National Toxicology Program

Board of Scientific Counselors

April 19, 2022

National Institute of Environmental Health Sciences
Research Triangle Park, NC

Summary Minutes

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1. Location of Background Materials, Written Public Comments, and Presentations

Background materials and presentations for the April 19, 2022, Board of Scientific Counselors meeting are available on the National Toxicology Program (NTP) Past BSC Meetings page (https://ntp.niehs.nih.gov/go/meeting). No written comments were received from the public.

2. Abbreviations and Acronyms

BSC	Board of Scientific Counselors
DIR	Division of Intramural Research
DNTP	Division of the National Toxicology Program
GEO	Gene Expression Omnibus
GSEA	Gene set enrichment analysis
HTS	High-throughput screening
IPA	Ingenuity pathway analysis
KEGG	Kyoto Encyclopedia of Genes and Genomes
NIEHS	National Institute of Environmental Health Sciences
NTP	National Toxicology Program
QSAR	Quantitative structure-activity relationship
SRA	Sequence Read Archive
SVM	Support vector machine
Tox21	Toxicology in the 21st Century

3. Attendees[1]

Board of Scientific Counselors

Chair: David Eaton, PhD, University of Washington
David Berube, PhD, North Carolina State University
Eric Blomme, DVM, PhD, AbbVie
Weihsueh Chiu, PhD, Texas A&M University
Susan Felter, PhD, Procter & Gamble
Kathleen Gray, PhD, University of North Carolina, Chapel Hill
Devon Payne-Sturges, DrPH, University of Maryland, College Park
Mark Russi, MD, Yale University
Anne Ryan, DVM, PhD, Act 5 Ventures, LLC
Veena Singla, PhD, Natural Resources Defense Council
Susan Tilton, PhD, Oregon State University

National Institute of Environmental Health Sciences (NIEHS) Office of Acquisitions Staff

Julie Bardo
Melissa Gentry

[1]The meeting was webcast with the listed individuals attending by Zoom. NIEHS/DNTP staff are limited to those with a role in the meeting. Public attendees are not listed.

National Institute of Environmental Health Sciences/Division of the National Toxicology Program (NIEHS/DNTP) Staff

Brian Berridge
B. Alex Merrick
Mary Wolfe

Other Federal Agency Staff

Gonçalo Gamboa da Costa, U.S. Food and Drug Administration (BSC liaison)
Christina Lawson, National Institute for Occupational Safety and Health (BSC liaison)

Contract Support Staff

Lauren Fitzharris, ICF
Ernie Hood, Bridport Services
Jeanne Luh, ICF

4. Introductions and Welcome

The National Toxicology Program (NTP) convened a meeting of its Board of Scientific Counselors (BSC) on April 19, 2022, via Zoom for identified attendees noted above and webcast for public attendees. Dr. David Eaton served as chair. Dr. Mary Wolfe served as the Designated Federal Official.

Dr. Eaton called the meeting to order at 12:30 p.m., welcomed everyone to the meeting, and asked BSC members, Drs. Brian Berridge, Mary Wolfe, Gonçalo Gamboa da Costa, and Christina Lawson to introduce themselves. Dr. Wolfe read the conflict-of-interest policy statement and briefed the attendees on meeting logistics.

Dr. Eaton stated that there was one item on the meeting agenda. One of the roles of the board is to review and approve external contracts, which was the purpose of the meeting. Dr. Eaton noted that there were no written or oral public comments on this topic.

5. Contract Concept: Bioinformatics Support for the NIEHS

5.1. Instructions for Concept Review

Ms. Melissa Gentry from the National Institute of Environmental Health Sciences (NIEHS) Office of Acquisitions briefed the board on the process for reviewing the contract concept. A high-level discussion is required to identify the basic purpose, scope, and overall objectives of the work. The board was directed to consider the overall value and scientific relevance of the contract concept, and whether it supports the NIEHS goal of protecting public health. Consideration should be given to the significance of the goals of the proposed research activity, the availability of technology and other resources necessary to achieve those goals, the extent to which there are practical scientific or clinical uses for the expected results, and the adequacy of the proposed methodology. The board would then vote on the appropriateness of the use of a contract mechanism to support the proposed activities.

