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September 14, 2010

Dear SMRB Members,

Thank you for the opportunity to provide written comment on the detailed review provided by the SUAA Working Group. As the meeting date of the SMRB coincides with an important meeting of the international community on alcohol problems, ISBRA, many of the leaders in the field are at that meeting in Paris, either giving presentations or participating, and have only this venue to respond by written comment in the very small hours of the morning.

I agree that the SUAA Working Group should be congratulated on their diligent and hard work, and that their general conclusion that the status quo is not optimal is appropriate. The more fundamental question, however, is how to create optimal synergy between NIAAA and NIDA to provide the best science that can be applied to the prevention and treatment of all substance-use-related disorders.

My view is that a functional merger would achieve the goal of creating the optimal synergy in a focused manner that conserves resources, builds upon clear examples of success, and avoids the significant risks of a highly complicated, expensive, and untried attempt to do this through a structural process. From this vantage point, there are five important veins of consideration that need to be highlighted.

First, the promotion of the overarching view that all addictions simply fall within a known addiction circuitry of reward is rather overstated, and cannot be viewed as the “theory of everything” related to addiction. Notably, whilst this reward circuit appears to have support at the level of acquisition of addictions, once the disorder is established this is no longer necessarily the case. Indeed, advances in the neurosciences show clearly that circuits outside this traditional reward circuit become increasingly important with an established addiction, and that these vary for different drugs of abuse, including alcohol. Indeed, new knowledge on these neuromodulators of the addiction process shows that small molecules and neurohormonal circuits are particularly important, especially in the case of alcohol. Therefore, the addiction circuitry for alcohol has some overlap with that for other abused drugs but is far from being the same. Furthermore, despite several decades of this concept of a singular central addiction circuitry, there is no single

established medicine in humans that cuts across the treatment of all these disorders. Curiously, with regard to specific addictions, for example with opiates, we have not been able to develop any cogent non-opiate-related treatments based on this addiction reward theory. What appears to be emerging is that the neuropharmacological differences between alcohol and other drugs might actually hold the key as to the success of medications development for these different disorders. For example, with respect to alcohol, non-brain systems related to metabolism appear to play an important role in its intake. Hence, an identical neuroscientific approach to the treatment of alcohol dependence is unlikely to generalize well to that for drug dependence. Thus, a structural merger of institutes based upon a narrow focus on the addiction circuitry will not provide a comprehensive scientific understanding or treatment option for all addictions that we currently seek. Indeed, much more is likely to be gained by developing themes of collaborative research and a functional blueprint between the two organizations.

Second, the global perspective of the scientific and clinical communities points to a functional rather than a structural merger of the two institutes. Whilst it was emphasized that there are two separate scientific meetings, one for alcohol abuse and another for drug abuse in the U.S., this actually very much represents the global perspective. The global community recognizes the clear distinctions between these disorders and is organized as such. For instance, the end-organ focus of NIAAA that would have to be jettisoned to other NIH-related institutions is actually at the very core of the focus of the global scientific community for alcohol-related diseases. Indeed, these alcohol meetings around the world include as many liver experts, cancer specialists, and general physicians as those specifically related to the treatment of alcohol dependence. That important connection would be lost in a structural merger, thereby setting back important work and advances in liver disease, cancer prevention, and fetal alcohol syndrome (one of the most common acquired congenital disorders). With respect to training, whilst it is important to teach overlap, it would not be feasible for any trainee to become an expert across all these fields, interact with all the specialists, and attend all the important scientific meetings. Focused training in these individual specialties would best protect the respective fields of alcohol and drug addiction, with attention to the points of overlap.

