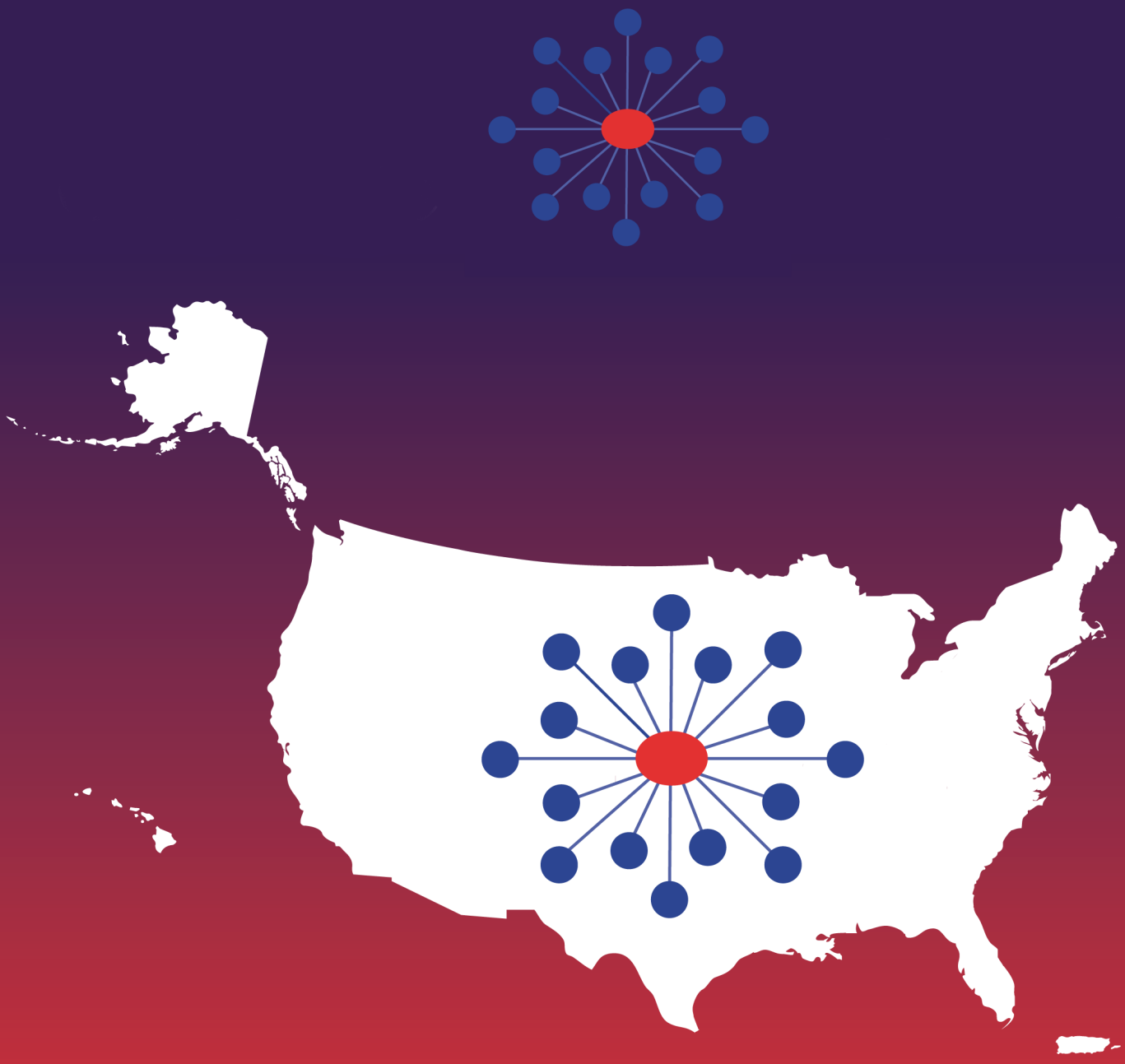
Report and Recommendations of the Clinical Trials Network Work Group



NIDA NATIONAL INSTITUTE ON DRUG ABUSE

National Institutes of Health
U.S. Department of Health and Human Services

JOIN TOGETHER
A National Resource for Communities Taking Action Against Substance Abuse and Gun Violence

David L. Rosenbloom
Director

Janice Ford Griffin
Deputy Director

December 5, 2003

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse
6001 Executive Boulevard
Bethesda, MD 20892

Dear Dr. Volkow:

I am pleased to transmit the draft report and recommendations of the Clinical Trials Network (CTN) Work Group that was created at your request by the National Advisory Council on Drug Abuse at its meeting on May 21, 2003. The report and recommendations reflect the unanimous view of the Work Group members. We take full responsibility for the contents. We remain available to meet with you and/or members of your staff to discuss our conclusions and recommendations, though we hope the report makes our views and thinking clear on its own.

The Work Group is enormously impressed with the hard work and solid achievements of the NIDA CTN staff and the hundreds of professionals involved throughout the Network. We think you and everyone at NIDA should be proud of the CTN and hopeful about the enormous potential it holds to improve drug treatment.

To be sure, we heard about the growing pains of the CTN, but remembered that no one learns to walk without falling. We were impressed that the CTN operating structures have taken time and energy to learn from their early experiences and have made adjustments as they move the CTN forward. The Work Group has also focused on the future, as well as the opportunities that exist to strengthen and expand the foundation that has been built. We have also placed emphasis on improving the levels of collaboration throughout NIDA, other Institutes, and the CTN.

The members of the Work Group and I would like to thank Denise Pintello, Ph.D., M.S.W., and Sarah Michaud for their support throughout the process. They helped mightily by monitoring the Work Group's progress and played major roles in editing the draft report. Thank you for this opportunity to support NIDA's mission.

Sincerely,

David L. Rosenbloom, Ph.D.
Chairman
Clinical Trials Network Work Group

Major funding is provided by a grant from the Robert Wood Johnson Foundation to the Boston University School of Public Health.

National Institute on Drug Abuse
National Institutes of Health

REPORT AND RECOMMENDATIONS OF THE CLINICAL TRIALS NETWORK WORK GROUP

TABLE OF CONTENTS

Clinical Trials Network Work Group
Draft Report and Recommendations

I. PREFACE

The members of the Clinical Trials Network (CTN) Work Group would like to acknowledge the admirable work of the National Institute on Drug Abuse and CTN staff as well as the CTN Node participants for their creativity and diligence in fulfilling the goals of the Network since its inception nearly 5 years ago. Since 1999, the CTN has gone through a steep learning curve, inventing new procedures, often through long and complex committee work. The CTN Work Group hopes that its efforts in compiling the following recommendations and the continuing growth of the CTN will lead to an even more productive Network in which the talents of the academic and community partners are focused on improving treatment and prevention of substance use disorders in their communities without undue administrative burden.

II. EXECUTIVE SUMMARY

The National Institute on Drug Abuse (NIDA), an Institute within the National Institutes of Health (NIH), provides national and international leadership for research on drug abuse and addiction. Over the past three decades, findings from NIDA's research efforts have produced advances in understanding drug abuse and addiction, which has led to the development of new treatment and prevention approaches. Despite the development of science-based advances, only some of the research findings were reaching patients in the community-based settings where most drug abuse treatment is provided.

In 1998, the Institute of Medicine (IOM)/National Academy of Sciences published a report titled *Bridging the Gap Between Practice and Research: Forging Partnerships With Community-Based Drug and Alcohol Treatment* (Lamb et al., 1998). The IOM report recommended the creation of a research infrastructure to test the effectiveness and usefulness of new and improved treatments in real-life settings with diverse populations. NIDA established the Clinical Trials Network (CTN) in 1999 to enhance the delivery of scientifically based treatments to drug-abusing patients in community-based settings. The CTN now has 17 Nodes (research centers) and 116 participating Community Treatment Programs (CTPs). (See map in Appendix A.)

The CTN Work Group, created by the NIDA Director, Nora D. Volkow, M.D., in 2003, comprised members from the National Advisory Council on Drug Abuse and distinguished leaders from the drug abuse and addiction field. The purpose of the CTN Work Group was to review the CTN program and advise NIDA on its future development. The NIDA Director charged the CTN Work Group to address the mission, scope and vision, achievement of goals, and operational efficiency of the CTN. The Work Group was asked to assess the role of the CTN in prevention, treatment, training, HIV/hepatitis C research, involvement with the medical community, and collaboration with other Institutes.

This final report from the Work Group includes a background review of the CTN portfolio since its inception, recommendations to fortify the current CTN research mission, examination of the organization and management of CTN and its interactions with other NIDA Divisions and Centers, and the potential of the CTN as a platform for other research and training efforts. The Work Group makes one core recommendation as well as recommendations in six areas of concern.

CORE RECOMMENDATION

The CTN Work Group recommends that the Network be continued and that it become a central strategic element in the future plans of NIDA, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute of Mental Health (NIMH) to diffuse research to improve the quality of treatment for substance use disorders in communities throughout the country.

OUR UNDERSTANDING OF THE MISSION OF THE CTN IN THE FUTURE

The Work Group believes that the unique mission of the CTN differentiates the Network from other NIDA and NIH clinical research efforts. The primary mission is:

- To study the impact of evidence-based practices when they are broadly disseminated in diverse settings and populations; and
- To study the impact of evidence-based practices modified to be more readily adoptable.

