Policy and Procedures for Adding Non-Cancer Health Conditions to the List of WTC-Related Health Conditions

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***Note for May 1, 2019 Update*:** This version incorporates non-substantive changes to update the definition of "9/11 agents" and describe the Inventory of 9/11 agents as established in the "Development of the Inventory of 9/11 Agents," published July 17, 2018.

Note for September 11, 2019 Update: This version incorporates non-substantive changes to describe the process by which the Science Team evaluates the quality of scientific evidence, adds descriptions of the select Bradford Hill criteria used by the Science Team to evaluate causality, and provides an additional bibliographic reference.

Note for July 5, 2023 Revision: This version has been revised to include the following substantive and non-substantive changes: reorganization of the methodology to better reflect the chronology of the procedures; clarification of the five categories of likelihood of causal association and the evaluation criteria used to assess each; additional descriptions of the Bradford Hill criteria used in the Science Team's evaluation; revision of the discretionary secondary evaluation procedures to allow a supplemental review of highly-relevant, peer-reviewed, published scientific information regarding 9/11 agents in non-9/11 exposures; and further explanation of the nature of the rationale that provides the basis for the WTC Health Program Scientific/Technical Advisory Committee (STAC) recommendations. As directed by the Zadroga Act, these revisions were presented to the WTC Health Program STAC for review.

Note for August XX, 2024 Update: This version incorporates non-substantive changes to add a definitions subsection to Section I made up of terms previously introduced in other WTC Health Program documents or in footnotes in previous versions of the *Policy and Procedures*. A new subsection IV.A.C. is added to clarify that the Science Team revisits limitations in assessing the weight of the evidence during their evaluation of the evidence in identified high-quality studies. It also provides additional information on how the literature search is conducted based on

information previously published in *Federal Register* Notices for individual petition evaluations and makes other language revisions to clarify the process applied by the Science Team.

TABLE OF CONTENTS

I. Introduction

A. Authority

The *Policy and Procedures for Adding Non-Cancer Health Conditions to the List of WTC-Related Health Conditions* is based on the James Zadroga 9/11 Health and Compensation Act of 2010 ("Act")[1] and the World Trade Center (WTC) Health Program regulations.[2]

B. Definitions

- **9/11 agents** means chemical, physical, biological, or other hazards reported in a published, peer-reviewed exposure assessment study of responders, recovery workers, or survivors who were present in the New York City disaster area, or at the Pentagon site, or the Shanksville, Pennsylvania site, as those locations are defined in 42 C.F.R. § 88.1, as well as those hazards not identified in a published, peer-reviewed exposure assessment study, but which are reasonably assumed to have been present at any of the three sites. Known 9/11 agents are established in the WTC Health Program's *Development of the Inventory of 9/11 Agents*.[3]

- **9/11 exposure** refers to those hazards to which responders, recovery workers, and survivors may have been exposed but which may not have been identified or measured at one of the 9/11 disaster areas. The WTC Health Program considers 9/11 agents to be a subset of 9/11 exposures and has published an inventory of recognized 9/11 agents.[4]

- **9/11-exposed population** means, for the purposes of this *Policy and Procedures*, those persons who can be reasonably assumed to have been exposed to hazards resulting from the September 11, 2001, terrorist attacks, including those 9/11

[1] Title I of Pub. L. 111-347, as amended by Pub. L. 114-113, Pub. L. 116-59, Pub. L. 117-328, and Pub. L. 118-31, codified at 42 U.S.C. § 300mm *et seq*.
[2] 42 C.F.R. Part 88.
[3] *See* WTC Health Program, published July 17, 2018, available at: https://www.cdc.gov/wtc/pdfs/research/Development_of_the_Inventory_of_9-11_Agents_20180717.pdf.
[4] *See supra* note 3.

agents identified in the Program's *Development of the Inventory of 9/11 Agents*, within the geographic areas identified in the WTC Health Program's eligibility criteria; such populations may include, but are not limited to, WTC Health Program members.

- **Causal association** means, for purposes of this *Policy and Procedures*, a causal discovery based principally on measures of association in high-quality epidemiologic studies. A causal association asserts a causal relationship between exposure and the health condition, and is interpreted by using qualitative evaluation criteria, such as strength, consistency, temporality, biological gradient, plausibility, and coherence of the observed measures of association.[5]

- **Hazard** means a chemical, physical, or biological agent, or an experience that may cause psychological harm.[6]

- **High-quality study** means, for purposes of this *Policy and Procedures*, those studies within the identified peer-reviewed, published, epidemiologic studies[7] of the health condition of interest in the 9/11-exposed population that the Science Team has determined are informative regarding the causal association between 9/11 exposure and the health condition of interest and of appropriate study quality based on an assessment of validity indicators to merit further evaluation.

