



From the editor's desk:

Clinical trials – old but not benign

By Elise Langdon-Neuner

The theme of this issue is clinical trials. Clinical trials are as old as the hills or at least the Old Testament according to Susanna Dodgson's article on their evolution published in this issue. Nevertheless today some interventions still remain unevaluated. Take for example parachutes. Gordon Smith and Jill Pell were unable to identify a single trial in their systematic review of randomised controlled trials to determine whether parachutes are effective in preventing major trauma related to gravitational challenge. Alarmed by this oversight, they called for volunteers to participate in a clinical trial to assess the effect of jumping out of a plane with a parachute as against the placebo of 'no parachute' [1]. Although that article was designed to snipe at protagonists of evidence-based medicine, the integrity of evidence secured by clinical trials and of its reporting is of paramount importance to everyone's health.

In clinical trials the new product being tested needs to be tested against something, perhaps logically against no intervention, i.e. no parachute. The idea would then be that the placebo has no effect—however, the matter is not quite so simple. For example, in a clinical trial of dapoxetine (a therapy to increase time to ejaculation), men receiving placebo doubled their time to ejaculation, and did not suffer the side effect of nausea experienced by 20% of the men who received the highest dose of dapoxetine [2]. This is just one example of the well-known "placebo effect", which is one of the more important reasons for today's standard of double-blind, randomised, placebo-controlled trials. Most medical writers will be able to think of a long list of medications that were stunningly successful in open trials and failed miserably against placebo.

Care must be taken to ensure that clinical trials measure what needs to be measured. For example, in testing for lead poisoning, volunteers breathed and swallowed lead in large quantities. Measuring lead in their urine and faeces gave a negative result—not surprisingly, because lead is dangerous precisely because it is not excreted, but accumulates in bones and blood [3]. Failures of clinical trials to detect long-term consequences are increasingly causing pharmaceutical companies to move centre stage, in a gathering storm of lawsuits costing companies hundreds of millions of dollars in payment of claims brought by patients [4].

Not only do we need to know that to be an effective protection for patients clinical trials are properly designed but we also need to know that they are conducted on interventions that patients actually need. Do women need the seven new

products for sexual dysfunction (a disease not all experts agree exists) currently being developed? [5]. Why have no entirely new antibiotics been invented since the 1970s? Perhaps the answer is something noted in James Surowiecki's article in the New Yorker, "given the choice between developing antibiotics that people will take every day for two weeks and developing antidepressants that people will take every day for ever, drug companies opt for the latter" [6]. I have heard the same argument applied between vaccines against bird flu and Viagra.

Clinical trials are therefore not without controversies and these affect medical writers too. Medical writers' responsibilities are in the reporting of data from clinical trials to regulatory authorities and to the public. Clarity has not been promoted by the great restrictions that have traditionally been placed upon the divulgence of information to the public about the clinical trials. To combat this problem, the registration of clinical trials was proposed. Two articles in this issue of TWS look into the registration of clinical trials and ask what the medical writer needs to know about registration. Medical journals are reacting to what they see as their manipulation by the industry by dismissing industry-sponsored research with the serious danger that drugs that may help patients are not being prescribed [7]. Accusations frequently mention the inappropriate use of medical writers as ghostwriters of manuscripts submitted to journals. EMWA has tried to bridge the gap between the role of medical writers and medical journals by issuing guidelines (see box on page 5)

Articles in this issue which should further help medical writers in their everyday work include an article that asks whether experience with non-clinical drug development is important for medical writers, another article that gives some intriguing hints on how to do battle with clinical submissions and yet another on how to cope with the electronic Common Technical Document (eCTD). The eCTD is targeted for Europe-wide use by 2009 and is also the theme of the forthcoming EMWA conference in Lyon.

The Write Stuff welcomes suggestions. One has been that we should have more articles about English usage and grammar. In future a greater effort will be made to include at least one article on this topic in each issue. In this issue, we present the first of several articles in which Alistair Reeves will investigate English language myths.