The secondary mission of the CTN is:

- To serve as a platform for a broad variety of basic and applied research—both inside NIDA and perhaps outside the Institute—that is not yet ready for dissemination;
- To provide state-of-the-art examples of drug abuse treatment and prevention;
- To expose researchers, practitioners, and agencies to the benefits of mutual collaboration;
- To help inform NIDA about practical issues in need of research;
- To study how to disseminate evidence-based practices successfully; and
- To support the dissemination of scientific results to the practice community.

RECOMMENDATIONS RELATING TO THE PLACEMENT OF THE CTN WITHIN NIDA AND INTEGRATION WITH OTHER NIDA STRUCTURES, AND ITS RELATIONSHIP TO NIAAA AND NIMH

- The CTN should remain housed in NIDA's Office of the Director for the foreseeable future, with a senior officer, perhaps the Deputy Director, designated with clear final decisionmaking authority. To facilitate collaboration throughout NIDA, a coordinating structure should be created under the designated official to include the Center for Clinical Trials Network (CCTN) Director, NIDA Division Directors, and other senior officers whose work can impact or be impacted by the CTN.
- The Director of NIDA should create a formal mechanism for input and collaboration on CTN policy and operations from NIAAA and NIMH, with a goal of developing joint research and training projects using the diverse populations in the CTN.

RECOMMENDATIONS RELATING TO THE APPROPRIATE SIZE OF THE CTN

- As the re-funding cycle is addressed, the size of the CTN should be rationalized to ensure adequate access to the broad spectrum of Americans with substance use disorders in all regions of the country.
- There should be sufficient Nodes to plan a growing portfolio of research, training, and dissemination projects. At least some funding should be flexible enough to enable a Node to sponsor innovative work in collaboration with its CTPs that may lead to larger practical clinical trials.
- NIDA should announce a single competition covering the first two rounds of initial funding (11 Nodes). The announcement should clearly state the criteria for selection.

RECOMMENDATIONS RELATING TO AREAS OF APPROPRIATE RESEARCH FOR THE CTN AND STANDARDS FOR CONDUCTING RESEARCH WITHIN THE CTN

- The CTN should deliver its primary mission through practical clinical trials (PCTs) of interventions that have been shown to be effective through prior empirical research.
- Efficacy research that examines the impact of existing interventions that are modified so as to make them simpler, more clinically friendly, more cost-effective, or otherwise more useful in diverse practical settings may also be conducted in the CTN at appropriate scale.

- Research on how to disseminate empirically supported research at the appropriate scale and in support of the PCTs being investigated should be performed in the CTN as a means of supporting its primary mission.

- The Work Group believes that a wide variety of research is needed to examine how to disseminate empirically supported treatments successfully in diverse practical settings. Studies of this kind may involve the evaluation of innovative methods—such as new methods of training practitioners in empirically supported interventions and new means of modifying organizations to make them more receptive to adoption of empirically supported methods—that have relatively limited empirical support. However, because the level of analysis of such research is inherently larger (e.g., involving larger numbers of clinicians or agencies) and because methods of this kind are necessarily involved in mounting the more primary research purposes of the CTN, such studies logically belong within the funding and evaluation streams of the CTN.

- CTN trials can and should provide new information about the possible differential impact of interventions on various population groups by taking care to design these questions into the studies and recruiting participation from the heterogeneous populations within the entire range of participating CTPs.

- CTN dissemination-oriented research should include cost-benefit or cost-effectiveness analyses to assist treatment programs and funders in making decisions about implementing interventions.

- The Work Group recognizes that these kinds of analyses often raise complex measurement issues, especially in assigning costs to activities within existing entities and providing fully quantified measures of benefit. Nevertheless, the question of how much it will cost to implement a new treatment protocol and whether the result will be better than the benefits the program now gets is at the heart of many barriers to widespread dissemination of new approaches.

- Over time, the special characteristics of the CTN should enable it to emerge as an active participant in a wide variety of substance use disorder research. For example, the CTN has access to a huge and heterogeneous pool of genetic material—including families—that could speed collection and analysis of genetic markers. CTPs in the Network may be in a better position than traditional NIDA researchers to maintain long-term contact with patients and families for followup and longitudinal studies.

- The CTN can now be used as a vehicle for Phase III trials of drugs that will be submitted to the Food and Drug Administration (FDA) for NIDA approval. Phase III medication studies could be carried out in collaboration with other NIDA Divisions to provide them with access to the diverse populations served in the CTN. Data quality and monitoring standards for CTN protocols should be appropriate to the risks actually involved.

- The good clinical practice (GCP) model for randomized clinical trials being submitted to the FDA is not the only optimal model for selection for all protocols.

RECOMMENDATIONS RELATING TO CTN OPERATIONS AND BUDGETS

- To fulfill its mission, the CTN, over time, should become open to receiving and reviewing proposals to use the Network as a platform for research emanating from outside the CTN. In many cases, funding for such proposals will also come from outside the CTN; but in other areas that closely align with the primary mission of the CTN, consideration should be given to funding them from the CTN budget.

- The process for developing, reviewing, approving, and funding research protocols should be further simplified and made more transparent. The need for an external Protocol Review Board and an external Data Safety Monitoring Board (DSMB) should be carefully reexamined in light of

the CTN's actual experience. If NIDA determines that such external review will remain necessary, it should be integrated early in the process (as apparently happens in the U.S. Department of Veterans Affairs system), and actions should be transparent to the CTN to avoid wasted effort.

- Budgets should be developed and attached to protocols early in the review process and should cover the expected cost for the life of the protocol as long as progress is being made on the research plan. Currently, protocols are being approved for multiyear periods, but funded on a year-to-year basis. An appropriate accountability and monitoring system should be established to force corrective action or cancellation if progress on a particular protocol or in a particular study site is not being made.

- A single or limited number of Coordinating Centers should be established to manage all stages of protocol training, implementation, and data monitoring. An independent Coordinating Center should be selected through a competitive bidding process in close coordination with the CTN Steering Committee, and it should endorse the plans under the terms and conditions of the cooperative agreement.

RECOMMENDATIONS RELATING TO DISSEMINATION AND DIFFUSION OF CTN MATERIALS, RESULTS, TRAINING MODULES, AND OTHER WAYS TO IMPROVE THE QUALITY OF TREATMENT AND PREVENTION

- To fulfill the CTN's mission, planning and resources for dissemination should be included in all protocol development and review, not left as a matter to be addressed after the fact. Principal Investigators and their CTP colleagues should identify and address likely barriers to widespread adoption during the planning phase of a study, and they should test approaches to overcoming such barriers in the practical clinical trials supported in the CTN. NIDA should consider providing additional resources within its own operations and the CTN to promote broader dissemination of evidence-based treatments.

- NIDA and other Institutes should consider new research initiatives that address barriers to dissemination of effective treatment interventions.

- The CTN should work closely with NIDA and other agencies working on dissemination, especially the Addiction Technology Transfer Centers (ATTCs) network, operated by the Substance Abuse and Mental Health Services Administration (SAMHSA).

- NIDA and the CTN should establish a continuing collaboration with directors of State treatment and prevention agencies, perhaps through the auspices of the National Association of State Alcohol and Drug Abuse Directors (NASADAD), to foster dialogue about the CTN and NIDA research agenda and to enhance the probability of broad dissemination of effective treatment regimens.

III. THE NIDA CLINICAL TRIALS NETWORK

INTRODUCTION

The National Institute on Drug Abuse (NIDA), an Institute within the National Institutes of Health (NIH), provides national and international leadership for research on drug abuse and addiction. NIDA supports a comprehensive research portfolio that focuses on the biological, social, behavioral, and neuroscientific basis of drug abuse as well as its causes, prevention, and treatment. Over the past three decades, findings from NIDA's research efforts have produced dramatic advances in understanding drug abuse and addiction and have led to the development of new treatments and therapies to help individuals with drug abuse and addiction. Despite the development of these science-based advances, only some of the advances were reaching patients in the community-based settings where most drug abuse treatment is provided.

In 1998, the Institute of Medicine (IOM) and the National Academy of Sciences published a report titled *Bridging the Gap Between Practice and Research: Forging Partnerships with Community-Based Drug and Alcohol Treatment* (Lamb et al., 1998). The IOM report recommended the creation of an entity to facilitate two needs: (1) the creation of a research infrastructure to test the effectiveness and usefulness of new and improved treatments in real-life settings with diverse populations; and (2) the creation of a mechanism for the systematic study of processes and factors involved in the incorporation of new and improved interventions into community-based drug treatment.

Based on the IOM report, NIDA established the Clinical Trials Network (CTN) in 1999 to enhance the delivery of scientifically based treatments to drug-abusing patients in community-based settings. NIDA developed a pilot program based on the National Cancer Institute (NCI) model within NIH. The initial focus of the CTN was on integrating medication and behavioral therapies and translating these efforts to community treatment programs.

The CTN structure called for academic centers, or "Nodes," to link up with Community Treatment Programs (CTPs) to undertake research protocols. The CTN was established within the framework of a cooperative agreement, allowing NIDA to maintain a key role in the Network's management and administration, including the process by which protocols are implemented. The CTN currently comprises 17 research Nodes across the country with 116 CTPs across 27 states. Appendix A contains a map of CTN Nodes, and Appendix B provides definitions of CTN organizational structures.

