

# The CFIDS Association of America

*Working to make CFS widely understood, diagnosable, curable and preventable*

## **VIA ELECTRONIC DELIVERY**

June 26, 2009

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ATTENTION ADVOCATES

**Link to Action Alert to write to CDC:**

<http://capwiz.com/cfids/issues/alert/?alertid=13632546&type=CU>

RE: Comments on draft Five-Year CFS Research Plan

Dear Dr. King:

On behalf of the CFIDS Association of America, the largest and most active organization dedicated to solving CFS and the largest source of funding for CFS research outside the federal government, I am writing to provide comments on the proposed Centers for Disease Control and Prevention (CDC) "Five-year strategic research plan for chronic fatigue syndrome (CFS)."<sup>1</sup> Our organization is committed to establishing a new level of partnership with the CDC in advancing an integrated public health strategy for CFS.

We appreciate the opportunity to provide comment and feedback on the research plan presented at the May 27, 2009 meeting of the Department of Health and Human Services (DHHS) CFS Advisory Committee (CFSAC). Because this plan will form the blueprint for CFS research by the nation's public health agency for the next five years and reflects an institutional commitment to invest some \$20 million in research and education related to a condition that affects millions of Americans, we have carefully read and reviewed it, along with other planning and spending documents shared by CDC over the past three years. Our criticisms and recommendations are intended to help produce a refined plan that more appropriately leverages the 25 years of accumulated evidence and investment of more than \$100 million in pursuit of the agency's mission to protect the public health. This document reflects a strong consensus position that has formed and been articulated clearly by diverse members of the

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<sup>1</sup> References to the plan refer to the printed version distributed at the May 27, 2009 meeting of the DHHS CFS Advisory Committee.

external community, including researchers, clinicians, patients, family members and advocates, at the last two public meetings held at CDC and DHHS.

Overall, the draft five-year plan does not appear to make full use of existing knowledge or to appropriately address the community's most urgent needs. The plan is nearly identical to past program plans presented at public meetings, with few significant innovations or serious partnering efforts. Without any indication of relative or absolute priorities, it is impossible to discern which activities will actually be undertaken with available funds since the plan as a whole is not scaled to the program's projected budget. We believe there are several steps which should be immediately taken to ensure that the prior and anticipated taxpayer investments are marshaled toward clear public health program objectives.

### **Summary of Main Concerns**

While the primary goals of the CDC's research plan are laudable, its strategic and tactical plans for making progress toward these goals have failed to garner support or engender confidence in the CFS community. Following is a list of the main concerns about the plan:

1. Lacks meaningful innovation
2. Not actionable with present budget, staff, and leadership
3. Relies on flawed application of research definition ("empiric" definition) and is wholly dependent on just 113 CFS patients identified at baseline of the community-based study of CFS in Georgia
4. Bulk of activities described have already fallen behind previously reported timelines and have exceeded projected budgets, warranting closer examination of management's ability to execute plans
5. Overstates existing collaborations and branch's capacity for establishing and sustaining partnerships
6. Majority of projects are inconsistent with activities conducted in other branches within the division and coordinating center
7. Plan itself is laden with jargon and undefined terms; even the population to be studied is unclear (CFS vs. chronic unwellness)
8. Logic of plan is circular and does not leverage CFS research being conducted outside CDC or assets available within CDC
9. Plan does not clearly communicate priorities, weaknesses or contingencies
10. Threatens progress being made by other investigators in the field

### **Summary of Recommendations**

Despite 25 years of research conducted by the Centers for Infectious Diseases (CCID) at CDC and the profound, documented burden of CFS on the individual and on society, the cause of CFS is not known; there are no objective means of diagnosis and no effective interventions; there is little information on CFS available for providers and the public and there is still considerable stigma associated with CFS. The lack of progress in detection, intervention and control of CFS after 25 years of study is a clear indication of the need for realignment with a CDC center that has the necessary expertise and experience to deal with chronic disease intervention and prevention research. The CFIDS Association of America and the International Association for CFS/ME recommend the following in order to decrease morbidity and disability from CFS:

1. Align the CDC CFS program to ensure that there is the necessary expertise and leadership critical to establishing interventions to detect, control and prevent CFS.
2. Create and make publicly available a comprehensive, subject-oriented data warehouse containing epidemiologic, clinical and laboratory data from CDC supported CFS studies conducted by intramural and extramural scientists since 1984.
3. Support the establishment of a network of collaborative clinical research centers and biodiscovery centers to foster innovative and incisive extramural investigation.

