SCRIP MAGAZINE

Publish…but don't be damned

The probity of pharmaceutical research is called into question as medical journal editors justify their new editorial policy on publishing clinical trial data. Dr Michael Bowden, managing director, and Steve Mackenzie-Lawrie, director, of EU contract research organisation, Health Decisions, put the record straight

Dr Michael Bowden

By now most of the pharmaceutical industry will be aware of a new editorial policy on the publication of clinical trial data. As justification for this more stringent editorial stance, a number of charges were laid at the door of trial sponsors and contract research organisations (CROs). These are that investigators are excluded from much of the study process and are not allowed full access to the data or the right to publish without permission.[1,2] There have even been suggestions that CROs may skew enrolment to trials, compete unfairly with academic investigators for trial revenue and suppress the publication of unfavourable data.

From now on, the International Committee of Medical Journal Editors (ICMJE) has decreed that authors must disclose details of their own and their sponsors' roles in the study, accept full responsibility for the conduct of the trial, confirm they have full access to the data, and reveal who controlled the decision to publish.

The underlying sentiments behind this action – of securing objectivity, intellectual rigour, scientific integrity, publishing freedom and the accuracy of scientific records – are all laudable. They should already be an integral part of the process of communicating efficacy and safety of drugs to physicians as well as healthcare policy makers.

However, before you give three cheers for this action, we urge you to consider the accuracy of the charges made to justify the new policy. In the words of the UK Institute of Clinical Research these statements reveal "a lack of understanding of the operation of clinical research in the commercial world".[3]

Into perspective

First, the size of the problem needs to be put into context. Academia, sponsoring companies, government bodies, regulatory agencies, CROs, clinicians, investigators and patients all deplore malpractice in clinical trials and the publication of misleading data. Of course, it may happen occasionally – originating from either trial sponsors or from investigators in the healthcare sector or academia. But as the editor of the *British Medical Journal* stated, "Almost all new drugs are developed by the industry, and many companies have high ethical standards and will see no problem in complying with the new policies. Pharma companies become successful not through dubious publication or marketing policies but by developing important new drugs.''[2]

We all know that clinical trials are subject to mandatory stringent regulations and procedures as well as to both local and national reviews and approvals, in which patients' interests and safety are paramount. These regulations also stipulate that every study protocol must include a publication policy, which every investigator must sign in order to participate.

Therefore the implication that contractual agreements are denying investigators access to, or publication of, the data they generate creates a false impression. Although this may happen occasionally, in terms of the huge volume of research that is published, it is exceedingly rare in our experience.

A review of our own contracts with pharmaceutical sponsors and clinical investigators confirms this. As CROs, we have no control over the publication of data, neither do we expect to. And we were unable to find any contracts with investigators that denied them consent to publish their results.

In most cases, however, the contracts stipulate that the investigator should give a specified time before publication so that the sponsor can review and comment on the draft manuscript. The rational for this is to ensure that commercially sensitive information is not being disclosed and, if it is, to give the sponsor sufficient time to file patents and the like. In the vast majority of cases, 'current practice' does not support the notion of contractual agreements suppressing the publication of data.

False impression

The inference that investigators are excluded from study design, writing protocols and development is also misguided. It is misleading to suggest that these elements of the clinical trial process are completed by sponsors in isolation from investigators and other essential parties. In fact, in order to meet the current demands and pressures that drug developers face in today's marketplace it is shortsighted to believe that the intellectual input into clinical trials is the sole domain of sponsors or investigators and academic research centres.

As more and more data are required to support regulatory approval of new medicines, many expert disciplines must be brought together to conduct effective trials. Larger trials increasingly involve many countries and differing medical practices. Such trials demand expertise in project management, drug supply, regulatory affairs and logistics, as well as the clinical and therapeutic expertise of academic investigators, if they are to succeed.

In this environment it would be a very poor sponsor who did not seek systematically the essential input of academic investigators to the design and conduct of its clinical trials. This input is increasingly facilitated by the emergence of a new generation of e-clinical trial systems that allow rapid, real-time access to trial data as it is generated and which allow

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information and knowledge to be shared by all the parties involved.[4]

Indeed this approach is required by Good Clinical Practice as set out by the International Conference on Harmonisation. Sponsors are required to "utilise qualified individuals (eg, biostatisticians, clinical pharmacologists, and physicians) as appropriate, throughout all stages of the trial process, from designing the protocol and case report forms and planning the analyses to analysing and preparing interim and final clinical trial reports".

Unfair competition?

Another charge by the medical editors implied that academic investigators were faced with unfair competition for patients and trial revenues in the shape of CROs and, more recently, site management organisations (SMOs). Such companies have emerged in response to sponsors' efforts to meet the needs and demands of patients, governments, physicians and regulatory bodies. A lack of understanding of their roles is evident, for example the editors suggest CROs compete head to head with investigators and academic medical centres to enrol patients in clinical trials.

It is SMOs that enrol patients. These are usually companies providing a consortium or network of investigators (that is GPs or hospital consultants) operating on a commercial basis to co-ordinate single point of access to a large number of trial sites and patients. While SMOs may compete with individual investigators and academic medical centres to enrol patients, such organisations arose out of the need to 'improve patient recruitment processes' for larger trials and to meet the demands for faster development of new products and for a broader and wider demographic patient base to be included in clinical trials.

CROs are needed to effectively manage and coordinate the setting up and implementation of ever more complex trials. Acting as an agent for trial sponsors, they are an interface between investigator and sponsor and will often oversee and manage an SMO's activities in much the same way as they may manage those of an individual investigators' (academic, hospital or general practice-based) unit. CROs can provide the expertise and in-house skills to coordinate the broad range of disciplines vital for effective trials. These are resources which few, if any, academic medical centres or individual investigators have at their disposal or can provide in isolation. Far from diluting intellectual input into clinical trials, CROs have increased it by facilitating input from many disciplines, including biostatisticians, clinical pharmacologists, physicians and regulatory affairs. This is in accordance with the strict regulations governing drug trials, regulations which so far have not applied to non-commercial, purely academic research.

The *Lancet's* claim that CROs receive the lion's share of clinical trial revenue while academic trialists receive only 40% is also somewhat misleading. Although this percentage of revenues did go directly to academics last year, they also received a substantial proportion of the monies paid direct to CROs. The reality is that investigators deal directly with the CRO rather than the sponsor. In our own organisation, an average of 30-40% of the total study budget is paid to clinical investigator sites and institutions, often for the support of research staff.

It is not a question of competing for revenue or academics losing out. It is being aware of what is required for successful drug development and how budgets are allocated to achieve this. As this process has evolved, there has been a need to expand the range and type of resources required to perform clinical trials. CROs and SMOs are now an integral and effective part of the drug development process which academic medical centres and individual investigators could not deliver alone.

In the 'real world' the successful completion of clinical trials involves a team approach governed by strict regulations and guidelines. Perhaps now is the time for all of us involved in clinical trials – sponsors, CROs, regulatory agencies, clinicians and editors of medical journals – to re-affirm our shared goal of delivering high quality, safe and efficacious medicines to patients, and to ensure effective communication of the results of our endeavours to the wider scientific and medical community, and society at large. There is plenty of room for improvement in what we do, but at least let's not conduct the debate about those improvements without ensuring all the details are in the public domain and certainly not by slinging missiles over the walls at each other. SM

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