Since its inception, the CTN has reviewed and approved 26 protocols in three rounds of funding. The CTN released its first Request For Applications (RFA) on January 11, 1999, which resulted in the funding of seven protocols. Research began with the first protocol in January 2001. The Network released its second RFA on December 20, 1999, and accepted five protocols. The intention of the second RFA was to develop a geographically diverse and encompassing Network. The third RFA, released on November 20, 2001, resulted in nine new protocols for the CTN. The intention of the third wave was to expand the geographic distribution of CTN research, to encompass more subpopulations of racial/ethnic minority groups, and to broaden the range of treatment providers who work under varying systems of reimbursement and organization of care.

Topics covered in the first three rounds of CTN-funded protocols include AIDS/HIV, family therapy and treatment, motivational incentives, medication, motivational enhancement and interviewing, services and nontreatment, and 12-step programs. Twenty-one protocols are currently in various stages of implementation. Appendix C provides additional information on CTN protocols, including topic, Node, and lead investigator.

CTN grantees participate in the cooperative agreement between NIDA and the CTN to conduct and participate in coordinated multisite clinical trials of behavioral, pharmacological, and combined behavioral/pharmacological therapies for drug abuse and addiction, and to conduct research on practices (e.g., studies of factors that affect successful adoption of new treatments). The research is conducted in community-based treatment settings in collaboration with other awardees and with NIDA. Each awardee functions as a CTN research Node.

More than 3,500 patients are participating in these studies. Although it is too early to know if these protocols will lead to wide adoption of practices and technologies, several of the premises have been proven: CTPs are interested in participating in rigorous scientific research and are capable of implementing rigorous trials. Appendix D presents CTN budget expenditures for fiscal years 1999 through 2003.

The CTN currently uses the good clinical practice (GCP) model for data integrity for pharmacotherapy and various behavioral therapy studies—even when the goal does not involve conducting a pivotal study for FDA submission of a New Drug Application (NDA). Because the treatment community, not the FDA, is the audience and participants of the vast majority of CTN studies, it is logical that NIDA might not need to behave as if it were a pharmaceutical company going to the FDA for approval. The CTN has employed contractors to enforce the GCP model, which has been costly. To the Work Group's knowledge, no outside agency, regulatory body, or review group is imposing these costly standards on NIDA or the CTN.

The current Center for Clinical Trials Network (CCTN) is led by its Director, Betty Tai, Ph.D., who reports directly to NIDA's Office of the Director. She is supported by approximately 10 staff members and 8 full-time contractors. Dr. Tai has proposed a new structure for the CTN, which has been informally implemented. The new structure has four branches: program development, program operations, statistical services and informatics, and program dissemination.

THE CTN WORK GROUP

The CTN Work Group, created by the NIDA Director, Nora D. Volkow, M.D., comprises NIDA Advisory Council members and leaders from the drug abuse field. Appendix E presents the list of CTN Work Group members. The purpose of the CTN Work Group is to evaluate the CTN program and advise NIDA on strategies to maximize the transfer of research into practice, culminating in a final written report that includes a background review of the CTN portfolio since its inception, recommendations to fortify the current CTN research mission, examination of the organization and management of the CTN and its interactions with other NIDA Divisions and Centers, and the potential of the CTN as a platform for other research and training efforts.

Over the past 4 months, the CTN Work Group has held two meetings at which representatives from NIDA, the National Cancer Institute (NCI), the NIDA CCTN, and other CTN participants have delivered presentations and conducted discussions with the Work Group in open and in executive sessions (see Appendix F and Appendix G for the meeting agendas). The Work Group reviewed these discussions and documents and produced several drafts of the written report. The report was finalized through e-mail communication and conference calls. All recommendations in the final report reflect the consensus of the Work Group unless specifically noted otherwise.

CHARGE FROM THE DIRECTOR OF NIDA TO THE CTN WORK GROUP

The NIDA Director asked the CTN Work Group to specifically address the following ten questions:

1. What has been the mission of the CTN?

2. Is the mission adequate in specificity, scope, and vision?

3. How well has the CTN achieved its goals?

4. How efficiently has the CTN operated?

5. Where should the CTN be in 5 years?

6. Can the CTN play a role in prevention as well as treatment?

7. What is the role of the CTN in HIV/hepatitis C research?

8. What is the role of the CTN in training?

9. What is the role of the CTN in involving the medical community?

10. What is the role of the CTN in collaboration with other Institutes?

IV. FINDINGS IN RESPONSE TO THE CHARGE FROM THE DIRECTOR OF NIDA

The CTN Work Group's general conclusions are organized as responses to the Director's questions. These conclusions led to the detailed recommendations presented in the later sections.

1. What has been the mission of the CTN?

- The original mission was unidirectional, from NIDA to the communities. There was hope that research would provide a steady flow of new medications that could be tested in diverse community settings. However, the community treatment programs (CTPs) recruited to the CTN quickly expected that the flow of information and decisionmaking should be bidirectional.

- The mission statement of the CTN had two components: "(a) to conduct multisite clinical trials to determine the effectiveness of drug abuse treatment interventions in diverse community-based treatment settings and diverse patient populations, and (b) to transfer research results to treatment programs, clinicians, and their patients to improve the quality of drug abuse treatment throughout the Nation."

- The CTN was established and expanded rapidly with broad statements of research goals and areas, but few details. The Principal Investigators, Node directors, and a small number of NIDA CTN staff had to develop all the operating and rule-setting systems quickly to give life to the mission, too often in isolation from other NIDA Divisions. The Work Group was impressed with the results achieved.

2. Is the mission adequate in specificity, scope, and vision?

- The bidirectional communication and genuine partnership with CTPs evolved quickly and gave strength to the CTN with a broader mission. The establishment of a partnership between researchers and practitioners is essential to providing new treatments to address the critical needs and to provide suitable treatments for communities served by CTPs.

- CTN members invested an enormous amount of energy in developing and redeveloping processes to get the Network up and running. As stated, the current mission is too narrow methodologically and too broad conceptually to incorporate all of the CTN's goals and expectations. The mission provided no necessary link to previous research, nor did it differentiate aspects of the CTN mission that warrant multisite trials from those that do not. The mission provided little effective

guidance to the CTN and little reason for other NIDA Divisions to feel connected to the effort. The roadmap developed by the CTN was a step forward, but the Work Group felt that it would be helpful to make recommendations about questions asked by the NIDA Director if the group first spent time trying to state more explicitly the core mission of the CTN.

- The Work Group has listed specific recommendations in this report that will help refine the scope and vision of the CTN to go forward to achieve its original mission.

3. How well has the CTN achieved its goals?

- Although it is too early to know if CTN protocols will be disseminated widely, one of the key early questions about the CTN has been answered. It is clearly possible to engage CTPs in real research and to conduct rigorous trials in community treatment settings.

- It is clearly possible to establish strong working relationships with multilateral learning among the CTN, academic research sites, and community programs in the drug abuse area.

- Researchers report they are learning important lessons that improve the quality of their work.

- CTPs report that their staff members who are participating in particular protocols are being trained and learning new skills, which would not have been possible if the Network had not given CTPs a voice in developing new research to improve care.

- There is little evidence so far of dissemination beyond the actual participants. As the first CTN research protocol results have not yet been published, it is still too early in the process to evaluate dissemination efforts accurately.

- Although initial steps have been taken to initiate the plan for dissemination and training, it is now time to devote more resources to carry out these plans. The Work Group takes note of the work of the Dissemination Committees, especially in compiling a bibliography of past dissemination research. Specific recommendations concerning dissemination and training are made in Section V.

4. How efficiently has the CTN operated?

- Participants have experienced a steep learning curve, especially through three rounds of expansion in 4 years. The startup of the CTN was not necessarily conducted in the most efficient way possible. Lessons have been learned in the past 4 years, and the CTN has developed and implemented much more efficient review and planning processes.

- It is quite possible that the wheel has been reinvented several times within the CTN because of inadequate collaboration within NIDA. However, the Work Group feels the focus of the CTN should not be on this, but on the future instead.

- One result of the speed and complexity of the startup has been heavy reliance on outside contractors. The Work Group concluded that reliance on contractors should be carefully reviewed and audited to draw lessons for the future. The Work Group believes that if its recommendations are adopted, there will be less need for contractors in the future. In any event, the Work Group believes that all contracts should be competitively bid with clear deliverables and accountability to ensure that investigators and the CTN protocol development process retain substantive control.

- The CTN evaluation process needs to include adequate assessments of cost, time, and personnel to allow estimation of the cost of development and implementation as well as the probable community effectiveness of new therapies. Now that the CTN has established evaluation mechanisms for process measures (e.g., number of protocols approved, number of databases

locked), it is time to develop a mechanism to measure the dissemination and effectiveness of its efforts.

- The Work Group believes that its recommendations will improve the efficiency of the CTN and enable Principal Investigators, CTPs, and key NIDA staff to focus on important issues related to the mission.

5. Where should the CTN be in 5 years?

- The CTN should be at the core of NIDA, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute of Mental Health (NIMH) as a vehicle for translating research into practice and improving treatment processes and outcomes. The Network should be participating in key NIDA initiatives (e.g., genetic pooling) and providing important input to the entire research agendas of NIDA, NIAAA, and NIMH.

