Clinical trials in Sri Lanka: new Act at the behest of the pharmaceutical industry?

Article *in* Indian Journal of Medical Ethics · October 2013

DOI: 10.20529/IJME.2013.081 · Source: PubMed

2 authors, including:

Sisira H Siribaddana
Rajarata University of Sri Lanka
165 PUBLICATIONS **1,347** CITATIONS

SEE PROFILE

Clinical trials in Sri Lanka: new Act at the behest of the pharmaceutical industry?

SISIRA SIRIBADDANA[1], WASANTHA BANDARA[2]

[1]Foundation Professor and Chair, Department of Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura 500 08 SRI LANKA
[2]Dental Surgeon and Independent Management Consultant, 270/2(278/31) Colombo Road,Kurunegala 600 00 SRI LANKA. Author for correspondence Sisira Siribaddana e-mail: nipuna@stmail.lk

Clinical trials are defined as studies involving human participants, with the intervention being selected by the investigator (1). The intervention can be related to a new drug or device, or a new indication for an already approved drug or device. The intervention can also relate to different healthcare options, eg the trial may be aimed at comparing the management of a particular illness in the hospital to its management in the community.

The state regulatory body for drugs in Sri Lanka is the Cosmetics Drugs and Devices Regulatory Authority (CDDRA). The CDDRA's permission is required for the registration and import of new drugs. In January 2009, the ministry of health appointed a subcommittee on clinical trials (SCOCT) under the CDDRA. The SCOCT's regulatory approval is necessary for clinical trials. The SCOCT requires ethical approval by a recognised ethics review committee (ERC). Further, according to the regulations, registration in the primary World Health Organization clinical trial registry network is mandatory. The clinical trial registry, which is in the premises of the Sri Lanka Medical Association, is the only such registry in the country.

Recently, bureaucrats in the health and the finance ministries, as well as a few academics, have been pushing for a new Act on clinical trials (2). This paper highlights the various loopholes in this draft Act and describes how it may give the pharmaceutical companies opportunities to circumvent its provisions and exploit patients. The clinical trial industry has been perceived by these Faustian treasury economists as a magnet for foreign currency. The draft Act reflects an insouciant attitude to the patient's welfare and the free health system, which is unique to Sri Lanka. There were no consultations with the public or the stakeholders when this Act was drafted, and its provisions have still not been made known to academics, ERCs and the public.

The supposed aim of the Act is to regulate clinical trials in Sri Lanka, since the country lacks a legal framework to regularise clinical research. It is expected to cover the legal loopholes that arise during all phases of the conduct of clinical trials in drugs and devices. As in the USA, this Act will protect contract research organisations (CROs) and clinicians from law suits in case of an injury to a participant (3). Injuries such as multi-organ failure when injected with a biological agent (anti-CD28 antibody) in a highly publicised phase one randomised clinical trial (RCT) make it imperative to discuss mechanisms of compensating and treating research injury (4). Although the draft Act claims to follow the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines, there is ample evidence to show that even the ICH-GCP was formulated to safeguard the pharmaceutical industry (5).

The authors managed to get a copy of this draft Act forwarded by the attorney general's department to the secretary of the ministry of health. A copy was also sent to the attorney general for the issuance of a certificate of constitutionality. This is a common practice to verify whether an act is in harmony with the law of the land or constitution. The draft Act has a Preamble and 38 Articles. Its main objective is to establish the regulatory framework for randomised controlled trials (RCTs) and to facilitate the process of obtaining the licence and approvals required to conduct them. The other objectives are to ensure the implementation of the WHO's good clinical practice (GCP) guidelines, register all RCTs, support and protect study participants, provide accreditation and register CROs. Articles 3–6 relate to the policy and regulatory framework, while Articles 7–9 deal with ERCs. Articles 10–20 pertain to the licence for conducting clinical trials. Article 21 deals with the conduct of clinical trials and the payment of compensation. Informed consent is described in detail in Article 22. Articles 23, 25 and 26 discuss the responsibilities of the licence-holder and Article 27 is about adverse events. Article 24 discusses the conduct of clinical trials in emergency situations. Article 28 relates to amendments to the protocol, and Articles 29, 31 and 32 give details of responsibilities of sponsors and investigators. Article 33 describes offences and sets forth the pecuniary penalties, specifying the minimum and maximum limits. Article 34 describes the powers of the health minister, while Article 35 mentions regulations that should be included in the gazette. Articles 36, 37, and 38 deal with procedural aspects of the Act.

After the new Act is passed, the national policy on clinical trials will be drafted and reviewed every three years. The Act will be enforced mainly by the Clinical Trials Regulatory Division (CTRD), a new entity to be established under the CDDRA in the ministry of health (Article 4). The CDDRA has a history of scandals (6), the most recent one being related to an irregularity in a tender for surgical gloves (7). There is a belief that the CDDRA is under the influence of or being pressurised by Big Pharma (http://lankacnews.com/sinhala/main-news/45178/). Thus, it is likely that the CTRD will also be influenced by the pharmaceutical companies.