5.2. Contract Concept Review for Bioinformatics Support

Dr. B. Alex Merrick briefed the board on the contract concept. He stated that the purpose of the contract is to provide bioinformatics support for projects within the NIEHS research portfolio. The current bioinformatics contract provides biocomputational capabilities for NIEHS needs in diverse fields of study, including toxicology, genomics, structural chemistry, and high-throughput screening (HTS). The contract primarily supports DNTP, but also provides some support for the Division of Intramural Research (DIR). All branches and programs in DNTP use the current contract, which has a contract length of 5 years. To maximize the use of this contract, the new contract is proposed to last 7 years and will provide similar capabilities as the previous statement of work. The contractor is required to have flexibility to analyze numerous types of research data from different data streams such as gene expression and metabolomics. The work may involve multi-scale modeling and require tools and unique methods for data visualization. Given the collaborative nature of DNTP in addressing complex problems, delivery of contractor-developed source code that addresses programmatic needs will be a requirement for the new contract.

Technical capabilities will include omics analysis, computational modeling, cheminformatics, data display/data reduction, high content imaging/screening, source coding, and DIR support. Under these categories, capabilities will include:

- Analysis for next-generation sequencing data.
- Transcriptomics and toxicogenomics support including data reference, extraction, and deposits in public databases such as Gene Expression Omnibus (GEO) and Sequence Read Archive (SRA).
- High-throughput transcriptomics support.
- In vitro image analysis and pattern recognition related to in vitro methods including cellular and subcellular morphology in response to toxicants or environmental contaminants.
- Quantitative structure-activity relationship (QSAR) and read-across support for HTS assays to fill in data gaps for related chemicals in support of the Toxicology in the 21st Century (Tox21) program.
- Computational, biostatistical, and informatics methods including machine learning, data extraction from large data sources, multi-scale and mathematical modeling, and coding support.
- Informatics methods and data mining in support of systematic scientific literature reviews including machine learning, text mining, and natural language processing from government or public resources, or in scraping data from the internet.
- Computational and software support using Java, C++, and R for text mining, natural language processing, and machine learning methods.
- Study designs and pathway analysis support using data reduction methods, Kyoto Encyclopedia of Genes and Genomes (KEGG), Ingenuity pathway analysis (IPA), gene set enrichment analysis (GSEA), and support vector machine (SVM) analysis.
- Publication and meeting support including organizing data by means of graphs, tables and figures for publication, technical reports, and presentations.

Dr. Merrick described several representative bioinformatics projects and capabilities to be addressed under the contract. In summary, he asked the BSC members to review the concept for its overall value and scientific relevance in achieving NIEHS' goal of protecting public health. Consideration should be given to:

- The significance of the goals of the proposed research activity.
- The availability of technology and other resources necessary to achieve those goals.
- The extent to which there are practical scientific or clinical uses for the expected results.
- The adequacy of the proposed methodology.

Clarifying Questions

Dr. Weihsueh Chiu asked what was meant by "multi-scale modeling." Dr. Merrick replied that it means using different data streams and putting them together to use mathematical models for

prediction of chemical toxic events that may not emerge from just one data stream. He provided, as an example, the need to link transcriptomic data with genomic, epigenomic, and metabolomic data.

Dr. Chiu requested clarification on the precise role of this contract relative to what DNTP staff or other contractors are currently doing. Dr. Merrick said that the contract was conceived to address two aspects: first, to provide capabilities that DNTP and DIR staff can use for analysis; and second, to conduct projects like Orbitox, which are led by DNTP staff who provide broad direction to the contractor and work together with the contractor through an iterative process to accomplish the desired goals.