- The NIH Director Elias A. Zerhouni, M.D., recently established the NIH Roadmap Initiative for Medical Research. The NIH Roadmap is designed to accelerate medical research by identifying new research pathways, building research teams of the future, and re-engineering the clinical research enterprise. Within the NIH Roadmap framework, primary objectives include the integration of clinical research networks and the development of regional translational research centers. NIDA, in partnership with other NIH Institutes, should explore avenues for the CTN to participate and contribute to the Roadmap Initiative. The Work Group believes that the current CTN roadmap is a good start toward that contribution and recommends its further refinement.

6. Can the CTN play a role in prevention as well as treatment?

- The CTN could play a role in prevention dissemination research, but it is not well equipped to do so now. The Network currently plays a role where an overlap exists between treatment and prevention—for example, in family therapy studies and relapse prevention—but primary prevention has not been a focus of activity.

- Some CTPs have prevention programs, and a few current researchers have experience conducting prevention research; however, many do not.

- There is little connection between the CTN, school systems, community agencies doing prevention work, and other locations where research might need to be carried out. New network development would be needed to build a strong research platform for prevention issues.

7. What is the role of the CTN in HIV/hepatitis C research?

- Research in any specific area is now largely dependent on the interests of investigators in individual Nodes. Investigators should present the CTN with ideas for their particular areas of interest.

- The CTN also has established special interest groups of researchers and CTP partners to discuss and propose new areas for research. For example, three protocols have emerged from an HIV interest group.

- The Work Group found that the current "closed" nature of the CTN protocol development process is a potential weakness for future research areas. The Group was particularly concerned that there be a way for research ideas to flow to the CTN from all areas of NIDA. Specific recommendations are made to address this in Section V, Future Directions: Recommendations From the CTN Work Group.

8. What is the role of the CTN in training?

- During its meetings, the Work Group heard instances of very intense and high-quality training being provided in the context of implementing specific protocols from CTP members.

- The Work Group also has heard anecdotal evidence that staff members participating in trials are improving overall skills and are being retained in their organizations.

- The Work Group was unable to identify any resources dedicated to an overall training mission within the Nodes. If NIDA determines that it would be useful for the CTN to train new researchers in the Nodes or community providers in the Network, the Work Group believes additional funds will need to be targeted to these purposes.

- The Work Group also found no evidence of the impact on training beyond the participating centers, although some evidence suggested that contact with State agencies might lead to improvements in issues such as payment for supervision. This could have an important long-range impact on better training and outcomes.

9. What is the role of the CTN in involving the medical community?

- Most CTPs have minimal medical involvement. Therefore, the CTN is not currently a vehicle for involving the broader medical community in drug treatment.

10. What is the role of the CTN in collaboration with other Institutes?

- The Work Group noted a separation between the CTN and other NIDA Divisions in the effective use of the Network as a research platform.

- The Work Group learned that NIAAA representatives are starting to attend some meetings, but noted that, to date, there have been no examples of cross-Institute collaboration in the CTN. Recommendations that address this issue are included in Section V, Future Directions: Recommendations From the CTN Work Group.

V. FUTURE DIRECTIONS: RECOMMENDATIONS FROM THE CTN WORK GROUP

Please note that the recommendations made by the CTN Work Group are in italics.

CORE RECOMMENDATION

> *The CTN Work Group recommends that the Network be continued and that it become a central strategic element in the future plans of NIDA, NIAAA, and NIMH to diffuse research that improves the quality of treatment for substance use disorders in communities throughout the country.*

OUR UNDERSTANDING OF THE MISSION OF THE CTN IN THE FUTURE

The Work Group believes that the unique mission of the CTN differentiates the Network from other NIDA and NIH clinical research efforts. Clarifying this mission will provide a strong basis for better collaboration with other NIDA and NIH programs in the future.

The Work Group believes that the primary mission of the CTN is to help bridge the gap between science and practice, so as to treat and prevent substance use disorders more successfully. The Network accomplishes this mission primarily by conducting practical clinical trials and other forms of effectiveness research regarding empirically based, clinically relevant intervention and prevention programs. These programs will be for diverse populations recruited from heterogeneous settings, as assessed against a range of substance use disorders, mental health, physical health, social, cost, and organizational outcomes. CTN research can also help determine the processes through which these interventions produce their effects.

The Network also conducts research on how to modify existing empirically based interventions to make them more acceptable or practical with diverse populations and within heterogeneous practice settings, without unduly modifying their efficacy. In addition, the CTN conducts research on the training, professional, organizational, policy, or financial means necessary for successfully disseminating effective clinical treatments into diverse practical settings. Finally, the Network works with State, Federal, and other interested agencies and parties to transfer research results to treatment and prevention programs, providers, and consumers so as to improve the quality of drug abuse treatment and prevention.

The primary mission can be summarized as follows:

- To study the impact of evidence-based practices when they are broadly disseminated in diverse settings and populations; and

- To study the impact of evidence-based practices modified to be more readily adoptable.

The Work Group also believes that the CTN has a secondary mission, afforded by the processes and outcomes necessarily produced in service of its primary mission. The secondary mission of the CTN is outlined in the text below.

- A network of the kind needed to conduct practical clinical trials can provide a valuable platform for a vast variety of other kinds of research. Much of this research may be more central to the mission of other NIDA Divisions or other NIH Institutes, particularly NIMH and NIAAA. For example, a well-functioning CTN might enable the collection of important genetic databases. Research opportunities of this kind provide reasons to be hopeful about the positive impact of the Network on NIDA in general; however, other NIDA Divisions and NIH Institutes should not be confused with the primary mission of the CTN, and they should not necessarily be linked to the CTN's separate funding structure.

- The CTN also provides good examples of high-quality treatment in actual practical settings and develops a cadre of researchers, practitioners, and agencies that have been exposed directly to the benefits of collaboration. In the long run, these treatments could have a large impact on NIDA research and its dissemination efforts, and they can have a very positive impact on the practice base. These benefits are a side effect of the processes inherent in the CTN, however. If these goals were the primary mission, less costly methods of their achievement would probably be available.

- The active involvement of the CTPs helps NIDA identify crucial practical research questions that—although not yet ready for dissemination and effectiveness research and thus not yet ready for CTN testing—may nevertheless benefit from special forms of NIDA funding outside of the normal CTN funding.

- The Work Group noted that the CTN engenders a dynamic tension between research knowledge and practical needs that is both uncomfortable for some parts of NIDA and drug abuse treatment and helpful in the long run to the health of the Institute and to drug abuse treatment if the CTN is perceived correctly.

In summary, the secondary mission of the CTN is:

- To serve as a platform for a broad variety of basic and applied research—both inside and perhaps outside the Institute—that is not yet ready for dissemination;
- To provide state-of-the-art examples of drug abuse treatment and prevention;
- To expose researchers, practitioners, and agencies to the benefits of mutual collaboration;
- To help inform NIDA about practical issues in need of research;
- To study how to disseminate evidence-based practices successfully; and
- To support the dissemination of scientific results to the practice community.

RECOMMENDATIONS RELATING TO THE PLACEMENT OF THE CTN WITHIN NIDA AND INTEGRATION WITH OTHER NIDA STRUCTURES, AND ITS RELATIONSHIP TO NIAAA AND NIMH

> *The CTN should remain housed in NIDA's Office of the Director for the foreseeable future, with a senior officer, perhaps the Deputy Director, designated with clear final decisionmaking authority. To facilitate collaboration throughout NIDA, a coordinating structure should be created under the designated official to include the CCTN Director, NIDA Division Directors, and other senior officers whose work can impact or be impacted by the CTN.*

The Work Group discussed a wide range of possible alternatives for locating the CCTN function. Members recognized the strains on the CCTN Director's time and heard logical reasons why the CTN could be located within several existing NIDA Divisions. However, the Work Group noted the potential for additional strains and impediments to effective Institute and external collaboration in any of the alternatives. Therefore, members recommend that the CTN stay where it is in the Office of the Director.

The Work Group believes that the issues of internal and external coordination need more attention than they can get without new mechanisms at the Director's level and clear authority to set priorities and resolve disputes. These kinds of issues may become more acute in a period of slower budget growth and with a maturation of the CTN's ability to identify and conduct important dissemination research. The Work Group also believes such a coordinating mechanism will provide all NIDA Divisions with a place to engage in long-term strategic planning of a research agenda that clearly focuses on practical dissemination. A coordination structure that involves other Divisions may have longer-term intellectual benefits as well, such as bringing new findings into the CTN as well as developing and refining administrative vehicles for the use of the CTN as a platform.

> *The Director of NIDA should create a formal mechanism for input and collaboration on CTN policy and operations from NIAAA and NIMH, with a goal of developing joint research and training projects using the diverse populations in the CTN.*

Very large numbers of patients in CTP settings have co-occurring disorders associated with drugs, alcohol, and mental illness. As collaboration in research and administration among the Institutes increases, the

Network provides an excellent vehicle to reach these populations with interventions shown to meet their multiple needs.

RECOMMENDATIONS RELATING TO THE APPROPRIATE SIZE OF THE CTN

As the re-funding cycle is addressed, the size of the CTN should be rationalized to ensure adequate access to the broad spectrum of Americans with substance use disorders in all regions of the country.

