

**COMMENTS ON
DOCKET No. 2007-0489
FDA REPORT ON SCIENCE AND TECHNOLOGY**

We want to thank the authors of this historical undertaking and we want to acknowledge the powerful impact their work will have in strengthening the FDA and its mission to protect the health and wellbeing of Americans. It is a superb collection of work and represents a positive example of collaborative due diligence on behalf of concerned leaders and scientific advisors.

The following comments embody a collective viewpoint from various stakeholders in Arkansas, home to the National Center for Toxicological Research. From our perspective, more emphasis should be placed on how the capabilities at NCTR could, and should be utilized to strengthen the very weaknesses so accurately reported by the Science Advisory Board. We are pleased that there will be a more detailed review of the NCTR and hope this response will assist the Advisory Board members in reviewing the NCTR in terms of utility, purpose, and possibility.

The Report is accurate in the sense that distance and location of NCTR from other FDA operations has historically been a problem. We believe that NCTR's engagement through energetic and involved management, integrated communications technology, and an FDA-wide commitment to eliminating geographic barriers and bias would awaken the scientific and human potential of NCTR towards becoming an integral and vital component of FDA improvement, revitalization, and sustainability.

We also believe that the organizational culture and the scientific approach adopted by the NCTR should be examined for its excellence and utilized elsewhere as appropriate. The Report identifies weaknesses in peer review, in scientist retention, in morale, and in publication productivity. We do not believe NCTR suffers from these weaknesses in the same manner described in the Report. Peer review is both internal and external, covering protocol development, final report writing, publications, division programs, Center programs, and determining whether individual scientists may be promoted. Scientific turnover at NCTR is minimal, and although morale is impacted by a lack of adequate equipment, supplies, and travel budgets, the scientists and staff at NCTR enjoy their work and continue to strive for scientific excellence with the resources that are available to them.

The Report recommends that the NCTR Science Board become more proactive when learning about other FDA Center needs. We see this adjustment as relatively straightforward and readily accomplished. More structure is needed across the FDA in this regard, but sufficient infrastructure seems to be in place at NCTR to facilitate such an outcome.

There are a number of areas, both scientific and organizational, in which NCTR has already demonstrated the kind of acumen and leadership called for in the Report. Appendix G acknowledges that NCTR has created "Centers of Excellence in Toxicoinformatics, Metabolomics, Proteomics, and Functional Genomics – all integrated to address critical path needs, that is, integrating new technologies into the review process and assisting with the promotion of personalized nutrition and medicine. NCTR expertise and leadership in this area has provided the infrastructure (ArrayTrack system) upon which the VXDS program (CDER, NCTR and other Centers collaboration) has been developed." This is one of many positive examples of NCTR's contribution to FDA. By forming intra-agency collaborations, conducting relevant and applicable research, and by overcoming the distance and resource barriers, NCTR was able to accomplish breakthrough discoveries and is currently leading the FDA in several emerging areas of science and technology. Because of NCTR's vision and scientific leadership,

the FDA is positioned to address these critical path initiatives with more direction, more knowledge, and with a fundamental regulatory purpose that reflects the overall mission of FDA, to protect the health and well being of consumers.

This type of vision-minded leadership from NCTR is also evident from the advancements in computational molecular modeling, an area whose importance is stressed by the Report. NCTR's computational work with structure-activity relationships for natural and synthetic estrogens has been both important and pioneering. Moreover, as the Report so accurately cites the low level of research activity in the area of cosmetics, NCTR leadership was able to obtain much greater capability for FDA through partnerships with NIEHS to construct a phototoxicity capability; scientific resources unique to the government. The NCTR work on microdots and other cosmetics issues in this facility represents yet another capability FDA would not have were it not for the pioneering spirit of the NCTR. The NCTR capabilities in microbiology, in antibiotic resistance, and intestinal metabolism all seem to be areas that the Report indicates are needed to enhance the mission and objectives of FDA.

Looking at the table in Appendix G that indexes the many FDA-regulated compounds NCTR has studied through its partnership with NIEHS, we wonder how that relationship has over extended the NCTR and distracted from NCTR priorities. These projects seem to represent knowledge otherwise unavailable to FDA. Moreover, the work has had an enormous impact for providing funding of capabilities NCTR now possesses that otherwise would not have existed. The NCTR boasts a collaborative mindset and scientific culture that engages the priorities of NIH, leverages the innovations of private industry, and integrates the discipline and diversity of academia, promoting cooperative research partnerships that create a valuable entity whose leadership in these emerging areas of science is well recognized by government, industry, and academia alike.

The NCTR culture extends beyond the scientists. Animal care technicians are professionals who keep their certifications updated through the American Association for Laboratory Animal Science. Most of these individuals have been at their jobs for decades and exhibit a sense of pride and purpose uncommon indeed. The commitment of the animal care technicians combined with the unique animal capabilities of NCTR adds enormously to its overall value to FDA.

The Report to FDA cites the 1971 Executive Order creating NCTR, designating the Center as a non-regulatory FDA entity. Earlier foundational scientific committee work recommended that NCTR become a common meeting ground on which government, industry, and academia would come together to solve broad but relevant toxicological problems. Given the increasing demand for high-quality animal facilities and toxicology resources, the recent advancements and applications of toxicoinformatic frameworks, and the public/private collaborations that are central to NCTR culture, we believe NCTR could yet fulfill and even expand this vision by sharing and leveraging resources that would generate contract research income, provide orphan drug development resources, produce innovations in nano-toxicology that would form the baseline for regulating the nanotech industry, and continue to embrace emerging trends in personalized medicine, genomics, proteomics, and metabolomics. These are just a few of our ideas and we in Arkansas would like to cooperate with FDA in making that vision happen while strongly supporting NCTR and the other FDA scientific activities.