Dr. Chiu noted that the contract addresses both methods application (i.e., support to implement the pipeline for a particular project) and methods development (i.e., support to test hypotheses and develop approaches for data integration). Dr. Merrick confirmed that observation and emphasized that the process is a back-and-forth collaboration between staff and the contractor. The field of informatics is changing so quickly that being able to find and hire qualified personnel has become a challenge. The use of a contract mechanism addresses this challenge as DNTP can adjust the contract as needs change.

Dr. Chiu mentioned that it would seem challenging for a single contractor to be able to have the entire range of desired capabilities. Some of these capabilities are highly specialized, with perhaps only a handful of people in the world who have developed some of these methods. He asked how NIEHS would be able to access that diversity of expertise through the contract mechanism. Dr. Merrick replied that each part of the contract requirements could be considered a contract unto itself, but the management of the contract does allow and require some flexibility in terms of the kind and mix of talent to be offered by the contractor. The ability to use subcontractors is also included in the contract to fulfill the required needs.

Dr. Chiu asked about the systematic review aspects of the contract, such as text mining and literature-based machine learning, and how they would contribute to the delivery of systematic reviews, particularly given that there is a current, separate contract specific to systematic review work. Dr. Merrick acknowledged that DNTP has multiple contracts in a given area that sometimes overlap. DNTP staff are expected to collaborate and integrate their activities, and the same would be expected of contractors.

5.3. BSC Discussion

In considering the significance of the goals of the proposed research activity, Dr. Chiu, the lead discussant, stated that it is the larger goals of DNTP that are significant, and the contract includes approaches to help address those larger goals. In terms of the availability of technology and other resources, he observed that the purpose of the contract was to develop technologies and resources to achieve those goals. In terms of practical uses, it is the responsibility of DNTP staff to recognize when projects are more academic exercises versus those more applicable for use by decision makers. Regarding the adequacy of the proposed methodology, Dr. Chiu noted that without more details about the specific methodologies, it would not be possible to comment on their adequacy.

Dr. Chiu inquired whether a contract mechanism is appropriate, or whether some of the support requested might be more appropriately addressed as cooperative agreements or research grants, specifically for the stand-alone methods development projects.

Dr. Eaton asked about intellectual property issues related to instances where DNTP scientists work hand-in-hand with contractors to develop new methods and approaches. Dr. Merrick indicated this was an issue of active discussion within NIEHS. Because of the collaborative nature of many different types of projects, the contract will require that the government have distribution and ownership rights to any code that might be requested because it is in the public interest and is being paid for with public money. He said that the Office of General Counsel is comfortable with that as long as it is clearly defined to the potential vendors.

Referring to the question Dr. Chiu had raised regarding alternative approaches, Dr. Merrick noted that there are several ways to accomplish program goals, including contracts. The benefit of a contract is that it allows for an immediacy of exchange of information in a way that grants and cooperative agreements sometimes do not. He described some of the benefits offered by grants and cooperative agreements such as the ability to harness the creative solutions developed by those working in academia. He felt that contracts also allow for more precision direction and rapid changes in response to changing program needs.

Dr. Anne Ryan commented in support of the contract mechanism from the pharmaceutical industry perspective, citing her experiences at Pfizer.

Dr. Eaton noted that the growth in technologies and techniques in biology is of paramount importance, and it is gratifying to see DNTP at the leading edge in toxicology and environmental health sciences. Taking advantage of the specialized expertise offered by contractors is essential to the success of the field, he added.

5.4. BSC Action

Dr. Eaton called for a motion on whether a contract mechanism is the appropriate mechanism to support the proposed activities. Dr. Chiu so moved; Dr. Berube seconded the motion.

The Board voted unanimously in favor of the motion to approve the contract concept.

6. Adjournment

Dr. Wolfe thanked the board for their preparation and participation. She thanked all participants on behalf of Dr. Berridge, who had to leave the meeting early.

Dr. Eaton adjourned the meeting at 1:28 pm, April 19, 2022.

7. Approval of the Summary Minutes by the NTP BSC Chair

These summary minutes have been read and approved by the chair of the April 19, 2022 NTP Board of Scientific Counselors.

David Eaton, PhD, University of Washington

NTP BSC Chair

Date: May 20, 2022