

# Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

## Notice of Decision / Avis de décision

Application Number/Numéro de la demande: 369506

Committee Code/Code du comité: CFS

Applicants/Candidats: Alain Moreau

Institution paid/  
Établissement payé: Hopital Sainte-Justine (Montreal)

Title/Titre: C2ESAME - Network: Canadian Chronic Fatigue Syndrome / Myalgic Encephalomyelitis Network

Primary Inst./

Inst. principal:

Other Related Inst./

Autres inst. connexes:

<b>Competition Outcome/Résultats du concours:</b>	
<b>Number in competition/Nbre de demandes dans le concours:</b>	1
<b>Number approved/Nbre de demandes approuvées:</b>	0

<b>Decision on your application/ Décision sur votre demande:</b>	Not-Approved	Other offer
<b>Average annual amount/ Montant annuel moyen:</b>	\$0	
<b>Equipment amount/ Montant pour les appareils:</b>	\$0	
<b>Term/Durée:</b>	3 yrs/ans	0 months/mois

<b>Peer Review Committee Recommendation, for your information and use/ Recommandation du comité d'examen par les pairs, pour fins d'information et d'utilisation:</b>	
<b>Committee/Comité:</b>	Myalgic Encephalomyelopathy/Chronic Fatigue Syndrome (ME/CFS)
<b>Application rank within the competition/ Rang de la demande dans ce concours:</b>	4
<b>Percent Rank Within the Competition/ Rang en pourcentage au sein du concours:</b>	100.00%
<b>Rating/ Cote:</b>	2.65
<b>Recommended average annual amount/ Montant annuel moyen recommandé:</b>	\$0
<b>Recommended equipment amount/ Montant recommandé pour les appareils:</b>	\$0

<b>Additional Funding Opportunities/ Opportunités de financement additionnelles</b>	<b>Decision/ Décision</b>	<b>Competition Code/ Cote de concours</b>	<b>Application Number/ Numéro de la demande</b>
Myalgic Encephalomyelopathy/Chronic Fatigue Syndrome (ME/CFS)	Not-Approved	201605CFS	369506

\*\*\* Applications receiving a score of less than 3.5 on any evaluation criteria will not be considered for Funding. / Les demandes qui ont reçu une note inférieure à 3.5 pour n'importe quel des critères d'évaluation ne sont pas admissibles.

Institute of Aboriginal Peoples' Health

Institute of Aging

Institute of Cancer Research

Institute of Circulatory and Respiratory Health

Institute of Gender and Health

Institute of Genetics

Institute of Health Services and Policy Research

Institute of Human Development and Child and Youth Health

Institute of Infection and Immunity

Institute of Musculoskeletal Health and Arthritis

Institute of Neurosciences, Mental Health and Addiction

Institute of Nutrition, Metabolism and Diabetes

Institute of Population and Public Health

Institut de la santé des Autochtones

Institut du cancer

Institut des appareils circulatoire et respiratoire

Institut de la santé des femmes et des hommes

Institut de génétique

Institut des services et des politiques de la santé

Institut du vieillissement

Institut du développement et de la santé des enfants et des adolescents

Institut des maladies infectieuses et immunitaires

Institut de l'appareil locomoteur et de l'arthrite

Institut des neurosciences, de la santé mentale et des toxicomanies

Institut de la nutrition, du métabolisme et du diabète

Institut de la santé publique et des populations

Le 29 aout, 2016

Docteur Alain Moreau  
Centre de recherche du CHU Sainte-Justine  
Laboratoire Viscogliosi en génétique moléculaire  
des maladies musculo-squelettiques  
3175 Côte Sainte-Catherine  
Montréal, Québec H3T 1C5

Cher Docteur Moreau,

Merci d'avoir déposé votre demande de subvention : "C2ESAME – Network: Canadian Chronic Fatigue Syndrome/myalgic encephalomyelitis network", dans le cadre du programme de la « Subvention catalyseur : Subvention de réseaux de Réadapt. musculosquelettique et EM ou syndrome de fatigue chronique » avec l'Institut de l'appareil locomoteur et de l'arthrite (IALA) des IRSC.