- **List of WTC-Related Health Conditions (List)** means those conditions eligible for coverage in the WTC Health Program as identified in 42 C.F.R. § 88.15.

II. Initiation of the Process for Adding a Health Condition

A health condition may only be added to the List of WTC-Related Health Conditions (List) by rulemaking.[8] The Act provides two pathways to initiate the process of deciding whether to propose adding a health condition to the List—at the discretion of the Administrator or upon receipt of a petition from an interested party[9] requesting the addition.

A. Administrator's Discretion

The Administrator of the WTC Health Program may initiate the process of promulgating a proposed rule to add a health condition to the List at the

[5] *See generally* description of "associative causation," NIOSH [2020]. *Current Intelligence Bulletin 69: NIOSH Practices in Occupational Risk,* published at: https://www.cdc.gov/niosh/docs/2020-106/pdfs/2020-106revised032020.pdf?id=10.26616/NIOSHPUB2020106.
[6] *See generally supra* note 3.
[7] Epidemiologic studies include descriptive epidemiologic studies which describe the "what, who, where, when and why/how of a situation," as well as analytic epidemiologic studies which involve the use of a comparison group. *See* NIOSH [2020], *supra* note 5.
[8] *See generally* 42 U.S.C. § 300mm-22(a)(6); 42 C.F.R. § 88.16; the complete List is promulgated at 42 C.F.R. § 88.15.
[9] 42 U.S.C. § 300mm-22(a)(6)(E); 42 C.F.R. § 88.1 (an interested party is a representative of any organization representing WTC responders, a nationally recognized medical association, a WTC Health Program CCE or Data Center, a State or political subdivision, or any other interested person).

Administrator's discretion.[10]

B. Petition Request

Upon receipt of a valid petition[11] requesting that a health condition be added to the List, the Administrator of the WTC Health Program must initiate the process of evaluating whether to add the health condition to the List and take one of the following four actions within 90 days of receipt of the valid petition:[12]

- Engage the WTC Health Program Scientific/Technical Advisory Committee (STAC) (*see* Section VII.)
- Publish a Notice of Proposed Rulemaking (NPRM) to Add the Health Condition (*see* Section IX.)
- Publish a Notice of Insufficient Evidence (*see* Section IX.)
- Publish a Notice of Determination Not to Propose a Rule to Add a Condition (*see* Section IX.)

III. Science Team Identification of Evidence

A. Petition Review and Identification of Health Condition for Evaluation

Upon direction by the Administrator, the WTC Health Program's Science Team will review the information provided by the petitioner, including the medical basis, to determine the specific health condition that will be the subject of the scientific evaluation.[13]

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[10] 42 U.S.C. § 300mm-22(a)(6)(A).
[11] When the Administrator receives a written submission from an interested party to add a health condition to the List, the Administrator follows the steps outlined in *Policy and Procedures for Handling Submissions and Petitions to Add a Health Condition to the List of WTC-Related Health Conditions* (available at http://www.cdc.gov/wtc/policies.html) and determines whether the submission meets the requirements for a valid petition specified in 42 C.F.R. § 88.16(a)(1).
[12] 42 U.S.C. § 300mm-22(a)(6); 42 C.F.R. § 88.16(a)(2).
[13] For more information, see the Program's *Policy and Procedures for Handling Submissions and Petitions to Add a Health Condition to the List of WTC-Related Health Conditions* (available at http://www.cdc.gov/wtc/policies.html).

B. Identification of Studies of the Health Condition in 9/11-Exposed Populations

Once the health condition being evaluated is identified, the Administrator of the WTC Health Program will direct the Science Team to conduct a search of the scientific literature to identify all peer-reviewed,[14] published,[15] epidemiologic studies[16] of the health condition among 9/11-exposed populations. The literature search is conducted among relevant databases;[17] the Science Team uses professional judgment to identify key words to be searched in the databases, including but not limited to the health condition being evaluated.

The Science Team conducts an initial review of each reference located ~~identified~~ by the literature search to determine if it identifies any causal association(s) between 9/11 exposure(s) and health outcomes with the potential to provide a basis for deciding whether to propose adding the health condition to the List.

