excepted from Congressional Review Act reporting requirements prescribed under 5 U.S.C. 801 since it relates to agency management or personnel under 5 U.S.C. 804(3)(b).

V. Regulatory Flexibility Act

This final rule will not have a significant economic impact on a substantial number of small entities within the meaning of the Regulatory Flexibility Act, 5 U.S.C. 601, *et seq.,* because the changes are administrative in nature and only affect Government employees. Therefore, a Final Regulatory Flexibility Analysis has not been performed.

VI. Paperwork Reduction Act

The Paperwork Reduction Act does not apply because the changes to the Federal Travel Regulation do not impose recordkeeping or information collection requirements, or the collection of information from offerors, contractors, or members of the public that require the approval of the Office of Management and Budget under 44 U.S.C. 3501, *et seq.*

List of Subjects

41 CFR Parts 301–10, 301–70

Government employees, Travel and transportation expenses, common carriers.

Robin Carnahan

Administrator of General Services.

For the reasons set forth in the preamble GSA amends 41 CFR parts 301–10 and 301–70 as set forth below:

PART 301–10—TRANSPORTATION EXPENSES

■ 1. The authority citation for 41 CFR part 301–10 continues to read as follows:

Authority: 5 U.S.C. 5707; 40 U.S.C. 121(c); 49 U.S.C. 40118; Office of Management and Budget Circular No. A–126, ''Improving the Management and Use of Government Aircraft.'' Revised May 22, 1992.

■ 2. Revise § 301–10.309 to read as follows:

§ 301–10.309 What will I be reimbursed if I am authorized to use common carrier transportation or a rental vehicle and I use a POV instead?

You will be reimbursed the applicable POV rate on a mileage basis, plus per diem and related travel expenses, not to exceed the total constructive cost of the authorized method of transportation. Your agency must determine the constructive cost in accordance with § 301–70.105(a).

PART 301–70—INTERNAL POLICY AND PROCEDURE REQUIREMENTS

■ 3. The authority citation for 41 CFR part 301–70 is revised to read as follows:

Authority: 5 U.S.C. 5707; 40 U.S.C. 121(c); Sec. 2, Pub. L. 105–264, 112 Stat. 2350 (5 U.S.C. 5701, note); OMB Circular No. A–126, revised May 22, 1992; OMB Circular A–123, Appendix B, revised August 27, 2019.

■ 4. Amend § 301–70.105 by revising paragraph (a) to read as follows:

§ 301–70.105 May we prohibit an employee from using a POV on official travel?

* * * * *

(a) Limit reimbursement to the constructive cost of the authorized method of transportation, which is the sum of travel and transportation expenses the employee would reasonably have incurred had the employee traveled by the method of transportation deemed to be most advantageous to the Government. The calculation will necessarily involve assumptions. Examples of related expenses that could be considered constructive costs include, but are not limited to, taxi and TNC fares, baggage fees, rental car costs, tolls, ferry fees, and parking charges; and

* * * * *

■ 5. Amend § 301–70.506 by revising paragraph (b) to read as follows:

§ 301–70.506 How do we define actual cost and constructive cost when an employee interrupts a travel assignment because of an incapacitating illness or injury?

* * * * *

(b) Constructive cost is the sum of travel and transportation expenses the employee would reasonably have incurred for round-trip travel between the official station and the alternate location plus per diem calculated for the appropriate en route travel time. The calculation will necessarily involve assumptions. Examples of related expenses that could be considered constructive costs include, but are not limited to, taxi and TNC fares, baggage fees, rental car costs, tolls, ferry fees, and parking charges.

[FR Doc. 2023–00733 Filed 1–17–23; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 88

[Docket No. CDC–2022–0052; NIOSH–347]

RIN 0920–AA82

World Trade Center (WTC) Health Program; Addition of Uterine Cancer to the List of WTC-Related Health Conditions

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

ACTION: Final rule.

SUMMARY: In accordance with the World Trade Center (WTC) Health Program's regulations, which establish procedures for adding a new condition to the list of covered health conditions, this final rule adds malignant neoplasms of corpus uteri and uterus, part unspecified (uterine cancer) to the List of WTC-Related Health Conditions.

DATES: This rule is effective on January 18, 2023.

FOR FURTHER INFORMATION CONTACT: Rachel Weiss, Public Health Analyst, National Institute for Occupational Safety and Health, 1090 Tusculum Avenue, MS: C–46, Cincinnati, OH 45226; telephone: (404) 498–2500 (this is not a toll-free number); email: *NIOSHregs@cdc.gov.*

SUPPLEMENTARY INFORMATION:

Table of Contents

G. Executive Order 13132 (Federalism)
H. Executive Order 13045 (Protection of Children From Environmental Health Risks and Safety Risks)
I. Executive Order 13211 (Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use)
J. Plain Writing Act of 2010

I. Executive Summary

A. Purpose of Regulatory Action

In a notice of proposed rulemaking (NPRM) published in May 2022, the Administrator of the WTC Health Program (Administrator) and the Secretary of HHS proposed the addition of uterine cancer [1] to the List of WTC-Related Health Conditions (List) in 42 CFR 88.15.[2] In this final rule, the WTC Health Program summarizes and responds to both independent peer reviews and public comments on the NPRM and finalizes the addition of uterine cancer to the List.

B. Summary of Major Provisions

This final rule adds malignant neoplasms of corpus uteri and uterus, part unspecified (uterine cancer) to the List.

C. Costs and Benefits

The addition of uterine cancer to the List through this rulemaking is estimated to cost the WTC Health Program between $1,706,454 and $3,805,173 annually from 2023 through 2026. All of the costs to the WTC Health Program are transfers.[3] Benefits to current and future WTC Health Program members [4] are expected to include improved access to care and better treatment outcomes than members would have experienced in the absence of Program coverage.

The case numbers used to develop the cost estimates are, themselves, only estimates; the certification of individual cancer diagnoses will be conducted on a case-by-case basis, as required by the Zadroga Act. Interested parties should visit the WTC Health Program website for information about how to apply for enrollment in the Program [5] and about health condition certification.[6]

II. Background

Title I of the James Zadroga 9/11 Health and Compensation Act of 2010, as amended, revised the Public Health Service Act (PHS Act) to establish the WTC Health Program, which is administered by the National Institute for Occupational Safety and Health (NIOSH), within CDC, provides medical monitoring and treatment to eligible responders to the September 11, 2001, terrorist attacks in New York City, at the Pentagon, and in Shanksville, Pennsylvania, and to eligible survivors of the New York City attacks. In an NPRM published in May 2022,[7] the Administrator of the WTC Health Program and the Secretary of HHS proposed the addition of uterine cancer [8] to the List of WTC-Related Health Conditions in 42 CFR 88.15. In this final rule, the WTC Health Program summarizes and responds to both independent peer reviews and public comments on the NPRM and finalizes the addition of uterine cancer to the List in § 88.15(d).

A. WTC Health Program Statutory Authority

Title I of the James Zadroga 9/11 Health and Compensation Act of 2010 (Pub. L. 111–347, as amended by Pub. L. 114–113 and Pub. L. 116–59), added Title XXXIII to the PHS Act [9] establishing the WTC Health Program within HHS. The WTC Health Program provides medical monitoring and treatment benefits to eligible firefighters and related personnel, law enforcement officers, and rescue, recovery, and cleanup workers who responded to the September 11, 2001, terrorist attacks in New York City, at the Pentagon, and in Shanksville, Pennsylvania (responders), and to eligible persons who were present in the dust or dust cloud on September 11, 2001, or who worked, resided, or attended school, childcare, or adult daycare in the New York City disaster area (survivors).

All references to the Administrator in this document mean the Director of NIOSH, within CDC, or his or her designee. Section 3312(a)(6) of the PHS Act requires the Administrator to conduct rulemaking to propose the addition of a health condition to the List codified in 42 CFR 88.15.

B. Rulemaking History

In 2020, the Administrator received requests from WTC responders, survivors, and five of the WTC Health Program Clinical Centers of Excellence (CCEs) to add ''uterine cancer'' to the List. The letter from the CCEs raised important questions about the potential association between endocrine disrupting chemicals (EDCs) present at the WTC sites and uterine cancer, and noted that a previous WTC Health Program evaluation of the evidence regarding a causal association between endometrial cancer and 9/11 exposure did not address the potential role of EDCs. In response to the requests, the Administrator directed the WTC Health Program's Science Team to assess the available scientific evidence for adding uterine cancer to the List pursuant to the *Policy and Procedures for Adding Types of Cancer to the List of WTC-Related Health Conditions* (*Policy and Procedures*).[10]

The *Policy and Procedures* describes four methods for determining whether to add a type of cancer to the List, summarized below:

- *Method 1. Epidemiologic Studies of September 11, 2001, Exposed Populations:* A type of cancer may be added to the List if peer-reviewed, published, epidemiologic studies of cancers in the 9/11-exposed populations demonstrate a causal association between 9/11 exposures and that 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 peer-reviewed epidemiologic studies for a causal association between a health condition already on the List and that type of cancer.
- *Method 3. Review of Evaluations of Carcinogenicity in Humans:* A type of cancer may be added to the List if a 9/11 agent [11] included in the *Inventory of*

[1] For the purposes of this action, the WTC Health Program defines the term ''uterine cancer'' as ICD–10 code C54, including the following specific malignant neoplasms: isthmus uteri (C54.0), endometrium (C54.1), myometrium (C54.2), fundus uteri (C54.3), overlapping sites of corpus uteri (C54.8), and corpus uteri, unspecified (C54.9); and ICD–10 code C55, including only a single sub-category, malignant neoplasm of uterus, part unspecified.

