

Review of FDA Projects in Scientific Priority Areas: Report by the Science Project Review Subcommittee to the FDA Science Board

May, 2009

Purpose and Nature of Review: The Science Project Review subcommittee was established by the Science Board to review FDA research projects in areas considered by the FDA to be of high scientific priority. The subcommittee consisted of David R. Parkinson, MD (Nodality, Inc.), John Floros, PhD (Pennsylvania State University), and James Broach, PhD (Princeton University). In addition, Robert Nerem, PhD (Georgia Tech) aided the subcommittee as subject matter expert.

Project descriptions supplied to the subcommittee members were of approximately 3 pages in length, describing the project generally, outlining the hypothesis, detailing the methodologies to be used and the relevance of the studies, then listing the deliverables from the project, and their timelines. The subcommittee reviewers considered the projects, already representing the result of internal review and prioritization within each of the FDA centers, from the following perspectives:

- (i) Did the projects appropriately fall within the FDA's defined "Overarching Scientific Priority Areas", as described by the Science Commissioner? These scientific priority areas include:
 - a. Rapid detection
 - b. Adverse event detection and analysis
 - c. Biomarkers
 - d. Clinical trial design and analysis
 - e. Microbial ecology and contamination mitigation strategies
 - f. Manufacturing science
 - g. Personalized medicine and nutrition
- (ii) Were any of projects deficient, flawed in some manner, or of lesser apparent priority?
- (iii) Were there projects which stood out in terms of their particular importance scientifically, or their potential for contribution to the mission of the Agency?
- (iv) Amongst the projects, were there potential opportunities for synergy or creating internal Agency critical mass of technology or expertise?

A total of 32 projects were reviewed, contributed from 5 FDA Product Centers, the National Center for Toxicology Research, and the Officer of Regulatory Affairs. The subcommittee reviewed all of the projects; this report represents a recommendation to the Science Board based on teleconference discussions.

Results of Review: The subcommittee considered all of the projects to have scientific merit and to fall within the defined scientific priority areas. They clearly represented the results of robust internal project development and review processes, and the extensive breadth of science encompassed in the proposals reflects the wide range of science encompassed by the FDA mission. In formulating recommendations to the Agency about relative merit and prioritization of the proposed projects the subcommittee found it most useful to classify projects within three broad categories: (A) those which

were considered to be fundamental to the FDA public health mission, necessarily had to be conducted within the FDA, and potentially involved more than a single Product Center. These projects were considered to be of particular importance to the mission agency, and therefore of the highest scientific priority, (B) projects which were clearly mission-oriented but restricted in their application within a single Product Center, and finally, (C) those projects which although of scientific interest, were not as clearly directly Agency mission-oriented, and which it appeared to the subcommittee could alternatively be conducted by external academic or industry scientific collaborators. Given the lack of detail in the project descriptions, the subcommittee felt that it would not be appropriate to assign specific project ratings; however, comments about particular projects, alone or in groups, follow:

Specific Comments:

(A) Projects of Highest Priority Because of Their Particular Importance to the Mission of the Agency:

These projects, which in the view of the subcommittee represented the highest prior science-based proposals because of their criticality to Agency mission, fell into three categories (i) those related to the rapid detection of pathogens (ii) those related to pathogen detection and elimination in manufacturing and in products, as well as (iii) those related to the more rapid and efficient detection of adverse events,

(i) **Rapid Detection of Pathogens:** The following projects fell into this category:

CBER: Proactive identification, assessment, monitoring of and response to top priority pathogen threats to blood and tissue supply

Development of standards, reagents and assays to facilitate rapid response to emerging pathogens that threaten the blood and tissue supply

Harness new cutting edge science for pathogen detection to enhance prevention and rapid response to emerging and unknown threats and to improve product quality through in-process testing and process analytic technologies.

CFSAN: High throughput technology for identification and characterization of microorganisms: Field trial of IBIS biosensor

Rapid identification of food pathogens using high-throughput detection methods that target single-nucleotide polymorphisms (SNPs)

CVM: Simultaneous detection and identification of multiple foodborne bacterial pathogens isolated from animals and foods by Bio-Plex technology and microarray

NCTR: Validation of advanced technologies for rapid detection of bacterial contaminants

ORA: Enhanced preventive analytical capabilities

Comments: The project descriptions make compelling arguments for the introduction of rapid detection technology, and the new technology and instrumentation introduction make these goals achievable. A number of different instrument platforms involving a range of technologies are being evaluated, with overlaps in similar instrumentation evaluation by different Product Centers. In addition, different rapid detection tests for the same pathogens are being proposed by different Product Centers. **The subcommittee believes that these projects cumulatively should be assigned highest scientific priority, and that there are significant opportunities for more efficient cross-Center evaluation and implementation of these important new technologies, recognizing that different needs may result in utilization of particular technologies in different Centers.** We encourage formation of a cross-Center task force or equivalent to lead these efforts. These projects if realized would contribute significantly to more efficient evaluation of real and potential pathogen threats.

