DEPARTMENT OF HEALTH AND HUMAN SERVICES

OFFICE OF INSPECTOR GENERAL

WASHINGTON, DC 20201

January 18, 2013

TO: James M. Anderson, M.D., Ph.D.
Director
Division of Program Coordination, Planning, and Strategic Initiatives
National Institutes of Health

FROM: /Gloria L. Jarmon/
Deputy Inspector General for Audit Services

SUBJECT: Independent Attestation Review: National Institutes of Health Fiscal Year 2012 Performance Summary Report for National Drug Control Activities and Accompanying Required Assertions (A-03-13-00354)

This report provides the results of our attestation review of the National Institutes of Health (NIH) Performance Summary Report for National Drug Control Activities and accompanying required assertions for the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) for fiscal year (FY) 2012.

Each National Drug Control Program agency must submit to the Director of the Office of National Drug Control Policy (ONDCP) an annual evaluation of the progress by the agency with respect to drug control program goals using the performance measures established for that agency (21 U.S.C. § 1703(b)(13)). The Federal statute authorizes ONDCP to "monitor implementation of the National Drug Control Program, including – (A) conducting program and performance audits and evaluations." ONDCP may request "assistance from the Inspector General of the relevant agency in such audits and evaluations" (section 1703(d)(7)). Section 7 of the ONDCP Circular entitled *Drug Control Accounting*, dated May 1, 2007, provides the reporting requirements to comply with section 1703(b)(13). Section 8 of the ONDCP Circular requires that each report defined in section 7 must be provided to the Office of Inspector General to express a conclusion about the reliability of each assertion made in each Performance Summary Report for National Drug Control Activities.

As authorized by section 1703(d)(7) of the Federal statute, and in compliance with the Circular, ONDCP requested that we perform this review. Accordingly, we reviewed the NIH report entitled "FY 2012 Performance Summary Report for National Drug Control Activities" and accompanying required assertions, dated November 9, 2012 (Attachment A). We conducted our attestation review in accordance with attestation standards established by the American Institute of Certified Public Accountants and the standards applicable to attestation engagements

contained in *Government Auditing Standards* issued by the Comptroller General of the United States. A review is substantially less in scope than an examination, the objective of which is to express an opinion on management's assertions contained in its report; accordingly, we do not express such an opinion.

NATIONAL INSTITUTES OF HEALTH PERFORMANCE SUMMARY REPORT

NIH's combined report for NIDA and NIAAA included assertions for two measures of National Drug Control Activities. The two measures were (1) by 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies and (2) by 2015, identify three key factors influencing the scaling up of research-tested interventions across large networks of services systems such as primary care, specialty care, and community practice. The two performance measures represented drug control activities that accounted for $38.4 million for NIDA and $3.5 million for NIAAA.

In accordance with ONDCP requirements, NIH made the following assertions:

- the system for reporting performance was sufficient;
- the explanations for not meeting performance targets, and plans and recommendations for meeting targets, were reasonable;
- the methodology to establish performance targets was reasonable; and
- performance measures exist for all significant drug control activities.

We performed review procedures on the performance summary report and accompanying required assertions. In general, we limited our review procedures to inquiries and analytical procedures appropriate for our attestation review.

According to NIH officials, the prevention and treatment goals reported in FY 2012 are intended to be representative of the budget for prevention and treatment. However, in our related review, *Independent Attestation Review: National Institute on Drug Abuse Assertions Concerning Drug Control Accounting for Fiscal Year 2012* (A-03-13-00353), NIDA identified obligations totaling approximately $1.1 billion. According to NIDA and ONDCP officials, NIDA's entire $1.1 billion budget related to preventing or treating drug abuse. NIDA classified its obligations by function. For NIH's combined report, NIDA used the first measure, accounting for $23.5 million, to represent the $370.8 million obligated for prevention of drug abuse and used the second measure, accounting for $14.9 million, to represent the $681.6 million obligated for treatment of drug abuse.

The Performance Summary Report provided an evaluation of the agency's progress with respect to specific activities within the drug control program goals. However, the two measures only accounted for a total of approximately 3.7 percent of NIDA's $1.1 billion in funds obligated for preventing or treating drug abuse. The ONDCP guidance for FY 2012, dated June 17, 2010,

requested that NIDA revisit its performance measures and develop metrics that better reflect more of NIDA's drug control budget, which is all drug related.
Beginning in FY 2012, NIAAA was required to submit assertions for performance measures of National Drug Control Activities. In our related review, *Independent Attestation Review: National Institute on Alcohol Abuse and Alcoholism Assertions Concerning Drug Control Accounting for Fiscal Year 2012* (A-03-13-00359), NIAAA identified drug control obligations totaling $61.7 million out of a total budget of $459 million. NIAAA classified its drug control obligations by function. For NIH's combined report, NIAAA used the first measure, accounting for $0.8 million, to represent the $53.7 million obligated for prevention of drug abuse and used the second measure, accounting for $2.7 million, to represent the $8.0 million obligated for treatment of drug abuse.

The Performance Summary Report provided an evaluation of the agency's progress with respect to specific activities within the drug control program goals. However, the two measures only accounted for a total of approximately 5.7 percent of NIAAA's $61.7 million in funds obligated for preventing or treating drug abuse.

Accordingly, the current performance measures for NIDA and NIAAA may not meet ONDCP's expectation that the report reflect the complexity and scope of NIH's drug control activities.

OFFICE OF INSPECTOR GENERAL CONCLUSION

Based on our review, except for the fact that NIH's performance measures may not meet ONDCP's expectations for reporting the scope or complexity of NIH's national drug control program activities, nothing came to our attention that caused us to believe that NIH's Performance Summary Report for FY 2012 and management's assertions accompanying its report were not fairly stated, in all material respects, based on the ONDCP Circular.

NATIONAL INSTITUTES OF HEALTH COMMENTS

NIH stated that it did not have any comments on the report. A copy of its comments is included as Attachment B.

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Although this report is an unrestricted public document, the information it contains is intended solely for the information and use of Congress, ONDCP, and NIH. It is not intended to be, and should not be, used by anyone other than these specified parties. If you have any questions or comments about this report, please do not hesitate to call me, or your staff may contact Kay L. Daly, Assistant Inspector General for Audit Services, at (202) 619-1157 or through email at Kay.Daly@oig.hhs.gov. Please refer to report number A-03-13-00354 in all correspondence.

Attachments

ATTACHMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

DATE: November 9, 2012

MEMORANDUM TO: Director
Office of National Drug Control Policy

THROUGH: Norris Cochran
Deputy Assistant Secretary, Budget, DHHS

FROM: Director, Division of Program Coordination,
Planning, and Strategic Initiatives, NIH

SUBJECT: Assertions Concerning Performance Summary Report

In accordance with the requirements of the Office of National Drug Control Policy circular "Drug Control Accounting," I make the following assertions regarding the attached Performance Summary Report for National Drug Control Activities:

Performance Reporting System

I assert that NIH has a system to capture performance information accurately and that this system was properly applied to generate the performance data presented in the attached report.

