for their own training but also for that of the entire staff working on the research study. One of their paramount responsibilities is to follow – to the letter – the study protocol they have signed and which has been approved by a duly constituted oversight or research ethics committee.

So how does a physician investigator acquire the knowledge and commitment to conduct clinical research studies and follow the principles of GCP? As you might expect, there are several ways to accomplish this. It should not be difficult, as physicians go through school with the attitude of ‘see one, do one, teach one’. In addition, physicians believe that they think ‘scientifically’, and research is certainly science. This suggests, perhaps correctly, that one could learn what is needed by working with and following an experienced PI. This ‘apprenticeship’ type of learning is well known to all physicians who have completed an internship and residency. It may work, but the question of how to demonstrate proficiency in this area of specialised knowledge is left unanswered. Additionally, this approach does not provide standardised training for all investigators, and depends on the quality of the mentor.

The information needed to become familiar with the regulations is readily available, and the current certifying bodies all have guidelines as to what information needs to be known and understood (see Figure 1). In addition, ‘certification’ includes the requirement for experience over time (at least two years in most cases) in actual research in some capacity – preferably as a PI. In addition, many groups around the world have developed training courses for investigators.

Becoming a certified investigator

How can investigators provide the evidence that they have the required knowledge and are comfortable with the regulations, ethics, and rewards of clinical research? The goal of any certification process is to

evaluate systematically the professional knowledge of appropriately experienced members of the clinical research team. There are at least four broad areas in which the investigator must demonstrate knowledge and competence (see box opposite).

Certification programmes are well established among clinical research professionals. In 1985, the Society of Clinical Research Associates (SoCRA) developed a way to recognise formally clinical research professionals who met certain eligibility requirements (job experience) and who could demonstrate a standard level of job-related knowledge and skills. SoCRA held its first single examination for all types of research professional (designated CCRPs) in 1995.

The Association of Clinical Research Professionals (ACRP) set up its certification programme 1990 and held its first examination for certified clinical research co-ordinators (designated CCRCs) in 1992, followed by one for certified clinical research associates (designated CCRAs) in 1995 (see ‘Examining levels of competence’, page 24).

Since then some 17,400 CRCs and CRAs have been certified and this process has become the standard for non-physician study personnel. Sponsors often insist on, or at least give preference to, sites and CROs boasting CCRCs, CCRAs, and CCRPs on their staff. In addition, investigators have learned to rely heavily on these professionals. Few CROs or large sites conduct trials without at least some of the co-ordinators and/or research associates being certified. These knowledgeable staff make or break most studies conducted at the present time because they are often the only ones who do know the rules of research and have demonstrated that they have both the experience and knowledge to know what they are doing.

The story is different for physician investigators because, until recently, there was no formal way for investigators to demonstrate that they were qualified to take responsibility for all aspects of the conduct of an investigation involving human subjects. At the time of writing, four organisations have developed a process for investigator certification that requires both experience and an examination to test practical knowledge of GCP and the regulation of research and human subject protection (Figure 1). Of the groups, the American Academy of Pharmaceutical Physicians (AAPP) is on track for pharmaceutical medicine to become a medical specialty complete with an independent Board of Pharmaceutical Medicine. One of the tracks in this specialty will surely be clinical research competence.

Of the many thousands of individuals who are now certified as competent in the conduct of clinical research studies, only 380 are physicians. This is significant, as it is physicians who are most often the PI responsible for everything

| Certifying organisation | Letter designation | First exam | Involved in training? | Years to re-certification | Contact information |
|-------------------------|--------------------|------------|-----------------------|---------------------------|---------------------|
| AAPP | CPI | 2003 | Yes | Five | www.AAPP.org |
| ACRP | CCRI | 2002 | Yes | Two | www.ACRPnet.org |
| DIA | CCI | 2003 | Yes | Three | www.DIAhome.org |
| SoCRA | CCRP | 1995 | Yes | Three | www.SoCRA.org |

Figure 1: Physician certification guide.