Nous apprécions énormément tout le travail et l'intérêt que vous avez démontré dans le cadre de cette possibilité de financement; au cours de l'évaluation par les pairs mise en place par les IRSC votre demande a été considérée en lien avec les critères d'évaluation énoncés dans la possibilité de financement et les politiques et procédures afférentes. Malheureusement, votre demande n'a pu se qualifier pour une subvention suite au processus d'évaluation. Nous sommes sincèrement désolés de ce résultat.

Vous trouverez sur RechercheNet les résultats et les documents explicatifs en lien avec l'évaluation de votre demande. Si vous avez une quelconque difficulté à accéder aux documents, le centre de contact des IRSC se fera un plaisir de vous assister. Comme les IRSC ne communiquent qu'avec le candidat principal, nous sollicitons votre collaboration pour aviser vos collègues et leurs institutions respectives du résultat.

Pour toutes questions, vous pouvez communiquer avec le centre de contact des IRSC à l'adresse [support@cihr-irsc.gc.ca](mailto:support@cihr-irsc.gc.ca)

Veuillez agréer nos salutations distinguées,



Nathalie Gendron, PhD  
Gestionnaire, Exécution des concours  
Recherche Priorisé

<b>Review Type/Type d'évaluation:</b>	Committee Member 1/Membre de comité 1
<b>Name of Applicant/Nom du chercheur:</b>	Moreau, Alain
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**Assessment/Évaluation:**

The declared focus of the Canadian Chronic fatiguE Syndrome/myAlgic encephaloMyElitis network is to establish biomarkers of chronic fatigue syndrome (CFS). Specifically: “[The] C2ESAME-Network research priorities will be given to the development of a consensus regarding biomarkers correlated with clear changes in symptomatology and their evaluation in both genders through specific standardized experimental approaches in order to validate their clinical utility.” The Nominated Principle Applicant (Alain Moreau) is an associate professor in the departments of dentistry and biochemistry at the University if Montreal. A PubMed search of “Alain Moreau AND chronic fatigue syndrome” reveals no citations.

The application notes “The disease is challenging because the etiology and pathophysiology are not well understood.”; however, there is no evidence that CFS is a disease. Conditions such as CFS, fibromyalgia, multiple chemical sensitivity, irritable bowel syndrome, etc. are labeled on the basis of excluding known disease and as a group they have been designated as functional somatic syndromes or medically unexplained syndromes.<sup>1,2</sup> There is evidence that suggests labels assigned to medically unexplained syndromes are an artifact of medical specialization.<sup>3</sup> Diagnostic criteria for these syndromes frequently overlap, patients often meet the criteria for multiple syndromes, and similarities in patient characteristics, prognosis and response to treatment are common.<sup>4,5</sup>

Psychosocial factors are strongly associated with the development of CFS. For example, Hatcher and House reported the results of a case control study that found patients with CFS were more likely to experience severe events and difficulties in the 3 months (odds ratio [OR] = 9, 95% confidence interval [CI] 3.2 to 25.1) and year (OR = 4.3, 95% CI 1.8 to 10.2) prior to onset of their illness than population controls.<sup>6</sup> Individuals with CFS have been found to rate themselves higher than controls on the ‘hard-driving’ and ‘many outside interests’ of the Bortner type A personality scale.<sup>7</sup> Individuals with CFS have also been found to adopt confrontational coping styles and to rate themselves highly on an ‘action proneness’ scale.<sup>7,8</sup> CFS has been found to be associated with a Defensive High Anxious coping style,<sup>9</sup> which may directly affect physical well-being through the hypothalamic-pituitary-adrenal (HPA) axis<sup>10</sup>. Another study of 195 individuals diagnosed with CFS found that over 80% satisfied diagnostic criteria for Depression or Generalized Anxiety Disorder,<sup>11</sup> and depression is an established risk factor for development of CFS.

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**Assessment/Évaluation:**

Vercoulen et al. have developed and validated a model to explain the perpetuation of CFS.<sup>12</sup> Their model was able to account for the experience of fatigue amongst CFS sufferers through three factors: [1] focusing on bodily symptoms, [2] low physical activity, and [3] low sense of control. Patients with CFS are more likely than either depressed patients or normal controls to interpret symptoms (characteristic of CFS) in terms of physical illness, and least likely to interpret symptoms in terms of negative emotional states.<sup>13</sup> Attributing symptoms to underlying physical pathology results in low levels of physical activity, which in turn amplifies fatigue severity.

