



## Monitoring Clinical Trials: A Gratifying Experience

by *Farhad Handjani*

It was in the late 1990s that I was first invited to attend a workshop on Good Clinical Practices (GCP) conducted by members of the World Health Organization/Special Programme for Research and Training in Tropical Diseases (WHO/TDR) in Dizin, Iran. This was the first time I had heard about GCP. Up till then, all my thoughts had been centred on how I could become a better physician in my clinical practice. However, my attendance at the workshop opened my eyes to the concept of GCP and made me look in a new way at clinical trials and their conduct. In that workshop, I was introduced to the two basic principles of GCP, namely participant safety and credible clinical trial data. In addition, I learned about the principles of protocol writing, the responsibilities of sponsors, investigators and monitors, the formulation of standard operating procedures (SOPs), the role of ethics committees, the importance of the informed consent process, and the significance of data management procedures.

After the workshop, I was contacted by the WHO/TDR Clinical Coordination Unit to see if I would be interested in becoming a GCP clinical monitor for their unit. Being young and fairly energetic at the time, I quickly accepted. In a sense, it was a great chance to work for a non-profit international health organization on a temporary basis and at the same time be able to continue with my academic career back home.

I started off with monitoring leishmaniasis vaccine trials in Sudan and Iran. In the past few years, I have monitored both drug and vaccine trials in Kenya and Ethiopia (the Box on page 22 describes one of my days as a monitor in Ethiopia). I have also attended many monitoring refresher courses as well as workshops on ethics in health research and protocol writing.

As a clinical monitor, I am the link between the sponsor and the investigator. As soon as I get my assignment for a clinical trial, the preliminary study protocol, the case report form (CRF) and informed consent forms are sent to me for review. I then try my best to incorporate my monitoring experience in finalizing these documents. At the same time, I have to follow up with the investigator(s) on the issues of ethical clearances and regulatory body approvals regarding the trial. It is of paramount importance to have all ethical and regulatory body approvals before starting recruitment of trial participants.

In general, clinical monitoring involves four types of visits: the pre-trial monitoring visit, the initiation visit, the

monitoring visit, and the close-out visit. During the pre-trial monitoring visit, the monitor will assess the expertise, enthusiasm, and availability of the investigators as well as the overall management infrastructure and clinical setting for the particular trial. The monitor will also visit the laboratories and the pharmacy and inspect the equipment available for the trial. It is only after this visit that the sponsor can approve the site for that specific trial. The initiation visit will take place when all ethical and regulatory body clearances have been obtained and everything is in place to start recruitment. During this visit, a short summary of the principles of GCP will be given to the study team and the final protocol and major SOPs will be reviewed. It is also important to make sure that all study products are in place for the initiation of the trial. After this visit, the sponsor will give the go-ahead signal to the investigator to begin recruitment and initiate the study. During the monitoring visit(s), the conduct and progress of the trial is assessed, especially with regard to adherence to the protocol and GCP principles. All CRFs are cross-checked against the source documents and any generated queries are clarified with the investigators. It is a general principle of GCP that "if it is not documented, it does not exist." Special attention is paid to informed consents, making sure that all trial participants have signed (or had a witness sign for them) prior to enrolment in the trial. During the monitoring visit, the monitor will also specifically check for any adverse events and serious adverse events in order to ensure that all such events have been properly documented and reported. Lastly, product accountability is reviewed and the investigator file is checked in order to make sure that all essential documents are archived properly. The monitoring visit is a very important visit, and the monitor needs to clearly plan what s/he wants to accomplish at that visit. Checking various documents (on a 100% basis) can be very time-consuming and somewhat tedious, but is an integral part of clinical monitoring. The outcome of these visits are data that are then sent to the data management team to be entered into the trial database and processed. This may sometimes lead to generation of further queries that need to be resolved by the investigator.

The close-out visit is the last visit. It will involve a final product accountability as well as making certain that all documents archived in the investigator file are updated. It is during this visit that the monitor has to make sure that the final generated data are clean and to request locking of the database and final data analysis. During this visit,

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WHO/TDR publication policies and a request to submit a final report are conveyed to the investigator by the monitor.

On the more personal side of monitoring, it is a great chance to travel to distant and remote places in the world. To places that many may not travel to on their own. For me, this travelling experience has always brought to mind the sayings of one of Iran's greatest poets, Saadi, who said:

*“Of one Essence is the human race,  
Thusly has creation put the Base;  
One Limb impacted is sufficient  
For all others to feel the Mace”<sup>1</sup>*

Additionally, clinical monitoring gives one the chance to

meet many different investigators, both young and old, who are interested in overcoming a disease burden in their community. As a clinical monitor, it is very gratifying to be able to help them in this endeavour. It is also very fortunate to have them as new friends.

### Farhad Handjani

*Associate Professor of Dermatology  
and WHO/TDR Clinical Monitor,  
Shiraz University of Medical Sciences  
Shiraz, Iran  
hanjanif@yahoo.com*

<sup>1</sup>This verse also graces the entrance of the United Nations' building in New York

## A day in the life of a monitor

The trial was to be undertaken in Ethiopia and involved vaccinating 400 children and young adults in a rural area. Two small villages (kebeles as they call them in Ethiopia) were selected to recruit the volunteers. The villages had no electricity or purified running water, and their small huts were widely distributed across a magnificent green and serene landscape. The challenge for us was to screen the volunteers in this type of setting. Initially, one of the co-investigators and I visited one of the villages. We met the village chief and were taken to a place where there were two small huts and a larger one which was used to keep cattle. The two small huts were sometimes used as a make-shift health centre. We visited the place surrounded by young and excited children, who had left off playing soccer in the middle of the village to come and see what we were up to. The village chief informed us that some of the households would give us chairs, tables and benches, and we informed them that we would bring along the necessary medical equipment (for initial physical examination and pregnancy tests).

On the first day of trial enrolment, the large hut (with benches provided by the villagers) was used as our waiting area. Here, information regarding the trial was given to a group of 8-10 volunteers at a time by one of the investigators.

After they had received this initial information, the volunteers moved to a porch in front of the two smaller huts where a small table, provided by the villagers, was used as our reception desk so that the volunteers could be assigned a screening number. After that, the volunteers were weighed and their height was recorded. They were then asked to go into one of the huts where a physician was waiting for them. The physician again explained what the trial entailed and asked that the informed consent be signed by the volunteer or his/her legal guardian or a witness. After the volunteer had consented to participate in the trial, s/he was then examined and all information was documented on a screening form. For women who had started to menstruate, a urine pregnancy test was requested and a lab technician was at hand to do the test. After this stage, the volunteer moved back to the larger hut, where a photographer using a red background cloth hanging on the wall took a photo of the participant in order to prepare a photo ID on the next day. The volunteer was then escorted to one of our vans where s/he received a soda and a small pastry to overcome some of the energy lost in this half day endeavour! What was fascinating about all of this was the great enthusiasm that existed among both the participants and investigators which led to a very smooth and orderly flow of events. No doubt, this was an extraordinary day in the lives of the residents of one of Ethiopia's kebeles.



Surrounded by young and excited children



Meeting the village chief