The University of Arkansas for Medical Sciences (UAMS) has been partnering with NCTR since its creation. Some 35 of the NCTR staff hold adjunct professorships at UAMS, and UAMS toxicology students often conduct practical training exercises and thesis work on the NCTR campus. UAMS has a robust toxicology program as well as a strong overall interest in NCTR

and NCTR research. UAMS research programs often include interactions with NCTR staff. Similarly, the neurotoxicity of pediatric therapeutics has been studied together with Arkansas Children's Hospital creating regulatory guidelines and clinical practices that protect our children from harmful side effects. Nanotoxicology is currently the subject of meaningful and pertinent interactions between researchers at NCTR and the University of Arkansas at Little Rock (UALR) that will generate industry awareness for the possible health hazards with certain nanomaterials. The Donaghey College of Engineering and Information Technology at UALR is also a valued NCTR partner working together in areas of bioinformatics and supercomputing. We fervently hope that recommended centralizations of IT related activities recognize and support the kind of scientific computing developed at the NCTR. History has shown that some information technology centralization has hampered administrative activities at NCTR.

Private industry has also greatly benefited from CRADA research at NCTR. The most recent example is a collaborative project between a private company, the NCTR, the University of Arkansas for Medical Sciences, and Vanderbilt University showing how NCTR-generated technology has been adapted to create a novel approach to antipsychotic rational drug design using computational molecular modeling capabilities. As a result of these advancements in the field of computational modeling, industry, government, academia, and the American population as a whole could benefit from this cost-effective and rational approach to predictive toxicology. This NCTR innovation has shown to improve lead drug candidate selection, produces therapeutic candidates that are safer and more effective, and could help reduce the overall time and costs associated with discovering and developing new drug products. Safer and more effective treatments, translational software tools, and a scientific vision that promotes the advancement of pharmaceutical sciences as stewards and protectors of the health, safety, and wellbeing of Americans; the NCTR's impact and importance is undeniable.

Other industry representatives have communicated a desire to conduct more cooperative research with NCTR in combination with UAMS, UALR, and other academic institutions in Arkansas, particularly in developing orphan drug products and leveraging the animal capabilities of NCTR as a contract research resource. There is a productive collaboration with the University of Arkansas (Fayetteville) in understanding how to control microorganisms in poultry and in detecting antibiotic resistance and its sources. The University of Arkansas at Pine Bluff (UAPB), a land-grant institution, provides collaborative support in areas of aquaculture and agricultural sciences.

The point of these previous paragraphs is to show that with intelligent and creative planning, the collective support of public and private stakeholders, and an ongoing commitment to innovation and advancement of FDA priorities, the NCTR could not only serve as a core research capability for the FDA, but the NCTR could emerge as a leading national research center that leverages the innovations of private industry and the knowledge of academia to position the FDA as a proactive and visionary organization committed to the research, development, and regulation of emerging technologies in a global economy. It could become a vibrant campus directly engaged with the scientists at other FDA Centers. It could become a coordinated epicenter of innovation and scientific research within the FDA and linked to a defined set of goals and regulatory objectives. It could also help prevent duplicated efforts in various FDA laboratories. We urge the subcommittee to think beyond existing barriers to what the NCTR could become. What, with necessary "sunlight" provisions, along with industrial, academic, and government oversight participation, could the NCTR become for the FDA since it

does not have a direct regulatory role? Might it be so organized as to fulfill that original vision of a common meeting ground?

Finally, as Arkansans, we make another plea. We emphatically suggest that it is not the FDA's role or responsibility to make decisions based upon local economics. That stated, it would be just as wrong to make decisions based on a perception that *nothing good* (scientifically) *can come from Arkansas*. We in Arkansas are devoted to the advancement of science and technology and have recently contributed the leadership, policy support, and financial resources to help develop and manage new organizations and structures that support science and technology innovation through state government, private industry, and academic participation. This being said, **we need a strong NCTR and believe NCTR's participation is vital to the success of Arkansas' vision to expand and diversify our state economy**. We believe in an environment of transparency and communication **and if there were sufficient travel budgets**, participating FDA scientists could easily manage the geographic separation. Arkansas is currently 49th for receiving federal research funding, our *per capita* income is 76% of the national average, and we need to continue developing a research base around what NCTR provides. We are motivated to assure the success of partnering ventures.

With the pledged support of Arkansas stakeholders and in good conscience with strong resolve, we ask you to consider the NCTR's existing capabilities and objectively review NCTR's numerous contributions to the body of scientific literature and FDA priorities. More importantly, we ask that you embrace its potential with vision, responsiveness, and positive legislative action.

We appreciate this opportunity to respond and look forward to more positive interaction with the Subcommittee and with the FDA. Again...thank you!

- Jerry Adams-President, Accelerate Arkansas and Director, Arkansas Research Alliance
- John Ahlen, PhD-Director, Arkansas Science and Technology Authority
- William Carpenter-Founder and CEO, Consensus Biotechnology
- Michael Douglas, PhD-Director UAMS Bioventures
- Mary L. Good, PhD -Dean, College of Engineering and Information Technology, University of Arkansas at Little Rock
- Maria Haley-Executive Director, Arkansas Economic Development Commission
- James K. Hendron, PhD-Chairman, Arkansas Science Technical Engineering and Math Coalition
- Larry Milne, PhD-Vice Chancellor for Academic Affairs, University of Arkansas for Medical Sciences
- Lou Ann Nisbett, President and CEO, Economic Development Alliance of Jefferson County
- Art Norris-Retired NCTR Deputy Director
- I. Dodd Wilson, MD-Chancellor, University of Arkansas for Medical Sciences