Myths of another kind are explored in Ursula Schoenberg's

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“codes and quips” article. When I read ‘don’t let the bed-bugs bite’ my thoughts rambled on with the quip my children said back to me: ‘and if they do, squeeze them tight – they won’t come another night’. The article got me thinking about sayings from my own childhood such as ‘When one door closes another one opens’ and one from an old gardener ‘You have to eat a bit of dirt before you die’. As a child, I thought this meant that I shouldn’t worry as much about getting dirty as my mother would have done. Now, it seems more like a moral in immunology. I hope that Ursula’s article will evoke many reminiscences and favourite sayings to publish in future issues.

Finally, I should like to mention that the authors in this issue come from no fewer than seven countries: Sweden, Switzerland, the USA, the UK, Germany, Austria and Australia. But this is not unusual for TWS, except that the last is the result of a new co-operation with the Australian

Medical Writers’ Association (AMWA). I am particularly delighted to have received this article. The next issue, in June, promises even more international variety, with its theme of non-native English speakers and translation. Contributions on this topic are very welcome.

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“What should journal editors consider before they publish studies involving animal research?”

This question was considered in a plenary session at a seminar given by COPE (Committee on Publication Ethics, www.publicationethics.org.uk) in March this year. There is no international standard like the Helsinki agreement applicable to animals. As Angela Turner explained in her article on animal experimental regulations published in TWS (Vol. 13, No. 2, 2004, pages 43-45) researchers submitting papers to a journal are expected to have complied with their own national and local laws, and to have had their work reviewed by the local ethics committee where relevant. Often these regulations will be based on the ‘3 Rs’

- refinement of experimental techniques to reduce suffering
- reduction of numbers of animals used
- replacement of animals with non-animal methods.

Cultural attitudes towards treatment of animals however varies. The pallet ranges from the French (not the British) who are apparently the most sympathetic towards animal welfare among EU nationals and the Chinese who do not have national regulations for animal welfare.

Journal editors are faced with a problem when manuscripts are received from another country describing experiments conducted on animals in a manner acceptable for that country but unacceptable for the country where the editor resides. An example was given at the seminar where rats had been left to die after experiments had been completed rather than being killed immediately after the experiment. The editor refused to publish this research. The conclusion reached at the COPE seminar was that editors should judge experiments by their own ethics standards when deciding whether to publish. But

they may face the dilemma that publication of these experiments could be valuable in furthering research in humans. A point was also raised as to whether society owes a debt to those who partake in trials to publish the study results. The point is probably more applicable to human trial participants in negative trials but is one that is not currently taken into account in publication ethics.

Medical writers might not be party to decisions relating to methods used in experiments involving animals but we do have some control over words that appear in documents reporting the experiments. Here attempts at euphemisms can be deceitful and distasteful.

The word ‘sacrifice’ was widely used to describe the killing of animals after an experiment until stylebooks bitterly protested against it. Neville Goodman and Martin Edwards in their book *Medical Writing a Prescription for Clarity* write “A sacrifice is a religious rite, or (COD) the giving up of a valued thing for the sake of another that is more worthy or more important or more urgent. Do not use sacrifice when you mean kill. A similar debasement is likely to happen to assassinate if the media persist in applying it to the murder of hoodlums and terrorists”. I have yet to come across assassinated rats in the documents I edit but ‘euthanasia’ has crept in. Webster’s dictionary defines ‘euthanasia’ as “the act or practice of killing or permitting the death of hopelessly sick or injured individuals in a relatively painless way for reasons of mercy”. The spirit of this definition is hardly that the person responsible for the euthanasia also caused the sickness or injury. The truth is that animals are killed and this is the word to use. Murder and homicide only relate to humans and slaughter is to kill animals for food or to kill in a bloody and violent manner.

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