C. Evaluation of Quality of Scientific Evidence in Identified Studies

The Science Team will summarize each identified study that has the potential to provide a basis for a decision on whether to propose the addition of the condition based on observed causal associations of interest and evaluate each study for scientific quality. A high-quality study[18] will demonstrate that potential by exhibiting sufficient validity[19] indicators including, but not limited to, the following:[20]

- Possible confounders are identified and adequately addressed;
- Recruitment bias is adequately addressed;
- Exposures are reasonably assessed using methods that are reliable and reasonably reduce the potential for bias.
- A control group is used to compare exposures, and inadequacies of the

[14] The Administrator has determined that articles and reports published in CDC's *Morbidity and Mortality Weekly Report* (MMWR) are also eligible for review for their potential to provide a basis for deciding whether to propose adding a condition to the List. MMWR publications undergo a review process that has been independently evaluated and found to be similar or equivalent to peer review.
[15] Published studies also include those published online ahead of print.
[16] *See supra* note 7.
[17] Examples of relevant databases include the following: CINAHL, Embase, NIOSHTIC–2, ProQuest Health & Safety, PsycINFO, Ovid MEDLINE, Scopus, Toxicology Abstracts/ TOXLINE, and WTC Health Program Bibliographic Database.
[18] Studies of low-quality design are unable to be evaluated pursuant to the criteria described in Sec. IV. ~~Studies that do not fully meet the threshold to be identified as high-quality may be considered at the Science Team's discretion.~~
[19] "Validity is the quality of being logically or factually sound; the extent to which a measure describes that which is being measured; and the degree to which inferences drawn are valid." *See* NIOSH [2020], *supra* note 6 at 152.
[20] All of the indicators are aspects of study design.

control population(s) are addressed;

- Results are not selectively reported and there is no evidence of a strong bias that may fully explain the results; and

- Any conflicts of interest are identified and reported.

D. Study Quality Evaluation Outcomes

1. If the Science Team determines that any of the studies identified in the literature review are of high-quality, those studies will be reviewed pursuant to the criteria described in Section IV.A.

2. If the Science Team determines that none of the studies identified in the literature review are of high-quality, the Science Team will find that there is inadequate evidence to determine a causal association, pursuant to Section V.E.

IV. Science Team Evaluation of Evidence

A. Evaluation of Evidence in High-Quality, Peer-Reviewed, Published, Epidemiologic Studies of the Health Condition in 9/11-Exposed Populations

Studies identified as high-quality, as described above in Section III.D.1., will be further evaluated by the Science Team to determine if they provide a basis to support an addition to the List.

The Science Team will evaluate the information from the studies, individually and together, to characterize the evidence of a causal association between 9/11 exposures and the health condition. Upon evaluating the evidence, the Science Team will assign its findings regarding causal association to one of five categories, as described in Section V.~~: (1) substantial likelihood of causal association, (2) high likelihood of causal association, (3) limited likelihood of causal association, (4) no likelihood of causal association, and (5) inadequate evidence to determine the likelihood of causal association.~~

The scientific evidence evaluation will include consideration of the following:

1. Bradford Hill Criteria

The Science Team will utilize Bradford Hill criteria[21] to describe and evaluate the evidence across the high-quality epidemiologic studies:[22]

- Strength of the association between a 9/11 exposure and the health condition under consideration[23] and precision of the risk estimate;[24]
- Consistency of the association across multiple studies;[25]
- Specificity observed in the cause and effect; [26]
- Temporality of the cause and effect; [27]

[21] NIOSH typically evaluates observed associations against multiple factors to assess weight of evidence. One leading weight of evidence framework is known as the "Bradford Hill criteria," which comprises nine aspects of association. These aspects comprise strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy. *See* NIOSH [2020]*, supra* note 5 at 17–19. The criterion "experiment" refers to evidence from a successful intervention; that is, removing the cause results in removing or reducing its effects. Given that exposure to 9/11 agents cannot be controlled by intervention in human studies, experiment is not applicable to Science Team evaluations and has not been included in the criteria listed in the text. Evaluation of injury studies does not utilize the Bradford Hill criteria; such studies are instead evaluated for onsite occurrence, presence of known causative factors, and quality. *See generally* Baker SP, O'Neill, Ginsburg MJ, and Guohua L, [1992], *The Injury Fact Book* 2nd ed. New York: Oxford University Press (regarding causation); *see also* National Academies Press [1985], *Injury in America: A Continuing public health problem.* Injury studies that provide information about injuries recorded in contemporaneous medical records and studies and which when combined with known hazards and known connections between those hazards and injury may demonstrate concordance of an injury and 9/11 exposures, allow the Administrator to evaluate whether there is support for a causal association between those exposures and the injury.

[22] The last three Bradford Hill criteria, biological plausibility, coherence, and analogy, require reasonable knowledge of the biology of the health condition being evaluated as well as facts about disease etiology and potential established direct or analogous causal relationships. To establish such a scientific baseline for comparison, the Science Team may exercise professional judgment to refer to additional information from biologic, toxicologic, and epidemiologic research beyond the identified high-quality studies of the health condition in a 9/11-exposed population. Additional studies, including those outside of the 9/11-exposed population, may be identified from references cited in the high-quality studies or medical basis, or from a limited review of the literature to assess biologic plausibility, coherence, and analogy.

[23] It is generally thought that strong associations are more likely to be causal than weak associations; however, a weak association does not rule out a causal relationship. *See* NIOSH [2020]*, supra* note 5.

