

Human Research Subject Safety

Perception vs. Reality

With regard to research involving human subjects wherever they are conducted, few subjects are more in the regulatory as well as the public consciousness at this time than the **perception** that the safety of the subjects or study participants is more than occasionally compromised. After all, these subjects are undergoing what in their mind is “human experimentation”.

The **reality** is that it is far safer to be on any clinical study at any medical research site or in any university setting than to take any non-medically prescribed or over-the-counter medication or even some medications prescribed by a physician. In both of these instances, the “medication” is taken without supervision or control. This is especially so regarding the taking of additional or concomitant medications that may adversely interact with whatever else may be taken. In a research study or drug trial, any and all medications are taken with a great deal of supervision and control with the absence of concomitant medications unless they are required. Among the many other safety checks, there is always the Independent Review Board (IRB/IEC) comprised of unaffiliated lay and medical persons who additionally insure and safeguard volunteer study participant safety.

To change the perception of the lay public regarding this “unknown” requires education. This is attested to by the fact that any and all individuals who have ever been a study participant or any employee working for a research facility are very well aware that both the long term and the short term safety of study participants is usually paramount. Actually, it is in the interest of no one associated with a research study that any untoward event occurs during any clinical study. There are, actually, five groups committed to GCP (subject safety) and whose reputation depends on being judicious and careful. The groups most involved in pharmacovigilance include the following:

- The **Study Physician** whose reputation and medical license would be at stake and who is responsible for study participant safety is, as all physicians are, invariably committed to the safety of all persons in her/his charge.
- The **Research Facility** is only as good as its reputation and this counts on not only how well the clinical study is performed but also on the study being incident free. Only the very rare group would ever undertake a study with even the potential to harm study participants.
- The **IRB/IEC** spends most of its time reviewing and assuring themselves that the study participants are not placed at any unacceptable risk during a clinical study.
- The **Sponsor** (a pharmaceutical firm or the government usually) also has a lot on the line and has no interest in bringing medications to study that are unsafe to use in the study population. That some slip through attests to the importance of the other groups being involved
- The **Government** through the regulatory agencies is also in continuous review of not only the mechanics of clinical studies but also the impact on the health of study participants.

Specifically, a number of systems and processes are in place at research facilities (Private, university or MRO) to insure that there is no compromise in the safety of any study participant. Each and every protocol undergoes a thorough review, starting well before any study is initiated. The following different groups review the Protocol, for subject safety per GCP:

- The Principle Investigator reviews all protocols as a first step in the review process. Study participant (patient) safety is always the main consideration. Subject safety must be this physician's first obligation.
- Other non-medical scientific staff also review the protocol for scientific and study participant safety issues.
- The IRB/IEC reviews all protocols prior to the start of any study specifically for study participant safety issues
- There is on-site review of all Adverse Events (AE's) during and after dosing by the study physician and involved co-investigators.
- The study nurse and other staff throughout the course of a clinical study carry out continuous review and documentation of AE's.

Human beings being what they are, it must always be kept in mind that to expect the unexpected is far better than to assume or pretend that nothing can go wrong. For this reason, there are also systems and procedures in place and at ever ready to effectively handle any unexpected event. In the GCP sense, the elements of these safety measures must include the following:

- Trained and experienced medical personnel must be physically present at the time of dosing for all studies (unless the subject is required to take the medication at home). The purpose of being present to handle an unexpected AE such as an allergic reaction or other unexpected and unforeseen reaction to the medication.
- When required, arrangements must be made with appropriate specialists to be on-call when the study medication has even the slightest potential for some effect within the specialists' area of expertise.
- The presence of a fully equipped and functional "crash cart" of the type found in any hospital must be available and stocked for any emergency.
- Arrangements are always made, in advance of a clinical study, with a nearby hospital so that they are not caught off-guard should a study participant require hospital medical service.

From the above, it should be clear that volunteer study participants are considerably safer on a clinical research study at a physicians office, a university setting or at a medical research organization than they would be taking any medication from any source at their home.

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