FDA National Center for Toxicological Research

Science Advisory Board Meeting Summary

August 18-19, 2020

These summary minutes for the August 18-19, 2020 meeting of the National Center for Toxicological Research (NCTR) Science Advisory Board were approved on August 19, 2020. I certify that I attended the August 18-19, 2020 meeting of the NCTR Science Advisory Board and that these minutes accurately reflect what transpired.

____/s/_____ ____/s/_____

Donna L. Mendrick, Ph.D. Michael Aschner, Ph.D.

Designated Federal Official, NCTR Chair, NCTR Science Advisory Board

August 18-19, 2020

A verbatim transcript will be available and posted at https://www.fda.gov/advisory-committees/toxicological-research-science-advisory-board-national-center-toxicological-research/2020-meeting-materials-science-advisory-board-national-center-toxicological-research.

August 18, 2020. Meeting started at 9:00 am (Eastern)

The meeting was called to order by Chair of the Science Advisory Board (SAB), **Michael Aschner, Ph.D**., Professor of Molecular Pharmacology, Neuroscience and Pediatrics, Albert Einstein College of Medicine.

He welcomed the following **Science Advisory Board** (SAB) members:

1. **Michael Aschner, Ph.D**., Professor of Molecular Pharmacology, Neuroscience and Pediatrics, Department of Molecular Pharmacology, Albert Einstein College of Medicine, who joined us on December 4, 2019
2. **Mary Ellen Cosenza, Ph.D., DABT,** President, MEC Regulatory & Toxicology Consulting, LLC
3. **Patricia E. Ganey, Ph.D.,** Professor, Department of Pharmacology and Toxicology Michigan State University
4. **Charles Kaspar, Ph.D.,** Professor & Chair, Department of Bacteriology, University of Wisconsin
5. **Gregory M. Lanza, M.D., Ph.D.,** Professor of Medicine, Cardiovascular Division, Washington University School of Medicine
6. **Kenneth S. Ramos, M.D., Ph.D.,** Executive Director Texas A&M Institute of Biosciences and Technology, Texas A&M University
7. **John-Michael Sauer, Ph.D.**, Program Officer, Biomarker Programs and Executive Director, PSTC, Critical Path Institute
8. **Steven L. Stice, Ph.D.,** Professor, Georgia Research Alliance Eminent Scholar, Director of the Regenerative Bioscience Center, University of Georgia
9. **Alexander Tropsha, Ph.D.,** Professor, Associate Dean for Data and Data Science, UNC Eshelman School of Pharmacy, UNC-Chapel Hill

FDA Speakers Representing the Office of the Commissioner and other FDA Centers:

1. **RADM Denise Hinton,** Chief Scientist, Office of the Commissioner (OC)
2. **Emily Braunstein, Ph.D.,** Scientific Program Manager, Center for Biologics Evaluation and Research (CBER)
3. **Sruthi King, Ph.D.,** Supervisory Pharmacologist**,** Office of Generic Drugs and **Bernard Marasa, Ph.D.,** Review Microbiologist, Office of Pharmaceutical Quality, Center for Drug Evaluation and Research (CDER)
4. **Ed Margerrison, Ph.D.,** Director, Office of Science and Engineering Laboratories, Center for Devices and Radiological Health (CDRH)
5. **Suzanne C. Fitzpatrick, Ph.D., DABT, ET.,** Senior Advisory for Toxicology, Center for Food Safety and Applied Nutrition (CFSAN)
6. **Dana van Bemmel, Ph.D., MPH,** Chief, Research and Knowledge Management Branch, Office of Science, Center for Tobacco Products (CTP)
7. **Regina L. Tan, DVM, MS,** Director, Office of Research, Center for Veterinary Medicine (CVM)
8. **Judy McMeekin**, **Pharm.D,** Associate Commissioner, Office of Regulatory Affairs (ORA)

National Center for Toxicological Research (NCTR) Scientific Leaders and Speakers:

William Slikker, Jr., Ph.D., Director
Donna Mendrick, Ph.D., Designated Federal Official and Associate Director of Regulatory Activities
Tucker Patterson, Ph.D., Associate Director for Science & Policy
Frederick Beland, Ph.D., Director, Division of Biochemical Toxicology
Carl E. Cerniglia, Ph.D., Director, Division of Microbiology
Sherry Ferguson, Ph.D., Director, Division of Neurotoxicology
Steven L. Foley, Ph.D., Deputy Director of the Division of Microbiology
Robert Heflich, Ph.D., Director, Division of Genetic and Molecular Toxicology
William Mattes, Ph.D., DABT, Director, Division of Systems Biology
Anil Patri, Ph.D., Director of the Nanotechnology Core Facility
Bradley Schnackenberg, Ph.D., Associate Director, Office of Scientific Coordination
Weida Tong, Ph.D., Director, Division of Bioinformatics and Biostatistics

<u>Dr. Aschner (Chair)</u>

- Dr. Aschner opened the meeting by introducing the SAB members and providing an overview of the meeting.