[24] Precision of the risk estimate describes the random error ("chance") inherent in estimating the strength of association (the effect size) between exposure and the health condition. It is often expressed as a confidence interval illustrating a range of plausible values of the effect estimate given sampling error. A narrow confidence interval indicates a more precise measure of the effect and a wider interval indicates greater uncertainty. While precision is not a Bradford Hill criterion, the Science Team takes it into consideration to evaluate the extent of random error in study estimates. *See* NIOSH [2020]*, supra* note 5.

[25] Consistent findings are demonstrated when they have been repeatedly reported by multiple studies. *See* NIOSH [2020]*, supra* note 5. When assessing consistency, the Science Team also considers differences in study quality that could explain inconsistent study findings. If only a single study is available for evaluation, the Science Team will place more emphasis on evaluating the strength of the association and precision of the risk estimate.

[26] Specificity is the premise that an association is more likely to be causal if it is observed between one cause and one effect. In practice, epidemiologic examinations of health conditions in the 9/11-exposed population involve complex exposures to multiple 9/11 agents suspected of causing multifactorial diseases; therefore, specificity has a limited role in Science Team evaluations.

[27] Temporality is the condition that the 9/11 exposure must precede the health condition of interest and is typically assessed when considering aspects of exposure in the study design (*see* Section III.C.).

- Biological gradient, or exposure-response, relationships between 9/11 exposures and the health condition under consideration;[28]

- Biological plausibility of the studies with known facts about the biology of the health condition under consideration;[29]

- Coherence between a causal association and known disease etiology;[30] and

- Analogy with an established causal relationship.[31]

2. Representativeness Assessment

The Science Team will assess whether the studies, taken together, represent both WTC responder and survivor populations or, if only a subgroup of 9/11-exposed population is represented, whether the results can reasonably be extrapolated to the complete 9/11-exposed population of responders and survivors.

3. Consideration of Limitations

There are limitations inherent to all observational epidemiologic studies; even studies with sufficient validity indicators to meet high-quality threshold described in Section III.C. above may nevertheless have limitations that should be considered in weighing the evidence. The Science Team will assess the limitations among all studies evaluated, individually and together. In its assessment, the Science Team will consider the degree to which these limitations provide a reasonable alternative explanation of study findings. Study limitations to be weighed may include the following:

- Accounting for potential for mediation, modification, or confounding resulting from inadequate information on the relationship between 9/11 exposure, other factors, and the health condition.

[28] Studies establish an exposure-response relationship by demonstrating that increases in exposure (i.e., exposures of greater intensity and/or longer duration) are associated with a greater incidence of disease. A thorough evaluation of exposure-response requires analysis of multiple levels of exposure such that the investigator can demonstrate that the risk increases with increasing levels of exposure. *See* NIOSH [2020], *supra* note 5.

[29] Study findings demonstrate a basis in scientific theory that supports the relationship between the exposure and the health effect, and do not conflict with known facts about the biology of the health condition. *See* NIOSH [2020], *supra* note 5.

[30] Coherence implies that the interpretation of a causal association agrees with known disease etiology.

[31] Analogy is used to inform on biological plausibility and coherence by contrasting the evidence on the suspected causal association with that from an established association between similar (analogous) causes or effects.

- Accounting for potential selection or information biases, such as healthy worker effects, adequacy of the control group, ascertainment errors, exposure misclassification, and conflicts of interests.

V. Science Team Categorization of Evidence

Based on the evaluation of the totality of the scientific evidence described in Section IV., the Science Team will assess the degree to which the evidence supports a causal association between 9/11 exposures and the health condition.

The Science Team will assign the evaluated scientific evidence to one of the following five categories: (1) substantial likelihood of causal association, (2) high likelihood of causal association, (3) limited likelihood of causal association, (4) no likelihood of causal association, or (5) inadequate evidence to determine the likelihood of causal association.

If the Science Team determines there is a high, but not substantial, likelihood of a causal association between 9/11 exposures and the health condition, the Administrator may direct the Science Team to evaluate additional scientific evidence as outlined below in Section V.B.

A. Category I — Evidence Supports Substantial Likelihood of a Causal Association

Substantial likelihood of causal association means that the association is strongly supported by evidence from high-quality, peer-reviewed, published epidemiologic studies of the health condition 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.

The scientific evidence demonstrating that a causal association is *substantially likely* includes the following:

- Evidence supporting a causal association from more than one high-quality epidemiologic study;
- Available epidemiologic studies as a whole must have examined both groups of the 9/11-exposed population (e.g., responders and survivors);

  AND

- Available epidemiologic studies as a whole must consistently and precisely report increasing risk of the health condition with increased 9/11 exposures.[32]

B. Category II — Evidence Supports High Likelihood of Causal Association

[32] *See supra* note 25.