[2] 87 FR 27961 (May 10, 2022).

[3] Due to the implementation of the Patient Protection and Affordable Care Act in 2014, and as required under the authorizing statute for the WTC Health Program, all current and future Program members are assumed to have or have access to medical insurance coverage other than through the WTC Health Program; therefore, all projected treatment costs to be paid by the Program are considered transfers.

[4] Although this rulemaking refers, at times, to uterine cancer in females, the WTC Health Program recognizes that some individuals who identify as male also may be at risk for uterine cancer.

[5] *See* WTC Health Program, *How to Apply* web page, *https://www.cdc.gov/wtc/apply.html.*

[6] *See* WTC Health Program, ''Certifications and Covered Conditions,'' *Member Handbook, https://www.cdc.gov/wtc/handbook.html#certifications.*

[7] *See supra* note 2.

[8] *See supra* note 1.

[9] Title XXXIII of the PHS Act is codified at 42 U.S.C. 300mm to 300mm–61. Those portions of the Zadroga Act found in Titles II and III of Public Law 111–347 do not pertain to the WTC Health Program and are codified elsewhere.

[10] WTC Health Program [Nov 2021], *Policy and Procedures for Adding Types of Cancer Conditions to the List of WTC-Related Health Conditions, https://www.cdc.gov/wtc/pdfs/policies/WTCHP_PP_Addn_Cancer_11182021-508.pdf.*

[11] The WTC Health Program defines *9/11 agents* to mean chemical, physical, biological, or other hazards reported in a published, peer-reviewed

9/11 Agents [12] has been determined by the National Toxicology Program (NTP) to be a *known human carcinogen* or *reasonably anticipated to be a human carcinogen* and the World Health Organization's International Agency for Research on Cancer (IARC) has determined there is *sufficient* or *limited* evidence in humans that the 9/11 agent causes that type of cancer.

• *Method 4. Review of Information by the WTC Health Program Scientific/Technical Advisory Committee (STAC):* A type of cancer may be added to the List if the STAC recommends the addition and provides a reasonable basis for the recommendation.

The Science Team evaluated the available evidence and presented its findings to the Administrator in a white paper (2021 White Paper) [13] that was shared with the STAC and the public before the STAC's public meeting on September 28–29, 2021 (*see* discussion below). The 2021 White Paper concluded that insufficient evidence exists under Method 1 and Method 3 to support a decision to add uterine cancer to the List. The Science Team found that evidence considered under Method 2 supports the addition of uterine cancer to the List, but only for those WTC Health Program members who have a certified WTC-related estrogen-secreting tumor.[14] Finally, the 2021 White Paper included additional information for the STAC to consider in its deliberations, conducted pursuant to Method 4 and discussed below, including: mechanisms of endometrial cancer development; other evidence from studies of uterine cancer from exposure to the 9/11 agents 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), polychlorinated biphenyls, cadmium, asbestos, and chloroethane; sex disparities in occupational cohort studies; and other cancers causally associated with EDCs.

Pursuant to Method 4 of the *Policy and Procedures,* the Administrator exercised his discretion to request a recommendation from the STAC regarding whether the available evidence provides a reasonable basis for adding uterine cancer to the List. The STAC held a public meeting on September 28 and 29, 2021, during which it heard public comments and deliberated on the evidence, including the evidence presented in the Science Team's 2021 White Paper, and created a workgroup to write a report describing the STAC's findings on uterine cancer. In a subsequent public STAC meeting on November 18, 2021, the full Committee voted unanimously to approve the workgroup report and recommend that the Administrator add uterine cancer to the List.

In a letter received by the Administrator on November 29, 2021,[15] the STAC formally recommended the addition of ''all types of uterine cancer'' to the List. In its rationale, the STAC noted that the *Inventory of 9/11 Agents* includes certain 9/11 agents which are recognized as EDCs, and that EDC exposure-related imbalances in sex steroid hormones are a ''plausible mechanism'' for the development of uterine cancer among WTC responders and survivors. Moreover, the STAC argued that other hormone-related cancers thought to be caused by EDC exposure are on the List, including thyroid cancer, breast cancer, testicular and prostate cancers, and all other female reproductive organ cancers. Finally, the STAC commented on the likelihood that future epidemiologic studies in the extensively studied 9/11-exposed responder population may be unable to accurately capture uterine cancer incidence because of the small number of female responders.

The Administrator reviewed the available body of evidence, including the evidence presented in the Science Team's 2021 White Paper and the STAC's comprehensive rationale and recommendation, and concluded that the totality of the available information provided a sufficient evidentiary basis to propose adding uterine cancer to the List. Subsequently, the Administrator and Secretary of HHS published an NPRM in May 2022 proposing the addition of uterine cancer to the List in 42 CFR 88.15.[16] The NPRM described the methodology used by the Science Team to evaluate the scientific evidence and included a full discussion of the Science Team's 2021 White Paper, the STAC recommendation and rationale, and the Administrator's decision to propose the addition of uterine cancer to the List.

C. Public Participation

The NPRM was published on May 10, 2022. The Administrator provided a 45-day public comment period and invited interested persons and organizations to submit written views, opinions, recommendations, and data.[17] The Administrator received 27 comments in the rulemaking docket from the public, including current WTC Health Program members and non-members who experienced 9/11 exposures who have or have had uterine cancer; unaffiliated individuals; and the WTC Health Program Survivors Steering Committee. Concurrently, as required by statute, the Administrator solicited an assessment of the WTC Health Program's evaluation of evidence supporting the proposal to add uterine cancer to the List by three independent peer reviewers.[18]

Comments received from the three peer reviewers were de-identified and compiled into one document which was published in the docket on June 9, 2022, 30 days after the NPRM publication. This permitted the public an additional 15 days to comment on the peer reviewers' assessment of the proposed rulemaking. The three peer reviewers were asked to respond to the following questions:

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

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 CFR 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. *See* the *Inventory of 9/11 Agents, infra* note 12.

[12] The *Inventory of 9/11 Agents* is composed of those agents identified in Tables 1–4 of the document, *Development of the Inventory of 9/11 Agents,* published July 17, 2018, *https://wwwn.cdc.gov/ResearchGateway/Content/pdfs/Development_of_the_Inventory_of_9-11_Agents_20180717.pdf.*

[13] The WTC Health Program released a draft of the white paper, entitled *Scientific Considerations for Potential Addition of Uterine Cancer to the List of Covered Conditions by the World Trade Center Health Program: Preliminary Assessment for the World Trade Center Health Program Scientific/Technical Advisory Committee,* on August 20, 2021, followed by a revised draft on September 16, 2021. The September revision updated the August draft to include additional information concerning 9/11 exposures and reorganized one section for clarity but did not alter the findings or conclusions of the August draft. The September revision was shared with the STAC and public prior to the STAC meeting. All versions of the WTC Health Program Science Team's white paper referenced in this final rule are available at *https://www.cdc.gov/wtc/stac_meeting.html* and in the docket for this rulemaking.

[14] The most common type of estrogen-secreting tumor are granulosa cell tumors of the ovary. Another type of estrogen-secreting tumor is adrenocortical cancers. The findings in the 2021 White Paper related to estrogen-secreting tumors are described in detail in the NPRM, *see* 87 FR 27961, 27964.

[15] Letter from Dr. Elizabeth Ward, Chair of the STAC, to the Administrator, regarding the STAC's resolution on the addition of uterine cancer to the List of WTCHP Covered Conditions, received November 29, 2021. The letter from Dr. Ward, including the STAC's recommendation, is available in the docket for this rulemaking and on the WTC Health Program website, at *https://www.cdc.gov/wtc/pdfs/stac/STAC.Recommendation.Received.29.November.2021.pdf.*

[16] *See supra* note 2.

[17] Pursuant to the *Policy and Procedures, supra* note 10, the public comment period remained open for 45 days to allow the public an additional 15 days to comment after the independent peer reviews were posted to the docket.

[18] *See* PHS Act, sec. 3312(a)(6)(F).

2. Have the requirements of this *Policy and Procedures* [19] been fulfilled? If not, please explain which requirements are missing or deficient.

3. Is the interpretation of the available information 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.

The peer reviews and public comments are found in the docket for this rulemaking. Summaries of all peer reviews and public comments, as well as the Administrator's responses, are found below.

D. Issuance of Final Rule With Immediate Effective Date

The Administrative Procedure Act (APA) requires the publication of a rule ''not less than 30 days before its effective date,'' unless the agency finds and publishes with the rule good cause for such exception.[20] In the context of the requirement for notice and comment on rulemakings, the APA specifies that such procedures may be avoided if an agency ''for good cause finds'' that ''notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest.'' [21] To the extent that the same standard for establishing ''good cause'' applies to both excepting a rulemaking from notice and comment requirements and excepting a rulemaking from the 30-day post-publication effective date requirement, the ''impracticable'' and ''contrary to the public interest'' prongs of the good-cause exemption are particularly relevant to situations such as this, where the typical delayed effective date would defer the agency's ability to provide life-saving treatment and result in less favorable treatment outcomes and survival rates for covered individuals.

The purpose of the post-publication waiting period is to give affected parties time to adjust their behavior before the final rule takes effect. In this instance, however, the affected parties are current and prospective members of the WTC Health Program who need treatment for uterine cancer. Currently enrolled WTC Health Program members who have already been diagnosed with uterine cancer do not require an additional 30 days to ready themselves for implementation of this rule; indeed, any delay in effective date could result in postponed medical care for such members or necessitate their paying out of pocket for care in the interim.