<u>Dr. Mendrick (Designated Federal Official)</u>

- Dr. Mendrick read a statement that assured the attendees that all appropriate ethics regulations were satisfied.

<u>Dr. Slikker (Director of NCTR)</u>

- Dr. Slikker provided an overview of NCTR with a summary of NCTR staff and research goals. NCTR's main goal is to advance scientific knowledge and tools to support the FDA mission. He briefly discussed the work NCTR is doing with non-animal models. He introduced some of the work being done to address the COVID-19 pandemic and the use of Artificial Intelligence

approaches to address the needs of the regulatory centers. He provided a progress update on the new Perinatal Health Center of Excellence (PHCE) and an update on the meetings of the Global Coalition for Regulatory Science Research (GCRSR).

Discussion Highlights

- Dr. Aschner asked how the COVID-19 pandemic has affected the work being done at NCTR. Dr. Slikker spoke about the challenge of working in the time of this pandemic and noted that many manuscripts have been written. Some projects were continued during this time, particularly those that are long term studies. Dr. Slikker noted that as NCTR looks at the ability to have more investigators on campus, he hopes to start and complete new studies in the near future.

Subcommittee Review of the Division of Neurotoxicology (DNT)

- Dr. Aschner discussed the Subcommittee review of the Division of Neurotoxicology. Overall, they were very impressed with the leadership of this division by Dr. Sherry Ferguson. Some of the major comments included the following. The work is well aligned with the FDA mission and they were impressed with the many collaborations with our FDA centers. The division is working on both alternative and animal models; some of their work on the blood-brain barrier is unique and important to examine drugs. One area of improvement is the need to make sure the Subcommittee or SAB review protocols in the future. This will help strengthen NCTR research in general. Overall the research fits FDA needs, and the quality of the work is very impressive. The bioimaging area, particularly that run by Dr. Liachenko, is very impactful. They have made significant accomplishments in a short period of time and relevant to the Division's mission. They recommended more use of the imaging suite although acknowledged limited staff. This division has made great strides in risks of exposure to children to ketamine and other drugs. The division's work has great translational aspects.
  There was unanimous approval of the report.

Response to Subcommittee Review

- Dr. Ferguson spoke to the report and thanked the subcommittee for their favorable review. Due to the restricted time and other considerations of the review, not all their work could be discussed; for example, the work they are doing on developmental neurotoxicology of CBD. She responded to comments made in the report. Dr. Ferguson also described some new research being done and actions to hire additional personnel as suggested.

Discussion Highlights

- Dr. Aschner found this to be a thorough response but warned Dr. Ferguson not to stretch the division too thin. Dr. Stice agreed. He complemented the work and the update on all they are doing. He suggested they assist other centers by providing their expertise on protocols and execution of studies.

Statement from the Chief Scientist

RADM Denise Hinton, Chief Scientist, complemented the work being done at NCTR and its leadership. She thanked all lab workers at NCTR and across the agency. She noted that NCTR was one of the first entities in FDA to initiate research into COVID-19 back in March while continuing to do its part with

several ongoing projects related to opioid addiction and toxicity potential. She thanked NCTR for leadership within FDA and abroad

FDA Center Perspectives

Dr. Emily Braunstein provided an overview of the products regulated by CBER, their research goals and scientific expertise. She discussed some of the CBER-NCTR collaborations, described the need for the research, why CBER is working with NCTR and the potential impact of the work. The three areas of collaboration focus on metabolic and lipidomic analyses, evaluation of alternative in vitro assays and genomic evaluations. Examples included research related on fecal transplants, a possible in vitro assay for studying vaccine efficacy, and use of 3D tissue chips to study reproductive toxicology. She noted that some projects slowed down due to the pandemic.