Explanations for Not Meeting Performance Targets

I assert that the explanations offered in the attached report for failing to meet a performance target are reasonable and that any recommendations concerning plans and schedules for meeting future targets or for revising or eliminating performance targets are reasonable.

Methodology to Establish Performance Targets

I assert that the methodology used to establish performance targets presented in the attached report is reasonable given past performance and available resources.

Performance Measures Exist for All Significant Drug Control Activities

I assert that adequate performance measures exist for all significant drug control activities.

James. M. Anderson, MD, PhD

Attachment

FY 2012 Performance Summary Report for National Drug Control Activities

Decision Unit 1: Prevention

Measure 1 SRO-3.5: By 2013, identify and characterize at least 2 human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies.

Table 1: NIDA Annual Targets for Measure 1

FY 2008 Actual	FY 2009 Actual	FY 2010 Actual	FY 2011 Actual	FY 2012 Target	FY 2012 Actual	FY 2013 Target
SNP analyses identified a gene cluster predictive of treatment response to bupropion for smoking cessation and revealed additional genetic markers of addiction vulnerability.	Research has identified or verified genetic markers of nicotine dependence vulnerability or outcomes of smoking cessation therapies including: CYP2A6, CHRNB2, SLC6A3, and NR4A2.	Three studies confirmed the association of gene variants in Chrna5, Chrna3, and Chrnb4, on *chr15q25* with smoking frequency. Also, the first polygenic complex genetic score to significantly aid in predicting (in combination with other clinical attributes) success in smoking cessation was developed and tested.	Replicate/validate genetic markers that identify differences in treatment response and/or vulnerability to drug dependence in a minority population	Characterize the functional genetic variations associated with substance abuse	NIH researchers characterized the functional roles of genes previously identified as being associated with addiction to tobacco and other drugs, including those within the CHRNA5/A3/B4 gene cluster and A11G of the human mu opioid receptor gene.	Continue to characterize functional genetic variations associated with substance abuse

Table 2: NIAAA Annual Targets for Measure 1

FY 2008 Actual	FY 2009 Actual	FY 2010 Actual	FY 2011 Actual	FY 2012 Target	FY 2012 Actual	FY 2013 Target
Functional differences were identified for the A118 allele of the OPRM1 gene. Research was conducted on functional differences of haplotypes in the GABRA2 gene.	Functional differences related to alcohol dependence and treatment were validated for the A118G SNP of the OPRM1 gene.	Functional differences were characterized for sequence variations in genes encoding serotonin receptors and transporters, the oxidative stress enzyme SOD2, and nicotinic receptor subunits. (Target Met)	NIH researchers conducted functional studies of gene variants that are associated with increased risk for alcohol dependence through population-based research in European-Americans and African Americans.	Initiate replication and refinement of genome wide association and functional analysis data	NIH researchers replicated and extended the results of previous association studies in East Asian populations to populations of European and African ancestry.	Complete genome wide association and functional studies and identify potential genomic variants associated with risk for substance use and/or psychiatric disorders.

(1) Describe the measure. In doing so, provide an explanation of how the measure (1) reflects the purpose of the program, (2) contributes to the *National Drug Control Strategy*, and (3) is used by management of the program. This description should include sufficient detail to permit non-experts to understand what is being measured and why it is relevant to the agency's drug control activities.

NIH's growing knowledge about substance abuse and addiction (including tobacco, alcohol, illicit, and nonmedical prescription drug use) is leading to prevention strategies that are based not on anecdotal experience but on validated epidemiological, genetic, and neuroscience research. NIH-supported research is building the scientific knowledge base needed to advance our goal of developing effective tailored prevention strategies.

One key aspect of this knowledge base is inclusion of data on factors that enhance or mitigate an underlying propensity to initiate or continue substance abuse. This includes research on the influence of biological (e.g., genetic, gender) and environmental (e.g., socioeconomic, cultural) factors on substance abuse and addiction at various stages of development. Information about these contributors to substance abuse and addiction and the different ways biological factors operate in different individuals is critical to designing more effective prevention messages.

That is why NIH's genetics research is essential to preventing addiction. A person's genetic makeup plays an important role in his or her addiction vulnerability: approximately 40-60 percent of the predisposition to addiction can be attributed to genetics, including the impact of the environment on how implicated genes function or are expressed. Although the gene variants driving such increased risks are largely unknown, NIH-supported research is making strides in this area, harnessing new advances in science and technology to identify and characterize them. This measure, SRO-3.5, to identify and characterize at least 2 human candidate genes that have been shown to influence risk for substance use disorders, is representative of our overall approach to the development of targeted prevention programs—that is, identifying who is at risk and tailoring prevention programs to be most effective for them, thereby contributing to the ***National Drug Control Strategy Goal of Strengthening Efforts to Prevent Drug Use in Our Communities (Chapter 1)***.

The efficacy and cost effectiveness of primary prevention programs—designed to stop substance abuse before it starts, or prevent its escalation to abuse or addiction—can be enhanced by targeted efforts toward populations with specific vulnerabilities (genetic or otherwise) that affect their likelihood of taking alcohol or other drugs or becoming addicted. For example, prevention programs designed for sensation-seeking youth are effective for them, but not for their peers who do not demonstrate a high level of sensation seeking. High levels of sensation-seeking, and other traits known to be risk factors for substance abuse, may be identified early using genetic markers. Such identification would enable substance abuse prevention programs to target messages more accurately based on individual or group vulnerability markers, ultimately increasing their impact and cost-effectiveness. Combined with improved educational efforts to increase an individual's awareness of his or her personal risk, this preemptive prevention approach could empower people to make decisions that ultimately prevent substance abuse from starting or escalating.

Finally, genetic information can be harnessed for improving relapse prevention by personalizing treatments for optimal benefit. For example, individual differences seen in response to medications for nicotine and alcohol addiction suggest that genetic predictors of treatment response could lead to more efficacious and cost-effective relapse prevention strategies.

Indeed, the information gained from genetics research will lay the foundation for improved and tailored prevention efforts in the future. As genetic markers of substance abuse and addiction vulnerability (or protection) are identified, NIH will encourage researchers to use that information to better understand how biological factors, combined with environmental ones, contribute to abuse vulnerability, thereby enhancing its prevention portfolio. NIH would also encourage the scientific community to use this knowledge to develop and test targeted prevention interventions for populations with differing vulnerabilities to improve our Nation's intervention efforts, similar to the strategy now being used to prevent substance abuse in high sensation-seeking youth.

(2) Provide narrative that examines the FY 2012 actual performance results with the FY 2012 target, as well as prior year actuals. If the performance target was not achieved for FY 2012, the agency should explain why this is the case. If the agency has concluded it is not possible to achieve the established target with available resources, the agency should include recommendations on revising or eliminating the target.