As discussed in the economic analysis in Section VI.A. of this rulemaking, the WTC Health Program estimates that over 200 enrolled members currently have uterine cancer; the Program anticipates these members will submit requests for certification of their uterine cancers as WTC-related as soon as the rule is issued. It is in these members' best interest that treatment for their cancer is made available as soon as possible. Neither these members nor the WTC Health Program require additional time to prepare for the implementation of this rule.[22] Treatment of cancer at the earliest stages has been shown to result in the best outcomes and higher survival rates.[23] As such, there is no public interest served in further delaying the effective date of this rulemaking.

For the forgoing reasons, the Administrator and the Secretary of HHS find that good cause exists to make this rulemaking effective immediately on publication.

III. Summary of Public Comments and Independent Peer Reviews

The WTC Health Program has considered whether the public comments and the peer reviews of the evidence comprising the basis for the proposed rulemaking warrant any revision to the findings and determinations described in the NPRM. The public comments and the independent peer reviews are summarized below, followed by the WTC Health Program's response.

A. Summary of Public Comments

Twenty-seven public commenters submitted comments to the docket for this rulemaking. Twenty-six expressed unequivocal agreement with the addition of uterine cancer to the List. One commenter expressed displeasure with the WTC Health Program's process for adding health conditions to the List; that comment is outside the scope of this rulemaking and is not further addressed.

Of the 26 supportive public comments, one asked that the Administrator also consider adding fibroid tumors, endometriosis, and infertility to the List. Another of the supportive comments described concerns with inequities in the WTC Health Program's research agenda, faulting the Program for ''routinely pass[ing] over'' research proposals to study survivor cohorts. These comments are also outside the scope of this rulemaking but are discussed further below.

No public commenter suggested additional references to scientific evidence regarding causes of uterine cancer, nor did any commenter indicate that there were any flaws in the WTC Health Program's evaluation of the available evidence or the Administrator's determination.

B. Summary of Independent Peer Reviews

The de-identified peer reviewers were labelled as Reviewer A, Reviewer B, and Reviewer C; their reviews of the content of the NPRM are summarized below.

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

Reviewer A suggested that a study by Curtis *et al.* [2019] [24] should be included in the evaluation.

Reviewer B was not aware of any ''additional epidemiology studies that should have been considered using Method 1,'' nor any other studies using Method 2. Reviewer B described two concerns with the WTC Health Program's analysis of evidence pursuant to Method 3 of the *Policy and Procedures.* First, Reviewer B stated that the Science Team did not consider the Endocrine Society's definition of EDCs (''an exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action'') and noted that the list of EDCs found in the

[19] *See supra* note 10.

[20] 5 U.S.C. 553(d).

[21] 5 U.S.C. 553(b)(B). Courts differ on whether the good cause standard for waiving notice and comment announced in sec. 553(b)(B) of the APA is the same standard that should be applied in waiving the 30-day publication rule in sec. 553(d). *See* Cole JP [Jan 2016], *The Good Cause Exception to Notice and Comment Rulemaking: Judicial Review of Agency Action,* Congressional Research Service, No. R44356 at 3–4 (noting that some courts have indicated that these are two distinct standards and that the test for good cause to waive notice and comment is more stringent than that used to waive the 30-day rule).

[22] In anticipation of the potential addition of uterine cancer to the List of covered health conditions, the WTC Health Program has prepared internal procedures and has worked closely with the CCEs and Nationwide Provider Network, the contractors tasked with requesting cancer certifications for members where appropriate, to ensure all parties are ready to begin processing uterine cancer certification requests from Program physicians.

[23] The American Cancer Society reports a 96 percent 5-year relative survival rate for people diagnosed with uterine cancer that is still confined to the uterus (generally considered Stage I); the 5-year survival rate drops exponentially to 20 percent for people diagnosed with uterine cancer that has spread to distant parts of the body *(e.g.,* lungs, liver, or bones) (generally considered Stage IV). *See https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/survival-rates.html.*

[24] Curtis S.W., Cobb D.O., Kilaru V., Terrell M.L., Kennedy E.M., Marder M.E., Barr D.B., Marsit C.J., Marcus M., Conneely K.N., Smith A.K. [2019], *Exposure to Polybrominated Biphenyl (PBB) Associates with Genome-Wide DNA Methylation Differences in Peripheral Blood,* Epigenetics 14(1):52–66.

Inventory of 9/11 Agents ''is almost certainly incomplete.'' According to the reviewer, the WTC Health Program should have evaluated several other EDCs in the *Inventory,* including but not limited to benzo[a]pyrene, carbazole, chlordane, chromium, dibenzofuran, dieldrin, endosulfan, heptachlor, mirex, and oxychlordane. Second, Reviewer B found some of the references cited in the 2021 White Paper concerning U.S. Environmental Protection Agency (EPA) determinations of carcinogenicity to be too dated to be authoritative. Reviewer B ultimately found that the STAC's conclusions, pursuant to its review under Method 4, are supported by a ''large body of evidence.''

Finally, Reviewer C also indicated that the Method 3 review in the 2021 White Paper does not include EDCs that have ''estrogenic activity,'' but are not carcinogens, including: polyvinyl chloride, trichloroethylene, TCDD, and some pesticides. Reviewer C provided references to support that assertion and also asked that the WTC Health Program add a discussion of studies demonstrating the association between EDCs and uterine hyperplasia and other alterations to the uterine lining that may have a causal relationship with uterine cancer. The reviewer found the assertion in the 2021 White Paper that ''[n]one of the 9/11 Agents identified as EDCs have been found by NTP, IARC, or EPA to be known to cause or be reasonably anticipated to cause uterine cancer'' to be misleading because (1) the exposures studied by these organizations may not be comparable to the extensive exposures experienced by WTC responders and survivors; (2) the reviews conducted by NTP, IARC, and EPA are often outdated; and (3) many studies have been conducted in male mice, precluding examination of uterine cancer. Finally, Reviewer C indicated that ''women's health and women's health related cancers have been under examined and grossly understudied,'' and offered a reference [25] to demonstrate that breast and ovarian cancer are associated with EDCs and that the mechanisms of action through which EDCs can impair endocrine system function and cause those cancers are similar to the known causes of uterine cancer.

Question 2: Have the requirements of this Policy and Procedures been fulfilled? If not, please explain which requirements are missing or deficient.

All three peer reviewers found that the WTC Health Program's scientific evaluation and proposed rulemaking fulfilled the requirements in the *Policy and Procedures.*

Question 3: Is the interpretation of the available information 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.

Reviewer A agreed that it was appropriate for the Administrator ''to use Method 4 of the Policy and Procedures to include uterine cancer.'' Reviewer A argued, however, that the WTC Health Program should consider the addition of uterine cancer to the List pursuant to Method 2, based on the association of uterine cancer with estrogen-secreting tumors, which may themselves be associated with EDCs. Reviewer A also pointed to their own research on polybrominated biphenyl, a type of flame retardant, which is similar to a chemical found at the WTC site and shows ''considerable overlap with endogenous estrogen.''

Reviewer B stated that they believed the rationale used by the Administrator to support the addition of uterine cancer to the List was sound.

Reviewer C agreed that the interpretation of the available information was appropriate but thought that ''some important evidence of risk factors for developing uterine cancer were under identified.'' Reviewer C suggested EDCs and other toxins contained in WTC dust may lead to risk factors that, in turn, may lead to uterine cancer.

C. WTC Health Program Response to Public Comments

The WTC Health Program finds that the comment regarding the addition of other female reproductive health conditions (*i.e.,* fibroid tumors, endometriosis, and infertility) to the List to be outside the scope of this rulemaking, which only contemplates the sufficiency of the scientific evidence for the addition of uterine cancer to the List.

Although the comment about purported inequities in the WTC Health Program research agenda is also outside the scope of the rulemaking, the Administrator notes that the Program continually evaluates its research priorities and is committed to funding research that includes all 9/11-exposed populations. The WTC Health Program manages and solicits research on a broad range of health conditions related to the 9/11-exposed population of workers and community members, including health conditions among women, members of minority groups, and persons exposed as children. With input from researchers and community members, the WTC Health Program monitors the progress of each award cycle and adjusts solicitations as needed to promote an appropriate balance of health conditions and exposure cohorts.[26] All extramural research funded by grant or cooperative agreement is awarded under a competitive process following the widely accepted National Institutes of Health framework.[27] Each research proposal is rigorously reviewed by an independent panel of experts and is subsequently scored according to its merits, including aims that address health equity. The research portfolio has been and continues to be the product of the quantity and quality of the proposed research.[28]

The public comments were overwhelmingly supportive of the proposal to add uterine cancer to the List. Moreover, public commenters did not suggest any additional references or identify concerns with the evaluation of evidence presented in the NPRM or the Administrator's determination. Therefore, there are no changes to this rulemaking as a result of the public comments.

D. WTC Health Program Response to Independent Peer Reviews

The WTC Health Program has considered the independent peer reviews of the scientific and technical evidence presented in the NPRM. The peer reviewers favored the addition of uterine cancer to the List and offered supplemental evidence in support of the addition. Many of the reviewers' suggestions for improving the Program's evaluation of the evidence supporting the addition of uterine cancer to the List

[25] Rachoń D. [2015], *Endocrine Disrupting Chemicals (EDCs) and Female Cancer: Informing the Patients,* Rev Endocr Metab Disord 16:359–364.