High likelihood of causal association means that the scientific evidence, taken as a whole, demonstrates that the likelihood of a causal association is less than substantial, but definitively more than limited. Therefore, there is some meaningful likelihood that the association can be explained by chance, bias, confounding, or another alternative explanation. The scientific evidence supporting that a causal association is *highly likely* includes the following:

- Evidence supporting a causal association from more than one high-quality epidemiologic study;

- Available epidemiologic studies as a whole must have examined at least one group of the 9/11-exposed population (e.g., responders or survivors);

  AND

- Available epidemiologic studies as a whole mainly report increasing risk of the health condition with increased 9/11 exposures; however, a determination of "substantial likelihood" is precluded because there is some possibility that the association can be explained by chance, bias, confounding or any other alternative explanation.

1. Discretionary Secondary Evaluation of Additional Highly-Relevant Scientific Information Regarding Non-9/11 Exposures

If the Science Team evaluation characterizes the evidence available from high-quality, peer-reviewed, published epidemiologic studies of the health condition in 9/11-exposed populations as demonstrating a high, but not substantial, likelihood of causal association between 9/11 exposures and the health condition (Category II), the Administrator may, at their discretion, direct the Science Team to evaluate additional highly-relevant scientific information regarding exposures to known 9/11 agents in non-9/11 exposure scenarios.

a. Sources of Highly-Relevant Scientific Information in Non-9/11 Exposures

If directed by the Administrator, the Science Team will identify and review additional highly-relevant, peer-reviewed, published scientific information on exposures to known 9/11 agents in non-9/11 exposure scenarios. Information from authoritative scientific sources published by the U.S. government is considered highly-relevant. Such sources include:

- *Toxicological Profiles* published by the Agency for ToxicSubstances and Disease Registry (ATSDR); [33]

[33] For available ATSDR Toxicological Profiles, *see* http://www.atsdr.cdc.gov/toxprofiles/index.asp.

- *Monographs* published by the National Toxicology Program (NTP); [34] and

- *Human Health Risk Assessments* published by the Environmental Protection Agency (EPA). [35]

In addition, the Science Team may, at its discretion, supplement its review of U.S. government sources with additional highly-relevant, peer-reviewed, published scientific information, if all three of the following circumstances are met:

- The information available in the U.S. government sources listed above is outdated or inconclusive;

- The supplemental literature has been published more recently than the U.S. government sources listed above;

  AND

- The supplemental literature uses data expected to be included in future updates to the U.S. government sources listed above.

b. Evaluation of Additional Highly-Relevant Scientific Information Regarding Non-9/11 Exposures

The Science Team will evaluate highly-relevant, peer-reviewed, published, scientific information on exposures to known 9/11 agents in non-9/11 exposure scenarios to determine if it provides additional support for a causal association between 9/11 exposures and the health condition. Based upon its evaluation of the available highly-relevant scientific information about 9/11 agents in non-9/11 exposure scenarios, together with its findings from the evaluation of high-quality, peer-reviewed, published, epidemiologic studies of the health condition in 9/11-exposed populations, the Science Team will determine whether the totality of the evidence and information supports characterizing the support for causal association as either Category I (substantial likelihood) or Category II (high likelihood).[36]

[34] For available NTP Monographs, *see* http://ntp.niehs.nih.gov/pubhealth/hat/noms/index.html.
[35] For EPA Human Health Risk Assessment Products and Publications, *see* https://cfpub.epa.gov/ncea/risk/hhra/advSearch.cfm.
[36] The secondary review helps determine whether available scientific information regarding non-9/11 exposures fills important gaps in the evidence found in the initial evaluation of evidence using studies of only 9/11-exposed populations. If such gaps have been sufficiently filled, then recategorization of the level of support for a causal association between 9/11 exposures and the health condition is warranted. For example, a secondary review finding support for a causal association between 9/11 agents and the health condition in non-9/11 exposure

The evaluation of scientific information from the additional highly-relevant sources will include, but not be limited to, consideration of the following:

- Whether the information provides evidence that exposure to 9/11 agents is substantially likely to cause the health condition;

- Whether the evidence fills an important gap in establishing a causal association between exposure to 9/11 agents and the health condition;

- Whether the information mitigates the quality limitations found in peer-reviewed, published, epidemiologic studies of the health condition among 9/11-exposed populations; and

- Whether the information is inconclusive or outdated.

The review of scientific information from additional highly-relevant sources will include an evaluation of the similarity of the exposure characteristics to 9/11 exposure characteristics including, but not limited to, the following:

- The amount of exposure;

- Route of exposure;

- Physical form of the exposure to the 9/11 agent, *e.g.*, particulate, gas, fume, vapor, or solute;

- Duration and consistency of the exposure; and

- Whether the adverse health outcome arises from acute, sub-chronic, or chronic exposure.