NIDA

The target for FY2012 was met. Multiple genome-wide and targeted association studies have revealed significant associations between nicotine dependence and variants in the CHRNA5-CHRNA3-CHRNB4 (CHRNA5/A3/B4) gene cluster in subjects of European origin, with a recent study also demonstrating such associations among Korean smokers. Recent NIDA-funded studies have further characterized this association, narrowing it to a specific region that is the most likely candidate to alter risk for heavy smoking. A recent meta-analysis of 27 datasets, including those of European, Asian, and African American ancestry (n = 32,587), showed that only rs16969968 was associated with smoking in these three populations and was a marker of a larger "high risk" haplotype (a set of alleles of linked genes). Additional studies have demonstrated novel associations between other gene variants in this cluster with various smoking-related phenotypes, such as nicotine dependence symptoms, nicotine tolerance, smoking initiation, and comorbid conditions (e.g., regular drinking and depression)[1], these vulnerabilities being heightened in early onset smokers.[2] Another study demonstrated that carriers of the high-risk haplotype were three times more likely to respond to smoking cessation

[1] Broms U, Wedenoja J, Largeau MR, Korhonen T, Pitkäniemi J, Keskitalo-Vuokko K, Häppölä A, Heikkilä KH, Heikkilä K, Ripatti S, Sarin AP, Salminen O, Paunio T, Pergadia ML, Madden PA, Kaprio J, Loukola A. Analysis of detailed phenotype profiles reveals CHRNA5-CHRNA3-CHRNB4 gene cluster association with several nicotine dependence traits. Nicotine Tob Res. 2012 Jun; 14(6):720-33. Epub 2012 Jan 12.

[2] Hartz SM et al. Increased Genetic Vulnerability to Smoking at CHRNA5 in Early-Onset Smokers. Arch Gen Psychiatry. 2012 Aug; 69(8):854-861.

medications, making this haplotype of interest for personalized cessation therapies.[3] An editorial on this report adds that the chances of successfully quitting increase two-fold in patients with the high-risk variant if they are treated with nicotine replacement, bupropion, or a combination.[4]

Although these associations and related predictive treatment models show promise, biochemical analyses and further characterization are needed to understand the mechanism of action. To explore the effect of the rs16969968 SNP[5], different variants of the nicotinic α5 receptor subunit were examined in a cell line containing the nicotinic receptor α3α4*complex. One of these variants had a decreased response to nicotinic agonists (chemicals that act on nicotinic receptors) under specific conditions. Such a response points to additional research that must be done to characterize the function of this variant.[6] In other work, virus-induced expression of the α5 subunit risk allele in the medial habenula-interpenduncular nucleus, a brain region associated with nicotine withdrawal, resulted in reduced aversion to nicotine and, consequently, greater consumption of the drug.[7]

Another genetic variant, A118G in the human mu opioid receptor gene (MOR), has been associated with opioid, alcohol, and other drug addictions and with the need for higher morphine doses to achieve adequate analgesia. Recent work using animal- and human-cultured cell lines found that one form of this gene reduced N-linked glycosylation more than the other, which may account for the reduction of the MOR protein in certain brain regions and thus the associations observed.[8, 9] Other work has demonstrated differences between this genetic variants' effects on dopamine release after tobacco smoking, known to be associated with the pleasure a smoker feels.[10] These studies are consistent with literature on the association of MOR A11G with drug

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[3] Chen LS et al. Interplay of Genetic Risk Factors (CHRNA5-CHRNA3-CHRNB4) and Cessation Treatments in Smoking Cessation Success. Am J Psychiatry. 2012 Jul; 169(7):735-742.

[4] Lotrich FE. The Emerging Potential of Pharmacogenetics in Psychiatry. Am J Psychiatry. 2012 Jul;169(7):681-683.

[5] Single Nucleotide Polymorphisms (SNPs): DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered.

[6] Tammimaki A, Herder P, Li P, Esch C, Laughlin JR, Akk G, Stitzel JA. Impact of human D398N single nucleotide polymorphism on intracellular calcium response mediated by α3α4α5 nicotinic acetylcholine receptors. Neuropharmacology. 2012; 63:1002-1011.

[7] Fowler CD and Kenny PJ. Habenular Signaling in Nicotine Reinforcement. Neuropsychopharmacology Reviews. 2012; 37:306-307.

[8] Huang P, Chen C, Mague SD, Blendy JA, Liu-Chen L-Y. A common single nucleotide polymorphism A118G of the mu opioid receptor alters N-glycolsylation and protein stability. Biochem J. 2012; 441:379-386.

[9] Wang YJ, Huang P, Ung A, Blendy JA, Liu-Chen L-Y. Reduced Expression of the mu opioid receptor in some, but not all, brain regions in mice with *Oprm1* A112G. Neuroscience. 2012; 205:178-184.

[10] Domino EF, Evans CL, Ni L, Guthrie SK, Koeppe RA, Zubieta J-K. Tobacco smoking produces greater striatal dopamine release in G-allele carriers with mu opioid receptor A118G polymorphism. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2012; 38:236-240.

abuse and stress, yet continued research is needed to explore the implications of these findings and to link these mechanisms to drug abusing behaviors.

NIAAA

The target for FY2012 was met. Studies with high risk family, twin, and special populations continue to be instrumental in identifying the genetic determinants of alcoholism and other disorders. NIH researchers conducted genetic association studies within these populations and replicated a previously identified genetic association with alcoholism. In addition, NIH researchers conducted studies of signaling pathways in animals that likely contribute to the risk for alcohol dependence and which may reveal additional genomic variants in humans.

For more than two decades NIAAA has supported the Collaborative Studies on Genetics of Alcoholism (COGA), a large-scale national, multi-ethnic, high-risk family study, with the goal of identifying specific genes that can influence a person's likelihood of developing alcoholism. This has resulted in a very rich dataset and repository of phenotypic and neurophysiological data, cell lines, and DNA for current and future studies within COGA. A current focus of COGA is the study of adolescents and young adults from these families, to examine genetic effects across development and to understand the environmental factors that modulate genetic risk in this critical age range. Studies on youth from families with a high density of alcohol dependence will enable researchers to examine how genetic variants identified in one generation influence risk in the next generation and how this risk is influenced by various environmental factors. The research will also further explore if exposure to alcohol during key developmental stages causes epigenetic modifications, defined as changes to DNA structure without changes to the DNA sequence that alter gene expression, which may affect the long-term risk for alcoholism and its sequelae. Analyses will also examine the potential association between these epigenetic changes and patterns of alcohol use initiation.

