FDA's Draft Guidance on Pharmacogenomics

Scope and Depth of Agency's Interest

Pharmacogenomics is said to have been created with the 1955 presentation of re-search relating excre-tory levels of isoniazid to therapeutic results (Fruh & Gurwitz, 2004). In the fifty years since then, the number of published articles referencing pharmacoge-nomics or pharma-co genetics has grown to the thousands.

But this expansion inves-tigation of inter-individu-al variability of drug re-sponse has not produced any fundamental changes in product development or clinical practice. The sources of inhibitions within the pharmaceu-tical and biotech communities to embracing individualized drug therapy are probably legion.

However, one issue often referred to (and recognized by the FDA itself) has been uncertainty over testing programs during product development.

The one day meeting, held in collaboration with the Drug Information Association (DIA), PhRMA, Biotechnology Industry Organization (BIO), and Medical Technology Association (MDMA), and the Pharmacogenomics Working Group (PWG), was written to facilitate "scientific discussion and evaluation of many such tests, and to encourage" the Agency to "provide FDA with valuable information to consider during its own regulatory decision making because they are gener-ated through a well-character-ized analytical system. In addition, there exists an established scientific framework or body of evidence that explains their significance in measuring safety or efficacy. But tests belonging to the dis-tinctive class of such valid bio-markers are further distinguished as either "known" or "probable." As defined in the Draft Guidance, a known valid biomarker is one which has been accepted in the broad scientific community, while a probable valid biomarker appears to have predictive value but has not been widely accepted or has been independently replicated.

A probable valid biomarker is likely to be one for which a spon-

FDA described its primary pur-pose to be to "provide an interactive forum for discussing industry and other perspectives and experi-ence derived from the develop-ment of recently approved pharma-cogenomics products. ...and to provide FDA with valuable information to consider during development of guidance for industry on the co-development of pharmacogenomic combination products for therapeutic and diagnostic use.

The one day meeting, held in cooperation with the Drug Information Association (DIA), PhRMA, Biotechnology Industry Organization (BIO), and Advanced Medical Technology Association (ADVAMed), Medical Device Manufacturers Association (MDMA), and the Pharmacogenomics Working Group (PWG), is expected to lead to the eventual issue of a draft guidance on the co-development of pharmacogenomic combination products.

The FDA announced on August 11, 2004, that it had submitted the Draft Guidance and related mate-rials to the Office of Management and Budget (OMB) for review and clearance. On December 27, 2004, the Agency reported in the Federal Register that OMB had approved the submission. Release of the final guidance is expected in early 2005.

Goals

The FDA makes clear at the out-set of the Draft Guidance that it was written to facilitate "scientific progress in the field of pharmaco-genomics" and "the use of pharma-cogenomic data in informing regulatory decisions." If finalized as drafted, the Draft Guidance will apply to sponsors holding pending investigational new drug applications, new drug applications, and biological license applications. It will also give re-com-mendations to those sponsors on when to submit pharmacogenomic data during the product development and review process, the formats to use to submit that data and how the data will be used in regulatory decision making.

As used in the Draft, "pharma-cogenomics" specifically does not include proteomics, metabo-lomics, or genetic or genomic techniques for biological product characterization.

The Agency concedes in the Draft Guidance that uncertainties over its use of pharmacogenomic data in the drug application review process has discouraged sponsors from initiating pharmacogenomic testing programs during product development.

While acknowledging the experi-mental nature of many such tests, the FDA clearly believes that ful-filling the potential of pharma-cogenomics to individualize thera-pies that maximize effectiveness and minimize risk will require its active encouragement (and partici-pation in the evaluation) of these tests in the context of product development.

Consequently, a key element of the Draft Guidance is the pro-posed program for voluntary submission of pharmacogenomic test data, which is referred to as a VGDS (voluntary genomic data submission). As proposed, VGDSs would be referred to a cross-center Interdisciplinary Pharmacogenomic Review Group (IPRG), which would act as a clearinghouse and resource for further policy development.

At the same time, the submission of pharma-co-gentest data, even if experimental, would be required to the ther-apy isoniazid to therapeutic results (Frueh & Gurwitz; 2004). In the

Weblinks for this article

www.fda.gov/cder/notes/PRIMEDRUGS.html

(Documents for FDA/Industry Workshop on Pharmacogenomics/Pharma-
cogenomics Data Submissions (Documents for FDA/Industry Workshop on Pharmacogenomics/Pharma-
cogenomics Data Submissions (Documents for Science Board Meeting on April 9, 2003: agenda, presentations & transcript)

www.fda.gov/cder/calendar/ meeting/pharma52002/default.html

(Documents for FDA/Industry Workshop on Pharmacogenomics/Pharma-
cogenomics on May 16-17, 2002)

www.fda.gov/cber/dockets/ default.html (FDA Dockets link)


(CDRH 5150): Premarket Notification for the Aflametric geneshot IV)