C. Category III — Evidence Supports Limited Likelihood of Causal Association

Limited likelihood of causal association means the scientific evidence demonstrates that there is some evidence of a causal association between 9/11 exposures and the health condition, i.e., a causal association might exist but alternative explanations of the association such as bias, confounding, chance, or other alternative explanation, are also likely. The scientific evidence supporting *limited likelihood* of a causal association includes the following:

scenarios with high confidence that the association cannot be explained by chance, bias, confounding, or any other alternative explanation would permit the recategorization of evidence to Category I from Category II.

- Evidence supporting a causal association from at least one high-quality epidemiologic study;

- Available epidemiologic studies as a whole must have examined at least one group of the 9/11-exposed population (e.g., responders or survivors);

  AND

- Available epidemiologic studies more often than not report increasing risk of the health condition with increased 9/11 exposures; however, the evidence lacks sufficient consistency and precision to eliminate alternative explanations of the association, such as bias, confounding, chance, or any other alternative explanation.

D. Category IV — Evidence Does Not Support Causal Association

Does not support causal association means that the scientific evidence demonstrates that the health condition is substantially unlikely to be causally associated with 9/11 exposures. The scientific evidence supporting no causal association must include the following:

- Evidence supporting no causal association from more than one high-quality epidemiologic study;

- Available epidemiologic studies as a whole must have examined both groups of the 9/11-exposed population (e.g., responders and survivors);

- Available epidemiologic studies as a whole consistently and precisely report no increased risk of the health condition with increased 9/11 exposures;

- The evidence of biological plausibility is absent or is of low quality;

  AND

- There is high confidence that the evidence against a causal association is not explained by chance, bias, confounding, or any other alternative explanation.

E. Category V — Evidence is Inadequate to Determine a Causal Association

Inadequate likelihood of causal association means the scientific evidence fails to meet any of the likelihood standards described above

and is inconclusive with regard to a causal association between 9/11 exposures and the health condition.

VI. Science Team Advises Administrator of Evaluation Findings and Categorization of Evidence

At the conclusion of its evaluation, the Science Team will provide the Administrator with its findings regarding the potential causal association between 9/11 exposures and the health condition. The support for causal association will be described as falling within one of the following five categories: (1) substantial likelihood, (2) high likelihood, (3) limited likelihood, (4) no likelihood, or (5) inadequate evidence to determine the likelihood of a causal association.

VII. Engagement of the WTC Health Program Scientific/Technical Advisory Committee (STAC)

A. Administrator Requests a Recommendation of the STAC

Regardless of whether the process to add a health condition is initiated at the Administrator's discretion or a petition request, at any time, the Administrator may choose to engage the STAC and request a recommendation on whether to propose the addition of a health condition to the List.[37] For example, the Administrator may request a recommendation when the Science Team evaluation concludes that the evidence supports a high, but not substantial, likelihood of causal association between 9/11 exposures and a health condition (Category II).

B. Convening the STAC

The Administrator may send a letter to the STAC Chair requesting a recommendation from the STAC on whether to add a health condition, including the scientific and medical basis for the recommendation.[38]

C. STAC Meeting Procedures

The Designated Federal Official will work with the STAC to schedule meetings and assemble information needed to develop recommendations on whether 9/11 exposures are causally associated with the health condition.

D. Time Limits for STAC Recommendation

The STAC will submit its recommendation on whether to add the health condition to the Administrator no later than 90 days after the date of the Administrator's request or by such date (not to exceed 180 days from the

[37] 42 U.S.C. § 300mm-22(a)(6)(B)(i); 42 C.F.R. § 88.16(a)(2)(i).
[38] 42 U.S.C. § 300mm-22(a)(6)(B)(i) and (C).

date of the request) as specified by the Administrator.[39]

E. Administrator Actions after Receipt of a STAC Recommendation

1. Administrator Actions

a. If the STAC recommends the addition of the health condition to the List and provides a reasonable basis for the recommendation,[40] the Administrator may publish an NPRM in the *Federal Register* proposing adding the condition to the List via rulemaking (*see* Section IX.A.). To assist the Administrator in understanding whether the STAC's recommendation has a reasonable basis, the STAC must describe in detail the basis for its recommendation and, if applicable, any evidentiary sources used to support the recommendation.

b. If the STAC does not recommend the addition of the health condition to the List or is unable to provide a reasonable basis for the addition, the Administrator may publish a notice in the *Federal Register* of the determination not to propose a rule to add a condition and the basis for such a determination (*see* Section IX.C.).

2. Time Limits for Administrator Actions

Where the Administrator has requested a recommendation from the STAC, the Administrator will evaluate the STAC's recommendation(s) and take one of the actions outlined in Section VII.E.1., above, within 90 days after receipt of the recommendation.