[26] For example, a multi-year WTC survivor-only research solicitation was initiated in the most recent cycle in response to concerns raised by community members. *See https://grants.nih.gov/grants/guide/rfa-files/RFA-OH-22-004.html.*

[27] All WTC Health Program extramural research grant and cooperative agreement applications accepted for funding consideration: (1) are evaluated for scientific and technical merit by appropriate Scientific Review Group(s) convened by CDC/NIOSH in accordance with CDC peer review policy and procedures (*www.cdc.gov/os/quality/support/peer-review.htm*), the HHS Grant Policy Statement (*www.hhs.gov/sites/default/files/grants/grants/policies-regulations/hhsgps107.pdf*), and specific guidance contained in published research funding opportunity announcements (FOAs); (2) receive a second level of review for programmatic relevance and balance by a WTC Health Program Secondary Review Committee; and (3) compete for available funds with all other recommended applications submitted in response to an FOA. Additional information on the peer review process used can be found at *https://grants.nih.gov/grants/peer-review.htm.*

[28] For more information about the WTC Health Program's research priorities, *see https://wwwn.cdc.gov/ResearchGateway.*

were compelling. As a result, the Science Team has revised and finalized the White Paper (final White Paper) to address the peer reviewers' suggestions.[29] The final White Paper is included in the docket for this rulemaking. The WTC Health Program's evaluation of the supplemental evidence provided by the peer reviewers is discussed below.

Endocrine Disrupting 9/11 Agents

Upon careful evaluation of the information provided by all three reviewers in response to *Question 1,* the WTC Health Program has found that the scientific analysis described in the NPRM did not fully capture all of the 9/11 agents identified in the *Inventory of 9/11 Agents* that are known or potential endocrine disruptors. Accordingly, the Science Team has reevaluated whether the 9/11 agents that are included as known or potential EDCs in Table 3 of the 2021 White Paper[30] was comprehensive or if additional 9/11 agents may also be considered known and potential EDCs. Following the reevaluation, the Science Team concluded that 9/11 agents beyond those listed in the 2021 White Paper, might also exhibit endocrine disrupting properties. The Science Team's process and conclusion are described below.

In the absence of an internationally harmonized list of known and potential EDCs, the Science Team has evaluated 9/11 agents by comparing each 9/11 agent listed in the *Inventory* to publicly available lists of known and potential endocrine disruptors. Comparison lists included the following:

- The Endocrine Disruptor Lists published by the national authorities in six European Union (EU) member countries: *List of Substances Identified as Endocrine Disruptors at EU Level,* the L*ist of Substances Under Evaluation for Endocrine Disruption Under an EU Legislation,* and the *List of Substances Considered, by the Evaluating National Authority, to Have Endocrine Disrupting Properties,*[31] which altogether identify 194 chemicals recognized as known or potential endocrine disruptors. The EU lists are updated at least bi-annually and were most recently updated in June 2022.
- The United Nations Environment Programme's *List of Identified Endocrine Disrupting Chemicals,*[32] which identifies 45 chemical substances as endocrine disruptors and was last updated in July 2017.
- The Endocrine Disruption Exchange's *List of Potential Endocrine Disruptors,* a master list of 1,482 chemicals with at least one study demonstrating endocrine disrupting properties, last updated in September 2018.[33]
- The SIN (Substitute It Now) List developed by the non-profit International Chemical Secretariat (ChemSec).[34] ChemSec recommends ceasing use of 32 EDCs on the SIN List, last updated in 2014, because of their threat to human health and the environment.

As a result of this reevaluation, the Science Team has concluded that additional 9/11 agents and categories of 9/11 agents should be added to the 9/11 agents and categories previously listed in Table 3 of the 2021 White Paper as known or potential EDCs. Accordingly, Table 3 of the final White Paper now includes 136 individual 9/11 agents, one mixture (diesel exhaust), and 10 categories of 9/11 agents that may be evaluated as a group.

Of the 9/11 agents and categories of 9/11 agents that are now included in Table 3 and recognized by the WTC Health Program as known or potential EDCs, 78 have been evaluated by IARC for carcinogenicity. EDC 9/11 agents have been classified by IARC as follows:

- 12 EDC 9/11 agents and categories as *carcinogenic to humans* (Group 1),
- 8 EDC 9/11 agents and categories as *probably carcinogenic to humans* (Group 2A),
- 20 EDC 9/11 agents and categories as *possibly carcinogenic to humans* (Group 2B), and
- 38 EDC 9/11 agents and categories as not classifiable as to carcinogenicity to humans (Group 3).

The remainder—55 individual EDC 9/11 agents and three categories—have not been evaluated by IARC.[35] NTP classifies seven EDC 9/11 agents and categories as *known to be human carcinogens* and 23 EDC 9/11 agents and categories as *reasonably anticipated to be human carcinogens;*[36] the rest of the EDCs—101 individual 9/11 agents and 5 categories—have not been evaluated by NTP. For each cancer site, IARC identifies chemical, physical, and biological entities or exposure circumstances with *sufficient* or *limited* evidence of carcinogenicity in humans. IARC does not identify any EDC 9/11 agents, categories, or any other hazard included in the *Inventory of 9/11 Agents* as having sufficient or limited evidence in humans of causing cancer in the uterus.[37]

The Science Team also has acknowledged Reviewer B's concerns that the EPA classifications of carcinogenicity are not always up to date and should not be relied upon for current scientific knowledge. Some EPA evaluations of the carcinogenicity of 9/11 agents in the *Inventory* were conducted decades ago (*e.g.,* evaluations for phthalates such as benzyl butyl phthalates and dibutyl phthalate were last updated between 1987 and 1990) and some assessments are currently in development (*e.g.,* chloroform, chromium, cobalt, formaldehyde, mercury, naphthalene,

[29] Following review of public comments and peer reviews on the May 2022 NPRM, the WTC Health Program Science Team revised the 2021 White Paper twice. In an August 2022 revision of the white paper, the Science Team added the definition of EDC by the Endocrine Society and a reference to the Society's position statement on EDCs; revised Table 3 to include an additional 84 agents, mixtures, and categories of agents known and potential EDCs; and to exclude the EPA classifications of carcinogenicity found in the earlier drafts. In January 2023, the white paper was finalized and retitled *Scientific Considerations for Addition of Uterine Cancer to the List of Covered Conditions by the World Trade Center Health Program: Final Assessment and Follow-Up to November 18, 2021, Scientific/Technical Advisory Committee (STAC) Meeting.* In the final White Paper, the Science Team revised Table 3 to sort the 9/11 agents, mixtures, and categories in alphabetical order; revised the section named ''WTC Health Program's Actions after Receipt of the STAC Recommendation'' to clarify that the Administrator initiated this rulemaking to add uterine cancer to the List in response to the STAC recommendation; and added an appendix reflecting the discussion about mechanisms of endocrine disruption in the preamble of this rulemaking. Both the August 2022 revision and the January 2023 final White Paper are available at *https://www.cdc.gov/wtc/stac_meeting.html* and in the docket for this rulemaking.

[30] Table 3 includes a list of substances in the *Inventory of 9/11 Agents* that are known and potential endocrine disruptors and their reported carcinogenicity by authoritative bodies.

[31] The Endocrine Disruptor Lists are compiled by the national authorities of Belgium, Denmark, France, The Netherlands, Sweden, and Spain. *See https://edlists.org/.*

[32] United Nations Environment Programme, International Panel on Chemical Pollution [2017], *Worldwide Initiatives to Identify Endocrine Disrupting Chemicals (EDCs) and Potential EDCs, https://wedocs.unep.org/bitstream/handle/20.500.11822/25633/EDC_report1.pdf?sequence=1&isAllowed=y.*

[33] *The Endocrine Disruption Exchange (TEDX), https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list.*

[34] The International Chemical Secretariat, *Endocrine Disrupting Chemicals, https://sinlist.chemsec.org/endocrine-disruptors/.*

[35] World Health Organization, International Agency for Research on Cancer (IARC), *List of Classifications; Agents Classified by the IARC Monographs, Volumes 1–132, https://monographs.iarc.who.int/list-of-classifications.* Last visited August 22, 2022.

[36] National Toxicology Program (NTP), HHS, 15th Report on Carcinogens, *https://ntp.niehs.nih.gov/go/roc15.* Last visited August 22, 2022.

[37] World Health Organization, International Agency for Research on Cancer (IARC), *List of Classifications by Cancer Sites with Sufficient or Limited Evidence in Humans, IARC Monographs, Volumes 1–132, https://monographs.iarc.who.int/wp-content/uploads/2019/07/Classifications_by_cancer_site.pdf.* Last visited September 15, 2022.

perfluorodecanoic acid, perfluorohexanesulfonic acid, polychlorinated biphenyls, uranium, and vanadium).[38] Additionally, the Science Team has found that use of EPA references may be confusing since they are not required for review under any of the methods in the *Policy and Procedures* discussed above. To address these concerns, the Science Team has decided to remove the EPA carcinogenicity classification column from Table 3 of the final White Paper.