COGA researchers recently replicated and extended the results of previous association studies in East Asian populations to populations of European and African ancestry. Numerous gene variants have been associated with risk for alcohol dependence in different racial and ethnic populations using genome wide association studies (GWAS) and other approaches. Although many variants identified to date have been associated with increased risk for alcohol dependence and problem drinking, other variants have been associated with protection against alcohol use disorders. A variant in the alcohol dehydrogenase 1B gene, ADH1B-Arg48His, is common in East Asian populations, increases alcohol metabolism leading to elevated acetaldehyde levels and reduces risk for alcohol dependence. Because this variant is uncommon in populations of European or African descent, researchers combined datasets from three large case-control studies that focused on either alcohol dependence, nicotine dependence, or cocaine dependence in order to assess potential protective effects of ADH1B-Arg48His in these populations. Samples from more than 5,600 individuals with and without alcohol dependence were analyzed. The results indicated that ADH1B-Arg48His was significantly associated with reduced risk of alcohol dependence and associated with reduced alcohol consumption in both European Americans and African Americans. In addition to the adult sample described above, ADH1B-Arg48His was analyzed in an independent sample of 2,039 European American adolescents and adults age 12-

25, and was also found to be associated with reduced risk for developing future alcohol dependence in this group. [11]

A related project is integrating the study of twin populations with molecular and developmental approaches to advance our understanding of how genetic and environmental influences on alcohol use and related disorders interact across development. Twin studies are especially useful for characterizing the nature of genetic influences on alcohol use and related disorders and the findings will be used to identify gene associations in other family samples. Community-based samples of individuals studied longitudinally will then enable analysis of how risks associated with specific genes identified in the family samples may change across development and in conjunction with specific environmental factors.

Animal models are valuable for testing the effects and functions of genomic variants identified in human studies. For example, studies suggest that specific genes and their respective signaling pathways may prevent or delay the development of alcohol dependence by counteracting the adverse actions of alcohol and therefore malfunction of such pathways may increase an individual's susceptibility to developing alcohol dependence. For example, research has demonstrated that the bone derived neurotrophic factor (BDNF) pathway in mice has a protective effect against alcohol consumption and a variant in the human BDNF gene both impairs BDNF function and is linked to an increased risk for addiction and other psychiatric disorders. NIAAA supported researchers are currently testing this variant in a mouse model of drinking to determine if it disrupts the normally occurring protective effects of BDNF against the adverse actions of alcohol and thereby confers vulnerability to problem drinking. Other NIAAA-supported researchers are focused on elucidating the roles of neuropeoptide Y (NPY) and corticotrophin releasing factor (CFR) signaling in binge-like ethanol drinking in animals. Interestingly, recent studies have shown that neither of these pathways alters normal ethanol intake in non-alcohol dependent animals but both signaling pathways modulate excessive binge-like consumption in rodents.[12, 13] Studies underway will determine the effect of chronic heavy alcohol exposure on these pathways and how that may influence the transition from binge use to alcohol dependence.

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[11] Bierut LJ, Goate AM, Breslau N, Johnson EO, Bertelsen S, Fox L, Agrawal A, Bucholz KK, Grucza R, Hesselbrock V, Kramer J, Kuperman S, Nurnberger J, Porjesz B, Saccone NL, Schuckit M, Tischfield J, Wang JC, Foroud T, Rice JP, Edenberg HJ. ADH1B is associated with alcohol dependence and alcohol consumption in populations of European and African ancestry. Mol Psychiatry. 2012 Apr;17(4):445-50. doi: 10.1038/mp.2011.124. Epub 2011 Oct 4.
PMID: 21968928
http://www.nature.com/mp/journal/v17/n4/full/mp2011124a.html

[12] Sparrow AM, Lowery-Gionta EG, Pleil KE, Li c, Sprow GM, Cox BR, Rinker JA, Jijon AM, Pena J, Navarro M, Kash TL, and Thiele TE. Central Neuropeoptide Y Modulates Binge-Like Ethanol Drinking in C57BL/6J Mice via Y1 and Y2 Receptors. Neuropsychopharmacology (2012) 1409-1421.
PMID: 22218088
http://www.nature.com/npp/journal/v37/n6/full/npp2011327a.html

[13] Lowery-Gionta EG, Navarro M, Li C, Pleil KE, Rinker JA, Cox BR, Sprow GM, Kash TL and Thiele TE. Corticotropin Releasing Factor Signaling in the Central Amygdala is Recruited during Binge-Like Ethanol Consumption in C57BL/6J Mice. The Journal of Neuroscience (2012) 32(10): 3405-3413 doi 10.1523/JNEUROSCI.6256-11.2012
PMID: 22399763
http://www.jneurosci.org/content/32/10/3405.lon

The findings could potentially lead to the identification of NPY and CFR genomic variants that influence binge-like drinking behavior providing targets for medications development as well as identifying individuals who might benefit from treatment with such medications.

(3) The agency should describe the performance target for FY 2013 and how the agency plans to meet this target. If the target in FY 2012 was not achieved, this explanation should detail how the agency plans to overcome prior year challenges to meet targets in FY 2013.

NIDA

The FY2013 target is to continue to characterize functional genetic variations associated with substance abuse, building on the relationship between tobacco dependence and the nicotinic subunit receptor cluster on chromosome 15 (CHRNA5/A3/B4) and other genetic variations associated with addiction to other substances, such as A118G in MOR. NIDA will continue to support deep sequencing and functional analyses to understand how these genetic variants contribute to various addiction phenotypes.

NIAAA

The performance target for FY 2013 is to complete genome wide association and functional studies and identify potential genomic variants associated with risk for substance use and/or psychiatric disorders. As described above, the ongoing Collaborative Studies on Genetics of Alcoholism (COGA) has a major focus on adolescents and young adults and will use GWAS and other genomic data to identify genes and/or genomic variants that are associated with features of adolescent and young adult drinking behavior and other alcohol-related outcomes. In addition, studies described above will help elucidate how epigenetic changes resulting from alcohol exposure or other environmental factors modulate the expression of specific genes thereby reinforcing heavy drinking and contributing to the development of alcohol dependence.

(4) The agency should describe the procedures used to ensure performance data for this measure are accurate, complete, and unbiased in presentation and substance. The agency should also describe the methodology used to establish targets and actuals, as well as the data source(s) used to collect information.

Data Accuracy, Completeness and Unbiased Presentation

The research field is guided by standard scientific methodologies, policies, and protocols. Any variation from these proven methodologies generates criticism that negates findings. The scientific process also has several benchmarks within it to ensure scientific integrity. For instance, research designs, such as qualitative, quantitative, and mixed methods, have each been tested, with evidence-based strategies established to guide the implementation of all scientific research studies. In these processes, data collection, security, management, and structures are clearly defined to ensure optimum analyses.

Data analyses are guided by statistical methodologies, a mathematical science used to test assumptions. In addition, NIH has incorporated standardized policies and procedures for making

funding announcements, assessing meritorious science, monitoring progress of grantees and scientists in achieving the expected outcomes, and assessing performance at the project's conclusion. Researchers are also expected to publish findings in peer-reviewed journals, which offer another layer of assessment and validation of the findings. In addition, all studies involving human subjects must receive Institutional Review Board (IRB) clearance, yet another form of assessment that ensures the relevance of the study and the safety of the subjects. NIH's research activities implement and practice all scientifically relevant procedures to ensure data quality and to substantiate findings.

In implementing scientific research, NIH uses established tools to develop and oversee programs and improve their performance, proactively monitoring grants, contracts, and cooperative agreements and assessing their performance. The following briefly describes the NIH scientific process, which has been assessed by outside entities and is regarded as premier.