Paragraph 7 of Article 4 of the draft Act specifies that the CTRD will receive independent funding. However, there is no explanation regarding who will authorise payment from that fund and who or what organisations can give donations and grants to the fund. There is not a single sentence about the management of the fund. This gives an opportunity to various

foundations that represent the corporate social responsibility face of Big Pharma to manipulate the CTRD.

The draft Act requires the establishment of a regulatory review committee (RRC), which will include three pharmacologists and three clinicians, among others. The chairman of the RRC, who will be elected during the first meeting, need not be from the ministry of health or CTRD (Article 5, paragraph 3). If an influential clinician is elected as chairman, he/she will be able to manipulate the proceedings because of the enormous power that clinicians wield in developing countries such as Sri Lanka. Also, four clinicians have been co-opted as non-voting members to advise the committee. All of them are required to declare any conflicts of interest on a case-by-case basis (Article 5, paragraph 6). This may lead to further abuse as clinicians who have earlier been subtly involved with pharmaceutical companies can influence decisions. Sri Lanka has no law regulating the physician–industry relationship and no law on the transparency of such interactions. In a recent newspaper article, it was alleged that a medical consultant is paid as much as Rs 150,000 for recruiting a patient for a clinical trial.

The same medical consultants do their "rounds" in ethics committees, clinical trials registries and hospitals conducting RCTs, and are sometimes handsomely paid according to the number of patients they recruit for RCTs. Their collusion enables the conduct of RCTs at cheaper cost, in less demanding legal settings, and with less resistance from a less informed public (8).

A 12-member panel of experts has been appointed on the recommendation of the CDDRA to review applications for clinical trials (Article 6). If necessary, an expert may be consulted for his opinion (Article 6, paragraph 2). The expert has to give his feedback within 14 days of the receipt of the application. In the case of major disagreements, another expert has to review the application. The provisions are unsatisfactory, considering the review standards maintained by journals, funding agencies and ERCs, which deem that a minimum of two experts is mandatory. Also, the 14-day time limit is too short.

Article 7 of the draft Act discusses the accreditation of the ERCs. However, there is no mechanism for appeal if accreditation is denied. Currently, the ERCs of the major universities and professional organisations have a central body – the Forum of Ethics Review Committees, Sri Lanka (FERCSL) – which is under the patronage of the Sri Lanka Medical Association. Two ERCs in the FERCSL have received recognition from the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) through the Forum for Ethics Review Committees in Asia Pacific (FERCAP). Although the draft Act discusses the accreditation of ERCs and their standards, such as those related to ongoing monitoring of clinical trials, it does not mention the issue of increasing the capacity of the ERCs. ERCs do not have separate funding, secretarial or support staff, office equipment or stationery. They depend on the goodwill of the heads of the academic departments of universities to carry out their work. They are unable to monitor approved research due to lack of resources. Article 8 discusses the responsibilities of the ERCs, including site visits, if necessary (Article 8, paragraph 4). Presently, no site visits are being undertaken by ERCs in Sri Lanka due to lack of funding. Also, the Act devolves the responsibility of safeguarding the rights and ensuring the safety and well-being of trial subjects on investigators. In Article 21, the onus of dealing with research-related injury is placed on the investigator and the institution conducting the trial. The Article specifically requests the investigator to enter into an agreement with the sponsor of the trial about insurance and indemnity. Instances when compensation should not be paid are specified here. For example, the clause relating to the natural progression of the disease provides the sponsors of trials with an escape mechanism, helping them to avoid paying compensation (Article 21, paragraph 11). The draft Act proposes the establishment of an arbitration committee under the CDDRA to resolve disputes between the sponsor and the investigator about the compensation for trial-related injury.

The draft Act has other serious drawbacks as well. All the drug trials are not covered by it or by the CTRD. Non-commercial drug trials conducted by academic or healthcare institutions, collaborative groups and individuals, and cooperative establishments are not under its purview. This would make it possible for pharmaceutical companies to use proxy organisations to conduct research. Investigator initiated clinical trials, academic multicentre trials investigating non-drug therapies, exploration of drug therapies for neglected tropical diseases, and investigation of already established complementary and alternative medicines need to be encouraged. Increased paperwork and a complex procedure of regulatory review, together with additional administrative hurdles, are likely to further discourage local academic researchers (9). The wealthier foreign trial sponsors have the capacity and resources to produce the necessary paperwork that can clear the bureaucratic hurdles.

Another drawback is that pharmaceutical companies can apply to the CTRD and ERC simultaneously. If this draft Act is serious about protecting patients' rights, approval from the ERC should be a prerequisite for applying to the CTRD. The applicant can influence the ERC on the strength of the fact that he has obtained approval from the CTRD.