The stated goals of the proposed network are reasonable (i.e. create a research network, standardize care, provide education to researchers and clinicians, and host an annual meeting to develop collaboration); however, the strong focus on undiscovered physical pathology and failure to acknowledge the substantial literature that has established psychosocial factors as both a cause and perpetuating factor for CFS is concerning. Failure to attend to psychiatric co-morbidity can be devastating; individuals labelled with CFS are at higher risk of suicide than matched controls without CFS (age-standardised and sex-standardised mortality ratio = 6.85, 95% CI 2.22-15.98).<sup>14</sup>

The applicants advise that one focus of their educational strategy will be to “feature innovative diagnostic approaches”, but with no details of what such approaches would entail – an important detail given that CFS is a diagnosis of exclusion with no objective pathognomonic features. As noted by the 2016 Alberta TOP Guideline for CFS that the applicants refer to as “the first evidence based Clinical Practice Guideline for ME/CFS in Canada” – “*there is currently no definitive test or validated tool to diagnose ME/CFS*”.<sup>15</sup>

The applicants advise that “the ME/FM Action Network is one of our primary partners.” A review of this organization’s site (<http://www.mefmaction.com/>) reveals a focus on conceptualizing CFS as a physical disease best managed by rest and activity limitation. For example:

1. “[CFS] may result from a combination of factors including genetic predisposition. While it often appears to be triggered by a viral infection, like the flu, there are many other potential triggers including bacteria, parasites, immunization, trauma or environmental toxins... Consider including a naturopathic doctor as part of your health care team.”

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**Assessment/Évaluation:**

2. “Living within your “energy envelope” - the optimal zone of activity - means being as active as you are able without exceeding the limits that trigger your symptoms. Pacing involves careful observation of your energy limits, what time of day you function best, what activities trigger your symptoms.”

3. “Research suggests exercise or physical activity is not tolerated well by those with ME/CFS because the aerobic (long-term) energy system is impaired.”

<http://www.mefmaction.com/images/stories/Resources/ME-InfoSheet.pdf>

4. “Pace your physical and mental activities on the kind of day you're having”

[http://www.mefmaction.com/index.php?option=com\\_content&view=article&id=132&Itemid=139](http://www.mefmaction.com/index.php?option=com_content&view=article&id=132&Itemid=139)

There is no compelling evidence that any infectious agent is a cause of CFS<sup>16-22</sup> (a point highlighted by an article that the applicants have included in their submission: *No Evidence for XMRV Nucleic Acids, Infectious Virus or Anti-XMRV Antibodies in Canadian Patients with Chronic Fatigue Syndrome*), and the association between infection and development of CFS disappears when fatigue and psychological morbidity are adjusted for.<sup>23</sup> Regarding the evidence for optimal treatment of CFS, a 2016 Cochrane review has concluded: “Patients with CFS may generally benefit and feel less fatigued following exercise therapy, and no evidence suggests that exercise therapy may worsen outcomes. A positive effect with respect to sleep, physical function and self-perceived general health has been observed”.<sup>24</sup>

The 2001 Report of the Working Party on CSF/ME to the Chief Medical Officer for England and Wales concluded that graduated exercise therapy (GET) and cognitive behavioral therapy (CBT) were the most promising evidence-based strategies for management of CFS.<sup>25</sup> The report noted that “pacing”, which was advocated by patients’ organizations, was an option for sufferers but that “it has not yet been well defined or evaluated and should also be the subject of research”. This question has now been informed by a

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rigorously-conducted randomized controlled trial of 641 CFS patients that were allocated to receive specialist medical care (SMC) alone or with adaptive pacing therapy (APT), CBT, or GET.<sup>26</sup> This train found that, compared to SMC alone, the addition of CBT and GET produced improvements to physical functioning and fatigue and that pacing was ineffective.