Mechanisms of Endocrine Disruption

The Science Team also has evaluated the references provided by peer reviewers to supplement the STAC's discussion of some potential mechanisms of action [39] through which EDCs might cause uterine cancer in humans. Much of the available research on EDCs' mechanisms of action has focused on EDCs which are not also identified 9/11 agents in the *Inventory of 9/11 Agents.* Indeed, some of the specific chemicals and toxins identified as EDCs by the peer reviewers based on supplemental sources have not been identified by the WTC Health Program as 9/11 agents. The Science Team has recognized, however, that the list of 9/11 agents identified by the WTC Health Program in the *Inventory* may not be complete and that WTC-related uterine cancer may be associated with chemicals and toxins that exhibit estrogenic properties that may be identified as 9/11 agents in the future. Regardless of whether there are EDCs that may be associated with uterine cancer that may be added to the *Inventory* in the future, the Science Team has found it instructive to examine mechanisms of action for endocrine disruption even for those EDCs that have not been recognized as 9/11 agents. The supplemental references' descriptions of mechanisms of endocrine disruption illustrate the various ways in which exposure to EDCs could impact the female reproductive system and result in uterine cancer. The similar mechanisms of action for other EDCs help provide a complete picture of the possible causal relationship between the September 11, 2001, terrorist attacks, and uterine cancer among WTC responders and survivors.[40]

Most endometrial tumors are hormonally driven through estrogen signaling via estrogen receptors α and β acting as an oncogenic signal. The main risk factors (*i.e.,* estrogen therapy without progestins, tamoxifen for the treatment of breast cancer, parity, oral contraceptive use, age at menarche) and some treatment options (*i.e.,* progestin therapies) for endometrial cancer patients underscore a key role for estrogen signaling in the disease.[41] Estrogen-like chemicals have been shown to mimic the estrogen pathway and affect the normal function of female sex hormones. This mechanism is suspected to lead to carcinogenesis in women, including the development of endometrial cancer, breast and ovarian cancers, and prostate cancer in men.[42] EDCs can interfere with the function and metabolism of estrogen; breast and ovarian cancers are associated with EDCs and their current known mechanisms of action are similar to those of uterine cancer.[43] For example, experimental studies in animals exposed to endocrine-disrupting alkylphenols such as nonylphenol and oxylphenol, as well as a case-control study, suggest an association between exposure to EDCs and endometrial cancer.[44] Experimental animal and *in vitro* studies have shown that exposure to the EDCs bisphenol A (BPA) and 2,4-dichlorodiphenyltrichloroethane (DDT) result in changes that could lead endometrial cells towards malignancy.[45]

Studies in animal models show that exposure to some EDCs can cause endometrial hyperplasia (a proliferation of endometrial glands) and other alterations to the uterine lining.[46] Endometrial hyperplasia with atypia is of clinical significance because it may progress to, or coexist with, endometrial carcinoma. However, no human studies that showed an association between EDCs and endometrial hyperplasia were identified. Nonetheless, experimental animal studies have identified some evidence that suggests the likelihood of occurrence in humans.

EDCs such as di(2-ethylhexyl)phthalate (DEHP) and cadmium have also been associated with uterine leiomyoma (a benign smooth muscle tumor, also known as a fibroid, that causes symptoms such as uterine bleeding and severe pelvic pain, which may result in infertility or major surgery). A meta-analysis of five studies showed that urinary DEHP metabolites were statistically significantly associated with an increased risk of uterine leiomyoma, although the mechanism is still not well understood.[47] Moreover, an *in vitro* study showed that fibroid cells subjected to cadmium exposure for two months show enhanced migration potential, augmented anchorage-independent growth, and increased

[38] *See* U.S. Environmental Protection Agency (EPA), Integrated Risk Information System (IRIS) Assessments, *https://iris.epa.gov/AtoZ/?list_type=erd.*

[39] Mechanisms of action are the biochemical processes underlying the adverse response to exposure; these processes may lead to risk factors for or development of disease, such as cancer.

[40] The EDCs discussed in this section include:

- 9/11 agents: 2,4-dichlorodiphenyltrichloroethane (DDT); polyvinyl chloride plastics (which contain phthalates); trichloroethylene (and its major metabolites); TCDD; chlordane; dieldrin; endosulfan; hexachlorobenzene (HCB); lindane; heptachlor; metribuzin; mirex; cadmium; and WTC dust.
- Non-9/11 agents: alkylphenols (*e.g.,* nonylphenol and oxylphenol); bisphenol A (BPA); di(2-ethylhexyl)phthalate (DEHP); and polybrominated biphenyl (PBB).

[41] Rodriguez AC, Blanchard Z, Maurer KA, Gertz J [2019], *Estrogen Signaling in Endometrial Cancer: A Key Oncogenic Pathway with Several Open Questions,* Horm Cancer 10(2–3), 51–63.

[42] Deroo BJ, Korach KS [2006], Estrogen *Receptors and Human Disease,* J Clin Invest 116(3):561–570.

[43] *See supra* note 26.

[44] Zhang W, Yang J, Wang J, Xia P, Xu Y, Jia H, Chen Y [2007], *Comparative Studies on the Increase of Uterine Weight and Related Mechanisms of Cadmium and p-Nonylphenol,* Toxicology 241(1–2):84–91; Kim J, Cha S, Lee MY, Hwang YJ, Yang E, Ryou C, Jung HI, Cheon YP [2018], *Chronic Low-Dose Nonylphenol or Di-(2-ethylhexyl) Phthalate Has a Different Estrogen-Like Response in Mouse Uterus,* Dev Reprod 22(4):379–391; Wen HJ, Chang TC, Ding WH, Tsai SF, Hsiung CA, Wang SL [2020], *Exposure to Endocrine Disruptor Alkylphenols and the Occurrence of Endometrial Cancer,* Environ Pollut 267:115475.

[45] Scsukova S, Rollerovab E, Mlynarcikovaa AB [2016], *Impact of Endocrine Disrupting Chemicals on Onset and Development of Female Reproductive Disorders and Hormone-Related Cancer,* Reprod Biol 16:243–254.

[46] Singh P, Bhartiya D [2022], *Molecular Insights into Endometrial Cancer in Mice,* Stem Cell Rev Rep 18(5):1702–1717; Guerrero Schimpf M, Milesi MM, Zanardi MV, Varayoud J [2022], *Disruption of Developmental Programming with Long-Term Consequences after Exposure to a Glyphosate-Based Herbicide in a Rat Model,* Food Chem Toxicol 159:112695; Neff AM, Blanco SC, Flaws JA, Bagchi IC, Bagchi MK [2019], *Chronic Exposure of Mice to Bisphenol-A Alters Uterine Fibroblast Growth Factor Signaling and Leads to Aberrant Epithelial Proliferation,* Endocrinology 160(5):1234–1246; Nasiadek M, Danilewicz M, Sitarek K, Świątkowska E, Daragó A, Stragierowicz J, Kilanowicz A [2018], *The Effect of Repeated Cadmium Oral Exposure on the Level of Sex Hormones, Estrous Cyclicity, and Endometrium Morphometry in Female Rats,* Environ Sci Pollut Res Int 25(28):28025–28038; Padmanabhan R, Hendry IR, Knapp JR, Shuai Bin, Hendry WJ [2017], *Altered MicroRNA Expression Patterns During the Initiation and Promotion Stages of Neonatal Diethylstilbestrol-Induced Dysplasia/Neoplasia in the Hamster (Mesocricetus auratus) Uterus,* Cell Biol Toxicol 33(5):483–500; Wikoff DS, Rager JE, Haws LC, Borghoff SJ [2016], *A High Dose Mode of Action for Tetrabromobisphenol A-Induced Uterine Adenocarcinomas in Wistar Han Rats: A Critical Evaluation of Key Events in an Adverse Outcome Pathway Framework,* Regul Toxicol Pharmacol 77:143–159; Hendry WJ, Hariri HY, Alwis ID, Gunewardena SS, Hendry IR [2014], *Altered Gene Expression Patterns During the Initiation and Promotion Stages of Neonatally Diethylstilbestrol-Induced Hyperplasia/Dysplasia/Neoplasia in the Hamster Uterus,* Reprod Toxicol 50:68–86.

[47] Fu, Z, Zhao F, Chen K, Xu J, Li P, Xia D, Wu Y [2017], *Association Between Urinary Phthalate Metabolites and Risk of Breast Cancer and Uterine Leiomyoma,* Reprod Toxicol 74:134–142.

DNA synthesis, suggesting EDC-induced potential progression towards uterine cancer.[48]

In addition to interacting with estrogen receptors α and β, EDCs are known to bind to and activate the estrogen-related receptor gamma (ERRγ). BPA has weak estrogenic activity due to its limited capacity to bind to nuclear estrogen receptors α and β. Nonetheless, ERRγ is activated by BPA and interacts with the ligand domain of estrogen receptors.[49] Multiple studies show that BPA may increase the risk of estrogen-related cancers.[50]

EDCs are also known to play a role in endocrine disruption leading to epigenetic [51] changes. An instructive example is a study among Michigan residents accidentally exposed to the EDC polybrominated biphenyl (PBB). The study's authors found differences in epigenetic marks (chemicals which turn genes ''on'' and ''off'') that suggest that PBB acts similarly to estrogen and is associated with dysregulated immune system pathways. The authors also found evidence that PBB could be acting like an estrogen, impacting gene expression.[52] Furthermore, EDCs may increase uterine sensitivity to estrogens due to epigenetic alterations. Another example is a study in female mice in which BPA administered *in utero* increased the expression of the developmental homeobox gene *Hoxa10* that controls uterine organogenesis. Alterations in methylation of *Hoxa10* have been associated with several human cancers.[53]

