

## THE TIME IS COMING

Registration of many clinical trials seems increasingly likely to become mandatory. Proactive participation by the pharmaceutical industry in the establishment of an authoritative clinical trial registry could have benefits for all stakeholders in clinical research.

Why are clinical trial registries needed? Although this question has been brought to the fore recently by the controversy over unpublished data undermining the presumed safety of prescribing antidepressants to paediatric patients, the idea of registering clinical trials was first proposed 30 years ago. Speaking then to the US President's Cancer Panel, Mary Lasker asked the National Cancer Institute to publish a regularly updated book that would allow doctors to identify open cancer trials in which their patients could enrol.

Facilitating patient enrolment is one purpose of trial registries that has widespread acceptance. More recently, however, it is the potential of trial registration to reduce 'publication bias' by allowing all data associated with a given therapeutic intervention to be assessed that has provided impetus to the development of trial registries. It is clear that many trials that show negative or inconclusive results are never formally published, and this can influence medical practice adversely in several ways.

First, the non-publication of negative or inconclusive trials — as seems to be the case with some trials of antidepressants in paediatric patients — can result in the systematic reviews of available data that are used to aid medical decision-making being inappropriately skewed in favour of a particular therapeutic intervention. The multiple publication of trials with positive outcomes has also been shown to contribute to this problem. Second, if negative data are not made available, similar trials might unknowingly be repeated. The consequences in this case were tragically illustrated in the 1980s; during this decade, it has been estimated that the use of class I antiarrhythmic drugs with the aim of reducing mortality after heart attacks caused tens of thousands of premature deaths. Had the results of a trial indicating the hazards of this drug class been published when it was completed in 1980, rather than in 1993 as they eventually were, these deaths might well have been avoided.

Such examples of the need for trial registries have recently led the International Committee of Medical Journal Editors (ICMJE) to announce that next year they

will start to only consider papers reporting trial results for publication if the trial has been registered at its outset in a publicly accessible registry. The ICMJE identifies several other criteria that such a registry must meet, including the assignment of a unique identifier for all registered trials. This would help address publication bias by allowing those undertaking systematic reviews of trial data to assess whether all trials related to a particular intervention had been published, and to easily recognize cases of multiple publication.

At present, only one trial registry fulfils all of the ICMJE criteria: [www.clinicaltrials.gov](http://www.clinicaltrials.gov), which is sponsored by the US National Library of Medicine. But as critics have pointed out, many trials worldwide do not meet the current entry criteria for this registry, which is focused on studies funded by US federal agencies and private sponsors submitting data to the FDA.

However, in recent months, several other initiatives to set up trial registries have been announced or implemented by organizations including the American Medical Association and the World Health Organization. The Pharmaceutical Research and Manufacturers of America (PhRMA) has also begun to create a voluntary trial registry, as have several individual companies. But such voluntary databases are unlikely to find much favour with those who are already concerned about the industry's influence on the way clinical trials are reported. Furthermore, the continued proliferation of trial registries — of which there are already over 300 worldwide — and the lack of standardization in the nature of the entries within each adds further challenges for those seeking trial data.

Bearing in mind all of these issues, and imminent plans to introduce legislation that could make the public disclosure of trial data compulsory, an industry-wide drive to help establish an independent and authoritative source of trial information that reflects the needs of all stakeholders in clinical research could be timely. Such efforts would do much to restore the seriously damaged public trust in the industry and its regulation, and most importantly, could considerably improve the practice of medicine.

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