Third, there are clear examples of functional mergers within the NIH that have worked well but barely any clear examples of a successful structural merger of this scope and size. In these pressing economic times, there needs to be clearer understanding of the costs associated with the proposal of a structural merger, and I do not think we can operate as if there is an endless supply of funding. Have there been a feasibility analysis and a cost estimate? Has there been an analysis, even at a cursory level, of whether the large sums of money, which could reach billions of dollars to structurally merge these two institutes with uncertain results, could be best used in a targeted approach toward creating important fusions in projects with clear scientific objectives and goals? Would it not be prudent fiscally to try first a functional merger along the sequence provided by the SUAA in its report that can be more easily managed, monitored, and shaped? Has there been any planning given to personnel wastage that might ensue, the cost of retraining,

the colossal administrative work in identifying new leadership and leadership structures, and the formidable task of how to manage infrastructure across different states? Also, has there been consideration of the fact that the price of failure for a large structural merger—which would conservatively take up to a decade to be actualized fully—would be unacceptably high, both in economic and in human terms? Clearly, defined functional goals and themes within two separate institutes that can be managed appropriately within a known framework would render the optimal and most feasible outcome. At the very least, it would lay the necessary foundation and guiding principles for the consideration of a possible structural merger in future years as the institutes become closer.

Fourth, the data provided within the SUAA report also can be interpreted differently. Indeed, the report highlights the closer interaction between drug abuse and mental disease, which would point to a merger between NIDA and NIMH. If so, why has this not been considered even from the point of a preliminary investigation to increase the balance of the present report?

Fifth, I was puzzled by the statement that industry was not interested in developing drugs to treat drug addiction as a potential reason in favor of a structural merger. This is not quite the case. Indeed, industry is involved with developing medications for the treatment of opiate addiction where there has been clear success in identifying efficacious treatments. The same observation is evident for treatments related to nicotine dependence. Hence, if NIDA were to be successful with finding an efficacious medicine to treat stimulant dependence, it is most likely that industry would be interested in exploring that potential. Clearly, there are important lessons that can be learned from cross-talk between the medications development programs of both institutes, but since even the clinical endpoints are not the same for medications development, the concept of “one size fits all” would not work well.

In sum, I thank you for the time to read this note, which would have been shorter given more time, and for your thoughtful consideration of this most important matter.

My best wishes for the meeting,

Bankole A. Johnson, D.Sc., M.D.
Professor of Medicine
Professor of Neuroscience
Professor of Psychiatry and Neurobehavioral Sciences
Chairman, Department of Psychiatry and Neurobehavioral Sciences
Distinguished Fellow, American Psychiatric Association

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Public Statement Regarding Organizational Change/Merging Institutes
NAEVR Executive Director James Jorkasky
Scientific Management Review Board Meeting
May 18, 2010

Good afternoon. I am James Jorkasky, Executive Director of the National Alliance for Eye and Vision Research, or NAEVR, which serves as the privately funded ""Friends of the National Eye Institute (NEI)." I am providing these brief public comments about the potential broader impact of merging Institutes/Centers (I/Cs) within the NIH, as the SMRB's actions regarding a merger of the Drug and Alcohol Institutes could have far-reaching implications.

For the past year, I have attended the SMRB meetings and have listened intently and respectfully to all of the points that have been made, both pro and con. I am truly humbled by the thoughtful comments already expressed today by the panelists.

As background, NAEVR has long opposed the concept of "clustering" I/C budgets:

- Going back to the 2001 timeframe, NAEVR opposed the proposal by former NIH Director Harold Varmus to cluster the budgets/programs of the 27 I/Cs into six units, including a "Brain Institute," which would have incorporated the NEI.

- From 2005-2006, NAEVR opposed the budget cluster proposal within draft NIH reform legislation. In my extensive Capitol Hill visits to oppose this provision in the draft bill, I was initially met with support for clusters, based on an assumption of greater efficiency and scientific interaction. But after I discussed potential implications for the actual research involved, most offices expressed reservations—or, as Chairman Augustine has said, "this is more complicated than we thought." The fact that the cluster proposal was stripped from the final version of the bill, and that the SMRB was charged to comprehensively study the far-reaching scientific implications of such organizational change, has spoken volumes.

Having established this background, I offer the following observations:

- At the SMRB's April 27-28, 2009, inaugural meeting, Dr. Varmus spoke and recognized within his comments that numerous steps had already been taken through the 2006 reauthorization and administratively within NIH to foster trans-Institute research, meeting many of the goals of his cluster proposal.

