Regulatory Submission Process for Gene and Cellular Therapies

Gladice Wallraven, CCRA[1]; Phillip B. Maples[1], PhD.; John Nemunaitis, MD[1,2]

[1]Gradalis, Inc, Dallas, TX; [2]Mary Crowley Cancer Research Centers, Dallas, TX

In order to deliver a gene therapy product to the clinic, the sponsor of an agent must understand that recombinant DNA products must undergo review by four regulatory bodies. Intensive planning, group collaboration, and timing are essential elements in receiving FDA and NIH approval to implement a clinical trial. We will illustrate the processes utilized to submit and approve clinical trial use of a gene based product.

The FDA submission process is outlined clearly in the Code of Federal Regulations (CFR) and guidance documents. All components submitted are kept confidential between the Agency and the sponsor. An Investigational New Drug (IND) application must cover three broad areas: animal pharmacology and toxicology studies; chemistry, manufacturing, and controls information; and clinical protocols and investigator information. Details of each area must be carefully presented so that the FDA reviewers may easily identify the history, manufacturing, and safety of the product.

Contents of an IND Package include FDA Form 1571 (Cover Sheet), Table of Contents, Introductory Statement and General Investigational Plan, Investigator's Brochure, Protocols, Chemistry, Manufacturing, and Control Information, Pharmacology and Toxicology Information, Previous Human Experience with the Investigational Drug and Additional / Relevant Information.

As a part of the federal regulations, an investigator must ensure that Institutional Review Board (IRB) review is conducted and approved before commencing with the trial. This information must be submitted with the IND Package as part of the site selection process within the Protocols section.

Studies utilizing gene based products have additional review board(s) overseeing the conduct of a trial: the Recombinant Advisory Committee (RAC) and the Institutional Biosafety Committee (IBC). The RAC is part of the Office of Biotechnology Activities (OBA) of the National Institutes of Health (NIH). Institutes who receive federal funding for recombinant DNA research are required to submit for RAC review. However, though not all institutions are required to submit for RAC review, often times FDA deems that RAC review would be a necessary and appropriate step In addition to the protocol, the RAC requires an Appendix M to be submitted for review.

Appendix M is comprised of a series of questions regarding the design and submission of the protocol, including the potential safety risks imposed on individuals handling the product and product management. The IBC is a local body responsible for reviewing and approving recombinant DNA research and potentially biohazardous projects. The IBC sets containment levels in accordance with the National Institutes of Health (NIH) Guidelines and those of the Centers for Disease Control and Prevention (CDC).

We have repeatably demonstrated that approval from all regulatory bodies could efficiently be received from all parties within a 6 week timespan. Review of our process will be presented.