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BOARD OF SCIENTIFIC COUNSELORS

COMPUTATIONAL TOXICOLOGY SUBCOMMITTEE
CONFERENCE CALL SUMMARY

February 20, 2008
10:00 a.m. – 12:00 noon EST

Welcome and Overview

George P. Daston, Miami Valley Laboratories, The Proctor & Gamble Company, Chair, Computational Toxicology Subcommittee, Board of Scientific Counselors (BOSC)

Dr. George Daston, Chair of the Computational Toxicology Subcommittee of the Board of Scientific Counselors (BOSC), welcomed the participants to the teleconference. He stated that the purpose of this conference call was to discuss the letter report that was drafted following the December 17-18, 2007, meeting of the Subcommittee to review the National Center for Computational Toxicology (NCCT). Dr. Daston indicated that he had received the draft responses from all of the Subcommittee members with the exception of Dr. John Quackenbush. Dr. Quackenbush responded that he had completed his section and would be sending it to the members by e-mail before the completion of this conference call.

Dr. Daston said that he would prefer to go through the responses for each charge question and ask for the members' comments. He noted that there will be time for public comment at 10:45 a.m. Dr. Daston then asked Ms. Lorelei Kowalski to provide her remarks.

Designated Federal Officer (DFO) Remarks

Ms. Lorelei Kowalski, DFO for the Computational Toxicology Subcommittee, Office of Research and Development (ORD)/U.S. Environmental Protection Agency (EPA)

Ms. Lorelei Kowalski introduced herself and thanked the Chair and Subcommittee members for their participation in the teleconference. She identified the Subcommittee members on the teleconference, including Dr. Daston, Dr. James Clark (Exxon Mobil Research and Engineering Company), Dr. Richard Di Giulio (Duke University), Dr. M. Moiz Mumtaz (Agency for Toxic Substances and Disease Registry [ATSDR]), Dr. John Quackenbush (Dana-Farber Cancer Institute), and Dr. Cynthia Stokes. Staff from the NCCT also participated in the call and they are included in the list of participants attached to this summary.

Ms. Kowalski explained that the BOSC Computational Toxicology Subcommittee is a federal advisory committee that is subject to the requirements of the Federal Advisory Committee Act (FACA). As the DFO, her role is to ensure that all FACA requirements are met for this conference call. FACA requires that meetings and calls are open to the public if they involve substantive issues and include one-half or more of the members. Notice of this teleconference was published in the *Federal Register* and an electronic federal docket for the meeting was created and is accessible at http://www.regulations.gov, docket number EPA-HQ-ORD-2007-1148. She noted that the purpose of this conference call is to discuss the draft letter report

prepared by the Subcommittee following the review meeting held in December 2007. That was the third face-to-face meeting of the Subcommittee and it was held at the EPA facilities in Research Triangle Park (RTP), North Carolina. Ms. Kowalski distributed the draft sections of the report by e-mail to the members prior to the call. If the report cannot be finalized and approved by the Subcommittee on the call today, another conference call will be scheduled to do so. She mentioned that she had not received any requests to submit a public comment prior to the call. For the benefit of those participating on the call and for the accuracy of the notes, which are being taken by Beverly Campbell from SCG, Ms. Kowalski asked the members to identify themselves when speaking. The contractor will prepare a summary of the call and, once it is approved by the Subcommittee Chair, the minutes from this teleconference will be available on the BOSC Web Site.

In her role as DFO, Ms. Kowalski works with EPA officials to ensure that the relevant ethics regulations are satisfied. She reminded the Subcommittee members that they must inform her of any potential conflicts of interest regarding the topics discussed during the teleconference.

Dr. Daston thanked Ms. Kowalski for her comments and then turned to a discussion of the responses to the charge questions. Before initiating the discussion of the report, Dr. Daston noted that NCCT was created 3 years ago today. He congratulated the Center staff on what the NCCT had accomplished since it was established.