(ii) **Pathogen Detection/Elimination in Manufacturing and Products:** Projects from both CBER and CDER address evaluation of improved technologies to detect pathogens in manufacturing and product.

CBER: Harness new cutting edge science for pathogen detection to enhance prevention and rapid response to emerging and unknown threats and to improve product quality

CDER: Inactivation of resistant viral contaminants: Risk of human transmission & approaches for elimination

Comments: This was considered to be another area of high scientific priority, important to Agency mission; the proposals suggested opportunity for CDER/CBER collaboration.

(iii) **Detection of Adverse Events:** Again, projects from both CBER and CDER address the development of improved adverse event reporting:

CBER: Enhanced analytic capability: Develop tools to more quickly and reliably identify adverse events caused by administration of biologics

CDER: Analysis of medical product adverse events utilizing a distributed network

Comments: Introduction of improved adverse event reporting represents a clear national priority. Although the CBER proposal is focused more on vaccine event reporting, the subcommittees joint effort for a single reporting system, a project which should rank in the highest priority of Agency scientific goals.

(B) Projects Related to the Mission of Individual Centers: A number of projects were proposed around topics of importance to individual centers:

Biomarker and Personalized Medicine Studies: Biomarker and personalized Medicine proposals were submitted from CBER, CDER, CDRH, and NCTR. The proposals are wide-ranging, but in general seemed related to Agency mission.

Clinical Trial Methodology: CDER included 3 proposals related to clinical trial science; while all 3 were felt to be of merit, of particular interest to the reviewers was the “Development of a collaborative program between the FDA and the EMEA for good clinical practice inspection of clinical trials supporting drug development worldwide”

Manufacturing Science: Three projects were proposed by CDER in this area:

- (i) Rapid screening of pharmaceutical products and ingredients
- (ii) Implementation of Quality by Design principles and novel process analytical technologies for protein therapeutic manufacturing in the 21st century, and
- (iii) Harness new cutting edge science for pathogen detection to enhance prevention and rapid response to emerging and unknown threats and to improve quality through in-process testing and process analytic technologies

Comments: All three of these projects were considered to be of merit; the last two projects appear to present opportunities for cross-Center cooperation with some of the other pathogen detection proposals. Other Center-specific projects proposed included proposals from CFSAN around microbial ecology and contamination mitigation strategies (Ecology and Control of Salmonella on Tomatoes), and manufacturing science (High pressure processing as a new technology for producing safe shelf-stable foods). The projects seemed of significant merit and of high priority relative to the mission of the particular Product Center involved.

(C) Meritorious Projects of Less Clear Priority: A number of other projects were proposed which while of intrinsic scientific merit, represent work which committee members felt could potentially be conducted by academic or industry collaborators or by contractors. The subcommittee felt that as a result despite their merit these projects did fall into a different category of priority related to the stated Agency priorities, while acknowledging that each center involved would be most knowledgeable about the regulatory need in specific areas and would have to evaluate the best approach to addressing needs (i.e. whether conducted by academic, industry, or other collaborators). The following projects fell into this category:

- (i) **CBER:** Development and use of improved preclinical models to identify and assess biomarkers for the safety and efficacy of cellular therapies, including stem cells and engineered tissues
- (ii) **CDER:** Risk assessment of drug-induced phospholipidosis in the CNS
- (iii) **CDER:** Effect of proton pump inhibitors (PPIs) on the pharmacokinetics and pharmacodynamics of clopidogrel: Impact of CYP219 genotypes and PPI class effects

Additionally, one project was felt to be not clearly related to Agency mission in a manner comparable to the other submitted proposals. This project, The NCTR Healthy Challenge is an internal NCTR project related to staff health, and was felt not fit easily within this scientific evaluation process.

Concluding Summary: The submitted projects were of generally high level of scientific merit. The proposed A-category projects relating to pathogen detection technology evaluation and implementation, as well as the adverse event applications were considered to represent scientific opportunities which will greatly aid the Agency as it pursues its mission. Similarly, B-category projects were deemed to represent significant value to the scientific missions of the individual Product Centers. C-category projects were not deemed to be of the same level of priority based on the information provided to the subcommittee; other considerations which might modify this assessment include uniqueness of the scientific resource to conduct the study within the Agency or lack of corresponding resource availability within the Agency.

Respectfully submitted,

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