Have the ultimate benefits of clinical trials been maligned beyond repair?

'The pharmaceutical industry is totally dependent on the willingness and trust of the consumers around the world to volunteer for their clinical trials.'

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On Sunday, 1st April, 2001, *Sixty Minutes*, the high profile and number-one-rated news show in the US, reported yet another research scandal involving patients enrolled in clinical trials. On national television, they claimed that research patients are not being informed about the important safety information that is required for their participation in a clinical trial and that this practice is 'widespread'. Further, patients themselves reported being used as 'guinea-pigs' and abused by a system that is making 'millions' for the physicians conducting the research and the companies that are sponsoring it.

Is clinical research getting a 'bad rap'?

The recent portrayal of research scandals is called 'whistle blowing' by patients and, more frequently, employees peripheral to the research study, who inform the media of perceived misconduct by the researchers. This practice has escalated over the past two years, and has gained momentum after the public exposure of an 18-year-old research patient who died in a gene-therapy trial at the University of Pennsylvania (Pennsylvania, PA, USA) in 1999. His death pointed to flaws in the system for protection of patients and prompted a national debate on clinical studies. The father of the teen settled a lawsuit with the university and expressed his worry that many 'volunteers' are not being sufficiently protected[1]. Proper informed-consent is the foundation on which any person volunteers for experimental research. It is this foundation that is in question, in addition to the significant funding that the researcher and the academic institutions receive for conducting the research.

CenterWatch (Boston, MA, USA; http://www.centerwatch.com) reported that articles in the mainstream press have been steadily eroding that trust and goodwill. For example, in the fall of 2000, the *Boston Globe* ran a series of front-page stories describing the unethical and immoral treatment of institutionalized psychiatric subjects. In April 1999, the television series *48 Hours* ran a one-hour feature entitled 'Are You at Risk' in which negligent and unethical clinical-research practices were depicted as commonplace. The *New York Times* also ran an in-depth feature on Robert Fiddes – now serving time in prison – and his fraudulent practices at the Southern California Research Institute (Los Angeles, CA USA). The story documents, in vivid detail, the many deceptive and unethical ways in which he fabricated data and put lives at risk.

Furthermore, a story about Duke University (Durham, NC, USA) suspending its clinical trials culminated with a feature story in the 24 May 2000 edition of *US News and World Report*. Entitled 'Duke's Hazard: Did Medical Experiments Put Subjects Needlessly At Risk?', the article documented the failure of this prestigious university to respond to Institutional Review Board (IRB) problems identified by the federal government's Office for Protection from Research Risks (OPRR)[2]. Although misconduct and fraud are unacceptable and need to be reported and eradicated, the conduct of clinical trials has increasingly received a 'bad rap' over the past three years without an accurate counterbalance.

Whereas mainstream media tends to focus on the negative and the sensational, for more than a decade, industry professionals have failed to communicate the majority of experiences that are positive. Given the broad reach and influence of the media, the public is frequently left with a one-sided view that all clinical trials are unethical and unnecessarily risky. As a result, however, candidates for upcoming clinical trials could be turning-down an opportunity to access a potentially life-saving treatment, to use a novel therapy that is more effective and safer than a current medication, to help advance science and, ultimately, to benefit many people suffering from a given illness. As one industry professional commented: 'The negative publicity doesn't affect those subjects who have had experience participating in a clinical trial. They are very committed and won't be swayed. Bad press negatively impacts

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those subjects sitting on the fence, trying to decide whether to participate. Everyone loses. The subjects can't access a potentially promising treatment and industry fails to attract new study subjects.' Given the relatively low-level of eligible subjects participating in clinical trials today, industry needs to build public goodwill. Only an estimated five to six million study subjects – of 50 million North Americans with serious chronic illnesses – participate in clinical trials each year. Industry is failing to reach and to convince 90% of the eligible population of the importance, safety and benefits of clinical trial participation[3].

The costs and time will be devastating to study-sponsors

The repercussions of an unequal reporting of the infrequent occurrences of misconduct are complicating the difficult and expensive task of recruiting qualified patients for clinical trials of potentially successful therapies for disease. The effect is already being felt by many of the good clinical-trial sites that are finding it harder to obtain their patient's trust and recruit the needed volunteers for crucial studies.