VIII. Administrator's Determination

The Administrator will review the findings of the Science Team regarding the potential causal association between 9/11 exposures and the health condition and its categorization of the evidence of causal association (e.g., (1) substantial likelihood, (2) high likelihood, (3) limited likelihood, (4) no likelihood, or (5) inadequate evidence to assess the likelihood).

If the Administrator sought a recommendation from the STAC, the Administrator will also review the STAC's recommendation and the basis for that recommendation.

Based on the review of the findings and recommendations, the Administrator will determine whether there is sufficient evidence of causal association between 9/11 exposures and the health condition to propose adding the health condition to the List.

[39] 42 U.S.C. § 300mm-22(a)(6)(C); 42 C.F.R. § 88.16(b)(1).

[40] The STAC may base its recommendation and reasonable basis on criteria other than those outlined in Section IV.

A. Sufficient Evidence of Causal Association

The Administrator may determine that there is sufficient evidence of causal association between 9/11 exposures and the health condition based on at least one of the following:

1. The Science Team evaluation of high-quality, peer-reviewed, published epidemiologic studies of the health condition in 9/11-exposed populations supports a finding that the 9/11 exposures are substantially likely to be causally associated with the health condition (*see* Category I, Section V.A.);

2. The Science Team discretionary secondary evaluation of highly-relevant peer-reviewed, published, scientific information on exposures to known 9/11 agents in non-9/11 exposure scenarios (*see* Section V.B.), together with the evaluation of high-quality, peer-reviewed, published epidemiologic studies of the health condition in 9/11-exposed populations, supports a finding that 9/11 exposures are substantially likely to be causally associated with the health condition (*see* Category I, Section V.A.);

   OR

3. The STAC recommends adding the health condition to the List and the Administrator finds that the STAC provided a reasonable basis for the recommendation.

B. Insufficient Evidence of Causal Association

The Administrator may determine that there is insufficient evidence of causal association between 9/11 exposures and the health condition based on any of the following:

1. The Science Team advises that the literature review was unable to identify peer-reviewed, published, epidemiologic studies of the health condition in 9/11-exposed populations (*see* Section III.B.) and, therefore, further evaluation was not possible;

2. The Science Team advises that the peer-reviewed, published, epidemiologic studies were identified by the literature review do not meet the criteria to be considered high-quality (*see* Section III.C.) and, therefore, further evaluation was not possible;

3. The Science Team evaluation of the scientific evidence in high-quality, peer-reviewed, published, epidemiologic studies supports a finding of a high likelihood of a causal association between 9/11 exposures and the health condition (*see* Category II, Section V.B.),

   AND EITHER:

- The Administrator does not direct the Science Team to conduct a discretionary secondary evaluation of additional highly-relevant scientific information regarding 9/11 agents in non-9/11 exposure scenarios (*see* Section V.B.1.)

  OR

- The Administrator-directed discretionary secondary evaluation of additional highly-relevant scientific information regarding 9/11 agents in non-9/11 exposure scenarios does not provide additional support for a causal association between 9/11 exposures and the health condition (*see* Section V.B.1.b.)

4. The Science Team advises that the evaluation of the scientific evidence supports a limited likelihood of causal association between 9/11 exposures and the health condition (*see* Section Category III, Section V.C.);

   OR

5. The Science Team evaluation of the scientific evidence results in the finding that there is inadequate evidence to determine whether a causal association exists between 9/11 exposures and the health condition (*see* Section Category V, Section V.E.).

C. No Evidence of Causal Association

The Administrator may determine that there is no evidence of causal association between 9/11 exposures and the health condition based on any of the following:

1. The Science Team evaluation of high-quality, peer-reviewed, published, epidemiologic studies of the health condition in 9/11-exposed populations supports a finding that 9/11 exposures are substantially unlikely to be causally associated with the health condition (*see* Category IV, Section V.D.);

2. The STAC recommends not adding the health condition to the List and the Administrator finds that the STAC has provided a reasonable basis for not adding the health condition to the List;

   OR

3. The STAC recommends adding the health condition to the List but the Administrator finds that the STAC has not provided a reasonable basis for adding the health condition to the List of WTC-Related Health Conditions.

IX. Administrator Actions

Following the Administrator's determination regarding whether there is sufficient evidence of causal association between 9/11 exposures and the health condition to propose adding the health condition to the List, the Administrator will take one of the following actions:[41]

A. Publish a Notice of Proposed Rulemaking to Add the Health Condition

If the Administrator determines that there is sufficient evidence that 9/11 exposures are causally associated with the health condition, the Administrator will publish in the *Federal Register* an NPRM to add the health condition to the List of WTC-Related Health Conditions[42]

B. Publish a Notice of Insufficient Evidence

If the Administrator determines that there is insufficient evidence that 9/11 exposures are causally associated with the health condition (*see* Section VIII.B), the Administrator will publish in the *Federal Register* a determination of insufficient evidence.[43]