- At the same meeting, immediate-past NIH Director Dr. Elias Zerhouni spoke passionately about many aspects of the NIH that he would like to see changed. Merging or clustering I/Cs was not one of those priorities.

- In public comments at past SMRB meetings, including those immediately preceding me by Dr. Sanyal, researchers into liver function expressed concern that such research could "go away" or be minimized in a merged Institute. I would like to expand on this concern by providing a similar example from the vision space.

This past year, the National Eye Institute celebrated its 40th anniversary as a free-standing Institute. Prior to 1968, vision research was conducted in the then-National Institute of Neurological Diseases and Blindness (NINDB), accounting for less than 20 percent of the Institute's budget. In just the past couple of weeks, for example, NEI has released results from four major studies on visual impairment and eye disease, relating to both retinal, or "back of the eye" research, and corneal, or "front of the eye" research.

The concept of clustering I/Cs into a "Brain Institute," as Dr. Varmus proposed, may have initially sounded rational, based on the assumption that all neurological research is related. However, when we started to look at the potential implications for the actual research involved, we were alarmed. For example:

- Although 50 percent of NEI-funded research relates to the "front of the eye," it would only account for 7 percent of a total "Brain" cluster budget. Future funding for this research could be jeopardized, including that into corneal diseases, cataracts, and refractive errors that affect millions of Americans and cost tens of billions of dollars, with devastating consequences for public health, productivity, and quality of life.

- If "front of the eye" research were not adequately funded, the vision community could permanently lose key investigators. Eye researchers and clinicians are uniquely qualified to understand and treat eye disease, since neurologists do not necessarily have an understanding of corneal disease or cataract.

In closing, I know from this morning's discussion that the SMRB will carefully weigh what could be the consequences for a merged Drug and Alcohol Institute in terms of the actual research priorities that will be funded.

Thank you.

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Public Statement Regarding Clinical and Translational Research
Funded by the National Eye Institute (NEI)
NAEVR Executive Director James Jorkasky
Scientific Management Review Board (SMRB) Meeting
Translational Medicine and Therapeutics (TMAT) Working Group
September 14, 2010

Thank you, Chairman Augustine. I am James Jorkasky, Executive Director of the National Alliance for Eye and Vision Research, or NAEVR, which serves as the privately funded ""Friends of the National Eye Institute (NEI)." NAEVR is a research advocacy organization that does not speak for NEI, but about its accomplishments. I appreciate the opportunity to listen to these initial discussions about a comprehensive NIH plan for clinical and translational research.

Although the TMAT's discussions are in their infancy and will develop further during tomorrow's planned discussions, I did want to inform you about clinical and translational research initiatives in the vision space. I provide these comments for three reasons: none of the panelists scheduled to appear represent the vision space; although the NEI is a relatively small Institute, it has conducted numerous translational collaborations that have smartly and effectively expanded its research dollars; and NEI's translational research has resulted in drugs and devices─ and combinations thereof─as well as diagnostics and gene therapy approaches, reflecting what Dr. Varmus just stated about the promise of translational research to offer a "rich repertoire of patient solutions."

As the TMAT proceeds, I hope that it works with staff from all Institutes to become aware of the novel and effective translational collaborations. I wish to offer just a few examples of NEI collaborations within the NIH, across the Department of Health and Human Services (DHHS), with other government agencies, with private funding organizations, and internationally.

This past year the NEI celebrated its 40th anniversary. In June, it hosted a *Translational Research and Vision* Symposium on the NIH campus as the last of its educational celebratory events. At that meeting, Dr. Collins provided keynote remarks stating that, "The NEI has been central to advances in translational research. NEI's vision has allowed us to see farther and better and has enabled the NIH to attain its best vision. Most importantly, the best is yet to come." Within the meeting, several of NEI's collaborations were described, including:

Trans-NIH

- NEI's collaboration with the National Cancer Institute (NCI) and the National Heart, Lung and Blood Institute (NHLBI) into factors that inhibit new blood vessel growth has resulted in the first generation of Food and Drug Administration (FDA)-approved ophthalmic drugs to treat the "wet" form of Age-related Macular Degeneration (AMD).