## Explanation of concerns

1. Lacks meaningful innovation: Rather than using this strategic planning process as an opportunity to reconsider traditional paradigms and existing program plans, it appears that the process has been used to more fully document projects that have been presented publicly by branch leadership over the past five years. The plan is almost entirely consistent with program plans presented to the CFSAC at its May 16-17, 2007 meeting<sup>2</sup>. Of all the elements presented, only the concept of introducing intervention studies is new to the program, and those plans are cursory and based entirely on two well-studied therapies, cognitive behavioral therapy and Ampligen<sup>3</sup>. Ampligen has not been approved by the Food and Drug Administration, and it seems unusual for a public health agency to propose studying an intervention that is not available to the public.
2. Not actionable with present budget, staff, leadership: When asked by members of the CFSAC about what financial resources would be required to fully implement this plan, none of the CDC representatives could make an estimate, suggesting that a cost analysis had not been performed to ensure that all proposed projects were possible as presented. In the absence of such a financial representation of the plan, there will likely be choices among which of the proposed activities are implemented over the five-year period. This makes the plan as a whole unactionable, unless there are internal efforts being made to substantially increase the funding level for the program. The current staff of the Chronic Viral Diseases Branch (CVDB) lacks the expertise and experience necessary to capably undertake several aspects of the plan. The plan is devoid of a manpower plan to achieve its outcomes. Foremost among this is the leadership of the program, which has been widely criticized for being insular, narrowly focused and impervious to perspectives external to the group. The information provided to the CFSAC and the stakeholder community for 2005-2008<sup>4</sup> reflects a very different distribution of labor than would be required to implement the five-year plan. This suggests that different personnel will be needed to undertake the planned activities, yet only the addition of a single EIS officer has been included as part of the plan. In particular, there are no statements regarding recruitment of additional expertise needed to carry out the substantial education activities contemplated.
3. Empiric definition foundation: In spite of nearly unanimous objection, the strategic plan outlines studies based on the application of the flawed “empiric” definition<sup>5</sup> and the clinical and laboratory studies utilize the 113 CFS patients identified at baseline of the

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<sup>2</sup> [http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac070516min\\_pdf.pdf](http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac070516min_pdf.pdf), accessed June 17, 2009.

<sup>3</sup> Slide presentation by William C. Reeves, MD., on May 27, 2009 at CFSAC meeting.

<sup>4</sup> Documents from NCVZED

<sup>5</sup> Reeves, WC, et al. Chronic fatigue syndrome—a clinically empirical approach to its definition and study. *BMC Medicine* 2005;3:19.

community-based study of CFS in Georgia (as selected using the empiric definition). The proposed surveillance studies utilize this definition to identify patients for the registry and educational and clinical trials. However, the plan contains no efforts to compare patients selected from other geographic regions or by other methods. Concern about this very limited pool of subjects deepens when reflecting on repeated statements by the branch chief noting that “Georgia may not be representative of the U.S. as a whole” made at meetings of the CFSAC and in other public venues.

