Quality management

Research needs quality management system

Even the most ambitious clinical trials can unravel without rigorous quality controls. Strategic quality management is central to TDR’s quest to increase developing countries’ capacity to produce research needed to fight the infectious diseases of poverty.

The regulatory framework for clinical trials has changed in recent years with the addition of rigorous controls to ensure patient safety and data reliability. As the disease burden increased, there has also been a geographical shift, with increasing numbers of clinical trials being conducted in populations from Asia and Africa. TDR is therefore expanding its efforts to support strategic quality management in its partner clinical research institutions and in clinical coordination and training centres in disease endemic countries (DECs).

Until now, quality management was often fragmented. For instance, there was a quality check at the start of a new research project in the grant selection process, and another at the end through peer review publications. But during the balance of the research process, quality management was frequently left to researchers and their institutions.

“There is a clear need to implement the principles of strategic quality management in health research to prevent failure, maximize the utilization of available resources and ensure consistency and credibility of results,” according to Dr Juntra Karbwang, head of TDR’s new Strategic Quality Management (SQM) unit, which is accountable for the quality of TDR-supported studies. The activities include developing the necessary quality management tools and procedures, and providing training on good practices in TDR-supported research, as well as helping regional clinical coordination and training centres in disease endemic countries to develop their own quality management systems. In addition, SQM provides accountability for the quality and effectiveness of clinical laboratories and clinical monitors through GCLP and clinical monitor recognition programmes, respectively.

Emphasis on ethics

As part of its Strategic Quality Management efforts, TDR is seeking to strengthen the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER). This programme helps build in-country human subject protection programmes and provides accountability for the quality and effectiveness of ethical reviews worldwide. It is based on a partnership model that fosters a grassroots approach and emphasizes valuing local knowledge and cultural understanding.

A three-year certificate of recognition is issued to ethics committees meeting five standards:

- The committees’ structure, composition and skills must be appropriate to the amount and nature of research reviewed.
- Management and operational procedures must ensure optimal and systematic conduct of ethical review.
- Review of protocols and supporting documents must be timely and complete.
- Decisions must be effectively and adequately communicated to investigators.
- Documents and activities must be systematically archived.

In Asia, about 53 ethics committees have been recognized by the Forum for Ethical Review Committees in Asia and the Western Pacific and two in the Pan-African Bioethics Initiative. Other regional fora serving this function include the Forum for Ethics Committees in the Confederation of Independent States and the Latin American Forum of Health Committees in Ethics Research.
Good Clinical Practice

To ensure compliance with international scientific and ethics guidelines at the research site level, TDR also is training Good Clinical Practice site monitors. In February, Karbwang led a monitor training session at the Armauer Hansen Research Institute in Addis Ababa, Ethiopia, to help build a quality management system there.

Even the most ambitious clinical trial can unravel if it has one weak link. The SQM unit’s responsibilities thus include monitoring and quality assurance for major TDR trials to ensure the quality of every aspect of clinical trial conduct. Capacity for monitoring is usually very limited in disease endemic countries. Therefore the training and supervision of the TDR local monitors who are responsible for on-site monitoring is of critical importance.

The SQM unit’s Christine Halleux seeks to improve the competence of clinical monitors to prevent, detect and correct any deviations during clinical trials’ execution phase and to continuously improve their monitoring processes to ensure that quality is built into clinical trials from the start.

Auditing trials

Auditing is another quality management system process being routinely implemented in trials involving many patients, particularly trials with potentially large impacts on patients’ lives.

One such example is the trial on safety and efficacy of fixed-dose TB treatment (combining multiple drugs into a single pill) compared with loose TB drug formulations. The trial, which involves 1000 Nigerian and Ethiopian patients, has been audited to improve the quality processes of the study, and manage them properly to ensure the integrity and credibility of the data. Another example is the TB-HAART (highly active antiretroviral treatment) trial currently ongoing in four sub-Saharan African countries. This trial will involve 1800 patients and aims to elicit the survival benefit of early concomitant TB and HIV treatments compared with delayed treatment among HIV-infected TB patients. The trial has hit the halfway point for enrolment and it is hoped that by late 2010 researchers should be able to generate preliminary findings that can support policy recommendations. To do that, every aspect of the trial must conform to rigorous quality standards.

Good Clinical Laboratory Practice

Integral to quality management is adherence to Good Clinical Practice (GCP), an international ethical and scientific quality standard for designing, conducting and reporting trials involving human subjects. More recently, Good Clinical Laboratory Practice (GCLP) standards have also been established.

WHO/TDR’s Good Clinical Laboratory Practice Guidelines are based on those drawn up in 2003 by the British Association of Research Quality Assurance (BARQA). The guidelines help ensure that the laboratory has the systems in place to generate reliable and valid data in the course of a trial. They set a standard of good practices – which means that laboratories involved in analysis of samples from TDR-supported clinical trials should at least comply with these requirements, if not surpass them.

“It’s a very important initiative, because in the past it was rare for laboratories in Africa to be implementing consistent quality standards,” said Mihut. TDR’s first GCLP training session for laboratory surveyors took place in March with four participants from Africa and three from Asia. They are now expected to implement GCLP principles and standards in their laboratories and to spread the GCLP culture as far as possible. In addition, these trainees will be asked to assist in assessing laboratories that support TDR research.

TDR is developing a GCLP recognition scheme in which TDR surveyors will visit selected laboratories and recognize those meeting quality criteria. This will benefit all parties, as TDR and its partners can be confident that recognized laboratories are reliable and fulﬁl quality standards, while the laboratories will effectively be given a quality benchmark that will aid them in seeking research funding.

“We need all the links in the chain to be in place. Our colleagues in the training unit have trained the laboratories on GCLP and now we are training the surveyors who can audit the laboratories,” Mihut said.

“It is very important. Laboratories without quality systems have two major failings. It is more difficult to prove the validity of analytical data, and at the same time they are usually less efficient by having to redo a lot of their tests. That is called the cost of poor quality,” Mihut said.


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