Subcommittee Draft Letter Report
Dr. George Daston, Chair, Computational Toxicology Subcommittee

Charge Question 1: Does the scope and involvement of expertise in the project reflect activities consistent with the function of a Center?

Dr. Daston asked Dr. Jim Clark to present his response to Charge Question #1. Dr. Clark said that based on the materials presented and the discussions during the December meeting, he was confident that the NCCT staff and those involved in the program from outside the Agency are highly qualified in the various aspects of computational toxicology and the wide range of projects the Center has undertaken. The Center staff and collaborators have the appropriate expertise and insights needed to conduct the research. NCCT has made efforts to solidify formal agreements (memoranda of understanding [MOUs], cooperative research and development agreements [CRADAs]) with various organizations and this has presented the Center with diverse, quality opportunities to leverage and enhance ORD's efforts.

Dr. Clark suggested that the Center needs to move towards risk assessment as a unifying theme in applying NCCT's expertise. He added that NCCT should ensure that its data and tools are relevant to those conducting risk assessments. Some of the researchers seem to be searching for an application of the Center's sophisticated tools; they would benefit from gaining inputs from Agency staff practicing risk assessments (Office of Water and Office of Prevention, Pesticides, and Toxic Substances [OPPTS]).

Dr. Clark noted that the last paragraph of the response to Charge Question #1 could be moved to the response to Charge Question #2, which focuses on goals and milestones. He also was fine

with leaving it under Question #1. Dr. Richard Di Giulio agreed that it could go under either question. Dr. Daston suggested leaving it in the response to Charge Question #1, but also referring to it in the response to Question #2. Both Drs. Clark and Di Giulio agreed with this suggestion.

Dr. Daston suggested mentioning the recently signed agreement between EPA and the National Institutes of Health (specifically the National Institute of Environmental Health Sciences [NIEHS] and the National Human Genome Research Institute). This collaboration will leverage the strengths of each group in a new toxicity testing agreement to use high-speed, automated screening robots to test suspected toxicants using cells and isolated molecular targets. Dr. Daston agreed to send the February 14, 2008 press release on the agreement to Ms. Kowalski for distribution to the Subcommittee members. Dr. Daston also mentioned a recent paper published in *Science* entitled Toxicology: Transforming Environmental Health Protection. The paper is authored by Drs. Francis Collins, George Gray, and John Bucher and focuses on the shift from primarily *in vivo* animal studies to *in vitro* assays, *in vivo* assays with lower organisms, and computational modeling for toxicity assessments. He suggested that Dr. Clark cite the new agreement as well as the paper in the response to Question #1. Dr. Clark agreed to mention them in the revised response.

Charge Question 2: Are the goals and milestones suitably described, ambitious, and innovative?

Dr. Di Giulio stated that overall the answer to this question is yes. He added that the goals are well described, very ambitious, and innovative, but the milestones are somewhat more complex. In most cases, previous accomplishments and current activities are well described, but more detail concerning future milestones would be helpful. The Center has done a good job of achieving its goals and milestones to date so the lack of detail on future milestones is not a major concern.

The goal for ToxCast is suitably ambitious and well described. Progress on this project has been strong and the accomplished milestones are well described. Future plans for the project also are well described, although a more detailed timeline for milestones past 2008 would be helpful.

The Informatics/Data Management project is highly symbiotic with ToxCast and the success of one is highly dependent on the other. More importantly, the success of NCCT overall depends on the success of these two projects. This project is suitably ambitious and its goals and substantial progress are well described. Future plans are described in a general way, but more detail on future milestones (beyond 2008, which is well described) would be appropriate.

The Virtual Liver project is narrower in scope than ToxCast and Informatics/Data Management. Its fit with the goals of NCCT is perhaps less clear than these previous projects; it is more "visionary" in nature and less directly applicable to risk assessment. The goals of the project and the nature of the research to be performed to meet these goals are clearly described; however, milestones for tracking the project's progress are not apparent, particularly in later years (3-5).