- NEI has worked closely with the National Institute of Diabetes and Digestive and Kidney Disorders (NIDDK) through its Diabetic Retinopathy Clinical Research (DRCR) Network to study the best treatment practices for diabetic retinopathy.

- Both of these collaborations have resulted in ongoing Comparative Effectiveness Research (CER), which is an NIH priority. NEI is currently conducting the Comparison of AMD Treatment Trials study on AMD drug therapies, while the DRCR Network recently released results of a study which confirmed that laser treatments for diabetic macular edema, when combined with injections of the FDA-approved drug Lucentis, are more effective than laser treatment alone.

Across DHHS

- On September 24, the NEI and FDA will jointly host the fourth of a series of symposia to consider endpoints appropriate for use in clinical trials that support approvals for new ophthalmic drugs and devices. This meeting will be the second regarding clinical endpoints for Glaucoma, and previous meetings have addressed endpoints for AMD and Diabetic Retinopathy, as well as the use of Patient Reported Outcomes. This collaboration is very much in the spirit of the new NIH/FDA Joint Leadership Council to incorporate the latest science into the regulatory review process.

With Other Government Agencies

- NEI and the National Aeronautics and Space Administration (NASA) have collaborated on a diagnostic device for cataracts, which is the clouding of the natural lens. The compact fiber optic probe uses dynamic light scattering to measure the amount of the anti-cataract protein alpha-crystalline—the less light scattering from the protein, the more likely the individual is to develop cataracts.

- The Department of Energy, along with the National Science Foundation and the NEI, are supporting research into the development of an Artificial Retina—initial versions of which have enabled individuals completely blind to navigate their homes and community.

With Private Funding Organizations

- The collaboration between NEI and private funding organization Foundation Fighting Blindness (FFB) has resulted in successful gene therapy to treat the retinal degenerative disease Leber Congenital Amaurosis (LCA). In his April and May testimony before hearings of the House and Senate Labor, Health and Human Services, and Education (LHHS) Appropriations Subcommittees, respectively, Dr. Collins played a video entitled "Corey's Story," which featured a recipient of the gene therapy navigating a maze unsuccessfully prior to the procedure, then successfully after the procedure.

Internationally

- NEI recently established the International AMD Genetics Consortium to share information globally from Genome-Wide Association studies (GWAS) to determine the increased risk of developing AMD from gene variants. Once these pathways are understood, researchers can develop appropriate diagnostics and therapies. On September 23, my organization is sponsoring a Capitol Hill briefing acknowledging *International AMD Awareness Week* in which we will update Congressional staff on all of the basic, clinical, and translational research developments into AMD.

Thank you for this opportunity to comment so early in your discussions of this issue.

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Public Statement Regarding Organizational Change/Merging Institutes
NAEVR Executive Director James Jorkasky
Scientific Management Review Board (SMRB) Meeting
Substance, Use, Abuse, and Addiction (SUAA) Working Group
September 15, 2010

Thank you, Chairman Augustine.

I am James Jorkasky, Executive Director of the National Alliance for Eye and Vision Research, or NAEVR, which serves as the privately funded “”Friends of the National Eye Institute (NEI).” NAEVR is a research advocacy organization that does not speak for the NEI, but about its accomplishments.

Yesterday, in my public comments on translational research, I detailed NEI’s rich repertoire of patient solutions in clinical and translational research, including that in both the retinal (“back of the eye”) and corneal (“front of the eye”) research.

Why am I back up here commenting today on the potential merger of the Institutes on Drug and Alcohol Abuse?

NAEVR maintains that the breadth of NEI’s deliverables described yesterday could NOT have been accomplished had the NEI NOT been pulled out of the old National Institute for Neurological Disease and Blindness 40 years ago and made its own free-standing Institute. That especially relates to the “non brain” related research into front of the eye disease and vision impairment.