Discussion Highlights

- Dr. Aschner asked if most of the projects started in one center or another vs. a joint collaboration from the beginning. Dr. Braunstein noted that Drs. Wilson and Mendrick meet monthly and discuss research. Dr. Tropsha asked if their tissue models could be used to study vaccines. Dr. Wilson from CBER noted that they are pursuing all conceivable opportunities for possible insights into COVID-19 and how best to evaluate vaccines. However, there is a need for tissue models to have a full immune complement. Dr. Cosenza asked how one can further educate groups at both centers with cutting edge science. Dr. Braunstein noted that they share NCTR capabilities within CBER.

Drs. Sruthi King and Bernard Marasa presented from CDER. They discussed CDER's research goals, work being done to support the pharmacology and toxicology area of CDER and of the research being done in drug contamination with bacteria. Dr. King discussed joint research endeavors in areas such as FDALabel, improving review tools, facilitating the risk assessments and improving recommendations to industry. Dr. Marasa described collaborative work being done to develop methods to detect and characterize microbial contaminants in FDA-regulated products.

Discussion Highlights

- No questions from SAB members

Dr. Ed Margerrison, CDRH, presented the regulatory mandate of his center noting they are responsible for 190,000 types of products including medical devices, in vitro diagnostics and radiation emitting products. Their regulatory mandate excludes those that exert their effect by chemical actions in the body. Their research interests include far-ranging areas such as artificial intelligence and photoacoustics. They have aligned themselves in ~20 programs with the largest being artificial intelligence and machine learning. He listed potential areas of collaboration with NCTR including identifying at risk populations for rare adverse events.

Discussion Highlights

- Dr. Aschner asks about interactions between CDRH and FDA. Dr. Margerrison mentioned there are many areas but one particular close collaboration is the nanocore. Dr. Sauer asked about the form of external collaborations; i.e., will they be PPP or BAA? Dr. Margerrison noted that NSF and NIH overlap with their FDA needs and he could see a partnership with NIH that could

stimulate new medical imaging phantoms. Dr. Ganey asked about mask innovation for children. Is it provided so that moms can make better masks for their children or just for commercial entities? Dr. Margerrison said they want to be able to help both.

Broke for lunch at 1:04 pm eastern

Started again at 2:00 pm eastern time

No comments for the public session so continued with the meeting

Dr. Suzanne Fitzpatrick, CFSAN, discussed the Center's activities, partnership, research within CFSAN and with NCTR. This included the FDA's Alternative Methods Working Group and their current focus on microphysiological systems, the food-chemical toxicology public private partnership, CFSAN's use of in silico modeling and the organ chip program. Examples of collaborative research with NCTR include the study of CBD and tattoo inks.

Discussion Highlights

- Dr. Aschner asked for more details on collaborative work being done with NCTR. Dr. Ferguson noted that all cosmetics work is being done at NCTR. One example are tattoo inks as mentioned. They also want to look at zebrafish and arsenic to see differences between C elegans (work done within CFDAN), zebrafish and rodents. She noted that NCTR does excellent work

Dr. Dana van Bemmel, CTP, provided an overview of their public health goals which include reducing the number of people who start to use tobacco products, encouraging individuals to stop and reducing the adverse health impact for those who do use. She noted that science is central to their regulatory activities. Their interests align with NCTR in the areas of toxicity (e.g., identification of biomarkers of exposure and toxicological impact of flavors). Active collaborations include the development of a multi-pathway physiologically based pharmacokinetic model for nicotine in humans, aerosol exposure to both rodents and an in vitro model using the human air-liquid interface.

Discussion Highlights

- Dr. Lanza noted that COVID 19 impacts the convalescence cardiac and pulmonary disease. Is CTP looking at the potential for nicotine and tobacco products to potential such injury? Dr. van Bemmel said there are some in the research areas studying this, but she was not sure if CTP itself was investigating this.

Break from 2:52 to 3:00 pm eastern

Dr. Regina Tan, CVM, introduced us to their regulatory mandate and collaborations with NCTR in areas as broad as nanotoxicology, use of 3D tissue culture model systems to evaluate the virulence of bacterial pathogens and antimicrobial resistance. She also provided the impact of these collaborations.

Discussion Highlights

- No questions

Dr. Judy McMeekin, ORA discussed this Office and its relevance to FDA's mission in inspection, regulatory actions, recalls, response to complaints, etc. ORA protects public health by minimizing risk of all FDA products. She spoke to the challenges posed by the pandemic. ORA will continue to rely on collaborations with trusted partners such as NCTR.