Assessment to fund meritorious science (peer review). NIH uses state-of-the-art assessment to determine scientific merit and make funding decisions based on the best science. In general, project plans presented in competing grant applications and contract proposals are subject to three levels of review focused on the strength and innovation of the proposed research, the qualifications of the investigator(s), and the adequacy of the applicant's resources:

- The first level of review, called peer review, ensures that the most meritorious science, as determined by the scientific field's experts, is identified for funding. The NIH has over 11,000 external experts participating in peer review panels, each of whom is nationally recognized for his or her area of expertise. The applications are systematically reviewed and scored to inform funding decisions. The NIH is one of the few Federal agencies with a legislative requirement for peer review.
- The second level of review is the Institute's National Advisory Council, which is comprised of eminent scientists along with members of the general public. The Council serves as a useful resource to keep each Institute abreast of emerging research needs and opportunities, and to advise the Institute on the overall merit and priority of grant applications in advancing the research. All members of Council are appointed by the HHS Secretary.
- The third level of review is by the Institute Director, with input from Institute staff who have relevant expertise. The Director makes the final decision on whether an application will receive funding.

These layers of expert review assessing scientific methodologies and relevance to the field enable funding of the most promising research to advance the field. Consequently, funding decisions made at the agency level are conducted in a consistent, merit-based fashion, guided by scientific methodologies and relevance.

Performance monitoring of grants and contracts. Once an award is made, additional NIH policies and guidelines are implemented to ensure oversight of the proposed project aims and program goals. The NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps_2003/index.htm) provides the standardized protocols for monitoring performance-based grants and contracts. Although there are many procedures, a

few significant items include the timely submission of progress and final reports. These are assessed by NIH project officers and grants management staff to determine adherence to the approved scientific research plan and to appropriate cost principles and legislative compliance. Project officers may work closely with principle investigators to facilitate adherence, address barriers, and ensure quality programmatic achievements.

As a standard performance-based practice, the approved scientific aims and objectives formulate the terms and conditions of each grant award and become the focus of scientific monitoring. The NIH Grants Policy Statement, referenced as a term of every award, states the specific administrative requirements for project monitoring and enforcement actions when a grantee fails to comply with the terms and conditions of the award. NIH staff monitor scientific progress against the approved aims and scope of the project, as well as administrative and fiscal compliance through review of periodic progress reports, publications, correspondence, conference calls, site visits, expenditure data, audit reports (both annual institutional financial reports and project specific reports), and conference proceedings. When a grantee fails to comply with the terms and conditions of an award, enforcement actions are applied. These may include modification to the terms of award, suspension, withholding support, and termination.

A further checkpoint for programmatic assessment occurs when the applicant requests renewal support of continuation research. A peer review group again assesses the merits of future research plans in light of the progress made during the previous project period, and any problems in grantee performance are addressed and resolved prior to further funding. This process further demonstrates use of assessments to improve performance.

Review of manuscripts. Ultimately, the outcomes of any scientific research are judged based on published results in a peer-reviewed journal. The peer-review publication process is another point in which the quality and innovation of the science undergoes a rigorous evaluation. For most scientific journals, submitted manuscripts are assigned to a staff editor with knowledge of the field discussed in the manuscript. The editor or an editorial board will determine whether the manuscript is of sufficient quality to disseminate for external review and whether it would be of interest to their readership. Research papers that are selected for in-depth review are evaluated by at least two outside referees with knowledge in the relevant field. Papers generally cannot be resubmitted over a disagreement on novelty, interest, or relative merit. If a paper is rejected on the basis of serious reviewer error, the journal may consider a resubmission.

Additional controls specific for genetics projects. For all genetics projects (i.e., both contracts and grants), a three-tier system ensures data accuracy. This system is based on sound, proven scientific methodology internally governed by the larger scientific research community (as described above). First, gene expression levels are validated using highly quantitative methods to measure ribonucleic acid (RNA) levels. Second, each study builds in a replication design using subsets of the study population or, sometimes, different study populations. Third, the information gleaned from these studies is compared against previous animal data or, if not available, replicated and validated in newly generated animal models more suited to evaluate the implications of the genetic findings.

Every effort is made to acquire complete data sets; however, several factors conspire against doing so. These factors are either intrinsic to the type of data being collected (inability to collect from all drug abusers, all ethnic minorities, every developmental stage, every comorbid association, etc.) or linked to the incompleteness of genetic information databases (considerable gaps in SNP[14] collections, many genes yet unidentified or without known function, etc.). Some level of data incompleteness mires all human genomic programs in which population sampling, limited by cost considerations, must be used. These obstacles, however, do not necessarily jeopardize data quality, since many powerful post-hoc standard protocols are available and being deployed to clean the data sets and ensure accuracy and replicability.

Methodology Used to Establish Targets/Actuals

The targets are established based on the state of the science in a particular field and knowledge of the scientific process by which advances are made. For example, NIDA relies on the latest findings of biochemical and other (e.g., neuroimaging) experimental evidence suggesting that a particular gene might be involved in the addiction process and on whole genome association scans, an *unbiased* strategy for identifying genetic variations within large experimental populations, to identify genes that may confer substance abuse vulnerability. Genes putatively associated with addiction are subjected to further characterization and validation, typically through animal models. The targets are established based on where the field stands in this process and on the next logical scientific step for moving the field forward.

Data Sources

As described above, each grantee provides an annual progress report that outlines past-year project accomplishments, including information on patients recruited, providers trained, patents filed, manuscripts published, and other supporting documentation, depending on the goals of the study. This information allows NIH to evaluate progress achieved or to make course corrections as needed.

Decision Unit 1: Treatment

Measure 1: SRO-8.7 By 2015, identify three (3) key factors influencing the scaling up of research-tested interventions across large networks of services systems such as primary care, specialty care and community practice.

[14] Single Nucleotide Polymorphisms (SNPs): DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered.

Table 1: NIDA Annual Targets for Measure 1

FY 2008 Actual	FY 2009 Actual	FY 2010 Actual	FY 2011 Actual	FY 2012 Target	FY 2012 Actual	FY 2013 Target
Identified characteristics of facilities that predicted their use of evidence based programs (EBPs) and which EBPs they used.	12 Research Centers identified a state or local criminal justice partner in preparation for protocol development	Collaborative protocols have been developed to test 2 implementation models in CJ-DATS – MATTICCE and HIV-STIC.	2 studies have been fielded to test 4 implementation strategies for incorporating research-supported treatment interventions in the criminal justice system.	Collect data in 2 studies designed to test 3 implementation strategies for incorporating research-supported treatment interventions in the criminal justice system using collaborative implementation protocols.	All research centers have either begun or completed the implementation protocols for the 2 studies.	NIDA: Continue ongoing data collection in 2 studies designed to test 3 implementation strategies for incorporating research-supported treatment interventions in the criminal justice system using collaborative implementation protocols.