4. Activities being continued are behind schedule and conducted at a very high per-subject cost: The plan proposes continuation of the Georgia study, the Georgia registry, the Emory GCRC study and several meetings that have been proposed in the past. Comparison to past program reports and stated timelines reflects considerable delays in getting these activities under way. The baseline Georgia surveillance work was conducted between September 2004 and July 2005. The first follow-up is scheduled to be completed by July or August 2009, 4-5 years after the baseline survey. However, when discussing the Georgia study at the May 2007 CFSAC meeting, Dr. Reeves stated that, “Once you lose the cohort that you have picked up in a population survey and several years lapse, you cannot go back to it.”<sup>6</sup> In contrast, the second follow-up is scheduled to begin within months of the first follow-up study. At the May 2007 meeting, he also stated that the first follow-up would begin in August or September (2007), meaning it is nearly two years behind schedule. There are no contingencies to account for the potential difficulty re-contacting the original cohort at either the first or second follow-up time, in spite of the delays that have occurred.

Concerns raised by the CFIDS Association<sup>7</sup> about the sole-source contracts with Abt Associates and Emory University document that these projects consume a large percentage of the annual budget and have fallen behind schedule. Contracts with Abt Associates conducted between 2005-2008 have consumed \$7.3 million (33%) of total program costs. The in-hospital study being conducted with Emory’s General Clinical Research Center has cost \$5.6 million since 2005 when “protocol development” was the sole task of Emory and Abt contractors<sup>8</sup>. The first subject was enrolled in May 2008, by which time millions had already been obligated for the study. (Dr. Reeves was quoted at the May 2007 CFSAC meeting as projecting the in-hospital study to cost \$1.5-2 million.) The patient registry, which did not begin enrolling patients until September 2008, has already cost \$2.1 million. It will accept referrals for one year and will provide patients with neither diagnosis nor treatment. There have been no reports of how many patients have been enrolled, or what enrollment capacity is, in order to assess the per-subject cost. The proposed international workshop on clinical management has been reported at several past meetings. Now it is stated that it will be held in summer 2009, yet the top clinical researchers in CFS have not been contacted, making it likely that this time estimate will slip again. These budgeting decisions and planning problems deepen concern about the five-year plan as presented, with no cost projections or timelines for management to adhere to.

5. Overstates existing collaborations: We have attempted to independently verify the collaborations reported over the past year by CDC representatives. Investigators with

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<sup>6</sup> [http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac070516min\\_pdf.pdf](http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac070516min_pdf.pdf), accessed June 17, 2009.

<sup>7</sup> Testimony delivered October 28, 2008 available at <http://www.cfids.org/advocacy/testimony-mccleary-oct2008.pdf>

<sup>8</sup> CDC CFSRP Budget Estimate (October 2008) and CDC CFSRP Extramural Budget Estimate History (July 2008)

whom CDC has reported working were consistently surprised to be listed as collaborators, and replied that either their own inquiries had been unanswered or initial interest from CDC was short-lived and not acted upon. The branch has a long history of burning bridges with and otherwise distancing individuals who express differing viewpoints. Only those held in favor are considered as potential collaborators. This past pattern of behavior will make several planned activities very challenging to implement fully in a truly collaborative manner. This issue was raised by the CFSAC at its May 2009 meeting, during discussion of the plan with CDC. Of the 14 activities listed under the “Four Coordinated Complementary Goals” (page 4), six contain the words “collaborative” or “consensus.” Given the lack of success the branch has demonstrated in establishing successful collaborations, Division and/or Center leadership should undertake an independent review of the proposed collaborations to determine their validity, the reported collaborators’ true interest in engaging in work with the branch (under the typical contractual terms used) and branch leadership’s capacity to execute these strategies with success. It has been our own experience that the branch often defines activities that are inconsistent with best practices and prioritizes compliance with failed strategies rather than process innovation. It should be noted that the lack of CDC sponsorship and the notable absence of their CFS research program leadership at the 2009 IACFS/ME international conference in Reno, Nevada was very troubling for this field.

