

## BIORESEARCH MONITORING and SURVEILLANCE of GENE TRANSFER STUDIES

The mission of the Bioresearch Monitoring (BIMO) Program in FDA is to ensure the quality and reliability of data submitted to FDA in support of a marketing permit, i.e., an IND, BLA, IDE, NDA, PMA etc., and to ensure the protection of the human subjects' rights and welfare.

There are four compliance programs associated with the BIMO program:

Good Laboratory Practices...for animal studies  
Clinical Investigator.....for studies in humans  
Sponsor/Monitor/ CRO....for sponsor obligations  
Institutional Review Board...for IRB obligations re: local oversight

They cover the product development from the initial testing in animals through the final efficacy trials in humans. All five Centers in FDA have a BIMO program and follow the same compliance programs. Inspections are generally conducted by FDA field-based investigators, occasionally accompanied by a CBER expert.

The CBER BIMO staff become involved when a BLA has been submitted, a complaint about an investigational product is received, CBER review staff have concerns regarding a clinical study, or for routine surveillance. (Most inspections are conducted after the studies have been completed.) An assignment is issued to the field, they conduct the investigation, write a report of their findings and send it to CBER. Headquarters reviews the report, determines if significant violations were found, and develops the appropriate correspondence.

For reports with no significant violations found, a non-titled letter is issued describing the minor deviations from the regulations and requesting a description of what was done or will be done to prevent the recurrence of the violations. For reports documenting significant violations (classified as "Official Action Indicated"), we issue a Warning Letter (WL) or a Notice of the Initiation of Disqualification Proceeding and the Opportunity to Explain (NIDPOE) letter. This classification is used when FDA is prepared to take an administrative or regulatory action, usually when the clinical trial data is affected by the conduct of the study or the rights or welfare of the subjects have been violated.

### GENE TRANSFER THERAPY

After the problems uncovered in clinical trials using gene therapy in Philadelphia and Boston, CBER decided to take a look at how the community investigating gene therapies was conducting their research. At the time, CBER had 211 active INDs for gene therapies. The random sample of 30 INDs was taken and all identifiable principal investigators from each IND were selected for inspection. This amounted to 70

investigators. A general assignment (attached) was issued to instruct FDA field investigators what to cover during each inspection. The reports were reviewed and classified. The results are included in the attached slides. The fear was that since gene transfer was a relatively new field and many of the studies were at the Phase 1 or Phase 2 level, that we might find a significant number of violations. As can be seen in the slides, the findings indicated the studies were being conducted with fewer violations than the typical investigated trials.