The contours of clinical research in India

SACHIN NIKARGE

Centre for Studies in Ethics and Rights, 501, Dalkhania House, 'B' Wing, Vakola, Santacruz East, Mumbai 400 055 INDIA e-mail: sachinikarge@yahoo.com

Introduction

The Clinical Trials Registry-India (CTR-I), set up by the Indian Council of Medical Research's National Institute of Medical Statistics, is a freely available and searchable primary register. Anybody wishing to conduct a clinical trial in India must declare 20 items of registration data set as required by the World Health Organization's International Clinical Trial Registry Platform, in addition to items required by the Indian registry such as ethics committee approval status and regulatory clearance by the Drug Controller General of India (DCGI), etc, before the enrolment of the first patient. While this register is meant primarily for trials conducted in India, the CTR-I also accepts registration of trials conducted in other countries in the region.

The CTR-I was formally launched on July 20, 2007 (1) with the aim of paving the way for improved transparency, accountability, and reporting of results of all clinical trials in India and in the south or southeast Asian region (2). A total of 324 clinical trials were registered in this registry, over a period of about two years. On June 15, 2009, the DCGI made registration mandatory for every new trial (3, 4). Incidentally, this mandate coincided with the publication of the first factsheet in the October-December 2009 issue of this journal.

Trends

The factsheet collates data published in the public registry to present them in a more concise and accessible form. The fields of information for analysis are CTR-I ID, brief study title, study status, trial location, ethics committee details, sponsor, disease condition, trial start date, DCGI approval, and study type. Certain text-heavy fields like exclusion and inclusion criteria are left out.

The second factsheet published in the April-June 2010 issue of this journal reflects the effect of the DCGI's mandate; the number of trials registered increased to 689 in the six month period from June 15 2009 to Dec 31 2009. That is, the six-monthly period since the mandate came into effect shows registration of twice as many trials as the number voluntarily registered over a two-year period from the launch of the registry (5).

A large number of registered studies (292) are phase 3 studies. 128 studies are from phase 2 and 41 studies belong to phase 1 (Fig.1). Contrary to the assumption that India lacks a culture of phase 4 studies, 85 registered studies belong to phase 4. Some studies do not have clearly defined phases: these include 20 phase1/2 studies, 42 phase2/3 studies, and 16 phase 3/4 studies. A large number of studies (436) are currently recruiting participants, 96 trials are not yet recruiting, while another 81 are active and not recruiting. A total of 498 studies are sponsored by pharmaceutical companies.

Although the number of registered trials has substantially increased since the DCGI mandate, the two published factsheets have similar patterns. For example, in Factsheet 2, an overwhelming majority of trials registered in the register are drug trials. 501 of 689 registered trials are drug trials. Other types of trials are those related to devices, procedures, dietary supplements, radiation, biological, and behavioural trials. The most prominent disease categories continue to be neoplasms (110), endocrine, nutritional and metabolic diseases (77), diseases of the circulatory system (73) and lastly bacterial infections, intestinal infectious diseases and sexually transmitted diseases (69) (Fig. 2). Approximately one-third of the trials registered on CTR-I (219/689) are placebo-controlled, while another one-third (222/689) comprise active controlled trials (Fig.3). This pattern is reflected in the first factsheet as well.

Conclusion

The recent mandate to register clinical trials has increased accountability and transparency in the system. However, it is not known whether strict and timely action will be taken in cases of unregistered, illicit trials.

The registry allows for updates to trial information, but these updates cannot be tracked. Another primary register, clinicaltrials.gov , records and archives the "history of changes" made to each trial from the date of its registration. Clinicaltrials.gov also provides space for enlisting publications and uploading trial reports. No such provision has been made on CTR-I.

Only CTR-I requires the names of all ethics committees, approval status, site addresses and names of contact persons for each site. This helps in conforming to the ethical standards set by the ICMR.

Almost all trials registered on CTR-I are primarily conducted in India, restricting the impact of CTR-I to the Indian context.