6. Projects are inconsistent with activities conducted in CCID and NCZVED: Two of the four “Public health research goals” (page 3) relate to education and mainstreaming CFS. CCID’s mission is related strictly to infectious diseases. There is not a single reference to CFS as an infectious disease in the five-year plan, and the activities related to the study of infectious agents that may trigger or perpetuate CFS are minimal. NCZVED’s stated purpose is to provide “national and international scientific and programmatic leadership addressing zoonotic, vector-borne, foodborne, waterborne, mycotic, and related infections to identify, investigate, diagnose, treat, and prevent these diseases.”<sup>9</sup> “(NC)ZVED’s vision is to improve health by reducing the impact of infectious diseases using a comprehensive approach focused on the human-animal-environment interface.”<sup>10</sup> It is unclear how the CFS program fits within this context and benefits from inclusion among conditions that have known vectors and control and prevention measures. The outbreak-response capacity in CCID and NCZVED would have been an enormous asset to the study of CFS in the mid-1980s, but now seem to provide little advantage for developing an appropriate public health response to a prevalent, disabling chronic condition of unknown etiology.

The proposed activities related to education and mainstreaming CFS are highly consistent with the stated vision of the National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP): “All people living healthy lives free from the devastation of chronic diseases” and its mission: “To lead efforts that promote health and well-being through prevention and control of chronic diseases. ... Program activities include one or more of our major functions: supporting states’ implementation of public health programs; public health surveillance; translation research; and developing tools and resources for stakeholders at the national, state, and community levels.”<sup>11</sup> These

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<sup>9</sup> <http://www.cdc.gov/about/organization/ccid.htm>, accessed June 17, 2009.

<sup>10</sup> <http://www.cdc.gov/nczved/>, accessed June 17, 2009.

<sup>11</sup> <http://www.cdc.gov/nccdphp/about.htm>, accessed June 17, 2009.

activities bear striking similarity to the goals set in the five-year CFS research plan, yet there has historically been no attempt by the branch to coordinate its efforts with NCCDPHP, and none appear to be planned. The 2007 Blue Ribbon Panel<sup>12</sup> recommended that the branch explore integrating CFS into the National Health and Nutrition Examination Survey (NHANES) as a more effective means of conducting surveillance activities. This recommendation has also been made by the NIH representative at past CFSAC meetings. However, the five-year plan continues to support the limited geographic focus of all past CFS surveillance efforts (San Francisco, Wichita, Georgia) without any means to expand localized findings to national or international patterns. Indeed, the NHANES information pages on the CDC web site<sup>13</sup> address several influences illustrated in the plan's "CFS Interactive Biosystems Model" (page 1) such as genes, diet, nutrition, lifestyle, immune activation and stress. The Public Health Genomics program within NCCDPHP would also offer some important linkages to past and current studies of genetic polymorphisms in CFS, an opportunity within CDC that has again been ignored by the branch in its five-year plan. Another program of tremendous potential housed within the NCCDPHP is the Prevention Research Centers. Its logic model<sup>14</sup> represents a much better approach to the study of CFS than the one presented by CVDB.

7. Plan is laden with jargon and undefined terms: Most strategic plans employ a defined hierarchy of terms such as mission, goal, objective, strategy, outcome and tactic. These terms are employed throughout the five-year plan without any pattern as to hierarchy, making the accountabilities challenging to trace. Page 2 lists "3 coordinated complementary tactical components" of the strategy. Page 4 lists "4 coordinating complementary goals" of the strategy. Neither of these lists is tied back to the "CFS Interactive Biosystems Model" on page 1, which is said to serve as the program strategy. The term "interactive biosystems model" is itself an example of jargon used throughout the plan; it is meaningless on its face and does not relate to other models published in the literature. On page 3, the 25-year history of the program is summarized as, "Program strategy has successfully focused on obtaining baseline information necessary to plan clinical and educational interventions and to quantitatively measure outcomes associated with intervention efforts." This kind of glossy but meaningless language is used throughout the plan to replace direct, clear statements about what is planned for the future. Even the population to be studied is unclear (aside from the aforementioned problems with the empiric definition). According to the CDC's web pages for the patient registry<sup>15</sup>, providers are requested to refer patients with unexplained fatiguing illness of one month or longer. The description of the registry clearly states that patients will not be diagnosed or treated when brought into the clinic; however, the 5-year plan anticipates using these registry patients for intervention trials and other studies. Page 7 refers to "CFS and associated illnesses" without identifying those associated illnesses.
8. Logic of plan is circular and ignores CFS research being conducted outside CDC and assets available within CDC: The logic model on page 3 attempts to construct a logical flow of activity from left to right. Close inspection reveals several basic deficiencies that

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<sup>12</sup> External Blue Ribbon Panel Report, January 30-31, 2007, page 7.

