



Policy and Procedures for Adding Types of Cancer To the List of WTC-Related Health Conditions

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Note for May 11, 2016 Revision: This version (1) clarifies that a type of cancer can be added if the criteria of *any* of the four methods are met; and (2) adds peer review procedures when the Administrator proposes to add a type of cancer to the List of WTC-Related Health Conditions.

I. Authority

The *Policy and Procedures for Adding Types of Cancer to the List of WTC-Related Health Conditions* is based on the James Zadroga 9/11 Health and Compensation Act of 2010 (“Act”),¹ the Final Rule, “*World Trade Center Health Program: Addition of Certain Types of Cancer to the List of WTC-Related Health Conditions*,”² and the World Trade Center (WTC) Health Program regulations.³

II. Introduction

The Act provides two pathways to initiate the process of deciding whether to propose adding a health condition, including types of cancer, to the List of WTC-Related Health Conditions (“List”). These pathways are: (1) the Administrator of the WTC Health Program initiates the process at

¹ Pub. L. 111-347, as amended by Pub. L. 114-113, codified at 42 U.S.C. § 300mm *et seq.*

² 77 Fed. Reg. 56138 (Sept. 12, 2012). See <http://www.gpo.gov/fdsys/pkg/FR-2012-09-12/pdf/2012-22304.pdf>

³ 42 C.F.R. Part 88.

his own discretion;⁴ or (2) the Administrator initiates the process after receiving a petition⁵ by an interested party.⁶ A health condition may only be added to the List by rulemaking.

III. Review of Scientific and Medical Information and Administrator Determination

Once the process of determining whether to propose adding a type of cancer to the List is initiated, the WTC Health Program's Science Team reviews the scientific literature to determine if the available scientific information has the potential to provide a basis for a decision on whether to add the type of cancer to the List.

A. Systematic Literature Search

Where a cancer is being considered, the systematic literature search includes gathering information about the following:

1. Studies regarding the type of cancer among 9/11-exposed populations;
2. Studies regarding potential causal association between that cancer and a condition already on the List; and
3. The most recent classifications of the World Health Organization's International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP) *Report on Carcinogens*.

B. Literature Evidence Review

Scientific information in studies obtained in the systematic literature search⁷ is first evaluated for relevance. For studies regarding the type of cancer about 9/11-exposed populations, information is determined to be relevant if it is presented in peer-

⁴ 42 U.S.C. § 300mm-22(a)(6)(A).

⁵ When the Administrator receives a submission from an interested party to add a health condition to the List, he follows the steps outlined in the "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 petition specified in 42 C.F.R. § 88.17(a)(1).

⁶ 42 U.S.C. § 300mm-22(a)(6)(B).

⁷ Any medical basis provided in the case of a petition is included in this evaluation. See 42 C.F.R. § 88.17(a)(iii); see also "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>).

reviewed,⁸ published,⁹ epidemiologic studies¹⁰ of the cancer in 9/11-exposed populations; for studies regarding the potential causal association between the cancer and a condition on the List, information is determined to be relevant if it is presented in peer-reviewed, published, epidemiologic studies. The quantity and quality¹¹ of relevant studies are then reviewed for their potential to provide a basis for deciding whether to propose adding the type of cancer to the List. The findings of the review, including any information about IARC classifications and the NTP *Report on Carcinogens*, are documented and discussed with the Administrator.

C. Administrator Determination

The Administrator determines whether the evidence available in peer-reviewed, published, epidemiologic studies about the type of cancer among 9/11-exposed populations has the potential to provide a basis for a decision on whether to add the type of cancer and whether to proceed with an assessment of that information.

1. Where the Administrator determines that the evidence does not provide a sufficient basis for a decision:
 - a. The evaluation is documented and archived according to document management requirements; and
 - b. If the evaluation was initiated by a petition, then the Administrator:
 - i. Publishes a determination in the *Federal Register* that the available information is insufficient to take action,¹² and
 - ii. Notifies the petitioner in writing of the decision simultaneously to the determination being published in the *Federal Register*.

⁸ 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.

⁹ Published studies include those published online ahead of print.