The pharmaceutical industry expected to spend more than US$35 billion on R&D worldwide, US$12 billion on clinical trials, US$10 billion on marketing to physicians and consumers and in excess of US$600 million on each new drug marketed. However, those most affected by the results of crucial and successful medical research are consumers, patients and providers, and the medical community as a whole. Within the next few years, the pharmaceutical industry expects to see a 65% increase in the number of new compounds emanating from their labs. The advances in genomics will place a major strain on resources within the clinical-trial industry predicting that new chemical entity (NCE) launches will go from an average of one per year to >four per year[4]. Furthermore, the current revolution in science that is leading to 'personalized medicine' will exacerbate difficulties in the clinical-trial process, especially in patient recruitment. The recruitment of experienced investigators and qualified study patients for participation in the growing number of studies is just the tip of the iceberg of what is needed to overhaul a complex and inefficient process that slows time-to-market. It is an often-repeated truism in the clinical trials industry that poor patient recruitment is the primary reason why clinical trials are delayed or fail. Eighty percent of clinical trials do not meet the target recruitment and enrollment deadlines. Twenty-seven percent of clinical development-time is spent enrolling subjects. Traditionally, sponsors rely on the clinical sites to meet the patient-recruitment goals. Clinical sites are expected to develop successful patient-recruitment strategies, and it is usually not until trials begin to fail, that worried sponsors start to react to slow patient accrual. Costs associated with poor patient recruitment are iterated repeatedly in the industry at an estimated loss of US$1.3 million a day in sales for every day that a new drug approval is delayed.

Enrollment and retention of the patient for the duration of the study is key to the success of any clinical trial. It is estimated that in excess of US$1 billion is currently being spent solely on the recruitment of patients for clinical trials. This figure is a moving target because there are no published, comprehensive data on patient recruitment costs, thus far.

An obvious solution

Factors that inhibit subject participation in clinical trials are consistent throughout the general population. Lack of education and access concerning clinical trials by both patient and their physicians is the primary barrier to recruiting volunteers for important studies. On the other side of the equation, volunteers are truly benefiting from participation in clinical trials. Experience shows that, once in a study, patients return repeatedly to volunteer for more. The primary reason is not that they might receive some payment for their time or transportation cost. It is because of the extreme care and diligence that is afforded them by highly qualified study personnel. Research shows that:

- Most patients feel that they have been better treated, regarded and educated in clinical trials than by their primary care physician;
- A patient's medical history and visits, procedures, and treatment results are generally tracked more efficiently than in private practice; and
- Medical care is free to patients in most studies.

Because of the tremendous confusion about the benefits and risks of clinical trials, the public continues to relate participation in clinical trials to being a 'guinea pig'; the acceptance of clinical research as a mainstay of general medicine is overdue. Not only should patients know of, and have access to, important trials, but so should their physicians, but this is not happening.

Industry needs to take responsibility

This author challenges an industry, that is beyond comparison in the innovation of new drugs, to take the lead in educating the public and medical profession regarding the conduct and positive effects of clinical research on mankind. The pharmaceutical industry's lack of response to the media scandals is an example of a 'head in the sand' attitude about public perception and power over their studies. The sponsorship of educational programs via interactive media would be a good start in putting forth all

the good that is being done in the name of clinical research. When this author approached P*h*RMA with a possible solution to neutralize the negativity in the media, although the representative validated the issue and agreed something needs to be done, the ultimate response was that there are 'too many other fish to fry' and this is not a priority of the association. If no one steps up to neutralize the infrequent negative reports that are painting broad brush strokes about clinical research, the projections by the pharmaceutical industry to increase and expedite NCEs will be just that; projections. Without the efficient recruitment and enrollment of qualified patients into their clinical trials, their NDAs will be severely delayed. If the status quo is followed, in this instance, the pharmaceutical industry will respond only when there is a crisis that forces action.

The pharmaceutical industry is totally dependent on the willingness and trust of the consumers around the world to volunteer for their clinical trials. If the public's perception of lessening integrity on the part of the sponsors and physicians conducting research continues to grow unfettered, the pool of qualified study volunteers will continue to dwindle and so will the ability to successfully complete pivotal trials.

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What do YOU think about the media reporting of these clinical research 'scandals'?

What do you think the industry should do to try to avoid further escalation in the number of negative and sensational reports?

How do you think we should try to counteract the impact of these reports on clinical trials recruitment?

How else do you think we can reduce the level of concern from patients enrolling in clinical trials?

Please send your comments to Dr Rebecca Lawrence, News & Features Editor, *Drug Discovery Today*, e-mail: Rebecca.Lawrence@current-trends.com

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