There should be sufficient Nodes to plan a growing portfolio of research, training, and dissemination projects. At least some funding should be flexible enough to enable a Node to sponsor innovative work in collaboration with its CTP partners that may lead to larger practical clinical trials.

NIDA should announce a single competition covering the first two rounds of initial funding (11 Nodes). The announcement should clearly state the criteria for selection.

RECOMMENDATIONS RELATING TO AREAS OF APPROPRIATE RESEARCH FOR THE CTN AND STANDARDS FOR CONDUCTING RESEARCH WITHIN THE CTN

The CTN should deliver its primary mission through practical clinical trials (PCTs) of interventions that have been shown to be effective through prior empirical research.

The original CTN mission statement spoke only of multisite trials and did not specifically mention empirically supported interventions. The Work Group believes that this should be corrected. The primary mission will indeed require multisite randomized controlled trials, but these should be focused on PCTs with empirically supported interventions (Tunis et al., 2003). By their very nature, PCTs involve comparative evaluations of interventions used with diverse populations and in diverse practical settings. Insofar as possible, these trials should be designed to answer questions about whether the proposed intervention is better than currently used interventions. Although PCTs are randomized controlled trials, implementing a program of PCTs also requires other research methods or designs. For example, PCTs may need to compare an empirically supported treatment not to another well-defined treatment, but to treatment as usual.

Very difficult empirical issues must be faced in documenting and measuring treatment as usual—issues that the CTN is well suited to help solve for the entire field. The research methods needed in this area are not randomized controlled trials. Similarly, by definition, PCTs focus on broader and longer-term health outcomes. In some cases, these outcomes might be characterized using methods other than randomized controlled trials. For example, simple descriptive studies might examine the course of health outcomes produced by empirically supported treatments over a long-term followup. The Work Group's point is that, although PCTs should form the core of the CTN portfolio, accomplishing its primary mission may also require assessment development, evaluation research, services research, cost-benefit analyses, organizational research, and so on—some of which may properly belong within the CTN funding and project approval stream, despite the fact that these studies are not multisite randomized controlled trials.

Efficacy research that examines the impact of existing interventions that are modified so as to make them simpler, more clinically friendly, more cost-effective, or otherwise more useful in diverse practical settings may also be conducted in the CTN at appropriate scale.

Early efficacy research should normally be conducted on a small scale, not at multiple sites. Although most of this kind of research will be conducted outside the CTN, it makes sense for some of it to occur

within the Network. However, the precise compromises that might need to be tested to comport with practical needs require a healthy negotiation between equal partners, such as that afforded between the investigators and CTPs within the CTN. Ideally, modifications will be tested against existing methods delivered in a fashion that has known efficacy before being deployed in multisite trials, although other methods (e.g., examination of within-group effect sizes) may provide an adequate empirical basis for such deployment.

Research on how to disseminate empirically supported research at the appropriate scale and in support of the PCTs being investigated should be performed in the CTN as a means of supporting its primary mission.

The Work Group believes that a wide variety of research is needed to examine how to disseminate empirically supported treatments successfully in diverse practical settings. Studies of this kind may involve the evaluation of innovative methods—such as new methods of training practitioners in empirically supported interventions and new means of modifying organizations to make them more receptive to adoption of empirically supported methods—that have relatively limited empirical support. However, because the level of analysis of such research is inherently larger (e.g., involving larger numbers of clinicians or agencies) and because methods of this kind are necessarily involved in mounting the more primary research purposes of the CTN, such studies logically belong within the funding and evaluation streams of the CTN.

CTN trials can and should provide new information about the possible differential impact of interventions on various population groups by taking care to design these questions into the studies and recruiting participation from the heterogeneous populations within the entire range of participating CTPs.

The Work Group noted that the NIDA Diversity Plan makes specific reference to the CTN as an important element in its strategy to ensure that research is relevant to all-important subgroups in the population. The Work Group believes that this objective can be achieved and that important, clinically relevant information learned by explicitly planning trials to include minority populations that may have been underrepresented in the original efficacy trials. The value of doing research in diverse settings is diminished if issues of diversity are not addressed in the research design.

CTN dissemination-oriented research should include cost-benefit or cost-effectiveness analyses to assist treatment programs and funders in making decisions about implementing interventions.

The Work Group recognizes that these kinds of analyses often raise complex measurement issues, especially in assigning costs to activities within existing entities and providing fully quantified measures of benefit. Nevertheless, the question of how much it will cost to implement a new treatment protocol and whether the result will be better than the benefits the program now gets is at the heart of many barriers to widespread dissemination of new approaches.

Over time, the special characteristics of the CTN should enable it to emerge as an active participant in a wide variety of substance use disorder research. For example, the CTN has access to a huge and heterogeneous pool of genetic material—including families—that could speed collection and analysis of genetic markers. CTPs in the Network may be in a better position than traditional NIDA researchers to maintain long-term contact with patients and families for followup and longitudinal studies.

The CTN can now be used as a vehicle for Phase III trials of drugs that will be submitted to the FDA for NIDA approval. Phase III medication studies could be carried out in collaboration with other NIDA Divisions to provide them with access to the diverse populations served in the CTN. Data quality and monitoring standards for CTN protocols should be appropriate to the risks actually involved.

The good clinical practice model (GCP) model for randomized clinical trials being submitted to the FDA is not the only optimal model for selection for all protocols.

The issues of using the GCP model for data integrity appear to have come under the most strain when applied to various behavioral therapy studies, but can be equally questioned for many pharmacotherapy studies when the goal does not involve conducting a pivotal study for FDA submission of a New Drug Application (NDA). Because the vast majority of CTN studies have the treatment community, rather than the FDA, as their audience and participants, it is logical that NIDA might not need to behave as if it were a pharmaceutical company going to the FDA for approval.

This flexibility to move outside of the box of highly regulated NDA studies is perhaps a fundamental distinction between the trials networks of NIDA and NCI. The NCI network has allowed new medications for very rare diseases to be brought to market when multiple community sites are required to get a sufficient number of patients for a Phase III FDA submission of an NDA. This mission of NDA submissions is probably not a realistic part of the CTN at this stage of its development because few, if any, medications in the substance abuse disorders field merit this type of GCP monitoring and associated cost, and behavioral interventions neither require nor would benefit from the FDA or other regulatory approval.

Cost considerations may be an important point in this discussion, but the other consideration involves the broader mission of the CTN to move successful new treatments into realistic clinical settings and routine clinical practice. Many aspects of GCP procedures and monitoring are not related to goals that are embraced by the CTN, including providing good clinical care, using cutting-edge therapies, collecting high-quality data, or attaining cost-effective assessments of treatment. Particular GCP procedures that are not relevant to these goals cannot be extensively listed here, but include the typical tracking procedures for protocol deviations, the extensive onsite monitoring of every case report form, and signoffs by investigators on many documents and data collection instruments for each subject at every visit.

The issue of using the GCP model for data integrity is critical in the allocation of limited resources and in clearly defining the mission of the CTN. The Network is not a contract research organization, and NIDA has other mechanisms in other Divisions to address such a need, if that need arises for a particular treatment.

Many very high-quality studies have introduced clinical innovations and improved practice without adopting the detailed procedures of the GCP model that are typically supported by extensive and expensive monitoring organizations. In the field of substance use disorders, examples include the NIDA Cocaine Collaborative study (Crits-Christoph et al., 1999), Project MATCH (Project MATCH Research Group, 1998), the acupuncture study (Margolin et al., 2002), and the Marijuana Treatment Project (MTP Research Group, in press), all of which were multisite studies.

Later in this report, the Work Group recommends the establishment of a Coordinating Center to manage the many quality assurance tasks that go along with multisite research, but this Coordinating Center must be flexible in developing the level of monitoring and data management that is appropriate for the particular study. The current structure appears to use an outside contractor to make every study meet current interpretations of FDA standards for a pivotal study of an NDA submission by a commercial sponsor of a new pharmaceutical. The Work Group believes this structure is simply too rigid. The CTN can be in the vanguard in developing reasonable and valuable standards for application to clinical research, rather than

simply applying the very costly approach of current interpretations of GCP standards. No outside agency, regulatory body, or review group is imposing these costly standards on NIDA or the CTN, and no one will reward NIDA for imposing this relatively inefficient standard on its work.

The Work Group believes a more reasonable goal for the CTN will be a major service to the field of substance use disorders and to the field of practical day-to-day medicine, where we do need to test effective new therapies and determine how to realistically adapt them so that the broader treatment community will then adopt them.

It may be necessary to convene an expert group of clinical investigators to work with the CTN and NIDA leadership to detail all the minimal standards needed for reasonable studies. This group could provide realistic standards for various measures of treatment process and outcome such as the Addiction Severity Index and the Composite International Diagnostic Interview for psychiatric diagnoses and the time periods over which outcomes will be measured. This group could also review, in conjunction with the appropriate CTN committee's standard operating procedures, business rules for data acquisition and verification, and criteria for considering a priori outcome criteria. The Work Group further believes that much of the work involved in meeting this recommendation might be adopted from existing organizations such as the Veterans Administration (VA) Cooperative Studies Program or the other NIDA Divisions involved in clinical research.

In summary, some new ground is being broken in finding a hybrid model for clinical research that is more efficient than having each new multisite study redesign its operating procedures. However, the current iteration of this process needs to become more efficient than the current business of GCP monitoring, which was designed for a different purpose than the mission and promise of the CTN.

