

# PATIENT PARTICIPATION IN NEW PRODUCT DEVELOPMENT

## A Patient's Advocate's View

### CRITERIA FOR EVALUATION OF NEW THERAPIES : THE NEED FOR A PATIENT PERSPECTIVE

THE fundamental judgment that determines whether a new product will reach the market (consumers) is the tradeoff between the risks (safety) versus the benefits (efficacy) of the treatment. Information from the patient perspective is necessary to ensure that all of the important factors are considered in this evaluation.

Who takes the risks and who receives the benefits? Industry certainly takes risks, Companies invest hundreds of millions amounts in R&D over long periods of time and Scientists invest significant proportion of their career to develop a single product that can and often does fail, even in late stages. Companies also get rewards commensurate with the risks if they make to the end of the pipeline and into the market. Pharmaceuticals are among the USA's most profitable industries.

The ultimate decision is up to the FDA whose performance is judged by industry, politicians, consumer groups, as well as patient groups with widely varying agenda's. While FDA officials are certainly of high moral character, the pressures must be enormous, and at the end of the day few people applaud and many are eager to criticize. Nothing short of a perfect safety record is acceptable to some. Many Consumer protection groups appear to measure their success by how much they slow the process and how many drugs they get off the market because of a side effect or a rare but significant adverse event.

What about the patient with a degenerative chronic disease? Time is not neutral for a serious or life threatening illness and clinical research necessary to prove that the therapy is safe and effective is an inherently slow process. Two to four years to repeat a study with a design flaw that causes it to fail to reach primary end points may mean the difference between life and death or disability. Yes patients take risks to participate in clinical research and take powerful medicine and they benefit from the outcomes of science.

The difference for these three groups is the perspective of the patient is not represented in the critical design phases and assessment phases of development. All the discussions between the sponsors and the regulators are bilateral. The laws are set up to protect proprietary company information and hence to promote free market competition, not to allow a patient to say what is an important clinical outcome or give another perspective on the judgment call at the end.

Discussions about the criteria and standards for evaluation of new therapies would likely be different if there were independent patient advisors to both industry and regulators, who participated fully in discussions and key meetings during the evaluation phases of

regulatory review in addition to advisory committee review, as is commonly done now. The problem of lack of participation by patients in the design process of evaluation of new therapies can challenge the validity of the entire result.

For example, the primary specialty for the treatment of Parkinson's disease is Movement Disorders. Although PD was first identified in 1817 only very recently did PD professionals place a major emphasis on the non motor effects including autonomic functions such as swallowing and digestion and cognitive and psychological factors such as memory and mood effects of the disease. It was only when the medical profession started asking patients about the symptoms that were most troubling that these non-movement factors have begun to receive more attention. Most clinical trials focus on primary movement factors for measures of efficacy. Recent evaluations of several new treatments have "failed" to reach primary movement endpoints. Yet anecdotal testimony from trial participants indicates some improvements in the non-motor symptoms. While many factors may have an impact on the outcomes for any one study, it is possible that measuring a broader range of clinical outcomes based on input from patients could yield different results.

#### PATIENT ADVISORS AND PATIENT CENTERED PROCESSES SEEKING PATIENT PERSPECTIVES

The changing perspective in the healthcare system towards more patients' centered approaches opens up a complex set of issues regarding ways to actually achieve valid patient input. Currently patient participation is linked to the advisory group process. Patient representatives are recruited to serve on advisory groups and patients testify at advisory group hearings. Decisions about safety and efficacy are based on statistical outcome measures from controlled experiments, however, not on the anecdotal data from testimony. The details of the experimental design therefore play critical roles in the process. The judgment calls about what to measure, how to administer the treatment, and how long to run the trial are made during the design phase with very little opportunity to adjust the protocol based on the feedback from participants. Often questions arise during the design about what patient participants will or will not do at the request of the researcher. Assumptions are made with no input from the patient that can greatly affect outcomes. Positive contributions in the design phase of the research by a patient representatives would have an impact on the results of the studies and hence, on the ultimate decision to bring the treatment to market.

In my experience as an advocate I find that patient participation in the process of developing new medical treatments is often acknowledged but much less actually practiced. It appears that the sponsors, the clinical researchers, and the FDA are ambivalent or extraordinarily cautious about inviting full participation of patient advisors in the regulatory process. We need to know more about the reasons that sponsors and regulators and even foundations are concerned about inviting the patient's as partners in their in the quest for improved therapies

Participation on advisory panels is but one way to represent the patient perspective in the evaluation of new medical treatment. The Office of Special Health Initiatives was established to manage the patient input in to the process of drug evaluation and approval. The training offered and the ongoing interaction with other patient representatives has developed a cadre of experienced advocates. These pioneer patient representatives could lead the way to a larger and more meaningful role

#### EXPANDING PATIENT PARTICIPATION INDEPENDENT PATIENT ADVISORS

Fostered by the Office of Special Health Initiatives (OSHI), patient input to the processes and decisions of the FDA has been growing. AIDS and Cancer demonstrate the value added to the process of review and approval of new therapies from patient participation. To date relationships between patients in both sponsors and regulators have been bilateral. AIDS Community Advisory Panels assist sponsors with design of studies from a patient perspective and with recruitment of human subject research participants. Oncology patient advisors consult to the FDA address trial design, end points, and expanded use protocols.