References

1. World Health Organization country office for India. Launch of the Indian Clinical Trial Registry. WHO India highlights. [Internet]. 2007 Jul. [cited 2010 Jun 19]. Available from http://www.whoindia.org/EN/Section2/Section435_1439.htm
2. Clinical Trials Registry-India, National Institute of Medical Statistics (ICMR). *CTRI Bulletin*. [Internet]. 2007 Jul (1). [cited 2010 Jun 19]. Available from http://www.icmr.nic.in/ctri/2007/july.pdf
3. Nikarge S, Pamnani D. Clinical Trials Watch. *Ind J Med Ethics*. 2009; Oct-Dec; 6(4): 228-31.

4. Clinical Trials Registry-India, National Institute of Medical Statistics (ICMR). Trial registration set to become mandatory. [Internet]. 2009 May 19. [cited 2010 Jun 19]. Available from: http://www.ctri.in/Clinicaltrials/do/login1?action=toArchiveevents
5. Ravindran D, Nikarge S. Clinical Trials Watch. *Ind J Med Ethics*. 2010 Apr-Jun; 7(2):127-9.

Fig. 1 Phases Comparative

Culled from Factsheet 1 (3)

Phases	Year missing	2006 and prior	2007	2008	2009
0					
I				4	9
II		2	16	26	14
III		13	25	53	40
IV		5	5	17	19
I/II	2		3	6	
II/III		1	9	6	5
III/IV			4	2	
Not applicable		4	8	18	5
Not given	3				

Fig. 1 Phases Comparative

Culled from Factsheet 2 (5)

Phases	Year missing	2006 and prior	2007	2008	2009
0					
I		1		7	33
II	2	6	22	45	53
III	2	22	39	90	139
IV		7	8	27	43
I/II		4	1	5	10
II/III		4	13	12	13
III/IV		2	6	2	6
Not applicable		8	11	23	23
Total	4	54	100	211	319

Fig. 2 Disease Conditions Comparative

Culled from Factsheet 1 (3)

Disease conditions	Year missing	2006 and prior	2007	2008	2009
Bacterial infections, intestinal infections, STDs		3	7	12	10
Neoplasms		2	21	20	14
Endocrine, nutritional, and metabolic		1	1	19	11
Mental and behavioural diseases					
Diseases of the nervous system			3	11	5
Diseases of the circulatory system		2	5	12	14
Diseases of the respiratory system			3	10	10
Diseases of the digestive system		3	5	6	6
Diabetes					
Double disease condition		5	5	5	5
Other		10	6	8	21
Disease conditions not known	8				

Fig. 2 Disease Conditions Comparative

Culled from Factsheet 2 (5)

Disease conditions	Year missing	2006 and prior	2007	2008	2009
Bacterial infections, intestinal infections, STDs	1	4	10	17	37
Neoplasms		10	28	34	38
Endocrine, nutritional, and metabolic		4	5	30	38
Mental and behavioral diseases		3	1	4	18
Diseases of the nervous system		3	6	16	18
Diseases of the circulatory system		2	9	27	35
Diseases of the respiratory system	2	2	3	12	18
Diseases of the digestive system		4	11	10	14
Diseases of the musculoskeletal system and connective tissue		3	4	7	22
Diseases of the eye and adnexa		3	2	6	11
Diseases of the genitourinay system		2	4	5	16
Pregnancy, Childbirth and the puerperium		4	5	7	3
Double disease condition	1	6	4	12	11
Other		3	5	22	37
Disease conditions not known		1	3	2	4

Fig. 3 Type of control comparative

Culled from Factsheet 1 (3)

Control	Year missing	2006 and prior	2007	2008	2009
Active		10	17	38	38
Case control					
Cohort					
Cross sectional					
Dose comparison					
Historical					
Longitudinal					
Placebo		8	28	44	29
Uncontrolled		2	3	12	14
Multi-arm		2	8	13	9
Crossover		2	2	4	6
Other		3	7	17	2
Not given	6				

Fig. 3 Type of control comparative

Culled from Factsheet 2 (5)

Control	Year missing	2006 and prior	2007	2008	2009
Active		19	25	63	115
Placebo	3	19	43	71	83
Uncontrolled		3	4	22	48
Multi-arm		5	13	17	19
Crossover		2	2	5	19
Other	1	6	12	29	34
Control not known			1	4	2