The applicants highlight the 2016 Alberta TOP Guideline for management of CFS/ME, but many of the recommendations do not appear evidence-based, and this is even somewhat acknowledged within the Guideline itself: “Activity management: pacing or graded exercise as appropriate; Symptom self-management (sleep hygiene, active pain management); Nutrition (e.g., treat intolerances, ensure adequately nourished); Cognitive behavioural therapy (CBT) (web-based/in person/telephone options) if mood/anxiety and/or coping issues identified; Complementary alternative medicine (CAM) if helpful and patient preference (no evidence for effectiveness in ME/CFS)”.<sup>15</sup> On review of this Guideline, I cannot determine who was involved (aside from “representatives of family medicine, psychiatry, psychology and patients”), if any conflicts of interest were managed, how they acquired the evidence that was used, or the process used for arriving at recommendations. Accordingly, this document would fail almost all criteria proposed by the Institute of Medicine for Standards for Developing Trustworthy Clinical Practice Guidelines.<sup>27</sup> Dr. Elenanor Stein’s April 2016 newsletter does note that she served as “the content expert on the [guideline] committee” (<http://www.eleanorsteinmd.ca/newsletters/>). This same Guideline lists Dr. Eleanor Stein - one of the Principal Applicants of the current grant proposal – as an additional resource for telephone consultation or for her 10-week patient program.

One specific goal of the application is to validate the Hexoskin, a wearable vest that monitors different body positions (lying, sitting, and standing), walking speed, heart rate, heart rate variation,

heart rate recovery, ECG, breathing rate (RPM), minute ventilation (L/min), activity intensity, peak acceleration, steps, cadence and sleep positions. It is not clear why validating the Hexoskin (i.e. confirming that it is measuring what it says it measures) is important to the management of CFS patients, and I would be cautious of providing real-time feedback of all these measures to a population that is defined by unhelpful vigilance to physical symptoms and somatic attribution.<sup>12</sup>

The network team is comprised of individuals with expertise in immunology, infectious disease,

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hematology, epigenetics, informatics, family medicine, and psychiatry, and includes patient representatives.

This network grant application focusses on an important issue – improved education and research into CFS, and optimizing care of patients with CFS. My concern lies with the lack of details regarding what the applicants refer to as best care for CFS or what their educational program will involve, the very limited attention to the role of psychosocial factors in CFS, reliance on the Alberta CFS Guideline which appears to have serious methodologic limitations, and the apparent strong focus on unidentified physical pathology as causative of CFS.

#### References

1. Barsky AJ, Borus JF. Functional somatic syndromes. *Ann Intern Med.* 1999;130: 10-21.
2. Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet.* 1999; 354: 936-9.
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4. Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities. *Arch Intern Med.* 1994; 154: 2049-53.
5. Aaron LA, Buchwald D. A review of the evidence for overlap among medically unexplained clinical conditions. *Ann Intern Med.* 2001; 134: 868-81.

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**Assessment/Évaluation:**

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[www.topalbertadoctors.org/download/1930/MECFS%20Summary.pdf?\\_20160611123635](http://www.topalbertadoctors.org/download/1930/MECFS%20Summary.pdf?_20160611123635)

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**Assessment/Évaluation:**

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<b>Review Type/Type d'évaluation:</b>	Committee Member 2/Membre de comité 2
<b>Name of Applicant/Nom du chercheur:</b>	Moreau, Alain
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## Assessment/Évaluation:

### 1. Network Vision and Rationale:

The C2ESAME application clearly delineates an achievable vision of strengthening existing Canadian research, clinical care, and education in ME/CFS. Building on the pre-existing registry coordinated by the MF/FM Action Network and creating a research network around the topic of biomarkers addresses one aspect of research in the field of ME/CFS. The focus on standardizing clinical care, enhancing education of ME/CFS, and developing a national meeting would help to achieve their goals of strengthening and harmonizing collaborations in this field.

This Network would be a new network partnering with the National ME/FM Action Network. The emphasis on developing evidence –based best practices, creating educational platforms including national case-based rounds, webinars, and educational portals for providers and family would provide tremendous value to Canadians and the health care community. The collaboration with primary stakeholders, researchers across Canada, and Canadian industry provides additional value to the proposal.