Discussion Highlights

Dr. Lanza asks how much of the NCTR research initiatives driven by regulatory centers vs. areas of NCTR expertise such as the nanocenter. Dr. Slikker said that we get requests from regulatory centers, SAB and other areas. These ideas go through multiple levels of review both within NCTR and appropriate regulatory centers. Dr. Lanza mentioned that presentations have discussed AI in different ways, some are very basic. Could the Centers send funds to NCTR to develop their expertise more and enable them to serve all of FDA vs. repeating within all Centers. This was done with the nanocenter. Dr. Slikker said the FDA is a large and multipurpose type of agency working under different regulatory mandates. There is opportunity to build alliances and collaborations such as the AI Working Group that cross all of FDA. Thus, there are opportunities for collaborations yet some of the expertise needs to remain within the centers. Dr. McMeekin said that meetings such as this SAB meeting are important to learn where the expertise lies and use this information to create research teams.

Presentations from NCTR Research Divisions

Dr. Frederick Beland, Division of Biochemical Toxicology, described their staff, outreach and mission. Their focus is on cancer causing agents; they perform animal studies and mechanistic studies to identify if what is seen in animals is pertinent to humans. They also do a lot of modeling. The top three accomplishments during 2019 included the BPA bioassay, arsenic pharmacokinetics in rodents, and the use cytochrome P-450 stably transcribed overexpressing HepG2 cells. Some current and future projects include 1) tattoo pigments, 2) CBD and 3) COVID-19. He would welcome advice on these projects.

Discussion Highlights

- Dr. Aschner asked about the sewage screening project. The French were doing this months ago. Are there similar programs in US? Dr. Beland said that it would be good to find sewage samples pre pandemic but he cannot find any in US. The study they are doing has blood samples that pre date COVID. Dr. Aschner asks if they will be able to maintain the workforce or will need to shrink because of funding challenges. They have been able to recruit some postdocs this year. Dr. Cosenza asked if they have done PK, etc. work on CBD. Dr. Beland said they have not but will consider it. Dr. Stice asked about tattoo inks and the use of multiple species. What results would trigger studies in higher species? Dr. Beland explained that they are working with cosmetics experts in CFSAN and will first start with a mouse model and then could consider moving to minipigs.

Dr. Weida Tong, Division of Bioinformatics and Biostatistics, presented the leadership and outreach activities, cross-center collaborations and research accomplishments. They continued to work on toxicity, toxicogenomics, precision medicine, etc. Primary focus areas are bioinformatics and biostatistics and thus they need AI. They apply AI to drug and food safety, genomic biomarkers, and FDA regulatory documents. Applications include its use for FDA documents. 2020 projects highlighted include AI for COVID-19, AI for toxicogenomics and AI interpretability. Future projects include further work on TG-GATEs database with toxicogenomic data from rodents and primary hepatocytes from humans and rodents. They also will have AI read tissue images and will generate miRNA data.

Discussion Highlights

- Dr. Tropsha noted that AI methods don't provide value over simpler methods in all areas. Dr. Tong noted they conduct systematic analysis and do not look just at one method. The simpler methods can be more easily explained. If data are very diverse (e.g., multiple types of omics data), it is difficult to use simple methods. There was a question from Dr. Ramos on use of cancer cell lines to predict liver toxicity. Cancer cell lines lose metabolic capability and he wondered if that affected predictivity. Dr. Tong noted that they will not capture all biological aspects yet sometimes need to capture only some of the biology for good predictions.

Dr. Robert Heflich, Director, Division of Genetic and Molecular Toxicology, provided an overview of their staff, outreach, mission and vision. Their recent top accomplishments were 1) using error-corrected next generation sequencing for mutation assessment for both *in vivo* and *in vitro* assays and 2) regulatory acceptance of the *in vivo* erythrocyte *Pig-a* assay. This division is working with alternative models such as the human airway interface model. They are using this model to study toxicity of tobacco smoke, etc. They have been working to get the *Pig-a* assay accepted for regulatory use for multiple years. In April 2020 OECD accepted the large amount of data for validation and asked them to develop a test guideline. Future emphasis will be placed on FDA needs for genetic toxicology expertise and data, develop relevant in vitro test systems and development of advanced methods for genetic analysis relevant for human disease.