As you heard me testify at the May 18, 2010, SMRB meeting, NAEVR opposed the merger of the Drug and Alcohol Institutes and urged the SMRB to carefully consider the impact on the actual research being funded by those Institutes. Based on my attendance at all prior SMRB meetings and my review of the Substance Use, Abuse, and Addiction (SUAA) Working Group’s excellent written report, NAEVR urges the SMRB to recommend to Dr. Collins Option 2, which is the SUAA’s recommendation for a functional change to the operation of these two Institutes through the creation of a trans-Institute Addiction Blueprint.

Thank you for this opportunity to provide these public comments.

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March 26, 2010

William L. Roper, MD, MPH
Substance Use, Abuse, and Addiction Workgroup, Chairman
Scientific Management Review Board, OD, NIH
Building 1, Room 103
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Roper:

On behalf of the over 1,700 scientists, associates, and researchers represented by the Research Society on Alcoholism (RSA), we have frequently expressed our objections to a proposed merger between the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and National Institute on Drug Abuse (NIDA). RSA deeply appreciates the interest and attentiveness which you have paid to our concerns.

RSA has monitored SUAA's deliberations closely and it occurred to us that the views of the scientists and researchers who are "on the ground" conducting critical research may not have been fully aired.

To address this issue, RSA recently conducted a poll of its members over a two-day period in order to gauge the sentiment of its members about the potential merger. The survey asked whether the respondents agreed with or opposed the following resolution:

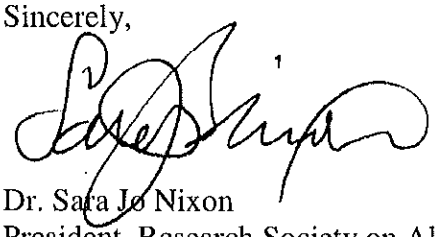
> "RSA strongly opposes any structural reorganization at NIH that results in the elimination of NIAAA as an independent Institute dedicated to all aspects of alcohol research. Moreover, RSA strongly supports the study of a functional reorganization of basic and clinical research across NIH Institutes to better address commonalities in alcoholism, substance abuse, obesity, gambling, and their co-morbid mental health disorders."

The results showed overwhelming opposition to the elimination of NIAAA as an independent Institute—597 respondents supported the proposition while only 18 opposed it, a 97 percent majority. This same majority, however, also endorsed a study of a functional reorganization of basic and clinical research across NIH Institutes.

We appreciate your diligent work to fully deliberate and review all aspects and potential outcomes of this important matter.

RSA stands ready to assist you and the SUAA Working Group as you work through the remainder of this process.

Sincerely,



Dr. Sara Jo Nixon
President, Research Society on Alcoholism

May 17, 2010

Dr. Francis Collins
Director
National Institutes of Health
Building 1
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Collins:

We the undersigned organizations – representatives of diverse patient communities and in many cases funders of medical research – share the common goal of translating the promising discoveries coming from basic science into new treatments and cures for the patients we serve. For that reason, the following 87 organizations support new approaches that maximize the resources of our nation's medical research enterprise and support collaboration among all the stakeholders involved. The National Institutes of Health (NIH) is, of course, at the center of that enterprise, and a key component of NIH's investment is the research effort on its own campus, the Intramural Research Program (IRP).

We have been pleased to see the NIH's Scientific Management Review Board (SMRB) take up the issue of the organization and management of the IRP, and specifically the fiscal sustainability and utilization of the Clinical Center. We are writing to offer our support for one of the actions we understand is under consideration by the Board and the NIH, and that is opening up the Clinical Center facilities for greater use by the external research community.

As you are well aware, the Clinical Center is the largest dedicated research hospital in the country, and its existence in the IRP represents one of NIH's most unique resources. It provides some of the nation's best imaging equipment, phenotyping expertise, and access to a wide range of clinical research specialists. As a world-class facility, it has the potential to excel in research efforts focused on rare and orphan diseases and on pre-clinical and methods research essential to building tools, platforms, and protocols for the entire clinical research enterprise.