The Virtual Embryo project is at an earlier stage than the Virtual Liver project. The issues for goals and milestones are essentially the same as those for the Virtual Liver project.

The Arsenic Biologically Based Dose Response (BBDR) Model is a relatively new effort. The goals of the project are very clear and well described. The milestones, however, are not stated and may be particularly important for this project, which has a clear deadline (2011) in order to be useful for the 2012 Safe Drinking Water Act review cycle.

Dr. Clark suggested that the response to Question #2 reinforce the suggestion that the Center make its organizing theme risk assessment applications for these tools. Dr. Di Giulio said he could add that at the end of the response. It would be similar to the last paragraph in the response to Question #1.

Dr. Stokes expressed her concern that some of the Center's goals may be overly ambitious. She mentioned this concern in the response to Charge Question #3. Should that be moved to this question? Dr. Di Giulio commented that he would rather see the Center err on the side of being overly ambitious than being under ambitious. Perhaps the Subcommittee should recommend that NCCT prioritize what will be done first. Dr. Mumtaz thought it was good to be optimistic but the Center must be realistic given projected budgets.

Dr. Daston asked if anything should be added to the response to Charge Question #2. Dr. Di Giulio asked the Subcommittee members to identify which projects were overly ambitious. Dr. Stokes responded that she thought the Virtual Liver project was overly ambitious. Dr. Mumtaz commented that NCCT has indicated it will develop a robust model in 3-5 years. The Center may not be able to accomplish this and what is considered robust now may not be considered robust in 3-5 years. This timeframe may be too optimistic.

Charge Question #3: Are there significant gaps in the approach that can be pointed out at this point in the evolution of the project?

Dr. Stokes stated that data acquisition for ToxCast is well underway. The main gap noted is that the structural specification of the database for compilation and rigorous quantitative analysis of the ToxCast data remain unclear. Because the data types are highly heterogeneous and the dataset is very large, developing these structural specifications will be a challenge that should be addressed as soon as possible. This gap is relevant to both the ToxCast and Informatics/ Information Management projects. One suggestion in her response is that the ToxCast team compile a list of some specific use cases, e.g., specific questions the team intends to address with the database. This will help solidify the needed database attributes that will allow the analysis for the chemical prioritization that is the end goal of the ToxCast project.

The major gap noted for the Informatics/Information Management project is the same as that described for the ToxCast project. In addition, finding an efficient and effective methodology for extracting data from text sources was a concern for the Subcommittee. A trial of natural language processing for pulling information into some of the databases was described by NCCT staff. This method has been attempted rather unsuccessfully by various research groups over probably 2 decades so the Subcommittee would encourage the exploration of other possible approaches as well.

The big-picture vision of the Virtual Liver project should be balanced with some very specific goals, milestones, and timelines for the next couple of years that are clearly attainable with the expected resources to assure some useful concrete outcomes. In a project with this possible magnitude, it can be tempting to try to do everything, both in terms of the various project approaches as well as the scope within any one approach, which may lead to ending up with little actually completed. One suggestion is that the team develop a short prioritized list of specific scientific research questions that are relevant to EPA's goals that they desire to address as soon as possible, and use this to focus first iterations of development of both the knowledgebase and model(s). More explicit milestones and goals for these highest priority questions then can be developed. Later iterations of knowledgebase development and modeling then can add scope (breadth/depth) to allow addressing additional research questions. Beyond managing compatible coding, the team is encouraged to actively plan for and manage on an ongoing basis the specifications that must be shared among models so as to produce compatibility when it is needed. Because the means of using resulting Virtual Liver models for actual risk assessment at EPA is unclear, the Subcommittee encouraged the staff to give some thought along these lines, in collaboration with program office personnel who conduct such assessments.