### STRENGTHS:

- Engagment nationally with a broad range of stakeholders
- Comprehensive including education, clinical practice, advocacy, and research collaboration
- Wearable device research has the potential of providing insight into quality of life and additional factors that may be contributing to symptomatology and function ie., sleep quality, vital sign variability, activity

### WEAKNESSES:

- Research focus on biomarkers is likely to provide limited additional value
- Clear description of steps to ensure that education and research remain scientifically sound and evidence-based

### 2. Network Impact and Knowledge Translation:

The C2ESAME application has the potential of making a significant impact on clinical practice and health outcomes in multiple ways. Firstly, by establishing best practice principles, clinical providers in Canada will be able to access up to date education and tools to assist in diagnosis and treatment options. This is especially

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important for this disorder given the lack of knowledge of most clinicians about ME/CFS. An evidence-based work-up protocol and treatment approach will help to ensure that warranted testing is obtained but potentially costly unwarranted testing be minimized. Additionally, avoiding potentially harmful interventions would have a great impact on meaningful outcomes such as quality of life and employment. Secondly, educational platforms will expand the knowledge of practicing clinicians and allied health workers as well as patients, families, care givers, and policy makers. Thirdly, providing opportunity for collaboration, networking, and sharing of research will enhance the national stage in the understanding of ME/CFS and keeping clinical care at the cutting edge. Fourthly, the Network has the potential of doing the same within research regarding biomarkers. This is any area of interest in the study of ME/CFS and a national biobank may help to facilitate research progress in this area. However, restricting to biomarker research is too narrow a focus and it would be recommended to expand the research to include additional research needs.

This application has the advantage of partnering with the pre-existing FM/ME Network and having ME/CFS registries that exist in Canada. They are planning to use the PREMMIUM platform to promote coordination of research and collaboration amongst researchers which may help in establishing partnerships with researchers across Canada. This could also enhance research efficiency if consultants will be available with the PREMMIUM platform to help provide guidance in study design, data collection, and analysis. If the intent is to develop a registry of ongoing research, and data, such a network could potentially facilitate improved dissemination of research findings and potential collaboration for multisite studies. They have focused primarily on biomarker research which is one area but its impact on quality of life for persons with ME/CFS would be quite indirect and current research remains very unclear whether this will add any value to diagnosis or management of individuals with ME/CFS. The application also intends to study the utility of using the health monitoring tool, HEXOSKIN, a wearable device developed by Canadian researchers. Data obtained through these sensors could potentially expand the population of potential participants given the home bound status of so many with this chronic condition. Collaborating and having funding support of HEXOSKIN and PREMMIUM are both positive components of this application. However, they have not described how the wearable vest might be specifically studied and whether data would be transmittable directly to researchers or be used as a feedback device for participants, the later of which may be detrimental.

The application demonstrates the potential for members to achieve greater impact through collaboration by making available the PREMMIUM platform but they haven't delineated specifically how this might be

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**achieved – team based rather than PI based? Data sharing vs funding sharing? Sharing of research resources such as investigational methodology advice, data analysis, etc? Knowing more specifically what the platform offers and who would have access to the platform would strengthen the application.**

**The Network would offer opportunity for education through webinars, web portal, and potentially the annual meeting. However, a mechanism for recruiting and inviting new investigators to collaborate with existing researchers within different research environments and through interactions across the network it not defined. The intent is to invite and fund 60 members to attend an annual meeting however, it is unclear who might be funded for attendance to the annual meeting and the selection process.**

**Although there is the potential of extensive advancement of knowledge translation through the education portals, webinars, and the annual meeting, the application does not discuss ways to recruit and provide support for trainees and junior researchers which is a strong concern.**

### **STRENGTHS:**

- Developing best practices and educational opportunities will have the potential of significantly impacting clinical care and outcomes for patients who often feel misunderstood and ostracized
- Partnering with key stakeholders nationally
- Using the FM/ME Action Network as a foundation with a pre-existing registry and including a patient advocacy contingent in the Network
- Making use of the PREMMIUM platform

### **WEAKNESSES:**

- There is not clear description of how the Network will ensure that the best practices are evidence-based and scientifically sound
- Given that a significant proportion of the budget will be spent for the annual meeting (25% of total budget, 45% of CIHR funding), the planning committee's roles, responsibilities, and accountability should be clearly described, and the selection process for attendees should be defined.
- What the PREMMIUM platform has to offer and how it will be used and by whom is not fully defined
- Lack of opportunity and support for trainees and junior investigators

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#### 3. Feasibility:

The application has a broad range of Canadian researchers, clinicians, and other stakeholders engaged in ME/CFS research or care. The plan proposed seems reasonable for both development and implementation. The investigators have secured support and funding from outside sources to help achieve their objectives which should help with engagement, ownership, and sustainability. However, using 25% of their total budget (45% of CIHR funding) to bring together 60 selected individuals (selection criteria not defined and selection panel not identified) for a 2 day meeting in Toronto each of 3 years may work against them for sustaining the Network.