<sup>13</sup> <http://www.cdc.gov/nchs/nhanes.htm>, accessed June 17, 2009.

<sup>14</sup> <http://www.cdc.gov/prc/pdf/PRC-Logic-Model.pdf>, accessed June 18, 2009.

<sup>15</sup> <http://www.fatigueregistry.org/sites/fatigueregistry/default.aspx?pid=711>, accessed June 17, 2009.

are not addressed elsewhere in the plan. The short-term outcomes are identified as being KAB and credibility. There is no description anywhere in the five-year plan of what messages will be provided to whom and by which mechanisms to influence KAB and enhance credibility, yet all the interim outcomes flow from forward-progress on these two short-term outcomes. As indicated earlier, there is no expertise within the group to develop a marketing strategy or marketing materials based on evidence, and the recruitment of such expertise is not identified in spite of its centrality to accomplishing the short-term objectives. Also, the logic model does not directly address the biological issues identified in the interactive biosystems model. There is nothing in the logic model to address the need for more objective means of diagnosing CFS, and no recognition of the dynamic states of KAB and credibility. Much of the community feedback about the CDC's plans reflects beliefs that CDC has diminished the credibility of CFS rather than enhancing it; without addressing and resolving this tension, it is unlikely that the moderators represented in the logic model by "advocacy groups" and "patients" will be anything less than problematic.

Speaking purely theoretically, this plan appears better suited to an independent, privately funded research institution, a "Dharma Initiative"<sup>16</sup> of sorts. It attempts to recreate several frameworks that presently exist within other centers at CDC, ignores the role of other HHS agencies (particularly NIH), and repeats CFS research already conducted and published by academic centers. While its language emphasizes collaboration and partnership, its design reinforces the isolated conduct of one small group of investigators, working at the direction of the branch chief without connection to colleagues inside the agency and at other institutions. The tight focus on patients recruited from the Bibb County/Macon (Georgia) region conversely makes the plan more suitable for a local department of public health than for the nation's public health agency in light of only passing references made to expand activities beyond this small regional population. The plan also ignores emerging trends in public health research already being influenced by health care reform legislation under consideration by Congress.

9. Plan does not clearly communicate priorities, weaknesses or contingencies: It is said, "When everything is important, nothing is important." In 2007, Dr. Reeves reported that, "We can complete the studies that I listed, but there will be insubstantial money to do anything like that in the future."<sup>17</sup> He was referring to the surveillance, registry and in-hospital studies initiated in 2005 which still comprise the core of the five-year plan. According to statements made by CDC representatives in May 2009, the funding level of \$4.3 million allocated in 2007 remains the same today. How then, can leadership expect to initiate other field studies, intervention trials and educational activities with a flat budget? This leads to the fiscal necessity to extend timelines for some activities and abandon others. Without indication of which projects take priority it is impossible to institute any system of performance measures or accountability since the moderator of "funding" excuses any diversion from the plan as written. The near-universal lack of trust and confidence expressed in the branch leadership prohibits leaving this critical element to the program's discretion. Listing vague outcomes is insufficient to overcome

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<sup>16</sup> The Dharma Initiative, also written DHARMA (Department of Heuristics and Research on Material Applications), is a fictional research project conducted on a remote island featured in the ABC television series *Lost*.