The Virtual Embryo project is very early in its development, and already shows interesting progress. Because the data needs of the proposed models may be significant, the Subcommittee noted that it will be critical to identify and enlist appropriate supporters and collaborators to provide such data. The track record of the principal investigator suggests this will develop naturally.

No specific technical gaps in the approach were noted for the Arsenic BBDR project. Because the goal is to use the project's resulting model(s) for the next cycle of review under the Safe Drinking Water Act, the Subcommittee encourages continuous communication with the appropriate program office personnel so that concerns, objections, and skepticism can be addressed early and on an ongoing basis.

Dr. Daston asked if there were any comments on the response to Question #3. Dr. Clark said he liked the write-up and thought it fit well with the responses to Questions #1 and #2. Dr. Daston asked if the second paragraph under ToxCast and the third paragraph under Virtual Liver should be moved to Question #1. Dr. Stokes thought it might fit better under Question #1 because they are not really gaps. Dr. Clark said that he could weave the two paragraphs into the response to the first question.

Noting the parenthetical questions in Dr. Stokes' draft response about what database and who was using it, Dr. Daston stated that he thought DSSTox was being used by the Office of Pesticide Programs (OPP). Dr. Kavlock indicated that the Toxicological Reference Database (ToxRefDB) is being used by OPP to look retrospectively at study design to see the results in the F2 generation that were not seen in the F1 generation.

Dr. Stokes said she tried to summarize the Subcommittee's concerns about using the data set in the response. She asked Dr. Quackenbush if she correctly captured the concerns. Dr. Quackenbush indicated the he had not received the response to Question #3. He asked if someone could send him the response by e-mail. Dr. Mumtaz said that he did not receive the

responses for Questions #1 and #3. Ms. Kowalski agreed to send them the responses immediately.

Charge Question 4: Does the work offer to significantly improve environmental health impacts and is the path toward regulatory acceptance and utilization apparent?

Charge Question 4a: In addition, specifically for the Arsenic BBDR project: Does the proposed computational model have the potential to identify and reduce uncertainties with the risk assessment process? Will the model be able to help identify susceptible populations and compare potential risks in those populations with less susceptible groups? Is coordination between model development and associated data collection sufficient to avoid problems with models being either over- or under-determined?

Dr. Mumtaz stated that the proposed computational models do offer to identify and reduce uncertainties with the risk assessment process. They might not provide all the answers but will move EPA forward in the right direction. Developing a universal arsenic model describing several cancer endpoints is a formidable challenge, so NCCT's proposed step-wise approach is appropriate. Initially, a generic model for cancer will be developed that will incorporate key steps of the mode of action commonly shared for multiple cancer types such as oxidative stress. This model will serve as an engine to develop specific cancer models as the need arises and resources become available. Appropriate experiments have been proposed to fill the research needs to develop a realistic model.

The initial generic model development exercise will allow the identification of issues such as mechanisms that operate in the general population versus sub-populations (e.g., susceptible populations) with varying degrees of arsenic methylation. Such issues could be the subject of workshops to explore the extent of polymorphism in human populations.

In the short-term (1-2 years), a coordinated program of laboratory research will generate essential data needed to develop a BBDR model that will increase confidence in the predictions. Model development will be initiated with available data. Work proposed includes multi-stage clonal growth modeling and target tissue dosimetry and methylated metabolites of arsenic.

In the long-term (3-5 years), the goal of developing a robust version of the model may be too optimistic. Five to 10 years may be a better timeframe. As the project gets underway, new questions and issues might be identified that will require additional laboratory research and continued resources. The project has a good future as it can be easily adapted to the National Academy of Sciences' (NAS) vision for toxicity testing in the 21st century that recommends systems biology and computational tool integration.

The coordination between model development and associated data collection is sufficient to avoid problems with models being either over- or under-determined. It is desirable to see what health effects are caused at lower doses and avoid potential compromise in setting the arsenic standard based on the cost-benefit analysis. Cost-benefit alone should not dictate what is done to protect public health.