See FDA on page 22
FDA

Continued from page 18

BioAdvance Grants Seed Capital to Biotech Firms

BioAdvance (Philadelphia), the biotechnology Greenhouse of Southeastern Pennsylvania, selected seven life science companies to receive a total of $3.5 million in seed capital in the first round of its Greenhouse Fund’s third investment cycle. The Greenhouse Fund aims to help entrepreneurs move promising products and technologies to the next stage where traditional venture or corporate funding is available. Since 2002, the fund has committed $9 million to 20 enterprises. Each company will receive $500,000:

- Avad RadioPharmaceuticals, for the development of a new diagnostic tool for Alzheimer’s disease.
- Marillion Pharmaceuticals, for developing methods to make chemotherapy safer and more effective.
- InfraScan, for methods to diagnose bleeding in the brain.
- Galleon Pharmaceuticals, for applying technologies to convert intravenous infusions into oral treatments.
- Jerin Discovery, for the development of obesity treatments.
- Mellor Discovery, for finding new uses for drugs and drug candidates using proprietary technologies.
- SanSrosa Pharmaceuticals, for the development of an approach to treat the disfiguring symptoms of rosacea.

“These new Greenhouse Fund recipients once again demonstrate the blend of established scientific strength and innovative proficiency in the Greater Philadelphia region,” says Barbara S. Schilberg, managing director and CEO of BioAdvance.

“Investing in funding is just the beginning of our relationship with these emerging companies, as we continue to help them obtain a range of resources needed at each critical stage of development.”

Bioterrorism Project

Corgenix Medical (Denver) established a research program to develop a rapid detection system for viral hemorrhagic fevers, a disease category recognized for its potential as a bioterrorism agent and included in the high priority “Category A” group of biological diseases as defined by the CDC.

“Bioterrorism defense is an important issue in this day and age, and we are confident that our collaboration with key industry and academic scientists will show meaningful results in a short period of time,” says Douglas Simpson, president of Corgenix.

Patents Granted

Aastrom Biosciences (Ann Arbor, MI) received U.S. patent 6,833,566, which covers expandable angioplasty technology that is intended to support the healing of human dendritic cells produced in cell culture. Aastrom is currently engaged in ongoing clinical trial collaborations at Stanford University to evaluate dendritic cells produced with this technology.

Dyonogen Pharmaceuticals (Waltham, MA) was awarded U.S. patent 6,846,823 related to the use of DPP225, formerly known as MCI225, for the treatment of lower urinary tract disorders. The patent covers the use of a broad class of thieno[2,3-d]pyrimidine derivatives, including DDP225, for the treatment of urinary frequency, urinary urgency, nocturia (nighttime urination), and enuresis (bedwetting).

The claims of this patent also protect the mechanisms of action by which the compound acts. The patent is directed toward the 3 receptor antagonist in combination with any NARI for the treatment of frequency, urgency, nocturia, and enuresis.

Antigen Express (Worcester, MA) was granted U.S. patent 6,583,382 B2. The patent covers the use of IL-2/IL-27 cytokine homologs for their use in treating cancer, which has the potential as a treatment for autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, and diabetes mellitus.

Scientists at Antigen Express discovered hybrid peptides in which the immunoregulatory IL-2/IL-27 cytokine is linked covalently to antigenic epitopes. By controlling the presentation of antigen peptides to the immunoregulatory IL-2/IL-27 helper cells, new classes of drugs can be developed to suppress autoimmune disease.

The Antigen Express compounds can either enhance or block presentation of antigenic epitopes to immunoregulatory T cells. In laboratory studies, such IL-2/IL-27 hybrid enhance presentation of the antigenic peptides in mice to small business innovative research (SBIR) grants, and make vaccines in animals about 10 times more potent.

FDA Approvals

The FDA approved Abbott’s (Abbott Park, IL) UroVysion™ DNA probe assay for use as an aid in the initial diagnosis of bladder cancer in patients with hematuria (blood in urine) suspected of having bladder cancer. UroVysion is a gene-based test for both diagnosis and monitoring of bladder cancer recurrence. The test is designed to detect genetic changes in bladder cells in urine specimens using fluorescence in situ hybridization (FISH).

Sinclair Pharma (Godalming, U.K.) says the FDA approved its OTC mouth ulcer treatment, Alclair® spray, as a medical device. The spray of Alclair is one of three delivery systems, including an oral gel and an oral rinse solution, which are already approved and marketed in the U.S. and EU.

Grant Awarded

Wilson Wolf Manufacturing (New Brighton, MN) was awarded a two year, $1,000,000 Phase I small business innovative research grant to study potential treatments for Diabetes and Digestive and Kidney Diseases. The grant will focus on a novel device that can improve the self implantation process. The device is designed to be smaller than flasks, according to Wilson Wolf, and has been capable of culturing up to 4,000,000 cells at 2 cm² at high viability, high oxygenation capacity and novel geometry.

Genetic Engineering News  |  Volume 25, Number 4, February 15, 2005 | 22

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