Discussion Highlights

- Dr. Aschner asked where he sees the division going. Dr Heflich thinks the most exciting science is happening now. Dr. Ramos noted the utility of the mutational based targeted assay for broad screening for chemicals is compromised in that you are neglecting a sea of other genomics changes. Dr. Heflich agreed and said they are looking at low hanging fruit.

The public meeting was adjourned at 6:01 pm eastern time

August 19, 2020. Meeting started at 9:03 am

Dr. Aschner welcomed everyone.

Dr. Carl Cerniglia, Director, Division of Microbiology, described the division staff, outreach, mission, vision and strategies to meet this mission. The focus areas of accomplishment include: 1) the evaluation of the impact of antimicrobial agents, food contaminates, etc. on the microbiome, 2) developing methods to detect and characterize microbial contaminants and 3) determining antimicrobial resistance and virulent mechanisms. Details of all three accomplishments were provided. Future research strategies were discussed. Among the top accomplishments of the year were multiple pathogen detections in support of CFSAN, CDER, CBER and CTP. Ongoing and future projects include work on COVID-19.

Discussion Highlights

- Dr. Kaspar asked which area he thinks is important yet are not investigating in the next 1-5 years? Dr. Cerniglia said it is difficult as there are many avenues of research. They are looking more about how AI can be applied, etc. Dr. Cosenza complimented the presentation and noted they were prepared for COVID pandemic as you have a division member with expertise on such viruses. How can you prepare for future pandemics that are not related to COVID? Dr. Cerniglia noted that they hope to expand their team and work closely with experts in other Centers. Dr. Aschner asked if there was a directive from the top on work specific divisions should be done. Dr. Cerniglia noted that the work has been initiated internally and interactions with other Centers.

Dr. John Talpos, Division of Neurotoxicology, described the division staff, outreach, mission and vision. A major accomplishment in 2020 was the completion of a decade long study of the use of methylphenidate in the non-human primate. They will continue to expand the in vitro work such as the development of a blood-brain barrier and Alzheimer's disease brain on a chip. He also discussed ongoing work on CBD and future studies on biomarkers, etc.

Discussion Highlights

- Dr. Aschner is impressed with the breadth of research. Dr. Stice likes microphysiological systems but noted they do not possess all cell types. Drs. Stice and Ramos mentioned that there are many commercial and academic sources of models and questioned why the Division is building their own. Dr. Talpos responded that they are testing platform to learn about their limitations and will use them as warranted to answer questions. Dr. Mendrick reminded the group that Dr. Fitzpatrick spoke yesterday about FDA's Alternative Methods Working Group. This group brings in external speakers on various platforms and has a research group discussing new approaches. Dr. Stice asked what they do next with the methylphenidate study closed. Dr. Talpos noted they are looking at exposure of anesthetics in NHP and focusing on imaging work. Dr. Aschner asked about the process to alert regulatory centers when they see something. Dr. Talpos said they regularly interact with the Centers of which they generally have collaborators and they publish their data.

Dr. William Mattes, Division of Systems Biology, spoke about the division staff, outreach, mission and vision. He listed collaborations of note both with FDA Centers and the USDA. He provided details on the goals, strategies, and themes of this division. The latter are response to COVID-19, biomarker discovery, technology development, assay development and precision health. Molecular modeling of opioids was an example of past accomplishments. Current projects were highlighted such as mass spec fingerprinting of viruses and the use of patient-specific iPSC-derived cardiomyocytes for precision medicine.

Discussion Highlights

- Dr. Sauer asked about their biomarker's strategy. What is your strategy to identify individual susceptibility? Will you be doing animal studies, clinical studies, etc.? Dr. Mattes pointed to the doxorubicin study where you do discovery followed by a targeted approach. You then can do a full clinical investigation if warranted. Dr. Tropsha is interested in biomarker discovery and asked about issues related to cohort size. Dr. Mattes said it is small as it clearly was an initial discovery study. This was a collaboration with UAMS, and these are the patients they had. One could confirm the biomarkers in the same samples with another technology and then move to a

larger trial. Dr. Ganey noted you are looking at genetic differences and asked if he is accounting for environmental effects as well. Dr. Mattes believes genetics plays a role but not the only role in individual variability. He likes metabolomics studies as they can capture both. She now does only in vitro and wonders if there is a process to test relevance of in vitro or in silico findings in animals and/or humans. Dr. Mattes said that such translational work is exactly what he would like to do in all experiments, particularly those done in microphysiological platforms. Dr. Lanza suggested they start using bioimaging as that will replicate what is being done clinically. He suggested he contact Dr. Fred Epstein is at the University of Virginia and would be a good collaborator. Imaging is becoming integrated as a therapeutic guide. Dr. Sauer asked if NCTR is doing any work looking at gene and cell therapies. Dr. Mattes noted that there is a new division member who has a background in oligonucleotide therapies and there are protocols in development.