Dr. Daston stated that he interpreted the third question concerning the sufficiency of coordination between model development and associated data collection differently. He thought it referred to how well coordinated the program is relative to the larger effort that was mentioned during the review. Dr. Mumtaz said he could revise his draft response to add that. He mentioned that last week, Dr. Jerry Blancato attended a colloquium at ATSDR. Dr. Blancato discussed the coordination of EPA's program with those of other agencies working in this area. It is clear that NCCT is working on coordinating with and informing others of the Center's work.

Dr. Daston though Dr. Mumtaz had done a good job in addressing Question #4a, but a response to the broader Question #4 was needed. This question was: Does the work offer to significantly improve environmental health impacts and is the path toward regulatory acceptance and utilization apparent? The response to this question needs to go beyond the Arsenic BBDR project to encompass the entire program. Dr. Mumtaz agreed to draft a response to Question #4.

Public Comment

At 10:45 a.m., Dr. Daston asked if there was anyone on the call who wanted to make a comment. No comments were offered so the discussion of the report resumed.

Subcommittee Draft Letter Report (Continued)
Dr. George Daston, Chair, Computational Toxicology Subcommittee

Charge Question 6: How would you assess the outreach to other groups in executing the project?

Dr. Daston stated that NCCT has done an admirable job reaching out to other groups, both inside and outside the Agency. NCCT has been successful at developing partnerships at several levels. Within ORD, the Center has developed partnerships with other ORD laboratories, which can conduct experiments and supply data for analysis and modeling by NCCT scientists. NCCT also has developed three Communities of Practice (CoPs) in chemi-informatics, biological modeling, and categorization and prioritization. NCCT has reached out to EPA program offices, especially OPP. This office is supplying data that are being used as part of the ToxCast project and OPP is likely to be an early adopter of the tools being developed by the Center. NCCT is doing a good job of joining forces with others outside the Agency, particularly with NIEHS. The National Toxicology Program (NTP) has a strong interest in high-throughput methods for predicting toxicity. NCCT and NIEHS have done a good job of information sharing and have developed a constructive working partnership in which data and analysis methods will be shared. NCCT also is establishing collaborations internationally, coordinated through the Organisation for Economic Co-Operation and Development (OECD). In summary, NCCT is doing an excellent job at outreach, which is enhancing its ability to fulfill its mission.

Dr. Daston said he would add a sentence that encourages continued outreach to the program offices to ensure that the tools developed by NCCT are useful for those conducting risk assessments. Dr. Mumtaz suggested adding a sentence about encouraging program office attendance at the next Subcommittee review. Dr. Daston asked Dr. Clark to add Dr. Mumtaz's sentence to the response to Question #1.

Charge Question 5: Have appropriate data management and analysis tools been incorporated into the project?

Dr. Quackenbush stated that this response mirrors what Dr. Stokes wrote in the response to Question #3. With regard to ToxCast, NCCT has made great progress in the past 18 months in hiring bioinformatics and computational biology scientists and staff to establish the infrastructure necessary to begin meeting the needs of the program. The Center is in the process of capturing a lot of data and bringing it into a central repository. The construction of the warehouse remains an open question. Ultimately, a database is a model of the interactions that exist in the underlying data and the relationships relevant to the analysis that will be performed. The diversity of the data, representing a wide range of *in vivo* and *in vitro* assays coming from multiple species, makes building such a model a significant challenge. The project seems to lack a set of analytical objectives necessary for building the relevant use cases that will inform the process of database construction and ultimately determine its utility. ToxCast needs to begin to define analytical outcomes in order to set goals and milestones with regard to developing and validating analytical protocols. This will help anchor future development and make it relevant as well as help define the requirements of the interfaces that are built to access the data.

