Informed Consent 'Not up to Scratch'

By Kirsty Barnes

18/07/2007 - **A recent survey of clinical trial participants in the US has revealed worrying signs that the informed consent process is 'not up to scratch'.**

Outsourcing-Pharma.com decided to address the issue after reviewing a subset of data presented at the recent Drug Information Association (DIA) annual conference in Atlanta.

The data was from the '2007 CenterWatch National Survey of Study Volunteers,' conducted in April and May this year on 620 previous US trial participants, the majority of who had been a participant in the last two years.

Probably the most disturbing thing to emerge from the survey was that 3 per cent of participants (18.6) claimed they did not receive an informed consent form prior to starting the study. While 3 per cent may sound like a small number, it is still unacceptable, and completely against International Conference on Harmonisation (ICH) good clinical practice (GCP) guidelines.

One of the main principals of ICH GCP states that *"freely given informed consent should be obtained from every subject prior to clinical trial participation."*

In addition, only 88 per cent of those who received a consent form said they read it completely. 9 per cent only read it partially and 3 per cent admitted they did not read it at all.

86 per cent of those who read it said they understood it 'very well,' 13 per cent said 'somewhat well,' and 1 per cent said 'not at all.'

"This number [86 per cent] decreased to 75 per cent in those who earned less than $30,000 a year, indicating that socioeconomic factors may need to be taken into account when going through informed consent forms," said CenterWatch analyst Paul Dewberry, who presented the study data.

"They often have a different motivation and level of understanding when participating in the informed consent process," he said.

Furthermore, a staggering 27 per cent of survey respondents said that no-one reviewed the informed consent with them, while 4 per cent said a family member did. 39 per cent indicated they had help from a nurse, 18 per cent said a doctor, 10 per cent said a research/study coordinator and 2 per cent listed 'other staff.'

Again, these figures are unacceptable and should raise cause for concern in the industry. The ICH GCP guidelines clearly state:

"The investigator, or a person designated by the investigator, should fully inform the subject… of all pertinent aspects of the trial including the written information and the approval/favourable opinion by the IRB/IEC."

"Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject… ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject…"

Moreover, on the issue of placebo, 19 per cent of participants said they did not realise they may receive a placebo instead of the investigational medicine and 6 per cent said they 'weren't sure'. 24 per cent said they did not understand that neither they, or their doctor, would know what

medication they were receiving during the study.

21 per cent said they did not realise that their study would carry 'additional risks and discomforts', while 4 per cent of those surveyed did not realise they could quit the study at any time, and 10 per cent said the information they received prior to the trial 'did not match their actual experience' or that they had in fact received 'no prior information'.

These are all further unsettling signs that in practice at least, the informed consent process is still not as robust as it must be. The ICH GCP guidelines clearly state:

"Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following: That the trial involves research; the purpose of the trial; the trial treatment(s) and the probability for random assignment to each treatment; the trial procedures to be followed, including all invasive procedures; the subject's responsibilities; those aspects of the trial that are experimental; the reasonably foreseeable risks or inconveniences to the subject…; and the reasonably expected benefits."

Outsourcing-Pharma.com spoke to Stuart Young, executive vice president of Clinical Monitoring at international clinical research organisation (CRO) Chiltern, who described some of the responses revealed in the survey as *"worrying."*

"The doctor [investigator] involved in the trial should sit with every trial participant themselves and talk to them about all aspects of the trial such as the science and the medical issues etc., including the fact that they may receive no treatment at all (i.e. a placebo), and then give them ample time [preferably in advance] to consider the information and then ask questions before full informed consent [in the form of a patient signature] can be obtained," said Young.

"The doctor then has to sign and date the consent form saying they have correctly obtained full informed consent, as well as write this in the patient's clinical notes."

Young said that Chiltern routinely conducts *"spot audits"* on 20 per cent of its clinical sites in order to *"police it [the clinical trial process] as carefully as we can."*

"Following GCP and ensuring patient protection is key in a clinical trial," he said.

At Chiltern, if there is any suspicion raised that an investigator is not strictly following the rules, an escalation team is immediately sent to the site to investigate the concern and the first thing they concentrate on is informed consent, said Young.

Most pharmaceutical companies and large CROs have a team of senior people who deal with issues such as this, he added, although he was unsure of the *"policing methods"* that smaller pharma firms and CROs, as well as academic institutions use.