This is a proposal to go beyond the bilateral relationships of the FDA and Sponsors with patient advocates by adding a third leg to the stool by establishing "Independent Patient Advisors" who consult both with to the FDA and to industry sponsors of new therapies for neurological conditions. In an era of user fees and necessary flexibility in regulations to serve the interests of public health, the design decisions and consultations between industry and the FDA are ever more crucial. As the ultimate consumer for the FDA and industry sponsors, patient advocates can bring a unique perspective to the pre-approval regulatory decisions of the FDA.

Patient representation is relatively new for neurological conditions. Three years ago OSHI recruited me as a patient representative for Parkinson's disease. Subsequent training and interactions with other patient representatives as well as with officials in FDA and industry has added depth to my understanding of the processes of development of new treatments and critical role that patient advocates have in that process. The proposal is:

The FDA will establish a task force including patient representatives and industry representatives to recommend policies and criteria to qualify independent patient advisors and to establish recognized patient organizations to recruit and train patient advisors

Patient advisors and advisory Panels recruited by patient organizations will provide consultation and input to both the FDA and individual companies including participation at key meetings in the pre-approval stages of an IND.

While the interests of patients are the ultimate goals of both FDA and Industry, additional interests of the agency or companies patients do not always coincide with either. In order

to represent patient concerns for safe, effective, and "timely" new treatments patient organizations need to have a strong and independent voice with respect to the FDA and Industry. An independent voice for patients can benefit both FDA and industry by offering independent political support of their efforts that benefit patients.

Parkinson's disease is well-suited as a test case for the independent patient advisors. There are sufficient numbers of well-educated professional PWP (persons with Parkinson's) who are early enough in their disease to be relatively unimpaired. Parkinson's research is quite active and increasing numbers of new therapies are expected to enter the pipeline.

#### MAINTAINING INDEPENDENCE CONFIDENTIALITY AGREEMENT

The legal mechanism to establish an independent patient advisor is the confidentiality agreement that companies use to establish a formal working relationship with any consultant. Proprietary information can then be shared with the consultant and be kept confidential under SEC regulations for publicly traded companies.

Independence is established by adding a clause to the agreement that acknowledges that the patient advocate is an advisor for the patient perspective, not an agent for the company. No fees are charged for this consultation other than reimbursement for reasonable expenses in order to maintain independence. This allows the FDA to consult independently with the advisor and gives an added degree of credibility to advocacy positions taken.

Funding to cover costs of recruiting, training and maintaining a cadre of skilled patient advisors will come from the voluntary and not-for-profit organizations in the PWP community. Addition funds may be raised by Industry through grants that maintain the discretion by of the patient groups, much like the FDA maintains independence from industry even though half the budget is user fees.

The PPP has tested these concepts over the past 3 years. Relationships have been established with a half dozen companies where our patient advocates have worked with sponsors in an advisory capacity, and have agreements recognizing our independence. The FDA has not to date taken advantage of our offers for input into decision-making on design and conduct of clinical studies.

#### INFORMING PATIENT REPRESENTATIVES AS ADVISORS

Until now, this discussion has focused on the importance of the patient perspective in making judgments from data on risk and benefit tradeoffs. Patient advisors for FDA and sponsors are recommended to speak for the patient population as Representatives in deliberative discussions because of the interactive nature of those discussions. Although No one patient or even several patients perspective is representative of the views of all

patients, a patient advocate who is well-informed about their patients views can be a representative for the group

And effective patient representative would be someone who is in contact with large numbers of patients to understand their preferences. This is firsthand knowledge can be supplemented through “market” research and other social science methods to obtain a more accurate picture of the views of the group.

Making a judgment about a risk and benefit trade-off for a population of patients is a complex issue. There is variability in the risk tolerance of individuals over time and across individuals and groups. Information on the actual perspective of patients as a group will better inform the overall judgment to be determined by the FDA and its advisory panels. Social science methods for ranking group preferences have been widely used in marketing and other social contexts. Given the multidimensional nature the issue, the best advice is to address the problem with multiple methods. There for some combination of patient representatives to deliberate with sponsors and regulators and market research to determine the range and frequency of the preferences is desirable.

#### MULTIFACITED ISSUE = MULTIPLE SOLUTIONS

Variability in the patient perspective over time and between groups

Risk tolerance

Subjective assessment of benefit

+ Weighting of relative value of multiple outcomes and side effects

+ Individual vs Group perspective - representative or qualitative...

+ Factors -- itemized & distributed vs synthesized – summation