The ToxCast group should be encouraged to release the data and databases at the earliest possible time and consider a Critical Assessment of Microarray Data Analysis (CAMDA)-like workshop in which the research community is offered access to the data with the challenge of using them to effectively predict endpoints. Dr. Quackenbush noted three advantages of releasing the data and databases at the earliest point: (1) it will help to drive creation of relevant use cases that will further database development; (2) it will assist in evaluating data access protocols and tools to assure the greatest utility to the research and regulatory community; and (3) it will accelerate the development of predictive algorithms to combine the data to make predictions about relevant phenotypic outcomes.

The Virtual Liver project is a very ambitious project. Dr. Quackenbush applauded NCCT for its decision to limit the scope of the project initially by focusing on nuclear receptor-mediated non-genotoxic liver cancer. This will focus the project sufficiently to ensure that it can make progress. The starting point and first challenge will be the construction of a liver knowledge base (KB). This is a non-trivial problem and ultimately will require linking information in the literature and a host of public data resources. The use of publicly available resources and tools and the commitment to making the KB available is commendable not only because it will be widely useful to the broader community, but also because it will accelerate the development and curation of the information with the KB.

The use of natural language processing probably is not the best solution for populating the KB. It does not work well with the scientific literature and its application in this domain remains an area of active research. Other methods, including expert or community curation, should be explored.

The greatest potential problem will be linking each of the domain-specific models to build a predictive system. This remains an area of active research and one that may present significant barriers to developing verifiable solutions. The greatest challenges will be to validate any

models that emerge from the analysis. NCCT needs to develop standards for interactivity and try to interface with developing standards within the community.

The Virtual Embryo project is in its early stages so it still is not well integrated with the overall NCCT program, and in particular ToxCast. Integration with other projects as well as internal and external initiatives needs to be resolved. It appears that this project could provide an opportunity to explore the results emerging from ToxCast and may help direct selection of the next generation of compounds for analysis in ToxCast.

Dr. Daston asked if there were any comments on the response to Question #5. Dr. Stokes noted that there is overlap between this response and the one she prepared for Question #3. Dr. Daston replied that he did not mind redundancy as long as the two responses are consistent. Both Drs. Stokes and Quackenbush agreed that the two responses are in agreement.

Final Draft Letter Report—Next Steps
Dr. George Daston, Chair, Computational Toxicology Subcommittee

Dr. Daston said he will prepare an opening section and a summary concluding section for the letter report and he asked the members to revise their assigned sections as discussed during this call.

Ms. Kowalski indicated that Dr. Robert Kavlock, Director of NCCT, had a few comments to make. Dr. Kavlock asked that the Subcommittee articulate more clearly what is meant by moving toward risk assessment in the response to Question #1. The suggestion is not clear and he would like to understand it better so the Center can respond. The second item focused on the comments regarding better defining out-year goals and milestones for the Virtual Liver and Virtual Embryo projects. He explained that the Center deliberately focuses on the next 1-3 years because it is very difficult to identify milestones beyond that timeframe. Dr. Kavlock's third comment was that the Center sponsored a peer consultation on the Arsenic BBDR project a few weeks ago. The comments received from that consultation will be incorporated into that project.

Dr. Daston asked Dr. Clark to be more explicit regarding the suggestion that risk assessment be the organizing theme for the Center. Dr. Clark agreed to clarify this suggestion in the response to Question #1.

Dr. Kavlock stated that the Center plans to hold a meeting with the program offices in March 2008. This meeting will focus on ToxCast and its use by the program offices. Dr. Daston thought this upcoming meeting should be mentioned in the report.

With regard to Dr. Kavlock's comment regarding the difficulty in identifying out-year milestones, Dr. Daston thought the report should acknowledge this difficulty and state that the Center should specify the project's long-term vision and goals so that it is clear where the project is heading and that it is making progress; it should be stated, however, that goals and milestones may be modified in the later years as the project progresses. It should also state that the Subcommittee recognizes the need for flexibility. Dr. Di Giulio thought the additional of that statement in the response to Question #2 was reasonable.