<sup>17</sup> [http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac070516min\\_pdf.pdf](http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac070516min_pdf.pdf), accessed June 17, 2009.

concerns about how absolute or relative priorities will be established, how alternative plans will be defined and how weaknesses that emerge will be accommodated.

10. Threatens progress being made by other investigators in the field: All of the preceding objections culminate with this point – CDC’s insularity and lack of cooperation with other CFS researchers (including those whose studies have been funded by NIH) have impeded progress that might have been possible under a more unified approach. CDC has set out to develop its own field through its sole adoption of new research criteria for CFS, pursuing only those studies that reinforce the contributions of early life stress and allostatic load (to the exclusion of other factors identified in its own biosystems model) and planning interventions such as CBT that fit its own perspectives. Asserting this particular viewpoint will do little to advance objective diagnosis and effective treatment since early life stress and allostatic load are common features of many chronic illnesses<sup>18</sup>. Because of CDC’s imprimatur within the scientific community, its choice of this path will prematurely and unjustly chill other paths to identifying biomarkers and reducing morbidity.

### **Explanation of recommendations**

1. Align CDC CFS program with necessary agency leadership and projected resources: It is essential to make these changes in order for the program to be placed on a pathway to deliver meaningful public health benefits. Specifically, we suggest the following activities:
  - a) Incorporate key CFS indicators (e.g., post-exertional relapse) into national surveys (e.g., BRFSS and NHANES);
  - b) Issue a funding opportunity announcement for a CFS Special Interest Project under the Prevention Research Centers program through a competitive, peer-reviewed process; and
  - c) Develop and market educational materials for patients, caregivers and health care professionals about the identification, diagnosis and management of CFS.
2. Leverage unique data assets to support global public health and research efforts: CDC should create a comprehensive, subject-oriented data warehouse containing epidemiologic, clinical and laboratory data from CDC supported CFS studies conducted by intramural and extramural scientists since 1984 to serve as an online, evidence-based CFS data resource available to health professionals, the scientific community and the public at large to develop evidence-based screening approaches for CFS as well as evidence-based research on genetic and environmental risk factors of CFS that would expedite development of objective diagnostic tests to define the spectrum of CFS and improve interventions.
3. Support clinical research network: The CFS community is developing a framework for collaboration among the leading CFS research and clinical sites in the United States. CDC, along with other HHS agencies, should partner with this initiative to foster innovative and incisive investigations that help define the pathophysiology, identify

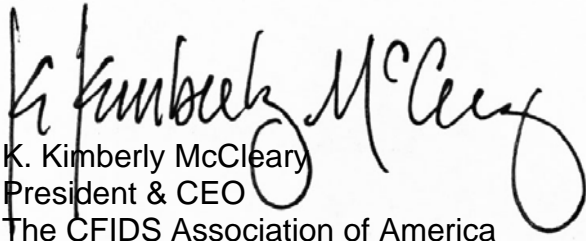
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<sup>18</sup> See “Stress and the Architecture of the Brain” at [http://www.developingchild.net/pubs/persp/Stress\\_Architecture/Stress\\_Architecture.html](http://www.developingchild.net/pubs/persp/Stress_Architecture/Stress_Architecture.html) and proceedings from a November 2007 NIH-sponsored workshop on allostatic load at <http://www.nia.nih.gov/NR/rdonlyres/AF0997F6-0C16-4A76-96C0-D3780F00E6D4/8839/AllostaticLoadBackgroundMaterials.doc>.

biological markers and risk factors, and ultimately to establish curative therapies and prevention strategies for CFS.

In conclusion, we cannot more strongly state our view that implementation of the proposed plan is highly unlikely to yield meaningful advances in reducing the burden of illness posed by CFS. We are committed to working with agency leadership to address these concerns and to seize the very real opportunities that exist for progress through a strategic public health initiative. Thank you for your careful consideration of these views. Please contact me for any further input through the contact listed below.

Sincerely,

A handwritten signature in black ink, reading "K. Kimberly McCleary". The signature is fluid and cursive, with a large loop at the end of the last name.

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