Yet the Clinical Center is an underutilized facility, and its potential as a national resource for the public health is not being fully realized. We believe that allowing and promoting greater use of the facility by external researchers is an important way for the Clinical Center to not only increase its utilization but to achieve its vision to "lead the global effort in training today's investigators and discovering tomorrow's cures."

We would like to see the NIH:

- Create streamlined mechanisms by which external researchers can more fully use the Clinical Center for projects in collaboration with the IRP. This might include giving the Clinical Center and/or Institutes the flexibility and authority to negotiate broader collaborative agreements or public-private partnerships, taking into consideration ethics rules and intellectual property rights;

- Explore the possibility of the Clinical Center controlling a pool of funds to make use of the facility feasible for investigators who otherwise could not afford it, for example through a program similar to the existing Bench-to-Bedside Awards.

We thank you for the opportunity to provide this input, and we look forward to working with you to ensure that the Clinical Center's resources are being put to their highest and best use.

Sincerely,

Accelerate Brain Cancer Cure
Accelerated Cure Project for Multiple Sclerosis
Aeras Global TB Vaccine
Alliance for Aging Research
Alpha-1 Foundation
Alzheimer's Foundation of America
Alzheimer's Association
American Autoimmune Related Diseases Association
American Institute for Medical and Biological Engineering
ARPKD/CHF Alliance
Autism Society
Beyond Batten Disease Foundation
Bonnie J. Addario Lung Cancer Foundation
Breast Cancer Network of Strength
Californians4Cures
Cancer Research Institute
Celiac Disease Center at Columbia University
CHDI Foundation, Inc.
Children's Neurobiological Solutions
Children's Rare Disease Network
Children's Tumor Foundation
Chordoma Foundation
Coalition for Pulmonary Fibrosis
Coalition of Heritable Disorders of Connective Tissue
Colon Cancer Alliance
COPD Foundation
Cure Alzheimer's Fund
Curing Kids' Cancer
Cutaneous Lymphoma Foundation
Cystic Fibrosis Foundation
Damon Runyon Cancer Research Foundation
Detroit Medical Reserve Corps
Dr. Susan Love Research Foundation
Epilepsy Therapy Project
FasterCures/The Center for Accelerating Medical Solutions
FOD Family Support Group
Foundation for Prader-Willi Research
Foundation for Sarcoidosis Research
Genetic Alliance

International AIDS Vaccine Initiative
Jacob's Cure
Jeffrey Modell Foundation
Joubert Syndrome and Related Disorders Foundation
Kidney Cancer Association
Klinefelter Syndrome and Associates
Life Raft Group
LIVESTRONG
Lung Cancer Alliance
Lung Cancer Circle of Hope
Medicines for Malaria Venture
Melanoma Research Alliance
Mesothelioma Applied Research Foundation
MHE Research Foundation
Michael J. Fox Foundation for Parkinson's Research
Multiple Myeloma Research Foundation
National Eczema Association
National Foundation for Ectodermal Dysplasias
National Health Council
National Indian Health Board
New York Stem Cell Foundation
Pachyonychia Congenita Project
Parkinson's Action Network
Partnership for Compassionate Use Therapies
Prader-Willi Syndrome Association (USA)
Progeria Research Foundation
Prostate Cancer Foundation
Pulmonary Fibrosis Foundation
PXE International
Rare Disease Foundation
Reflex Sympathetic Dystrophy Syndrome Association
Rett Syndrome Research Trust
Royal National Institute for Deaf People
Sarcoma Foundation of America
Seattle Biomedical Research Institute
Society for Women's Health Research
Solving Kids' Cancer
The AIDS Institute
The Alzheimer's Drug Discovery Foundation
The Leukemia & Lymphoma Society
The Nicholas Conor Institute for Pediatric Cancer Research
The RARE Project
The Sturge-Weber Foundation
Translational Genomics Research Institute
Tuberous Sclerosis Alliance
Van Andel Research Institute
VascularCures - The Foundation for Accelerated Vascular Research
VHL Family Alliance