The draft Act is full of clauses and exclusions that can be used by multinational pharmaceuticals companies which have abundant resources, including their teams of lawyers, ethicists and researchers, to circumvent the Act's provisions and exploit patients. As in the case of India, "mere guidelines will not suffice" and the need for stronger legal oversight cannot be overemphasised (1). The fact that the provisions of the draft Act have not been made known to everyone, lobbying by the economists who are regulating the monetary policy in Sri Lanka and the lack of transparency, which is reflected in the absence of debate and discussion in open forums, have caused concern. The draft should be available in the public domain and a mechanism of transparency should be put in place to solicit the views of all stakeholders, encourage debate and aid the process of reaching a consensus. A sufficient amount of

time should be devoted to the implementation of these steps as there is no urgent need to rush the legislation. Meanwhile, the ERCs can be strengthened by injecting more resources into them and enhancing the capacity of their members. The FERCSL should be encouraged to expand its role of providing guidance and increase its efforts in the sphere of capacity-building. It is important to distinguish between clinical trials initiated by local investigators, those initiated by Big Pharma and those by foreign academics and institutions, and the same set of guidelines should not be used to regulate all of them (10). There are other intricacies, too, that need to be taken care of. These include local investigator-initiated trials that test new food products, complementary and alternative medicine therapies and biotechnological products, which need to be evaluated separately. The approval of some such trials may need to be expedited, considering their importance to the national economy.

Meanwhile, the absence of any law is the preferable option till the ERCs have the capacity to stand alone confidently. As the new Act seems to have assigned the ERCs a pivotal role in the regulation of RCTs, it is essential to enhance the capacity of their members and expand the infrastructural support available to them before the draft Act sees the light of day. In the short to medium term, it seems that RCTs can be monitored well enough by the existing channels, such as the ERCs, Sri Lanka Clinical Trials Registry, the approval process of the CDDRA, the country's vigilant media and the outspoken, whistle-blowing academics. In the long term, ensuring transparency and full consultations with the public might reduce exploitation, but this is not a foolproof option. Increasing the science, health and research literacy of ordinary people, in addition to improving their living standards and reducing poverty would be the best method of preventing the exploitation of poor patients by the "clinical trials industry".

Acknowledgement

We would like to express our gratitude to Dr Sammani Gunasekare.

References

1. Laine C, Horton R, DeAngelis CD, Drazen JM, Frizelle FA, Godlee F, Haug C, Hébert PC, Kotzin S, Marusic A, Sahni P, Schroeder TV, Sox HC, Van der Weyden MB, Verheugt FW. Clinical trial registration — Looking back and moving ahead. *N Engl J Med*. 2009 Jun 28; 356(26): 2734-6.
2. Ministry of Justice, Sri Lanka. The Clinical Trials Bill, 2012. Legal Draftsman's Department, Ministry of Justice, Sri Lanka; 2012.
3. Elliott C. Justice for injured research subjects. *N Engl J Med*. 2012 Jul 5; 367(1): 6-8.
4. Suntharalingam G, Perry MR, Ward S, Brett SJ, Castello-Cortes A, Brunner MD, Panoskaltsis N. Cytokine storm in a phase 1 trial of the anti-CD28 monoclonal antibody TGN1412. *N Engl J Med.* 2006 Sep 7; 355(10):1018-28.
5. Abraham, J. Drug trials and evidence bases in international regulatory context. *BioSocieties.* 2007 Mar;2(1):41–56.
6. Madurawala S. Corruption risks in the provision of pharmaceutical drugs in Sri Lanka. *Talking Economics blog*. Colombo: Institute of Policy Studies of Sri Lanka; 2010 Mar 4 [cited 2013 Sep 3]. Available from: http://www.ips.lk/talkingeconomics/2010/03/corruption-risks-in-the-provision-of-pharmaceutical-drugs-in-sri-lanka/
7. Perera S. Bribery probe into awarding gloves tender to unregistered supplier [Internet]. *The Island Online*. 2012 Sep 15[cited 2013 Sep 3]. Available from: http://www.island.lk/index.php?page_cat=article-details&page=article-details&code_title=61642
8. Karunanayake P. The banal face of medical research [Internet]. *The Nation.* 2012 Jan 22. [cited 2013 Jan 16]. Available from; http://www.nation.lk/edition/component/k2/item/1730-the-banal-face-of-medical-research
9. Lang TA, Siribaddana SH. Clinical trials have gone global: Is this a good thing? *PLoS Med*. 2012;9(6):e1001228. doi:10.1371/journal.pmed.1001228
10. Franzen SRP, Chandler C, Enquselassie, Siribaddana S, Atashili J, Angus B, Lang T. Understanding the investigators: a qualitative study investigating the barriers and enablers to the implementation of local investigator-initiated clinical trials in Ethiopia. *BMJ open*. (under review)