The Network has multiple ways in which it is designed to link members to accomplish the proposed project including: an annual meeting for networking opportunity, task forces to oversee each of the primary goals (research, clinical care, education, and advocacy), biological repository, international collaboration, partnership with the ME/FM Action Network, and partnership with industry. However, interim deliverables and outcomes for success have not been described.

#### STRENGTHS:

- Engagement and funding support from key stakeholders should help with sustainability given ownership and vested interest in its success
- Building upon the pre-existing ME/FM Action Network

#### WEAKNESSES:

- Plans for sustainability are not addressed by the application
- Interim evaluation of success with clear outcomes are lacking
- Large proportion of budget is to invite 60 individuals to an annual meeting for which the selection process has not been described

#### 4. Network Management:

The Network structure, governance, leadership, and administrative oversight is generally outlined. It appears appropriate for the proposed project but lacks detail. For instance, it does not describe how the PREMMIUM platform

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for data management is part of the Network structure and how it will be managed. The structure includes 4 task forces that will have oversight for each of the key objectives but the composition of these task forces is not described. The application would be strengthened if specific outcomes and time frames for completion are described, as well as plans for interim evaluations, analyses, and remedial plans if objectives aren't being met.

The Network would include extensive involvement of all levels of stakeholders across Canada. Having secured significant funding support to supplement the CIHR funding should help to retain engagement and to promote ownership and accountability.

The Network appears to be widely open to clinicians, researchers, and advocates although it does not indicate plans for recruitment or for the process of selection of the '60' invited members to the annual meeting and does not have plans for recruiting trainees and junior investigators. Strategies for internal and external communication have not been described.

A Governance Administration Committee will be tasked with the financial and administrative oversight. The Nominated Principal Investigator (Dr. Moreau), the President of the National ME/FM Action Network and the delegated administrator of Sibylla-Hesse Foundation will be permanent members of the committee. Delegated signing authority and accountability for all financial transactions and accounts will reside with the Nominated Principal Investigator and will be countersigned by the CEO of Sainte-Justine University Hospital (CHU Sainte-Justine).

The investigators have not detailed anticipated challenges with their approach nor considered alternatives.

**STRENGTHS:**

- Overall structure with task forces overseeing the 4 branches of the Network and a Governance Administration Committee to provide financial and administration oversight
- Extensive involvement by key stakeholders across Canada

**WEAKNESSES:**

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- Overall composition of task forces has not been described
- Membership eligibility has not been described
- Attendance at the annual meeting is a key component to the Network but objectives of the meeting, outcomes to achieve, and attendance inclusion has not been described
- The operational plan is described only in generalizations without clear descriptions of interim/annual goals, anticipated challenges, and strategies for managing alternative results
- Communication plans both internally and externally are unclear
- Interim outcomes for evaluation and plans to address challenges have not been discussed

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The committee's main concern with this application was that the focus on biomarkers (vs. psychosocial and non-biomarker influences) might produce information with limited value in terms of its impact on outcomes and care. The committee also would have valued more discussion about the literature, which has previously tried to explore many of the larger questions that the network is focusing on. In particular, describing how the previous literature helps or falls short in addressing important CFS issues would greatly strengthen the rationale for this proposal.

The committee also discussed other proposal areas where more information and details were needed. For example, the guidelines which this proposal mentions frequently need much more description (see for example, the IOM criteria for evaluating guidelines). The expected or demonstrated impact of the Hexoskin on a group which has been characterized as highly sensitive to somatic symptoms needs more explanation. The large amount of resources devoted to the annual meetings (and therefore not available for other network activities) was a concern as well as the need for a more complete evaluation plan. The training plan would also benefit from a more complete description.

Strengths noted by the committee included the use of an existing registry which supports a more focused approach to CFS, partnering with an existing international action-related network, the focus on standardizing care, creating a research base to support the development of evidence-based practice, and the national engagement with a broad range of stakeholders.

More attention to these committee concerns would benefit this application.