Table 2: NIAAA Annual Targets for Measure 1

FY 2008 Actual	FY 2009 Actual	FY 2010 Actual	FY 2011 Actual	FY 2012 Target	FY 2012 Actual	FY 2013 Target
Recognizing that the primary care and mental health care systems provide an existing structure through which effective treatment could be made available to large numbers of patients with alcohol dependence, NIAAA continues to promote and disseminate the updated Clinician's Guide: Helping Patients Who Drink Too Much. In 2008, NIAAA launched a new, online, interactive companion video training program on Medscape which offers continuing education credits to physicians and nurses.	NIAAA supported studies on strategies for the management of alcohol use disorders in primary care and other healthcare settings.	Products that promote assessing and managing problem drinking in different media formats were refined and/or pursued.	NIAAA has disseminated new multimedia products that promote implementation of screening and brief intervention in primary care and educate the general public about the health effects of alcohol. NIAAA also continued to support research on the implementation of screening and brief intervention in primary care.	Develop strategies for dissemination of the underage drinking screening guide and begin dissemination for use in primary care settings.	NIAAA developed strategies for dissemination of the underage drinking screening guide and began dissemination for use in primary care settings.	Refine the underage drinking screening guide based on feedback from primary care providers and develop strategies to encourage widespread adoption of the guide.

(1) Describe the measure. In doing so, provide an explanation of how the measure (1) reflects the purpose of the program, (2) contributes to the *National Drug Control Strategy*, and (3) is used by management of the program. This description should include sufficient detail to permit non-experts to understand what is being measured and why it is relevant to the agency's drug control activities.

Decades of research have led to today's improved understanding of addiction. Research has shown addiction to be a chronic, relapsing brain disease characterized by compulsive behaviors and caused by a tangle of genetic, social, environmental, and developmental factors. NIH supports multidisciplinary research addressing the myriad factors that can influence the development and progression of substance abuse and addiction, with the goal of informing and improving treatment strategies to facilitate abstinence and prevent relapse.

NIH recognizes that despite major strides in treatment research, only limited improvements have occurred in non-research settings. An unacceptable gap separates scientific discoveries from their integration into community and other practice settings. A scientific approach must be brought to bear on effectively testing and disseminating research-based treatments and understanding how health services systems and settings influence treatment implementation. Ultimately, NIH strives to make research-based treatments user friendly, cost effective, and available to a broad range of practitioners and their patients. NIDA and NIAAA highlight two approaches the NIH is taking to address the gap in implementing interventions in non-research settings (i.e., improving treatment integration in criminal justice and primary care settings).

Criminal Justice Setting

It is estimated that 70–85 percent of State inmates need drug abuse treatment, yet only about 13 percent receive it while incarcerated. About 600,000 inmates per year are released back into the community, often without having received drug abuse treatment in prison or linkage to community-based drug treatment for continuing care. Left untreated, drug-addicted offenders often relapse to drug use and return to criminal behavior. This situation jeopardizes public health and public safety and leads to re-arrest and re-incarceration, which exacerbates already high burdens on the criminal justice system. To better address public health and safety concerns, a treatment model within the criminal justice system is needed that fits the chronic nature of addictive disorders and ensures a continuity of treatment in line with the individual's needs. Such an integrated model should be designed not only to incorporate the best criminal justice practices and therapeutic services but also to use the best organizational practices to deliver them.

NIDA's treatment portfolio not only encompasses the development and testing of medications and behavioral therapies for drug addiction but ensures that effective treatment interventions are used by the communities that need them. In 2002 NIDA established a multisite research cooperative program, the national Criminal Justice Drug Abuse Treatment Studies (CJ-DATS). The CJ-DATS program aligns with NIDA's multi-pronged approach to rapidly move more promising science-based addiction treatments into community settings, to improve existing drug treatment for criminal justice populations and to inform the development of integrated treatment models. Since its inception, CJ-DATS has contributed to a significant body of research to describe existing treatment practices in the criminal justice system and to develop and test the effectiveness of specific interventions. Now in its second phase, CJ-DATS research is focused on the effective implementation and sustainability of improvements in the quality of drug abuse treatment for criminal justice populations.

SRO-8.7 is focused on testing implementation of and quality improvement strategies for effective treatment interventions within the criminal justice system. SRO-8.7 represents NIDA's long-term strategy for improving drug abuse treatment nationwide, thereby contributing to the ***National Drug Control Strategy's Goals of: Integrating Treatment for Substance Use Disorders into Healthcare and Expanding Support for Recovery (Chapter 3) by supporting Seek, Test, and Treat HIV in the Criminal Justice System; and Breaking the Cycle of Drug***

Use, Crime, Delinquency, and Incarceration (Chapter 4) by supporting Innovative Criminal Justice Research Programs.

Primary Care Settings

NIH has a strong focus on preventing and reducing underage drinking, recognizing the pervasive use of alcohol among young people and the association between early initiation of alcohol use and future alcohol problems. A major focus is to integrate screening and brief intervention for youth into primary care. Research shows that while many youth are willing to discuss alcohol use with their doctors when assured of confidentiality, too few clinicians follow professional guidelines to screen their young patients. Clinicians often cite insufficient time, unfamiliarity with screening tools, the need to triage competing problems, and uncertainty about how to manage a positive screen, as barriers to alcohol screening. They therefore miss the opportunity to express concern about early alcohol use, allow their young patients to ask knowledgeable adults about alcohol, and intervene before or after drinking starts, as well as before or after problems develop. In 2011, NIAAA released an alcohol screening guide for health care providers to identify alcohol use and alcohol use disorders in children and adolescents, and to identify risk for alcohol use, especially in younger children. The tools, including a brief two-question screener, tips, and resources, are designed to help surmount common obstacles to youth alcohol screening in primary care.

SRO-8.7 represents NIAAA's long-term strategy for improving alcohol abuse treatment nationwide, thereby contributing to the ***National Drug Control Strategy's Goal of: Seek Early Intervention Opportunities in health Care (Chapter 2)*** **by** ***Evaluating Screening for Substance Use in Healthcare Settings*** **and** ***Enhancing Healthcare Providers' Skills in Screening and Brief Intervention.***

(2) Provide narrative that examines the FY 2012 actual performance results with the FY 2012 target, as well as prior year actuals. If the performance target was not achieved for FY 2012, the agency should explain why this is the case. If the agency has concluded it is not possible to achieve the established target with available resources, the agency should include recommendations on revising or eliminating the target.

NIDA

The FY 2012 target was met. The CJ-DATS research protocols described in the FY 2010 target collected data in two studies in FY 2012.

The *MATICCE (Medication-Assisted Treatment Implementation in Community Correctional Environments)* protocol is testing implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies. Goals are to increase the number of persons in corrections who are linked with medication-assisted treatment (MAT) and to improve community corrections agents' knowledge and perceptions about MAT and their intent to refer appropriate individuals to community-based MAT services. The study randomizes correctional agencies to two implementation strategies: (1) a KPI (Knowledge, Perception, and Information) intervention where correctional staff will be trained

on use of medications in addiction treatment, including the effectiveness of MAT for reducing drug use and crime, for overcoming negative perceptions about MAT, and for providing information about local resources providing MAT; or (2) a KPI+Organizational Linkage (OL) intervention, which engages key representatives from the corrections and treatment agencies in a strategic planning process designed to facilitate interorganizational referral relationships, thereby redistributing offenders from community corrections into community-based treatment.