RECOMMENDATIONS RELATING TO CTN OPERATIONS AND BUDGETS

> *To fulfill its mission, the CTN, over time, should become open to receiving and reviewing proposals to use the Network as a platform for research emanating from outside the CTN. In many cases, funding for such proposals will also come from outside the CTN, but in other areas that closely align with the primary mission of the CTN, consideration should be given to funding them from the CTN budget.*

This approach to funding and to CTN development cannot ultimately be successful if the Network is impermeable. It is the nature of a network, as distinguished from a mere collection of performance sites, that projects must be conducted in a fashion that supports cooperation and mutual benefit. Thus, the Work Group is aware of the complex nature of using the CTN as a platform for basic research or for applied research by outside investigators. Nevertheless, the research opportunities the Network affords—and the perceived mutual benefit between the CTN and other NIDA Divisions, Centers, and Branches—requires that means be developed to access the Network using funding and project approval streams external to the Network and with investigators external to the Network.

It is important that this funding not be channeled entirely through existing Principal Investigators because to do otherwise will ultimately lead to a sense that the CTN is a closed shop operated for the benefit of a few. Furthermore, the infusion of outside ideas and funding will help ensure the long-term intellectual, political, and financial viability of the Network. Balancing these interests will take vision, cooperation, and communication, particularly by the CCTN leadership. The Work Group recommends that the CTN be tasked to develop ways to open the Network, beginning immediately in small ways and increasing over time as proper administrative methods are developed.

> *The process for developing, reviewing, approving, and funding research protocols should be further simplified and made more transparent. The need for an external Protocol*

Review and an external Data Safety Monitoring Board (DSMB) should be carefully reexamined in light of the CTN's actual experience. If NIDA determines that such external review will remain necessary, it should be integrated early in the process (as apparently happens in the VA system) and actions should be transparent to the CTN to avoid wasted effort.

Budgets should be developed and attached to protocols early in the review process and should cover the expected cost for the life of the protocol as long as progress is being made on the research plan. Currently, protocols are being approved for multiyear periods, but funded on a year-to-year basis. An appropriate accountability and monitoring system should be established to force corrective action or cancellation if progress on a particular protocol or in a particular study site is not being made.

As already noted, the Work Group believes that it is important to distinguish between the primary and secondary mission of the CTN as well as to distinguish both missions from funding issues. The Network has established its own parallel funding and project approval structure. The Work Group believes that this was a necessary step for the proper functioning of the Network because the considerations made in cooperative efforts of this kind could not be transferred to an outside body that was unfamiliar with the needed compromises. However, this justification does not apply equally to all aspects of the CTN mission.

The Work Group believes that the secondary mission of the Network does not require a separate funding or evaluation structure: Normal NIDA processes, including Program Announcements and targeted Requests for Applications (RFAs), can provide the necessary funding—even when the projects are to be conducted within the CTN. Even within the primary mission of the CTN, some kinds of research could be understood and fairly evaluated without a separate evaluation and funding structure. A good example is the training research initiative recently launched by NIDA's Treatment Research Branch. This kind of research is central to the primary mission of the CTN. Some of the studies funded by this RFA could certainly be conducted within the CTN. For that reason, within those topics relevant to the primary mission, the Work Group believes that CTN funding should be *primarily* focused on PCTs and their impact and *secondarily* on treatment modifications or contextual research that will logically lead to PCTs that may have good scientific, practical, and policy implications.

A single or limited number of Coordinating Centers should be established to manage all stages of protocol training, implementation, and data monitoring. An independent Coordinating Center should be selected through a competitive bidding process in close coordination with the CTN Steering Committee, and it should endorse the plans under the terms and conditions of the cooperative agreement.

The Work Group believes that reliance on such a Coordinating Center, as is often the case in other multisite trials, will significantly enhance efficiency in the CTN without supplanting the authority and responsibility of the Principal Investigator in the study. This approach will free senior investigators in the Nodes from burdensome administrative tasks and enable them and their CTP partners to focus their attention on scientific issues, training, and dissemination.

RECOMMENDATIONS RELATING TO DISSEMINATION AND DIFFUSION OF CTN MATERIALS, RESULTS, TRAINING MODULES, AND OTHER WAYS TO IMPROVE THE QUALITY OF TREATMENT AND PREVENTION

To fulfill the CTN's mission, planning and resources for dissemination should be included in all protocol development and review, not left as a matter to be addressed after the fact. Principal Investigators and their CTP colleagues should identify and address likely barriers to widespread adoption during the planning phase of a study, and

they should test approaches to overcoming such barriers in the practical clinical trials supported in the CTN. NIDA should consider providing additional resources within its own operations and the CTN to promote broader dissemination of evidence-based treatments.

Dissemination is an inherent purpose of the NIH, but it is remarkable how little is known about effective dissemination. Normally, documentation of dissemination involves the documentation of processes, not outcomes. For example, NIDA regularly documents its publications, conferences, Web site hits, and so on. From time to time, NIDA has also documented whether consumers or clinicians are aware of or are satisfied with scientific materials produced by NIDA. All these steps are worthwhile, but the mission of the CTN is outcome-focused. The IOM report that led to the creation of the CTN is the source of its primary mission: To help bridge the gap between science and practice, so as to prevent and treat substance use disorders more successfully. As measured against that goal, documentation of dissemination processes cannot be considered adequate.

Very little literature has been published on dissemination, and the Work Group notes with approval the considerable efforts of the CTN to summarize that literature. Unfortunately, this literature is relatively limited; often not experimental; rarely focused on substance use disorders or, more broadly, on behavioral health; and is sometimes grim in its implications—often documenting what does not work more than providing clear guidance to what does work. Indeed, some of the methods known not to have a strong influence on actual clinical practice are processes now being documented as forms of CTN dissemination. That does not mean that articles, presentations, manuals, or other formats of scientific information are unhelpful. Logically, it is necessary to successful dissemination: It is not possible to implement methods that one does not know exist. However, it is clear that information is rarely sufficient to make a practical difference in the lives of those suffering with the behavioral health problems NIDA is tasked to help solve.

NIDA and other Institutes should consider new research initiatives that address barriers to dissemination of effective treatment interventions.

The CTN strategic plan for dissemination identifies the issues fairly well, and the Work Group's recommendations are more a matter of concurrence, emphasis, and focus on the areas outside of the CTN that NIDA might consider. The Work Group believes that this suggests a need for (1) new funding initiatives in effective dissemination of evidence-based practices, (2) cooperation with other research agencies to begin to close that knowledge gap, (3) research on dissemination within the CTN, (4) use of the best available methods in CTN dissemination efforts, and (5) cooperation with other agencies in dissemination programs.

The extent of the need for new initiatives in evidence-based treatments has been recognized repeatedly in the CTN development process so far. For example, when the CTN began to ask about which empirically supported treatments to disseminate, it was quickly realized that no list of such methods exists, and no agreement has been reached regarding how to define them. Other areas of health research are far more advanced in the development of evidence-based practice guidelines, clinical pathways, or empirical summaries of evidence. These are complex matters, involving professional infighting, theoretical disagreements, philosophy of science issues, methodological preferences, funding issues, political concerns, statistical arguments, and the like.

NIDA should find ways—perhaps in cooperation with the Substance Abuse and Mental Health Services Administration (SAMHSA), NIMH, and NIAAA—to develop rapid, updateable, cost-effective, multidisciplinary, evidence-based ways to reach a broad consensus on lists of empirically supported treatments, practice guidelines, or clinical pathways that can then inform the CTN's PCTs and disseminate research within NIDA more generally.

The CTN should work closely with NIDA and other agencies working on dissemination, especially SAMHSA's Addiction Technology Transfer Centers (ATTCs) network.

The dissemination efforts of the CTN should be leveraged wherever possible. The CTN dissemination strategic plan recognizes this clearly. Although NIDA has a direct dissemination mission, other agencies—for example, SAMHSA's Center for Substance Abuse Treatment (CSAT) and Center for Substance Abuse Prevention—are even more focused on this mission, and the CTN should work with these agencies to amplify the Network's impact. The Work Group noted with satisfaction that NIDA is helping to fund dissemination efforts by CSAT's ATTCs. NIDA should build on this opening and should ensure that these efforts are evaluated or, in some cases (with NIDA cooperation and funding), formally empirically tested.

The focus of dissemination can be expanded in other ways, as is noted in the CTN external linkages plan. The Work Group would add that it might also be possible for the CTN to involve more CTPs without increasing costs, perhaps through the creation of a new category of CTPs that are informally linked to the CTN. Such "affiliate CTPs" perhaps could be linked to the ATTCs or to the CSAT Practice/Improvement Collaborative programs. Their primary purpose would not be involvement in PCTs, but involvement in dissemination efforts of the CTN.

Overall, the Work Group believes the CTN is making good headway in its dissemination plan, but that the Network will need help from NIDA at large to accomplish this mission more fully.

NIDA and the CTN should establish a continuing collaboration with directors of State treatment and prevention agencies, perhaps through the auspices of the National Association of State Alcohol and Drug Abuse Directors (NASADAD), to foster dialogue about the CTN and NIDA research agenda and to enhance the probability of broad dissemination of effective treatment regimens.