A discussion of NCTR research was held by the SAB Members

Dr. Aschner said there have been great presentations over the last 1.5 days. The breadth of research is impressive but suggests NCTR might focus a little more as one cannot do everything. NCTR should look outside for new methods instead of trying to build everything themselves. He is impressed with the increase in collaborative work over the years between NCTR and the other FDA Centers. He also would like clarification on how a signal seen at NCTR gets the attention of the regulatory centers. Dr. Sauer agreed these were great presentations and the Center presentations showing collaborations with NCTR. The interconnections within NCTR are difficult to identify and the Division Directors may need to change the slide format. Several programs are very proactive in that they are learning what the next steps should be. However, the majority of activities are reactive. There needs to be a better balance. Dr. Sauer would love NCTR to lead in the realm of toxicology including creating the tools. Overall, he thought it was a great SAB meeting. Dr. Ganey agreed that the presentations were good and applauded NCTR's move into COVID research. The scientific question should drive the science, not the technology. She is trying to understand next steps. They have heard about AI, etc. When you get results there, how do you know if they are relevant in whole organisms? NCTR is doing great, timely work. Dr. Cosenza thought it was a great review. We have learned a lot about collaborative work, what has NCTR learned about how to work and strengthen collaborations during the pandemic? Dr. Tropsha learned a lot as this is his first SAB meeting. Scientific rigor and breadth of ppt were top notch. Level of science is very high. He spoke about three areas. 1). A lot of research is interdisciplinary, and he would like to learn more about the connectivity within NCTR and the agency. 2). He thought there would be a larger portfolio with academics would be larger. Is this strategic? 3). A lot of interesting projects and it is important that NCTR is seen as leading in toxicology. Dr. Kaspar agreed with the positive comments and wanted to commend the division directors and the center to center communications among groups. He asked how one decides between PI driven vs center-driven work. Would be valuable to understand the 1 or 2 highest priority areas within division and how these are decided. An example was retaining a virologist which helps them lead in COVID research. Dr. Stice responded to questions on recruiting. At his university they have a large NSF research program for undergrads. This year they could not bring anyone to the campus so worked with them remotely. Gave them data to analyze, etc. This helps recruit scientists. Dr. Lanza agreed with previous comments. He noted that the COVID epidemic showed needs at FDA and thought an FDA modernization act could bring money into FDA that would enable the use of AI. This could lead to moving drugs faster to market but then better post market surveillance. NCTR could use AI, for example, to harness to improve post market surveillance and determine what adverse effects are being detected. Then NCTR could study if this is real. Maybe there is a larger strategic plan here. Dr. Ramos echo many of the comments so will focus on a few points. NCTR

is functioning at high level based on qualify of work. However, some synergies still not being realized within NCTR and thought they should focus on a strategic vision for the enterprise as a whole. It is not clear how priorities are identified now.

Dr. Slikker was asked to respond. He thanked all for their insightful comments. He only had 10 minutes to respond so grouped the questions in three areas.

1). One area of work is emerging technology where we compare the results with existing approaches such as whole animal exposures. Our point is to be able to actually run those new technologies in our lab and then to compare them to our in vivo results that have been completed, are being done concurrently, or will be done in the future. I had hoped some of the examples I presented in my Center overview would explain this.

2). Questions were asked regarding the focus of our research. We focus on current and future FDA needs. An example is bioimaging where one can perform longitudinal studies. Imaging biomarkers can be identified and used in whole animal imaging and the clinic.

3). We do training. For 25+ years we have had a summer undergraduate training program which is a 10 week intensive course. We bring in 25-30 undergraduates from within the US. I appreciate Steve's comments about using online training as this summer we canceled this program for the year. Our postdoctoral training program is alive and well with 60-70 postdocs at any one time. Recruitment is an issue, but we have been able to hire 16 individuals over the last 6-9 months. We would like to learn more about how to improve our recruitment.

The public portion of the meeting concluded at 12:40 pm eastern time