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John Howard, MD
Administrator, World Trade Center Health Program
Centers for Disease Control and Prevention (CDC)
National Institute for Occupational Safety and Health (NIOSH)
395 E. St, S.W.
Suite 9200
Patriots Plaza
Washington, D.C. 20201

Dear Dr. Howard:

I am writing in response to your request for the WTCHP STAC to review of substantive changes to *WTC Health Program Policy and Procedures for Adding Non-Cancer Health Conditions to the List of WTC-Related Health Conditions* and the specific charge to address two questions:

1. Does the revised language under Section IV.B. adequately clarify the five weight-of-evidence categories used for grading a causal association by the Science Team: (i.e., substantial likelihood, high likelihood, limited or inadequate likelihood; and no likelihood)?

2. Are the evaluation criteria established for each weight-of-evidence category clearly defined, reasonable, and appropriately linked to an action?

In this letter I will provide the four STAC recommendations approved by vote and the rationale for each.

Recommendation 1: In the Policy & Procedure for adding non-cancer conditions, with respect to the consideration of health conditions for which a high or limited likelihood of causal association is being assessed, the Science Team consider studies that go beyond peer-reviewed and published epidemiologic studies of 9/11-exposed populations and US Government authoritative scientific publications, to the extent feasible. This is to include peer-reviewed clinical, mechanistic, toxicologic, biomedical, and mental health literature that are relevant to the 9/11 exposures.

Rationale: The STAC has previously expressed concern with the restriction of the second-level review to US Government authoritative scientific publications. These documents are produced at different times for different reasons by various agencies and may have significant gaps when used as the only source to evaluate relationships between 9/11 agents and specific health conditions. There are over 300 recognized 9/11 agents, and it seems like a reasonable first step for the second-level review would be to find one or more sources, such as the IARC Monographs and the NTP Review on Carcinogens, to identify 9/11 agents which have been associated with the condition in humans for more detailed review. However, for many non-cancer conditions, there may be no government document, such as the NTP Review on Carcinogens, to identify relevant 9/11 agents. In such cases, it would be reasonable to utilize relevant chapters in occupational and environmental medicine textbooks and review articles for this purpose. The

STAC believes that the Science team should have discretion to use tools such as PubMed and the broader scientific literature, as is conventional in public health and medicine, to narrow and deepen the scope of their review as appropriate for each condition and relevant agents. The STAC does not disagree with using government documents, when available, as a primary source of systematic evidence for agents and health conditions of concern, but believes that the Science Team should have reasonable discretion to supplement this information as needed; for example, to update the literature review if there is a time lag between the publication date of the government publication and the review or to refer to mechanistic and toxicological studies that the support human epidemiologic evidence for a causal association. The STAC believes that this broader discretion is important in providing a strong scientific evidence basis for any proposal to add a health condition to the List of WTC-related conditions that will withstand a rigorous scientific peer review.

Recommendation 2: In IV.B.1.a. revise the highlighted phrase in the first sentence from "*Substantial likelihood of causal association* means that "the scientific evidence demonstrates that a causal association exists" to "the association is strongly supported by peer-reviewed evidence in 9/11-exposed populations" and there is high confidence that the association cannot be explained by chance, bias, confounding, or any other alternative explanation."

Rationale: Several STAC members found the differences between "substantial likelihood" and "high likelihood" categories to be difficult to remember, in part because the common language distinction between these terms is not clearcut. In reading through the document, the STAC noted that the most prominent distinction between the two categories in the initial evaluation is that the evidence supporting "substantial likelihood" is restricted only to epidemiological studies in 9/11 populations, so suggested that this difference be highlighted early in the definition.

Recommendation 3: The Committee recommends that the Program develop and add to the Policy and Procedures a table that clearly delineates the categories that will be used at various stages of the review process.

Rationale: Some of the discussion at the STAC meeting revolved around differing interpretations of the text in different parts of the document. Since clarity to the reader is so important, it would be very helpful to augment the text with a flowchart to illustrate the steps in the deliberation process and a table that helps to delineate the definitions used for the various categories of evidence.

Motion 4: The Committee endorses the use of five weight-of-evidence categories, and recommends that these five mutually exclusive categories be maintained in all sections of the Policy and Procedures, as appropriate.

Rationale: The STAC noted that the document is inconsistent in referring to four or five levels of evidence. In some sections the limited or inadequate likelihood categories are combined and in others they are distinct. The STAC believes that that there is an important distinction between limited and inadequate evidence (see, for example, the definition of these terms in the IARC Monographs preamble) and these should be maintained as separate weight-of-evidence categories throughout the document.

The STAC appreciates the dedicated work of the Science Team and Administrator to develop and clarify the weight-of-evidence categories and thresholds for Administrator actions in the *WTC Health Program Policy and Procedures for Adding Non-Cancer Health Conditions to the List of WTC-Related Health Conditions* and the opportunity to provide input to the program on this important document.

Sincerely,

Elizabeth Ward

Elizabeth Ward, PhD

Chair, World Trade Center Health Program Scientific and Technical Advisory Committee