The Work Group noted the successful initial meeting with a few State directors at the recent CTN program in Denver and urges the Network and NIDA to continue efforts to nurture a strong relationship. The State directors can have a powerful influence on adoption rates for more effective treatments through their financial and regulatory oversight of the public treatment system.

VI. REFERENCES

Crits-Christoph P, Siqueland L, Blaine JD, Frank A, Luborsky L, Onken LS, et al. Psychosocial treatments for cocaine dependence: Results of the National Institute on Drug Abuse Collaborative Cocaine Study. *Archives of General Psychiatry* 56:495-502, 1999.

Lamb S, Greenlick MR, McCarty D (editors). *Bridging the Gap Between Practice and Research: Forging Partnerships with Community-Based Drug and Alcohol Treatment* (Washington, DC: Committee on Community-Based Drug Treatment, Institute of Medicine, National Academy Press), 1998.

Margolin A, Kleber HD, Avants SK, Konefal J, Gawin FH, Stark E, et al. Acupuncture for the treatment of cocaine addiction: A randomized controlled trial. *Journal of the American Medical Association* 287(1):55-63, 2002.

Marijuana Treatment Project Research Group. Treating cannabis dependence: Findings from a multi-site study. *Journal of Consulting and Clinical Psychology,* in press.

Project MATCH Research Group. Matching alcoholism treatments to client heterogeneity: Project MATCH three-year drinking outcomes. *Alcoholism: Clinical & Experimental Research* 22:1300-1311, 1998.

Tunis SR, Streyer DB, Clancy CM. Practical clinical trials: Increasing the value of clinical research for decision making in clinical and health policy. *Journal of the American Medical Association* 290(12):1624-1632, September 24, 2003.

VII. APPENDICES

APPENDIX A: CTN NODES

Node	Affiliation	Primary Investigator
California/Arizona	University of California at San Francisco	James L. Sorensen, Ph.D.
Delaware Valley	University of Pennsylvania	George E. Woody, M.D.
Florida	University of Miami	José Szapocznik, Ph.D.
Great Lakes Region	Wayne State University	Charles R. Schuster, Ph.D.
Long Island	New York State Psychiatric Institute	Edward V. Nunes, M.D.
Mid-Atlantic	Johns Hopkins University School of Medicine	Maxine Stitzer, Ph.D.
New England	Yale University	Kathleen Carroll, Ph.D.
New York	New York University School of Medicine	John Rotrosen, M.D.
North Carolina	Duke University Medical Center	Robert L. Hubbard, Ph.D., M.B.A.
Northern New England	McLean Hospital	Roger D. Weiss, M.D.

Ohio Valley	University of Cincinnati College of Medicine	Eugene Somoza, M.D., Ph.D.
Oregon	Oregon Health Sciences University	Dennis McCarty, Ph.D.
Pacific Region	University of California, Los Angeles	Walter Ling, M.D.
Rocky Mountain	University of Colorado School of Medicine	Paula Riggs, M.D.
South Carolina	Medical University of South Carolina	Kathleen T. Brady, M.D., Ph.D.
Southwest	University of New Mexico	William R. Miller, Ph.D.
Washington	University of Washington	Dennis M. Donovan, Ph.D.

APPENDIX B: GENERAL CTN STRUCTURE DEFINITIONS

The CTN is a collaborative group of geographically diversified Regional Research Nodes working collaboratively with NIDA to conduct multisite and cross-regional clinical trials on promising behavioral, pharmacological, or integrated treatments.

NODES

A Node is a functional unit within the CTN consisting of the Regional Research and Training Center (RRTC) and its affiliated Community Treatment Programs. The RRTC serves as the coordinating core and promotes a bidirectional research partnership between the RRTC and the CTPs. There are currently 17 Nodes in the CTN.

REGIONAL RESEARCH TRAINING CENTER (RRTC)

The RRTC is the recipient of the cooperative agreement award. One of the two components of a Node, the RRTC resides in the Principal Investigator's research and prevention institute or organization's academic medical center. The Principal Investigators at these sites are recognized nationally and internationally as scientific experts in substance addiction treatment. The RRTC provides a core of administrative and study operations services as well as scientific leadership and management of clinical trials.

COMMUNITY TREATMENT PROGRAMS (CTP)

CTPs are drug abuse treatment programs in a community (typically non-university-based) setting that have a history of providing quality treatment to large and diverse patient populations and that have the capability for and interest in participating in controlled clinical trials. There are currently 116 CTPs in the CTN.

NIDA CENTER FOR CLINICAL TRIALS NETWORK (CCTN)

The Center for Clinical Trials Network is located within NIDA's Office of the Director and is responsible for the scientific, operational, administrative, and budgetary management of the CTN. There are currently 17 full-time and part-time staff members, not including the Director.

ADMINISTRATIVE AND LOGISTICAL SUPPORT

NIDA awards contracts to provide centralized support for the administrative and logistical functions of the CTN.

APPENDIX C: CTN PROTOCOL PORTFOLIO

Protocol Number	Title	Node	Lead Investigator	Start Date	Complete Date
AIDS/HIV Protocols					
CTN 0012	Characteristics of Screening, Evaluation, and Treatment of HIV/AIDS, Hepatitis C Viral Infections, and Sexually Transmitted Infections in Substance Abuse Treatment Programs ("Infections and Substance Abuse")	New York	Lawrence Brown	June 2003	4Q 2004
CTN 0017	HIV and HCV Intervention in Drug Treatment Settings	Rocky Mountain	Robert Booth	1Q 2004	TBA
CTN 0018	HIV/STD Safer Sex Skills Groups for Men in Methadone Maintenance or Drug-Free Outpatient Treatment Programs	Washington	Donald Calsyn	4Q 2003	TBA
CTN 0019	HIV/STD Safer Sex Skills Groups for Women in Methadone Maintenance or Drug Free Outpatient Treatment Programs	Long Island	Susan Tross	4Q 2003	TBA
CTN 0024	Reducing HIV Risk Behaviors Among Adolescents in Community-Based Substance Abuse Treatment Programs	Long Island	Jeffrey Wilson	TBA	TBA
CBT Protocols					
CTN 0015	Women's Treatment for Trauma and Substance Use Disorders	Long Island	Denise Hien	3Q 2003	4Q 2005
CTN 0026	Treatment of Depression in Adult Substance Abusers	South Carolina	Susan Sonne	TBA	TBA
Family Protocols					
CTN 0014	Brief Strategic Family Therapy for Adolescent Drug Abusers	Florida	Jose Szapocznik	2Q 2003	2Q 2006
CTN 0022	Family Management Skills for Opiate-Addicted Women in Treatment: A Double Impact Risk Reduction Intervention	Great Lakes	Robert Zucker	TBA	TBA

Protocol Number	Title	Node	Lead Investigator	Start Date	Complete Date
Incentives Protocols					
CTN 0006	Motivational Incentives for Enhanced Drug Abuse Recovery: Drug-Free Clinics	Mid-Atlantic	Maxine Stitzer	26 Apr 2001	28 Feb 2003
CTN 0007	Motivational Incentives for Enhanced Drug Abuse Recovery: Methadone Clinics	Mid-Atlantic	Maxine Stitzer	26 Apr 2001	28 Feb 2003
Medication Protocols					
CTN 0001	Buprenorphine/Naloxone versus Clonidine for Inpatient Opiate Detoxification	Pacific	Walter Ling	26 Feb 2001	27 Feb 2002 (IRB) 14 Aug 2002 (DSMB)
CTN 0002	Buprenorphine/Naloxone versus Clonidine for Outpatient Opiate Detoxification	Pacific	Walter Ling	05 Jan 2001	27 Feb 2002 (IRB) 14 Aug 2002 (DSMB)
CTN 0003	Suboxone (Buprenorphine/Naloxone) Taper: A Comparison of Taper Schedules	Pacific	Walter Ling	June 2003	3Q 2004
CTN 0009	Smoking Cessation Treatment With Transdermal Nicotine Replacement Therapy in Substance Abuse Rehabilitation Programs	New York	Malcolm Reid	21 Apr 2003	3Q 2005
CTN 0010	Buprenorphine/Naloxone-Facilitated Rehabilitation for Opiod-Dependent Adolescent/Young Adults	Delaware Valley	George Woody	2Q 2003	3Q 2005
MET/MI Protocols					
CTN 0004	MET (Motivational Enhancement Treatment) to Improve Treatment Engagement and Outcome in Subjects Seeking Treatment for Substance Abuse	New England	Kathleen Carroll	30 May 2001	2Q 2003