Dr. Daston summarized the changes to be made to each response. For Question #1, Dr. Clark will elaborate on the suggestion that the Center use risk assessment as its organizing theme. He will cite the February press release and recent *Science* article, and weave in the two paragraphs from the response to Question #3. He also will insert a sentence about the program office participating in the BOSC reviews of NCCT. Dr. Di Giulio will modify the response to Question #2 to include the acknowledgement that defining out-year milestones is difficult and the Subcommittee understands the need for flexibility. Dr. Stokes will specify that OPP is using ToxRefDB and remove two paragraphs. Dr. Mumtaz will elaborate more on the response to Question #4a and draft a response to the broader Question #4 about environmental impacts of the program. Dr. Daston will add a sentence to the response to Question #6 concerning the risk assessment theme. The response to Question #5 is fine.

Dr. Daston asked the members to revise their sections as soon as possible and send them to Ms. Kowalski. After confirming that there were no additional comments, he adjourned the meeting at 11:07 a.m.

Action Items

- ✍ Dr. Daston agreed to send the February 14, 2008 press release on the agreement between EPA and NIH to Ms. Kowalski for distribution to the Subcommittee members.

- ✍ Dr. Clark will cite the February press release and the recent paper published in *Science* in the response to Question #1.

- ✍ Dr. Clark will revise the response to Question #1 so that it is more explicit regarding the suggestion that risk assessment be the organizing theme for the Center.

- ✍ Dr. Clark will weave the second paragraph under ToxCast and the third paragraph under Virtual Liver to be moved from the response to Question #3 into the response to Question #1.

- ✍ Dr. Clark will insert a sentence in the response to Question #1 encouraging program office participation in the BOSC reviews of NCCT.

- ✍ Dr. Di Giulio will modify the response to Question #2 to include the acknowledgement that defining out-year milestones is difficult and the Subcommittee understands the need for flexibility.

- ✍ Dr. Stokes will remove the paragraphs mentioned above to be moved to the response to Question #1 from the response to Question #3. She also will specify that OPP is using ToxRefDB and move a couple of paragraphs.

- ✍ Dr. Mumtaz will elaborate more on the response to Question #4a and draft a response to the broader Question #4 about environmental impacts of the program.

- ✍ Dr. Daston will add a sentence to the response to Question #6 encouraging continued outreach to the program offices to ensure that the tools developed by NCCT are useful for those conducting risk assessments.

- ✍ Dr. Daston will prepare the opening and concluding sections of the letter report.

- ✍ Dr. Daston will ensure that the March 2008 meeting between NCCT and the program offices to discuss the uses of ToxCast is mentioned in the report.

- ✍ Subcommittee members will send their revised sections to the Ms. Kowalski who will distribute them to the Subcommittee.

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BOARD OF SCIENTIFIC COUNSELORS

COMPUTATIONAL TOXICOLOGY SUBCOMMITTEE
AGENDA
Wednesday, February 20, 2008
10:00 a.m. – 12:00 noon Eastern

CONFERENCE CALL
Participation by Teleconference Only

10:00-10:05 a.m.	Welcome and Overview - Purpose of Teleconference Call	Dr. George Daston, Chair Computational Toxicology Subcommittee
10:05–10:10 a.m.	DFO Remarks	Lori Kowalski, Office of Research and Development
10:10–10:45 a.m.	Subcommittee Draft Letter Report - Overview - Draft responses to charge questions - Discussion	Dr. George Daston, Chair, Computational Toxicology Computational Toxicology Subcommittee
10:45–11:00 a.m.	Public Comment	
11:00–11:45 a.m.	Subcommittee Draft Letter Report (Cont.) - Discussion	Dr. George Daston, Chair, Computational Toxicology Subcommittee
11:45-12:00 noon	Final Draft Letter Report - Next steps	Dr. George Daston, Chair, Computational Toxicology Subcommittee
12:00 noon	Adjourn	