In addition, endocrine disruption caused by some 9/11 agents alters reproductive and sexual development, and may lead to other health outcomes such as obesity and diabetes that affect the risk of uterine cancer development.[54] The following identified EDC 9/11 agents may pose such risks for the development of uterine cancer: polyvinyl chloride plastics, which contain phthalates; [55] trichloroethylene and its major metabolites; [56] TCDD, which is an EDC that has antiestrogenic properties; [57] and pesticides such as chlordane, DDT, dieldrin, endosulfan, hexachlorobenzene, lindane, heptachlor, metribuzin, and mirex.[58]

Finally, the development of most endocrine cancers is likely to be the result of low-dose exposures to complex chemical mixtures in the environment throughout a person's life.[59] WTC dust is a complex mixture of EDCs and other environmental chemicals. Exposure to WTC dust, when added to the usual low-dose environmental chemical exposures experienced in a person's lifetime, may directly or indirectly influence the development of uterine cancer. Combined exposures have simultaneous effects on the endocrine system that could affect the development of uterine cancer and its risk factors.[60]

E. WTC Health Program Science Team Conclusion

In response to the peer reviews, the Science Team has updated its analysis and issued the final White Paper [61] including the Endocrine Society's definition of EDC and a reference to the Society's position statement on EDCs; the final White Paper recognizes 84 additional 9/11 agents in the *Inventory of 9/11 Agents* as known or potential EDCs in Table 3. The Science Team has also clarified in the final White Paper that among all 9/11 agents that are known or potential EDCs and that have been evaluated for their carcinogenicity by NTP and IARC, none are currently *known to cause* or *reasonably anticipated to cause* uterine cancer. Finally, the Science Team has modified the final White Paper to incorporate an appendix reflecting the discussion about mechanisms of endocrine disruption in this preamble.

The evidence provided by independent peer reviewers is compelling. However, the additional information does not alter the evaluations and conclusions found in the Science Team's final White Paper because the scope of the White Paper was limited to an assessment of the evidence for adding uterine cancer to the List based on Methods 1–3 of the *Policy and Procedures* described above. The peer reviewers did not suggest any epidemiologic studies of uterine cancer in the 9/11-exposed population; therefore, no further analysis was conducted under Method 1. No studies were suggested to demonstrate support for a causal association between a health condition already on the List and uterine cancer; therefore, no further analysis was conducted under Method 2. Finally, Method 3 relies on: (1) an NTP finding that the 9/11 agent is *known* or *reasonably anticipated to be a human carcinogen,* and (2) an IARC finding that there is *sufficient* or *limited* evidence in humans that the 9/11 agent causes that cancer. Although some of the 9/11 agents identified as known or potential EDCs that have been added to Table 3 of the final White Paper are considered by NTP to be *known human carcinogens* or *reasonably anticipated to be human carcinogens,* IARC has not determined that there is *sufficient* or *limited* evidence in humans that any 9/11 agent EDC or any other hazard in the *Inventory* causes uterine cancer. Therefore, the Science Team has continued to find that there is insufficient evidence available to

[48] Yan Y, Liu J, Lawrence A, Dykstra MJ, Fannin R, Gerrish K, Tucker CJ, Scappini E, Dixon D [2021], *Prolonged Cadmium Exposure Alters Benign Uterine Fibroid Cell Behavior, Extracellular Matrix Components, and TGFB Signaling,* FASEB J 35(8):e21738.

[49] Hwang KA, Choi KC [2015], Chapter One: Endocrine-Disrupting Chemicals with Estrogenicity Posing the Risk of Cancer Progression in Estrogen-Responsive Organs, *in Advances in Molecular Toxicology, Volume 9,* (Fishbein JC and Heilman JM, eds., Elsevier).

[50] Soto AM, Sonnenschein C [2010], *Environmental Causes of Cancer: Endocrine Disruptors as Carcinogens,* Nat Rev Endocrinol 6(7):363–370.

[51] Changes in gene expression caused by environmental factors that do not involve alteration of the DNA sequence.

[52] Curtis SW, Cobb DO, Kilaru V, Terrell ML, Kennedy EM, Marder ME, Barr DB, Marsit CJ, Marcus M, Conneely KN, Smith AK [2019], *Exposure to Polybrominated Biphenyl (PBB) Associates with Genome-Wide DNA Methylation Differences in Peripheral Blood,* Epigenetics 14(1):52–66.

[53] *See* Scsukova S, *et al., supra* note 46; Bromer JG, Zhou Y, Taylor MB, Doherty L, Taylor HS [2010], *Bisphenol-A Exposure in Utero Leads to Epigenetic Alterations in the Developmental Programming of Uterine Estrogen Response,* FASEB J 24:2273–2280.

[54] Eales J, Bethel A, Galloway T, Hopkinson P, Morrissey K, Short RE, Garside R [2022], *Human Health Impacts of Exposure to Phthalate Plasticizers: An Overview of Reviews,* Environ Int 158:106903.

[55] Ohashi A, Kotera H, Hori H, Hibiya M, Watanabe K, Murakami K, Hasegawa M, Tomita M, Hiki Y, Sugiyama S [2005], *Evaluation of Endocrine Disrupting Activity of Plasticizers in Polyvinyl Chloride Tubes by Estrogen Receptor Alpha Binding Assay,* J Artif Organs 8(4):252; Bang DY, Kyung M, Kim MJ, Jung BY, Cho MC, Choi SM, Kim YW, Lim SK, Lim DS, Won AJ, Kwack SJ, Lee Y, Kim HS, Lee BM [2012], *Human Risk Assessment of Endocrine-Disrupting Chemicals Derived from Plastic Food Containers,* Compr Rev Food Sci Food Saf 11:453–70; Yan Y, Zhu F, Zhu C, Chen Z, Liu S, Wang C, Gu C [2021], *Dibutyl Phthalate Release from Polyvinyl Chloride Microplastics: Influence of Plastic Properties and Environmental Factors,* Water Res 204:117597; Mariana M, Feiteiro J, Verde I, Cairrao E [2016], *The Effects of Phthalates in the Cardiovascular and Reproductive Systems: A Review,* Environ Int 94:758–776.

[56] Tachachartvanich P, Sangsuwan R, Ruiz HS, Sanchez SS, Durkin KA, Zhang L, Smith MT [2018], *Assessment of the Endocrine-Disrupting Effects of Trichloroethylene and its Metabolites Using In Vitro and In Silico Approaches,* Environ Sci Technol 52(3):1542–1550.

[57] Boverhof DR, Kwekel JC, Humes DG, Burgoon LD, Zacharewski TR [2006], *Dioxin Induces an Estrogen-Like, Estrogen Receptor-Dependent Gene Expression Response in the Murine Uterus,* Mol Pharmacol 69(5):1599–1606.

[58] Mnif W, Hassine AI, Bouaziz A, Bartegi A, Thomas O, Roig B [2011], *Effect of Endocrine Disruptor Pesticides: A Review,* Int J Environ Res Public Health 8(6):2265–303.

[59] Darbre PD [2022], Chapter 8: Exposure to Mixtures of EDCs and Long-Term Effects, *in Endocrine Disruption and Human Health* (Darbre PD, ed., Elsevier, 2nd ed.).

[60] *See supra* note 26.

[61] *See supra* note 30.

support the addition of uterine cancer to the List pursuant to Method 3.

For the reasons discussed above, the Science Team's analysis and conclusion are unchanged: there continues to be no evidence to support the addition of uterine cancer to the List pursuant to Methods 1 or 3, but sufficient evidence supports the addition of uterine cancer to the List for qualified WTC Health Program members, pursuant to Method 2 (*i.e.,* only for those Program members who have a certified WTC-related estrogen-secreting tumor). However, the Science Team has found that the evaluations and supplemental information provided by the peer reviewers in response to the NPRM provide additional support for the STAC recommendation and rationale provided to the Administrator under Method 4.

IV. Administrator's Final Decision Regarding Uterine Cancer

The Administrator and Secretary of HHS proposed the addition of uterine cancer [62] to the List after reviewing the available body of scientific evidence describing the causal relationship between 9/11 exposures and uterine cancer, including certain 9/11 agents which are known or potential EDCs, as well as evaluating the STAC's comprehensive rationale and recommendation. In accordance with the WTC Health Program's Policy and Procedures, the Administrator evaluated the available information under the four methods developed for determining whether to add a type of cancer to the List. The Administrator's evaluation was discussed in full in Section III.E. of the NPRM.[63] During the NPRM public comment period, 26 public commenters and three independent peer reviewers expressed unanimous support for the addition of uterine cancer to the List based on the STAC's recommendation. Peer reviewers found that the totality of evidence points to a causal association between 9/11 agents that are known or potential EDCs and uterine cancer in the 9/11-exposed population.

The Administrator considered the public comments and peer reviews as well as the Science Team's description and evaluation of the supplemental evidence regarding mechanisms by which EDCs could affect the development of uterine cancer and its risk factors. First, the Administrator assessed whether there was sufficient evidence in peer-reviewed, published, epidemiologic studies of 9/11-exposed populations to support adding uterine cancer to the List under Method 1. The Administrator concurred with the Science Team's evaluation of the literature pursuant to Method 1 and found that the available literature did not provide sufficient support for the addition of uterine cancer to the List under Method 1. Because no peer-reviewed, published, epidemiologic studies of uterine cancer in 9/11-exposed populations were identified by peer reviewers or public commenters, the Administrator has determined that the evidence available under Method 1 is insufficient to support the addition of uterine cancer to the List.