Protocol Number	Title	Node	Lead Investigator	Start Date	Complete Date
CTN 0005	MI (Motivational Interviewing) to Improve Treatment Engagement and Outcome in Subjects Seeking Treatment for Substance Abuse	New England	Kathleen Carroll	12 Apr 2001	4 Oct 2002
CTN 0013	Motivational Enhancement Therapy to Improve Treatment Utilization and Outcome in Pregnant Substance Users	Ohio Valley	Theresa Winhusen	2Q 2003	4Q 2005
CTN 0021	Motivational Enhancement Treatment to Improve Treatment Engagement and Outcome for Spanish-Speaking Individuals Seeking Treatment for Substance Abuse (METS)	New England	Kathleen Carroll Jose Szapocznik	3Q 2003	TBA
Services/Nontreatment Protocols					
CTN 0008	Assessment of the National Drug Abuse Clinical Trials Network: A Baseline for Investigating Diffusion of Innovation ("Baseline Study")	Oregon	Dennis McCarty	1Q 2002	3Q 2003
CTN 0011	A Feasibility Study of a Telephone Enhancement Procedure (TELE) to Improve Participation in Continuing Care Activities	North Carolina	Robert Hubbard	08 Jan 2003	4Q 2004
CTN 0016	Patient Feedback: A Performance Improvement Study in Outpatient Addiction Treatment Settings	Delaware Valley	Robert Forman	3 4Q 2003	TBA
CTN 0020	Job Seekers Training for Patients with Drug Dependence	Mid-Atlantic	Dace Svikis	1Q 2004	TBA
CTN 0025	Community Reinforcement and Family Training to Increase Drug Abusers' Motivation for Treatment	Ohio Valley	Greg Brigham	TBA	TBA
12-Step Protocols					
CTN 0023	12-Step Facilitation as an Intervention to Increase 12-Step Activities and Improve Outcomes among Drug-Dependent Individuals	Washington	Dennis Donovan	TBA	TBA

APPENDIX D: CTN BUDGET EXPENDITURES

CTN Budget Expenditures 1999 Through 2003						
Fiscal Year	**Number of Nodes**	**Number of New Nodes**	**New Awards**	**Continuation Awards**	**Protocol-Specific Supplements**	**Total**
1999	5	5	$11,000,000			$11,000,000
2000	11	6	$13,200,000	$11,000,000		$24,200,000
2001	14	3	$6,600,000	$23,550,000	$650,000	$30,800,000
2002	17	3	$5,100,000	$25,200,000	$6,800,000	$37,100,000
2003	17	0	$0	$25,500,000	$11,900,000	$37,400,000
Totals:			**$35,900,000**	**$85,250,000**	**$19,350,000**	**$140,500,000**

Projection 2004	17	0	$0	$25,500,000	$11,900,000	$37,400,000

APPENDIX E: CLINICAL TRIALS NETWORK WORK GROUP

Work Group Members

David Rosenbloom, Ph.D., Chair
Director, Join Together
Boston University School of Public Health
441 Stuart Street, 7th Floor
Boston, MA 02116
(617) 437-1500
david@jointogether.org

Richard R. Bootzin, Ph.D.
Professor of Psychology and Psychiatry
Department of Psychology
University of Arizona
1503 E. University Boulevard, Bldg. 68
Tucson, AZ 85721
(529) 621-5705
bootzin@u.arizona.edu

Kathleen Burlew, Ph.D.
Professor of Psychology
Department of Psychology
University of Cincinnati
Mail Location 0376
Cincinnati, OH 45221

Nancy Hamilton, M.P.A., CAP, CCJAP
CEO
Operation PAR, Inc.
6655 66th Street North
Pinellas Park, FL 33781
(727) 545-7564
nhamilton@operpar.org

Steven C. Hayes, Ph.D.
Department of Psychology/296
University of Nevada, Reno
Mack Social Science, Room 314
Reno, NV 89557
(775) 784-6828 x2005
hayes@unr.nevada.edu

Yasmin Hurd, Ph.D.
Professor, Karolinska Institute
Department of Clinical Neuroscience
Psychiatry Section
Karolinska Hospital
Stockholm, Sweden SE-171 76
+46.8.517.72.379

Ron Jackson, M.S.W.
Executive Director
Evergreen Treatment Services
1700 Airport Way South
Seattle, WA 98134
(206) 223-3644
ronjack@u.washington.edu

Herbert D. Kleber, M.D.
Professor of Psychiatry
Director, Division on Substance Abuse
Columbia University
1051 Riverside Drive, P.I. Unit 66
New York, NY 10032
(212) 543-5570
hdk3@columbia.edu

Thomas R. Kosten, M.D.
Professor of Psychiatry and Medicine
Yale University School of Medicine
Deputy Chief of Psychiatry
VA Connecticut, Bldg. 35—151D
950 Campbell Avenue
West Haven, CT 06516
(203) 932-5711 x7438
thomas.kosten@yale.edu

Curtis Wright, M.D., M.P.H.
Executive Medical Director
Purdue Pharma L.P.
One Stamford Forum
Stamford, CT 06901
(203) 588-7414
dr.curtis.wright@pharma.com

Clinical Trials Network Coordinator

Denise Pintello, M.S.W., Ph.D.
National Institute on Drug Abuse
Office of Science Policy and Communications
6001 Executive Boulevard
Bethesda, MD 20892

Science Writer

Sarah E. Michaud
IQ Solutions, Inc.
11300 Rockville Pike, Suite 901
Rockville, MD 20852

APPENDIX F: CTN WORK GROUP MEETING AGENDA FOR AUGUST

National Institute on Drug Abuse
Clinical Trials Network Work Group

August 19-20, 2003

Marriott Gaithersburg Washingtonian Center
9751 Washingtonian Boulevard
Gaithersburg, MD 20878
301-590-0044

Day 1 – August 19, 2003

9:00 – 9:15 am	**NIDA's Strategic Plan: The Role for the CTN** *Nora D. Volkow, M.D., Director, NIDA*
9:15 – 10:00 am	**Opening Remarks; Work Group Questions** *David Rosenbloom, Ph.D., CTN Work Group Chair*
10:00 – 10:30 am	**Overview of the CTN; Work Group Questions** *Betty Tai, Ph.D., CCTN Director*
10:30 – 10:45 am	BREAK

10:45 – 5:00 pm	**EXECUTIVE SESSION**
10:45 – 11:00 am	**Clinical Trials Process at NCI**
11:00 – 12:00 noon	**Work Group Discussion** *David Rosenbloom, Ph.D., CTN Work Group Chair*
12:00 – 1:15 pm	LUNCH (on your own)
1:15 – 2:15 pm	**"Adopting Innovations Through the CTN: Using the CTN as a Platform for Services Research"**

Day 1 – August 19, 2003 (continued)

2:15 – 2:45 pm	**Work Group Discussion** *David Rosenbloom, Ph.D., CTN Work Group Chair*
2:45 – 3:00 pm	BREAK
3:00 – 4:00 pm	**NIDA Research Related to the CTN Portfolio**
4:00 – 5:00 pm	**Work Group Discussion** - Review the Day - Pose Questions - Make Requests for Possible Staff Presentations on Day 2 *David Rosenbloom, Ph.D., CTN Work Group Chair*

Day 2 –August 20, 2003

9:00 –12:00 noon	**EXECUTIVE SESSION**
9:00 – 9:15 am	**Genetics and the CTN**
9:15 – 10:30 am	**Addressing CTN Work Group Objectives** - Goals of Final Report - Implementation Steps - Additional Information Needs *David Rosenbloom, Ph.D., CTN Work Group Chair*
10:30 – 10:45 am	BREAK
10:45 – 12:00 noon	**Addressing CTN Work Group Objectives** (continued) - Timeline - Next Steps - Work Group Assignments *David Rosenbloom, Ph.D., CTN Work Group Chair*
12:00 noon	ADJOURN

APPENDIX G: CTN WORK GROUP MEETING AGENDA FOR OCTOBER

National Institute on Drug Abuse
Clinical Trials Network Work Group

October 7-8, 2003

Wyndham City Center
1143 New Hampshire Avenue, NW
Washington, DC. 20037
202-775-0800

Day 1 – October 7, 2003

9:00 – 9:20 am	**Opening Remarks; Summary of Current Status** *David Rosenbloom, Ph.D., CTN Work Group Chair*
9:20 – 9:40 am	**NIDA's Research Dissemination Efforts** *Timothy P. Condon, Ph.D., Associate Director, NIDA*
9:40 – 10:00 am	**CTN's Research Dissemination Efforts** *Jack Blaine, M.D., CTN, NIDA*
10:00 – 10:15 am	**Work Group Discussion** *David Rosenbloom, Ph.D., CTN Work Group Chair*
10:15 – 10:30 am	BREAK

10:30 – 5:00 pm	**EXECUTIVE SESSION**
10:30 – 10:45 am	**Data Management System**
10:45 – 11:45 am	**Work Group Discussion** *David Rosenbloom, Ph.D., CTN Work Group Chair*
11:45 – 1:00 pm	LUNCH (on your own)
1:00 – 1:30 pm	**CTN Process**

1:30 – 2:30 pm	**Work Group Discussion** *David Rosenbloom, Ph.D., CTN Work Group Chair*
2:30 – 2:45 pm	BREAK
2:45 – 5:00 pm	**Work Group Discussion and Objectives** - Review the Day Additional Information Needs *David Rosenbloom, Ph.D., CTN Work Group Chair*

Day 2 – October 8, 2003

9:00 –12:00 noon	**EXECUTIVE SESSION**
9:00 – 10:00 am	**Addressing CTN Work Group Objectives** - Goals of Final Report - Implementation Steps *David Rosenbloom, Ph.D., CTN Work Group Chair*
10:00 – 10:15 am	**Follow-up Discussion** *Betty Tai, Ph.D., CCTN Director*
10:15 – 10:30 am	BREAK
10:30 – 12:00 noon	**CTN Work Group Recommendations** - Timeline - Next Steps - Work Group Assignments *David Rosenbloom, Ph.D., CTN Work Group Chair*
12:00 noon	ADJOURN