MATICCE is a collaborative study involving nine academic research centers (RCs), each with two community corrections partner agencies. Within each research center, one agency was randomly assigned to one study condition/implementation strategy. The MATICCE study involves:

- a pilot data collection phase,
- IRB review and approval,
- baseline data collection (surveys and site records),
- training for the KPI intervention,
- randomization to (1) KPI or (2) KPI+ OL condition; and
- for those assigned to KPI+OL,
  - establishing a Pharmacotherapy Exchange Council (PEC),
  - performing linkage assessments,
  - creating a strategic implementation plan to improve linkages,
  - implementing the OL intervention, and
  - collecting data on progress and outcomes.

Progress in fielding the MATICCE study. In FY2012, all nine research centers completed the active implementation protocol—that is, the strategic planning intervention with the PEC. All sites completed the KPI training and collected follow-up data from participants 3 months later. In each experimental site, the PEC has completed all assigned protocol activities: an assessment/walkthrough process to identify agency needs, a collaborative strategic planning process to identify key goals for improving offender referrals, the implementation of activities needed to achieve those goals, the production of written summary reports and sustainability plans, and the disengagement from the research teams as planned. All research centers implemented the same study protocol and associated measures.

The research teams are currently engaged in end-of-intervention and follow-up data collection at all sites. This ongoing data collection includes records abstraction from offender case reports at the end of the intervention and at 6 months post-intervention to determine the extent to which offenders are referred to treatment and gains are sustained over time. Both will be compared to referral rates documented at baseline (collected in FY 2011). Data collection also includes a repeated assessment of staff opinions about MAT, to determine lasting impacts of the KPI training at 12 months post-training; measures of interorganizational relationships, to assess improvements in referral relationships over time from the collaborative strategic planning process; and monthly counts of the number of treatment referrals made by parole/probation officers in each study site.

While the final data collection activities continue, RCs are actively engaged in cleaning and analyzing baseline data. FY 2013 is entirely devoted to final data collection, analysis, and reporting of study findings.

The other protocol, *HIV-STIC (HIV Services and Treatment Implementation in Corrections),* is testing an organizational intervention strategy for more effectively implementing improvements in HIV services for preventing, detecting, and treating HIV in offenders under correctional supervision. The study randomized correctional facilities to one of two conditions: (1) a control arm that receives basic training on the fundamentals of HIV infection, prevention, testing, and treatment, as well as information about the HIV services continuum and its implications or (2) an experimental arm that will implement a process improvement approach to guide a Local Change Team (LCT) through a structured series of steps to improve HIV services. Such models have been found to improve health services implementation in other settings, but have not been tested in correctional settings or with HIV services.

HIV-STIC is a collaborative study involving 9 academic research centers (RCs) and 30 community corrections partner agencies (3 research centers have partnered with 2 community corrections agencies, and 6 research centers have partnered with 4 community corrections agencies). Within each research center, community correction agencies are randomly assigned to one study condition/implementation strategy. The HIV-STIC study involves:

- identifying study sites (participating prisons or jails),
- surveying the facility to determine HIV practices currently used,
- completing an orientation meeting for executive sponsors (who will determine which part(s) of the HIV continuum to focus on),
- completing IRB approvals,
- collecting baseline data (surveys and records),
- conducting baseline HIV training and collecting data associated with it,
- randomizing sites to (1) the baseline training only or (2) baseline training + LCT process improvement,
- training LCTs on process improvement procedures,
- implementing the LCT intervention, and
- collecting process and outcome data over the course of the implementation intervention.

A 9-month follow-up is planned to measure implementation and sustainability outcomes.

Progress in fielding the HIV-STIC study. In FY 2012, all nine research centers began the HIV training and Local Change Team Intervention. In FY 2012, all sites (experimental and control) at all RCs completed baseline data collection, baseline HIV trainings, and site randomization. The experimental sites (those sites implementing HIV training + LCT) at all nine RCs have completed their LCT process improvement training. Three RCs have completed the implementation phase of the intervention. The 9-month LCT implementation phase is in progress at five RCs. One RC is in the planning phase of the intervention. While the final data collection activities continue, all RCs are actively engaged in cleaning and analyzing baseline data. FY 2013 is devoted entirely to final data collection, analysis, and reporting of study findings.

NIAAA

The target for FY 2012 was met. NIAAA developed strategies for dissemination of the underage drinking screening guide and began dissemination for use in primary care settings. In collaboration with the American Academy of Pediatrics, the guide was distributed to the organization's entire membership; a total of 168,494 guides were requested from NIAAA in FY 2012. To encourage use of the guide, NIAAA also began discussions with Medscape about developing an online course to provide continuing medical education (CME) credits for physicians, nurses, and physician assistants. In addition, NIAAA issued a request for research applications to evaluate the guide in practice and funded four of these projects in FY 2012: one in a network of emergency departments, one in a juvenile justice setting, one in primary care, and one with youth who have a chronic condition (e.g. asthma, diabetes). These studies will determine appropriate settings for effective use of the guide and inform dissemination strategies in these settings.

(3) The agency should describe the performance target for FY 2013 and how the agency plans to meet this target. If the target in FY 2012 was not achieved, this explanation should detail how the agency plans to overcome prior year challenges to meet targets in FY 2013.

NIDA

FY 2013 target is to continue field research on the two studies described above so as to test implementation strategies for incorporating research-supported interventions in the criminal justice system. To meet this target, NIDA will continue to support CJ-DATS and its partners as they undertake the next steps towards evaluating and analyzing the data from these protocols designed to facilitate quality improvement strategies for medication-assisted treatment and for HIV prevention, testing, and linkage to care.

NIAAA

To meet the FY 2013 target to refine the underage drinking screening guide based on feedback from primary care providers and develop strategies to encourage widespread adoption of the guide, NIAAA will continue to support studies to evaluate the guide in clinical settings. The brief, two-question screener will be assessed in youth ages 9 to 18: both as a predictor of alcohol risk, alcohol use, and alcohol problems including alcohol use disorders; and as an initial screen for other behavioral health problems (for example, other drug use, smoking, or conduct disorder). These studies will provide feedback to NIAAA that will facilitate refinement of the guide and help identify settings where use of the guide is appropriate and effective thereby informing strategies for more widespread dissemination.

(4) The agency should describe the procedures used to ensure performance data for this measure are accurate, complete, and unbiased in presentation and substance. The agency should also describe the methodology used to establish targets and actuals, as well as the data source(s) used to collect information.

Data Accuracy, Completeness, and Unbiased Presentation

As described above, the research field (including services research) is guided by standard scientific methodologies, policies, and protocols to ensure the validity of its research results. NIH uses established tools for program development; for actively monitoring grants, contracts, and cooperative agreements; and for assessing performance of grants and contracts in order to oversee the program and improve performance. These tools have been described in response to question 4 above.