¹⁰ 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 Centers for Disease Control and Prevention, HHS, *Principles of Epidemiology in Public Health Practice* (3rd ed. 2012), at 1-46. The WTC Health Program reviews these epidemiologic studies to determine if they identify causal associations between exposures and health outcomes with the potential to provide a basis for deciding whether to propose adding a condition to the List.

¹¹ The evaluation of quantity and quality includes consideration of any limitations, such as bias or confounding, of the reviewed studies.

¹² 42 U.S.C. § 300mm-22(a)(6)(B)(iv).

2. Where the Administrator determines that the available evidence has the potential to provide a basis for a decision, the Administrator may:
 - a. Direct the Science Team to assess the scientific and medical evidence and provide input on whether the available information supports a causal association between 9/11 exposures and the type of cancer [see Section IV.A.], and
 - b. In addition, the Administration may request advice from the WTC Health Program Scientific/Technical Advisory Committee (STAC) [see Section V.B.].

IV. Assessment of Scientific and Medical Information

A. Assessment Process

1. Review Criteria

The Science Team conducts an assessment of the available evidence under the following methods for determining whether to add a type of cancer to the List. In determining whether to propose that a type of a cancer be included on the List, a review of the evidence must demonstrate fulfillment of at least one of the following four methods:

Method 1. Epidemiologic Studies of September 11, 2001 Exposed Populations.

The peer-reviewed, published, epidemiologic studies of 9/11-exposed populations are assessed by applying the following criteria extrapolated from the Bradford Hill criteria, as appropriate:

- a. Strength of the association between a 9/11 exposure and a type of cancer (including the precision of the risk estimate¹³);
- b. Consistency of the findings across multiple studies. If only a single published epidemiologic study is available for assessment, the consistency of findings cannot be evaluated and more emphasis will be placed on evaluating the strength of the association and the precision of the risk estimate;
- c. Biological gradient, or dose-response relationships between 9/11 exposures and the type of cancer; and

¹³ A precision of the risk estimate describes the uncertainty inherent in estimating the strength of association (the effect size) between exposure and health effect from observational data. It is expressed as a confidence interval illustrating a range of values that contains the true effect size. A narrow confidence interval indicates a more precise measure of the effect size and a wider interval indicates greater uncertainty.

- d. Plausibility and coherence with known facts about the biology of the type of cancer.

Method 2. Established Causal Associations.

A type of cancer may be added to the List if there is well-established scientific support published in multiple epidemiologic studies for a causal association between that cancer and a condition already on the List of WTC-Related Health Conditions.

Method 3. Review of Evaluations of Carcinogenicity in Humans.

A type of cancer may be added to the List under Method 3 only if both of the following criteria are satisfied:

3A. Published Exposure Assessment Information. 9/11 agents¹⁴ were reported in a published, peer-reviewed, exposure assessment study of responders or survivors who were present in either the New York City disaster area, or at the Pentagon, or in Shanksville, Pennsylvania¹⁵; and

3B. Evaluation of Carcinogenicity in Humans from Scientific Studies. NTP has determined that the 9/11 agent is *known to be a human carcinogen* or is *reasonably anticipated to be a human carcinogen*, and IARC has determined there is *sufficient* or *limited* evidence that the 9/11 agent causes a type of cancer.

Method 4. Review of Information Provided by the WTC Health Program Scientific/Technical Advisory Committee.

A type of cancer may be added to the List if the STAC has provided a reasonable basis for adding a type of cancer.

2. Discussion with Administrator

The Science Team ensures that the results of the assessment are documented and discussed with the Administrator.

B. Administrator Actions

¹⁴ 9/11 agents are chemical, physical, biological, or other agents or hazards reported in a published, peer-reviewed exposure assessment study of responders 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.

¹⁵ Definitions of these locations are provided in 42 C.F.R. § 88.1.

1. If the assessment was performed in response to a petition, the Administrator takes one of the following actions:¹⁶
 - a. If a review of the evidence demonstrates fulfillment of at least one of the four methods described in IV.A. above, the Administrator publishes in the *Federal Register* a notice of proposed rulemaking (NPRM) to add the type of cancer to the List;¹⁷ or
 - b. If a review of the evidence does not demonstrate fulfillment of at least one of the four methods described in IV.A. above and does demonstrate that 9/11 exposures are not causally related to the type of cancer, the Administrator publishes in the *Federal Register* a determination not to propose a rule and the basis for such determination;¹⁸ or
 - c. If a review of the evidence indicates the information is insufficient to take either of the actions in IV.B.1.a. or b. above, then the Administrator publishes that determination in the *Federal Register*.¹⁹
2. If the assessment was initiated by the Administrator, the Administrator may take one of the actions described in Section IV.B.1. above.

