BJCP British Journal of Clinical Pharmacology

DOI:10.1111/j.1365-2125.2008.03291.x

Letter to the Editors

Investigator-initiated pragmatic trials in developing countries – much needed but much ignored

Nusrat Shafiq, Promila Pandhi & Samir Malhotra

Department of Pharmacology, PGIMER, Chandigarh-160012, India

The last decade has witnessed clinicians in developing countries gaining recognition as investigators for many sponsor initiated multicentre rials. This is indeed a welcome change as it has provided an impetus for investigators in these countries to gear up and meet world standards. This is exemplified by the fact that the Ethics Committees across countries are increasingly becoming compliant with International Conference on Harmonization-Good Clinical Practice (ICH-GCP) guidelines, laboratories are making efforts for Good Laboratory Practice (GLP) accreditation, indigenous clinical trial registries have been set up [1] and programmes to train clinical research co-ordinators/monitors and investigators are being undertaken at various levels. Contributions have also been made by generating informed consent templates [2] and by producing teaching materials for clinical trial participants [3]. However, with the recent upsurge of sponsor initiated clinical trials, investigator initiated clinical trials have taken a back seat.

High on the agenda for pharmaceutical company-sponsored clinical trials are new drug development or expanding the indication profile of their drugs. Questions such as comparative efficacy of one drug over another or a medical management with surgical/interventional management, strategies to ease drug dosage schedules, quality of life issues, exploration of alternative systems of medicines are not frequently explored in these trials. These are objectives of concern in investigator-initiated trials and the findings of these trials have important bearing for practice and for making health related policies [4]. Many investigators have the keenness and also the know-how for initiating and conducting such trials. However, the task is not easy if GCP standards are to be maintained. Funds are a major crunch.

Government funding agencies/research groups/associations in the west have from a long time realized this need and have sponsored such investigator-initiated trials which have contributed significantly to furthering medical knowledge. Key examples would be the Diabetes Control and Complication Trial (DCCT), the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and Clinical Antipsychotic Trials of Intervention Effectiveness. There are some examples from the developing countries as well such as Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) [5], the SPEAR trial to compare chloramphenicol *vs* ampicillin plus gentamicin for community acquired very severe pneumonia in children in low resource settings [6], the ongoing CORONIS trial to compare various surgical techniques for Caesarean section. Interestingly the funding for such studies has come from agencies such as the World Health Organization, the Fogarty International Center of the National Institute of Health, Center of International Health and Development of Boston University and Johns Hopkins Bloomberg School of Public Health to name a few. This is indeed one of the options for investigators in developing countries but self-reliance should be the ultimate goal.

All this would need a great deal of commitment from government aided agencies not only for providing funds for the conduct of the studies, but also for establishing systems for overseeing and ensuring GCP-compliant conduct of these trials. A government agency or scientific societies could play a constructive role in this regard. To start with, investigators who have published pilot trials could be encouraged to evolve their studies into adequately sized (if need be multi-centre) studies. A list of unanswered questions addressing the indigenous needs could be prepared and a list of investigators with proven credentials could be drawn up. For this, investigators with a past track record of conducting and publishing their trials should be chosen. Furthermore, these investigators could be helped to develop final protocols with inputs even from various experts the world over. The trial registration should be ensured. Evaluation of reports of the monitors, data safety monitoring board and audit of the trial could help in paving the way for the conduct of GCP compliant trials.

Some problems are indeed expected. There could be concerns about the legal issues such as compensation to the participants in case of injury, insurance of the investigators, staff for ensuring quality control and quality

© 2008 The Authors
Journal compilation © 2008 The British Pharmacological Society

assurance, inter-departmental and inter-institutional collaborations. However, none of these is insurmountable. Successful models are available [7, 8] and benefits could be derived from them to suit the needs of our country.

Over a period of time sponsor-initiated trials conducted in developing countries have forayed into the medical literature and created their impact on medical practice. There is no reason why investigator-initiated pragmatic trials should lag behind.

Competing interests

None declared.

REFERENCES

1 Clinical Trials Registry India. National Institute of Medical Statistics (ICMR). Available at http://www.ctri.in:8080/Clinicaltrials/trials_jsp/index.jsp (last accessed: 3 June 2008).

2 Shafiq N, Sidhu S, Pandhi P, Malhotra S. Informed consent form template for investigators conducting clinical research. Bull PGI 2005; 39: 106–9.

3 Malhotra S, Shafiq N, Pandhi P. All that you wanted to know about clinical research. Mansa Print and Publishers Ltd, India. 2006: 184–206.

4 Tyndall A. Why do we need noncommercial, investigator-initiated clinical trials? Nat Clin Pract Rheumatol 2008; 4: 354–5.

5 Vaidya A, Saville N, Shrestha BP, Costello AM, Manandhar DS, Osrin D. Mother and Infant Research Activities (MIRA), Kathmandu, Nepal. Effects of antenatal multiple micronutrient supplementation on children's weight and size at 2 years of agen Nepal: follow-up of a double-blind randomised controlled trial. Lancet 2008; 371: 492–9.

6 Hazir T, Fox LM, Nisar YB, Fox MP, Ashraf YP, MacLeod WB, Ramzan A, Maqbool S, Masood T, Hussain W, Murtaza A, Khawar N, Tariq P, Asghar R, Simon JL, Thea DM, Qazi SA. New Outpatient Short-Course Home Oral Therapy for Severe Pneumonia Study Group. Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. Lancet 2008; 371: 49–56.

7 Sledgewort J, Derewlany L. Institution/investigator initiated clinical trials in Canada. Can J Clin Pharmacol 2006; 13: e236–9.

8 NHLBI Research at the Bethesda Campus. Available at http://dir.nhlbi.nih.gov (last accessed: 3 June 2008).

RECEIVED
9 June 2008

ACCEPTED
20 August 2008

PUBLISHED *Early View*
5 November 2008

CORRESPONDENCE
Associate Professor Samir Malhotra, Department of Pharmacology, PGIMER, Chandigarh-160012, India
E-mail: Samirmalhotra345@yahoo.com