Four areas in which certified investigators must demonstrate knowledge and competence

1. Rules, regulations, laws and guidelines governing research with human subjects

- Ethical guidelines from all sources (local, AMA, FDA, OHRP, etc)
- International Conference on Harmonisation (ICH) GCP Guidelines
- Applicable Titles of the Code of Federal Regulations, such as Titles 21 & 45
- FDA and NIH regulations
- Local and national legal standards regarding subject safety and privacy
- The history of the development of the above

2. Ways of protecting human subjects from all harm

- Rights of the research subjects
- Informed consent and the correct process of consent
- Development of quality assurance processes and SOPs
- Knowledge of how to evaluate the investigators' brochure
- Understanding of the importance of adverse event handling
- Methods to minimise risk in the conduct of a study through observation and the laboratory
- Familiarity with the Belmont Report and the Declaration of Helsinki

3. Ways to conduct a clinical investigation

- Evaluate a study design and protocol to ensure that the scientific method is not compromised

- Know how to evaluate a site (for capability and appropriateness) before a study commences
- Evaluate and train study personnel
- Set up SOPs and source documents and maintain a regulatory binder
- Set up a delegation process and know what and when to delegate
- Recruit subjects on time and strictly according to the protocol
- Know how to evaluate subjects for safety and manage adverse events
- Know when and how to deviate from the signed protocol
- Know how to set up, maintain, and secure all study records
- Know how to control, use and record study test articles (drugs or devices)

4. Knowledge to organise and manage a study site


- Identify and evaluate staff who will assist in the conduct of clinical trials
- Set up and supervise the training of research staff
- Evaluate subject population as to appropriateness for a given study
- Determine and minimise 'risk' at the site to ensure site solvency
- Set up the assessment and maintenance (including calibration) of test equipment
- Create or supervise the creation of the site SOP binder

about these same clinical studies/trials. Certainly all studies involving the testing of new drugs or devices in human subjects must have physicians involved, even if not as the PI. Surely this relatively small band of certified physicians are the smart ones, as their sites will inevitably be more appealing to sponsors and CROs.

Given that the acceptance of accreditation is widespread, not only for individuals but for organisations involved in research,¹ it is disappointing that so few investigators are demonstrating their commitment to certification. The reason cannot be the lack of courses or material on the web, but rather it is the mind-set and perceived needs of investigators. In the US, the AAPP, the ACRP and the DIA all offer courses of GCP training in addition to their respective annual meetings. Both the DIA and the AAPP have developed study manuals that put together most of the basic information in an easily read format. In the EU, the European Centre for Clinical Research Training (ECCRT) is active in training and is itself certified for what it does through the ISO 9001 process.

The matter is of such importance that we can expect in the not too distant future to see those groups now offering 'certification' getting together and setting a standard examination and process for PIs. The next step will be for the sponsors of research (the pharmaceutical industry and the NIH), the CRO industry, and the FDA to require this guarantee of quality. It is my belief

that some process of proving that the investigator knows what he or she is doing will be required as part of the drug development process.

Demonstrating one's competence in an area of knowledge by an examination set by one's peers and thereby 'certifying' that the individual has the knowledge and tools to be committed and comfortable with the whole process of research involving human subjects is laudable. 'Certification' will not be a panacea, but the benefits are clear. Investigator certification will improve the protection of humans involved in research across the global community, which will make research safer and go a long way to improve, preserve, and justify the public's confidence and trust in research. 

Reference

- 1 M Speers. 'All credit to clinical research', *Good Clinical Practice Journal*, 10, 12, pp9-11, December, 2003.

Charles H Pierce, MD, PhD, FCP, CPI

Vice-President, Medical Affairs for North America
Harrison Clinical Research Group
Cincinnati, OH, US
Tel: +1 513 681 4084
Fax: +1 513 681 4094
E-mail: Charles@Pierce1.net