Next, the Administrator reviewed whether multiple peer-reviewed epidemiologic studies establish a causal association between a condition already on the List and that type of cancer to permit an addition to the List under Method 2. In the NPRM, the Administrator agreed with the Science Team's finding that there is evidence of a causal association between estrogen-secreting tumors, which are considered rare cancers within the WTC Health Program, and uterine cancer. Thus, the Administrator found that uterine cancer may be proposed for addition to the List pursuant to Method 2, but such an addition would be limited to only those WTC Health Program members who have a certified WTC-related estrogen-secreting tumor. Neither peer reviewers nor public commenters provided studies refuting a causal association between estrogen-secreting tumors and uterine cancer. Therefore, the Administrator has determined that uterine cancer may be added to the List pursuant to Method 2, but only for those WTC Health Program members with a qualifying certified WTC-related estrogen-secreting tumor.

Pursuant to Method 3, the Administrator examined NTP and IARC evaluations of carcinogenicity of 9/11 agents. Method 3 permits an addition to the List if: (1) NTP has determined that a specific 9/11 agent is *known to be a human carcinogen* or *reasonably anticipated to be a human carcinogen,* and (2) IARC has determined that there is *sufficient* or *limited* evidence in humans that the 9/11 agent causes uterine cancer. As described in the NPRM, the Administrator concurred with the Science Team's conclusion that there was insufficient evidence to add uterine cancer to the List because IARC has not determined there is *sufficient* or even *limited* evidence in humans that any of the 9/11 agents in the *Inventory of 9/11 Agents* cause uterine cancer. Following publication of the NPRM, the Administrator also reviewed the 9/11 agents added to the list of EDCs in Table 3 of the final White Paper in response to the peer reviews. He agrees that 9/11 agents that are considered by NTP to be *known* or *reasonably anticipated human carcinogens* but that are not determined by IARC to have *sufficient* or *limited* evidence of uterine carcinogenicity in humans do not meet the requirements of Method 3. Because IARC has not identified any EDCs among the 136 EDC 9/11 agents and categories of EDC 9/11 agents now recognized in Table 3 of the final White Paper, nor any other hazard included in the *Inventory* as having sufficient or limited evidence in humans of uterine carcinogenicity, the Science Team's analysis and the Administrator's determination remains unchanged. Accordingly, the Administrator has determined that the evidence available under Method 3 is insufficient to support the addition of uterine cancer to the List but acknowledges that some 9/11 agents in the *Inventory* have never been evaluated for carcinogenicity by NTP or IARC.

The Administrator ultimately proposed adding uterine cancer to the List pursuant to Method 4, which permits an addition where the STAC recommends such an addition and provides a reasonable basis for the recommendation. As explained in the NPRM, the Administrator found that the STAC's recommendation provided a reasonable basis for the addition of uterine cancer under Method 4 and the recommendation was further supported by the supplemental information presented by the Science Team in the 2021 White Paper.

Specifically, the Administrator agreed with the STAC that mechanisms of initiation and progression of uterine cancer are similar to those for several other cancers on the List.[64] The Administrator agreed with the STAC's finding that the shared etiology and pathogenesis described in the scientific literature suggest it would be unlikely that uterine cancer would be the only cancer type not related to 9/11 exposures. The Administrator also agreed that an association between exposure to EDCs in WTC dust and uterine cancer risk is plausible.[65]

Following publication of the NPRM and upon review of the public comments and peer reviews and the Science Team's response, including the final White Paper, the Administrator has found that the supplemental scientific evidence complements the evidence provided by the STAC by comprehensively demonstrating the variety of mechanisms of endocrine disruption and providing additional general support for the addition of

[62] ICD–10 codes C54 and C55. *See supra* note 1.

[63] *Supra* note 2 at 27966.

[64] *See supra* note 2 at 27966 and *supra* note 15.

[65] *See supra* note 2 at 27967 and *supra* note 15.

uterine cancer to the List. Given the growing body of scientific evidence suggesting that exposure to EDCs may be a risk factor for female reproductive organ cancers, the Administrator has found that it is reasonable to assume that exposure to EDCs in WTC dust may contribute to uterine cancer risk, even in the absence of a robust body of evidence conclusively demonstrating EDC carcinogenic risks in occupational cohorts of women. The Administrator continues to recognize that the disproportionally low representation of women in the most studied cohorts of exposed responders makes it epidemiologically unlikely that a definitive association between 9/11 exposures and the occurrence of uterine cancer will be identified during the lifetime of even the most highly exposed WTC Health Program members.[66]

After final review of the analyses by the STAC in its recommendation, the WTC Health Program Science Team's 2021 White Paper, public comments on the NPRM, the independent peer reviews of the scientific and technical evidence comprising the basis for the proposed rule, the Science Team's response to those comments, and the final White Paper, the Administrator has concluded that evidence continues to support the addition of uterine cancer to the List. For the reasons discussed above, the Administrator has determined that there is insufficient evidence to add uterine cancer to the List pursuant to Methods 1 and 3 of the *Policy and Procedures.* Sufficient evidence exists for the addition of uterine cancer pursuant to Method 2, restricted to those members who have a qualifying estrogen-secreting tumor. Finally, pursuant to Method 4, because the STAC provided a reasonable basis for an association between 9/11 agents listed in the *Inventory of 9/11 Agents* and uterine cancer, the Administrator has determined that there is sufficient evidence to add uterine cancer to the List for all eligible members.

With this rulemaking, the Administrator and the Secretary of HHS finalize the addition of uterine cancer to the List of WTC-Related Health Conditions. Adding uterine cancer to the List in a final rule with an immediate effective date allows the WTC Health Program to begin offering treatment services as soon as possible to members whose uterine cancers are certified as WTC-related.

V. Summary of Final Rule

For the reasons discussed above, the Administrator amends 42 CFR 88.15 by adding a new paragraph (d)(15) to include ''malignant neoplasms of corpus uteri and uterus, part unspecified'' [67] on the List of WTC-Related Health Conditions. The existing paragraph (d)(15)—malignant neoplasm of the ovary—and the remainder of the cancer types identified in existing paragraphs (d)(16) through (24)—rare cancers—are renumbered paragraphs (d)(16) through (25), accordingly. Finally, in renumbered paragraphs (d)(24) and (d)(25), the terms ''Childhood cancers'' and ''Rare cancers'' are unitalicized but are otherwise unchanged.

In addition to the changes described above, the Authority citation for part 88 is revised to remove the Public Law citations, retaining only the U.S. Code citations.

VI. Required Regulatory Analyses

A. Executive Order 12866 (Regulatory Planning and Review) and Executive Order 13563 (Improving Regulation and Regulatory Review)

Executive Orders (E.O.) 12866 and 13563 direct agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). E.O. 13563 emphasizes the importance of quantifying both costs and benefits, reducing costs, harmonizing rules, and promoting flexibility.

This final rule has been determined not to be a significant regulatory action under section 3(f) of E.O. 12866, and therefore has not been reviewed by the Office of Management and Budget (OMB). The addition of uterine cancer finalized by this rulemaking is estimated to cost the WTC Health Program between $1,706,454 and $3,805,173 per annum for 2023 through 2026.[68] All costs to the WTC Health Program will be transfers due to the implementation of provisions of the Patient Protection and Affordable Care Act (Pub. L. 111–148) in 2014 and as required under the authorizing statute for the WTC Health Program.[69] The rule will not interfere with state, local, or tribal governments in the exercise of their governmental functions.

Population Estimates

The WTC Health Program estimates that approximately 84,000 WTC responders and approximately 34,000 survivors, or approximately 118,000 individuals in total, are current, living Program members. Of that total population, approximately 60,000 individuals were participants in previous WTC medical programs and were enrolled as ''legacy'' members in the WTC Health Program established by Title XXXIII of the PHS Act. For the purpose of calculating a baseline estimate of cancer prevalence only, the Administrator assumed that a steady rate of enrollment would continue, based on the trend in enrollees through September 2021.

According to WTC Health Program data, 12 percent of the current responder members (approximately 10,000 individuals) and 50 percent of survivor members (approximately 17,000 individuals) are female.[70] Finally, because there are no existing data on cancer cases related to 9/11 exposures at either the Pentagon or in Shanksville, Pennsylvania, the Administrator has used only data from studies of individuals who were responders or survivors in the New York City disaster area.

Cost of Uterine Cancer Treatment

The Administrator estimated the treatment costs associated with covering uterine cancer in this rulemaking in U.S. dollars. The costs of treatment are divided into three treatment phases: the first year of treatment following diagnosis; the intervening years or continuing treatment after the first year; and treatment during the last year of life. The first-year costs of cancer treatment are higher due to the initial need for aggressive medical (*e.g.,* radiation or chemotherapy) and surgical care. The costs during the last year of life are often dominated by increased hospitalization costs.[71] Therefore, three

[66] *Id.*

[67] *See supra* note 1.

[68] As discussed in this section, NIOSH estimated lower-and upper-bound estimates to reflect the uncertainty in the Agency's ability to predict the expected number of cancer cases in the three years after this rulemaking. The lower-bound reflects the general U.S. population cancer rate and uses undiscounted costs for 2023 and costs for 2024–2026 discounted at the 7 percent discount rate. The upper-bound reflects the estimated rate of uterine cancer among existing WTC Health Program members and uses undiscounted rates for 2023 and costs for 2024–2026 discounted at the 3 percent discount rate. Although, if added to the List, uterine cancer would be considered a covered condition for the duration of the WTC Health Program (currently authorized through FY 2090). The dates 2023–2026 were chosen to provide a snapshot of uterine cancer costs in the coming years.

[69] Because sec. 3331(c)(3) of the PHS Act requires WTC Health Program members to maintain minimum essential insurance coverage, all treatment costs to be paid by the WTC Health Program are considered transfers.