C. Publish a Notice of Determination Not to Propose a Rule to Add a Condition

If the Administrator determines that the evidence establishes that 9/11 exposures are not causally associated with the health condition, then the Administrator will publish in the *Federal Register* a determination not to propose a rule and the basis for such determination.[44]

X. Rulemaking and Peer Review

A. Notice of Proposed Rulemaking (NPRM)

If the Administrator decides to propose adding the health condition to the List, the Administrator will publish an NPRM in the *Federal Register*. The Administrator will solicit written public comments on the NPRM.[45]

B. Independent Peer Review

As required by the James Zadroga 9/11 Health and Compensation Reauthorization Act, the Administrator will conduct an independent peer review of the WTC Health Program's evaluation of the scientific and

[41] Where the evaluation by the Science Team is in response to a valid petition, one of these actions must be taken within 90 days of receipt of the petition. *See* 42 U.S.C. § 300mm-22(a)(6)(B); 42 C.F.R. § 88.16(a)(2). The statutory deadlines do not apply where the evaluation is conducted at the discretion of the Administrator.
[42] 42 U.S.C. § 300mm-22(a)(6)(B)(ii); 42 C.F.R. § 88.16(a)(2)(ii).
[43] 42 U.S.C. § 300mm-22(a)(6)(B)(iv); 42 C.F.R. § 88.16(a)(2)(iv).
[44] 42 U.S.C. § 300mm-22(a)(6)(B)(iii); 42 C.F.R. § 88.16(a)(2)(iii).
[45] 42 U.S.C. § 300mm-22(a)(6)(D); 42 C.F.R. § 88.16(b).

technical evidence supporting the addition of the health condition prior to issuing a final rule.[46]

1. Selection of Peer Reviewers

a. Prior to issuing a final rule adding a condition to the List, the Administrator will select three subject matter experts[47] for each health condition being proposed for addition to serve as peer reviewers.[48] In selecting peer reviewers to review the Program's evaluation of evidence regarding a specific health condition, the Administrator will balance the following factors:

(1) Medical and/or scientific expertise needed to evaluate the evidence relied on to propose adding the health condition, including the authorship of publication(s) concerning the respective health condition;

(2) Independence from the National Institute for Occupational Safety and Health (NIOSH) and the Centers for Disease Control and Prevention (CDC); and

(3) Previous service as a peer reviewer (rotation of peer reviewers).

b. The Administrator will apply Federal science agency conflict or bias prevention methods to:

(1) Limit potential conflicts of interest;

(2) Ensure that bias is minimized in the peer review process;

(3) Achieve a high level of credibility; and

(4) Balance extremes in scientific perspectives.

2. Charge to Peer Reviewers

a. Peer reviewers will be asked to review the evidence assessment for adding the health condition to the List within the context of this policy. Within 30 days of when the NPRM is published in the *Federal Register*, reviewers will be expected to provide a brief written report answering the following questions:[49]

[46] 42 U.S.C. § 300mm-22(a)(6)(F); 42 C.F.R. § 88.16(b)(2).
[47] At least every two years, the Administrator will request recommendations from the STAC regarding the identification of potential independent peer reviewers with medical and/or scientific expertise. 42 U.S.C. § 300mm-22(a)(6)(G)(ii).
[48] 42 C.F.R. § 88.15.
[49] The questions given to the peer reviewers may be modified by the Administrator, as necessary, for the specific health condition being considered.

(1) Are you aware of any other studies which should be considered? If so, please identify them.

(2) Have the requirements of this *Policy and Procedures* been fulfilled? If not, please explain which elements are missing or deficient.

(3) Is the interpretation of the available evidence appropriate, and does it support the conclusion to add the health condition, as described in the proposed regulatory text, to the List? If not, please explain why.

b. The peer reviews will be compiled and posted to the NIOSH rulemaking docket at the end of 30 days. Peer reviewers will be identified without individual attribution of their comments.

C. Public Comments

All public comments and peer reviews will be considered and responded to, as appropriate, in the final rule preamble. The public comment period will remain open no less than 45 days after publication of the NPRM in the *Federal Register* to allow the public an additional 15 days to comment after peer reviewers' comments are posted. The public comments will be posted to the rulemaking docket.

D. Final Rule

After considering the public comments and peer reviews, the Administrator will determine whether the rationale discussed in the NPRM is changed by the information supplied by commenters. The Administrator's final determination and rationale will be published in a final rule in the *Federal Register* as soon as possible after the close of the public comment period.

If the evidence continues to support the addition of the health condition:

1. The condition will be added to the List on the final rule's effective date; and

2. Implementation procedures will be developed, which may include:

   a. Exposure qualifications;

   b. Time intervals for diagnosis and/or symptom onset; and

   c. Other procedures as appropriate to the particular health condition.

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