Additional controls specific for CJ-DATS. CJ-DATS's priority is to study implementation approaches in criminal justice settings to facilitate the translation of evidence-based practices into routine care. Since the priority is collection of scientific data, CJ-DATS follows scientific guidelines and procedures in collecting, verifying, cleaning, analyzing, and reporting data. These procedures ensure that the data meet scientific standards and can reliably and effectively be used to advance NIDA's goal of improving substance abuse treatment. Towards this end, CJ-DATS requires a protocol that describes each study in sufficient detail to dictate what will be done: the major research questions and hypotheses to be tested, a sequence and timeline for planning and implementing the study, a list of instruments to be used, target population characteristics, and proposed sample size.

A thorough process is used to develop CJ-DATS protocols to ensure their capacity to provide valid, reliable, and useful data. Briefly, research concepts are proposed by CJ-DATS Research Centers and submitted to the Research Management (RM) Subcommittee of the Steering Committee (SC) for a critical review of the concept, focusing on scientific and technical issues (e.g., research design, measurement issues, analytic strategies, participation of criminal justice and drug treatment partners, study budget). The RM then makes a recommendation to the SC for approval or for other action related to the final concept. The SC evaluates whether the proposed protocol:

- Is within the scope of the research framework established by NIDA;
- Considers systems-level factors in the criminal justice system and, as appropriate, in the drug abuse treatment system;
- Furthers improvement of the quality of treatment services offered to offenders with substance use disorders during incarceration, during transition from incarceration to community reentry, and after reentering the community;
- Responds to stakeholder needs and priorities, including those of criminal justice administrators and staff, drug abuse, mental health, and primary health care providers, and policy makers;
- Creates generalizable evidence-based practices, processes, and procedures;
- Capitalizes on the CJ-DATS research infrastructure to increase knowledge about effective models of integration with criminal justice, public health and social service, and drug abuse treatment systems; and
- Uses rigorous study designs to yield valid and reliable findings.

Concepts approved by the SC may proceed to protocol development, which is also reviewed by the RM and SC.

For each study protocol, NIDA's CJ-DATS has an extensive process for ensuring the data are collected, verified, cleaned, analyzed, and reported in a systematic and consistent manner. CJ-DATS has a Data Management Committee (DMC) that includes one or more representatives from each Research Center, which develops data collection and processing rules and monitors compliance across all protocols. The CJ-DATS Coordinating Center (CC) implements those rules and works in collaboration with the DMC to ensure quality control in the collection, entry, verification, and documentation of data. NIDA staff actively monitors each study protocol and participate in regular meetings of the DMC and CC. Briefly, the process is as follows:

1. The DMC and CC worked collaboratively to establish overall data tracking, collection, and quality control procedures to ensure the collection of accurate data using reliable and valid measures consistently across all protocols. Any deviations from established data collection/entry protocols must first be approved by the DMC before being implemented.
2. The DMC developed data collection forms recognizable by TeleForm scanners (a commercial Optical Character Recognition software) and created templates for exporting scanned data into the statistical software system. Teleform eliminates the need for most hand-keying of data, thus improving accuracy of data entry.
3. The DMC and CC developed protocols for data quality checks to be followed by each Research Center before scanning data into the TeleForm system. Back-up procedures were developed for forms that could not be successfully scanned for any reason.
4. Research Centers upload new data on a no-less-than monthly basis to a secure online system monitored by the CC. After receiving data uploads from Research Centers, CC staff complete extensive verification procedures to ensure the data's quality. This process includes reviewing automatic alerts generated by the TeleForm software and manually verifying all data fields.
5. CC staff follows set protocols for communicating with personnel at each Research Center to verify and correct any mistakes identified in their manual review of scanned data.
6. After the CC verifies the accuracy of the data and corrects any mistakes, data files are made available to a data analysis subcommittee for each protocol. Each committee is led by an expert in quantitative analysis and includes staff from each RC. This committee reviews each data file in detail and completes a number of sophisticated analyses to check for possible errors (outliers, validation, etc.) that were not identified as part of the manual process described above. Errors, omissions, and other issues are documented for each RC, and corrections are requested within given time parameters.
7. Data files are considered ready for analysis only after the data analysis subcommittee and the CC complete all checks and are confident of the data's integrity. These "locked" files are then uploaded to a secure web-based file system where they are made available for analysis. A separate analytic file request/approval process managed by NIDA staff ensures documentation of the use of each analytic file—by whom and for what purpose. This process avoids duplication of effort and ensures that only the current version of an analytic file is in use, and that the use is appropriate given the measures in the data file.
8. The CC staff has also implemented a comprehensive inventory detailing the status and ultimate disposition of every form distributed to the RCs for data collection. Those data are used to calculate response rates and to ensure that every completed form is included in the analytic files.

In addition to the procedures outlined above, the DMC holds weekly calls to review any problems that emerge as part of this process. Key decisions or changes to procedures are documented and disseminated to the cooperative via the project's secure website. Logs are used to track the transfer of files among analysts.

Data collection is still in progress for CJ-DATS protocols. As analytic work begins in earnest in FY2013, structured procedures will be developed and implemented to ensure accurate calculation and reporting of response rates, consistent use of syntax and documentation for constructed variables, minimum requirements for computed variables (e.g., scale reliabilities and factor weighting), etc.

Methodology Used to Establish Targets/Actuals

The targets to date have been to establish the network and its collaborations, and to develop protocols for implementation. These targets were established based on the initial steps that must be taken prior to conducting a research study. Upcoming targets will be established based on the protocols currently under development. As discussed above, these protocols undergo a rigorous review process to determine which research areas hold the most promise for filling gaps and should therefore be prioritized for testing. The target values will be based on sound methodological procedures and related timelines set for each protocol. While these methodologies cannot precisely predict the course of a study, the likely path of implementation and timing is based on knowledge gained from earlier research and will be used to generate the targets for this measure.

Data Sources

Each site conducting a CJ-DATS study is responsible for the collection, cleaning, and documentation of data in that study. The data must conform to predetermined parameters described in the written protocols that establish how, what, and when the data are collected. The data are then transmitted to the coordinating center, which is responsible for monitoring data files. An Information Management (IM) workgroup provides oversight and direction for data management, cleaning, and archiving of data. The data are stored confidentially and provide the resource for data analysis to determine program success.

ATTACHMENT B

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

DATE: January 11, 2013

TO: Stephen Virbitsky
Regional Inspector General for Audit Services, HHS

FROM: Director, Division of Program Coordination,
Planning, and Strategic Initiatives, NIH

SUBJECT: NIH Review of Draft HHS Office of Inspector General (OIG) Report A-03-13-00354 on NIH's FY 2012 ONDCP Performance Attestations

Thank you for the opportunity to review the HHS OIG Draft Report Regarding NIH's FY 2012 ONDCP Performance Attestations. NIH does not have any comments about the report.

James. M. Anderson, MD, PhD