V. WTC Health Program Scientific/Technical Advisory Committee (STAC)

A. Convening the STAC

The Administrator may convene the STAC if he determines that its advice would be helpful. For example, where there is need of an interpretation of conflicting or inconclusive published scientific evidence, the Administrator may convene the STAC.

B. Meeting Procedures

If the Administrator decides to request a recommendation from the STAC regarding a type of cancer, the Administrator provides a charge to the STAC, and the Designated Federal Official (DFO) works with the STAC to schedule meetings and assemble information needed to develop recommendations on whether 9/11 exposures have a causal association with the type of cancer.

C. Time Limits

¹⁶ If the Administrator exercises his discretion to request review and recommendation from the STAC, he will also take the STAC's recommendation into consideration in determining which of the actions described in Section IV.B.1. to take [see Section V].

¹⁷ 42 U.S.C. § 300mm-22(a)(6)(B)(ii).

¹⁸ 42 U.S.C. § 300mm-22(a)(6)(B)(iii).

¹⁹ 42 U.S.C. § 300mm-22(a)(6)(B)(iv).

1. If a petition to add a type of cancer to the List has been received and the Administrator decides to exercise his discretion to convene the STAC, then the Administrator must make his request for a STAC recommendation within 90 days of receipt of the petition.
2. If the Administrator requests a recommendation from the STAC, whether following the receipt of a petition or as part of an Administrator-initiated review, the Administrator will send a letter to the STAC Chair requesting advice on whether to add the type of cancer and establishing a time period of 90 days, with potential extension up to 180 days, for the committee to provide recommendations and the scientific and medical basis for those recommendations.
3. After receiving the recommendations from the STAC, the Administrator evaluates the STAC's advice and takes appropriate action under Section IV.B. not later than 90 days after receipt of the recommendation.

Exception: The option found in Section IV.B.1.c. above is not an option for the Administrator when advice has been requested from the STAC in response to a petition.

VI. Rulemaking

A. NPRM

If the Administrator decides to propose adding the health condition to the List, he publishes an NPRM in the *Federal Register* to that effect. The NPRM solicits public comments. The Administrator also conducts an independent peer review of the Program's evaluation of the scientific and technical evidence supporting the addition of the condition.

1. Public comments. All public comments received are considered and responded to, as appropriate, in the final rule preamble. The public comments are posted to the rulemaking docket.
2. Independent Peer Review. The Program requests peer review from three subject matter experts for the health condition to be added.
 - a. Identification of peer reviewers. The Administrator identifies qualified peer reviewers who are outside of NIOSH, with input provided by the STAC.
 - b. Charge to peer reviewers. Peer reviewers are asked to review the evaluation of the evidence for adding the health condition to the List

within the context of this policy, and provide a brief written report answering the following questions:²⁰

- i. Are you aware of any other studies which should be considered? If so, please identify them.
 - ii. Have the requirements of this *Policy and Procedures* been fulfilled? If not, please explain which elements are missing or deficient.
 - iii. Is the interpretation of the available evidence appropriate, and does it support the conclusion to add the health condition, as described in the regulatory text, to the List? If not, please explain why.
- c. All peer reviewers' comments are considered and responded to in the final rule preamble. The peer reviews are compiled without attribution and posted to the rulemaking docket.

B. Final Rule

After reviewing the public comments and peer reviews, the Administrator determines whether the rationale discussed in the NPRM is changed by the information supplied by commenters. If the evidence continues to support the addition of the type of cancer:

1. A final rule is developed and published in the *Federal Register*;
2. The condition is added to the List; and
3. Implementation procedures are developed, which may include:
 - a. Exposure qualifications;
 - b. Time intervals/latency; and
 - c. Other procedures as appropriate to the particular type of cancer.

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²⁰ The questions given to the peer reviewers may be modified by the Administrator, as necessary, for the specific health condition being considered.