[70] *See supra* note 4.

[71] Yabroff KR, Lamont EB, Mariotto A, Warren JL, Topor M, Meekins A, Brown ML [2008], *Cost of Care for Elderly Cancer Patients in the United States,* J Natl Cancer Inst 100(9):630–41.

different treatment phase costs were used to provide a best estimate of treatment costs in conjunction with expected incidence and long-term survival rates for uterine cancer. Average 2022 treatment costs for uterine cancer, the last year for which complete data were available, are in Table A below.

TABLE A—AVERAGE COSTS OF TREATMENT FOR UTERINE CANCER, 2022 DOLLARS

Stage of treatment	Average cost (U.S. dollars)
Initial (first 12 months after diagnosis)	$41,283
Continuing (annual)	2,152
Last year of life (last 12 months of life)	122,954

These cost figures were based on a study of cancer patients from the Surveillance, Epidemiology, and End Results (SEER) Program maintained by the National Cancer Institute and using Medicare files.[72] The average costs of treatment described above are given in 2022 prices, adjusted using the Medical Consumer Price Index for all urban consumers.[73]

Incident Cases of Cancer

For the purpose of illustrating a lower-bound incidence estimate, the Administrator used the same baseline analysis described in the NPRM, calculating the number of cases of uterine cancer expected to be observed in the cohort of approximately 27,000 female responders and survivors in the WTC Health Program, based on U.S. population cancer rates.[74] Demographic characteristics of the cohort were assigned since the actual data are not available for individuals in the responder and survivor populations who have not yet enrolled in the WTC Health Program. Sex and age (at the time of exposure) distributions for responders and survivors were assumed to be the same as current members in the WTC Health Program. Because uterine cancer occurs only in females,[75] all calculations only consider female WTC Health Program members.

The Administrator assumed race and ethnic origin distributions for responders and survivors, respectively, according to distributions in the WTC Health Registry cohort:[76] 57 percent non-Hispanic white, 15 percent non-Hispanic black, 20 percent Hispanic, and 8 percent other race/ethnicity for responders; 50 percent non-Hispanic white, 17 percent non-Hispanic black, 15 percent Hispanic, and 18 percent other race/ethnicity for survivors. Registry follow-up for cancer morbidity for each person began on January 1, 2002, or at age 15 years, whichever occurred later. Age 15 was used because the cancer incidence rate file did not include rates for persons of less than 15 years of age. Follow-up ended on December 31, 2016, or the estimated last year of life, whichever was earlier. The estimated last year of life was used since not all persons would be expected to remain alive at the end of 2016. The estimated last year of life was based on sex, race, age, and year-specific death rates from CDC WONDER.[77] A life-table analysis program, LTAS.NET, was used to estimate the expected number of incident cancers for uterine cancer.[78] The Administrator calculated cancer incidence rates using data through 2018 from the SEER Program and estimated uterine cancer incidence in the WTC Health Program for 2002–2026.[79] The resulting sex, race, age, and year-specific cancer incidence rates were applied to the estimated person-years at risk to estimate the expected number of cancer cases for uterine cancer starting from year 2002, the first full year following the September 11, 2001, terrorist attacks, to 2026.

For the purpose of illustrating an upper-bound incidence estimate, the Administrator reviewed WTC Health Program records and Program Data Center monitoring exam questionnaires to identify self-reported uterine cancer diagnoses among current members. The Administrator found 254 self-reports of uterine cancer among members who filled out monitoring exam questionnaires from January 2013 to November 2022; of those members, 11 are now deceased. The limitations associated with the review of WTC Health Program data are that some of the reported cases of uterine cancer may have been diagnosed prior to 2001 and some members may have mistakenly self-reported uterine cancer. The Administrator calculated a WTC Health Program uterine cancer incidence rate based on the January 2013–November 2022 WTC Health Program data and used that rate to estimate incidence of uterine cancer among Program members for 2023 through 2026.

These case numbers are offered as estimates only; the certification of individual cancer diagnoses will be conducted on a case-by-case basis, as required by the Zadroga Act.[80] Please see the WTC Health Program website for information about how to apply for enrollment in the Program[81] and about health condition certification.[82]

Prevalence of Cancer

To determine the potential number of persons in the responder and survivor populations with cancer, the Administrator conducted two different analyses for the purposes of illustrating lower- and upper-bound cost estimates.

As discussed above and in the NPRM, for the lower-bound, baseline analysis, the Administrator used the number of incident uterine cancer cases expected, based on U.S. population rates, for each year starting with 2002 and estimated the prevalence of uterine cancer using SEER survival rate statistics for *corpus uteri* through 2026.[83] Using the incident cases and survival rate statistics, the Administrator estimated the lower-bound prevalence (number of persons living with cancer) of cases during the 23-year period (2002–2026) since September 11, 2001. The resulting Table B summarizes those results for each year from 2023 through 2026, the number of new cases estimated to have occurred in that year (incidence), the number of persons surviving up to 23 years beyond their first diagnosis (prevalence), and

[72] National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program, SEER*Stat Database: Incidence—SEER Research Data, 9 Registries, Nov 2020 Submission (1975–2018), released Apr 2021, *www.seer.cancer.gov.* Although patients who are Medicare members are age 65 and older, cancer treatment costs are not expected to vary with age.

[73] Bureau of Labor Statistics, *Consumer Price Index, https://www.bls.gov/cpi/data.htm.* Accessed on November 10, 2022.

[74] *See supra* note 2 at 27968.

[75] *See supra* note 4.

[76] Jordan H.T., Brackbill R.M., Cone J.E., Debchoudhury I., Farfel M.R., Greene C.M., Hadler J.L., Kennedy J., Li J., Liff J., Stayner L., Stellman SD [2011], *Mortality Among Survivors of the Sept 11, 2001, World Trade Center Disaster: Results from the World Trade Center Health Registry Cohort,* Lancet 378:879–887. Note: percentages may not sum to 100 percent due to rounding.

[77] Centers for Disease Control and Prevention, National Center for Health Statistics, Compressed Mortality File 1999–2016 on CDC WONDER Online Database, released June 2017. Data are from the Compressed Mortality File 1999–2016 Series 20 No. 2U, 2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. *http://wonder.cdc.gov/cmf-icd10.html.* Accessed May 29, 2021.

[78] Schubauer-Berigan M.K., Hein M.J., Raudabaugh W.M., Ruder A.M., Silver S.R., Spaeth S., Steenland K., Petersen M.R., and Waters K.M. [2011], *Update of the NIOSH Life Table Analysis System: A Person-Years Analysis program for the Windows Computing Environment,* Am J Ind Med 54:915–924.

[79] *See supra* note 73.

[80] *See supra* note 9.

[81] *See* WTC Health Program, *How to Apply* web page, *https://www.cdc.gov/wtc/apply.html.*

[82] *See* WTC Health Program, ''Certifications and Covered Conditions,'' *Member Handbook, https://www.cdc.gov/wtc/handbook.html#certifications.*

[83] *See supra* note 73.

the number of individuals who might be expected to have died from their cancer in that year.[84]

For the upper-bound estimate, the Administrator used the incidence rate calculated based on a review of data from the WTC Health Program and the Program Data Centers of self-reported uterine cancer diagnoses among current members, discussed above, and SEER survival rate statistics for *corpus uteri* to estimate uterine cancer prevalence during the 4-year period from 2023 through 2026.[85] The resulting Table C summarizes those results for each year from 2023 through 2026, including the number of new cases estimated to have occurred in each year, the number of persons surviving beyond their first diagnosis, and the number of individuals who might be expected to have died from their cancer in each year.

TABLE B—ESTIMATED INCIDENCE AND PREVALENCE OF UTERINE CANCER; U.S. POPULATION CANCER RATES AMONG ~27,000 WTC HEALTH PROGRAM MEMBERS

[2023–2026]

	2023	2024	2025	2026
Vital status:				
New cases	17.87	18.13	18.22	18.30
Live cases from previous years	85.50	87.58	89.50	91.08
Deaths	15.27	15.79	16.41	16.44
Total new and live cases	103.37	105.71	107.72	109.38

TABLE C—ESTIMATED INCIDENCE AND PREVALENCE OF UTERINE CANCER; WTC HEALTH PROGRAM RATES AMONG ~27,000 WTC HEALTH PROGRAM MEMBERS

[2023–2026}

	2023	2024	2025	2026
Vital status:				
New cases	243	25.84	30.90	31.90
Live cases from previous years	n/a	266.54	296.09	326.52
Deaths	1.07	1.23	1.35	1.47
Total new and live cases	244.07	293.61	328.34	359.89

Cost Computation

To compute the lower-bound costs for uterine cancer, the Administrator assumed that the rate of uterine cancer in the WTC Health Program is equal to the rate of uterine cancer in the U.S. population. The treatment costs for the first year of treatment (Table A, year adjusted) were applied to the predicted newly incident (Year 1) cases for each year (*see* Table B). Likewise, the costs of treatment for the last year of life were applied in each year to the number of people predicted to die from their cancer in that year. The costs of continuing treatment from Table A were applied to the number of individuals who had survived their cancers beyond their year of diagnosis, for each year of survival (years two to four). Because some of the members estimated to be living with uterine cancer may not meet the WTC Health Program's exposure [86] and latency [87] requirements as necessary for certification, the Administrator assumed that 11 percent of uterine cancer certification requests will not be approved.[88] Costs for future years are discounted at both seven percent and three percent to reflect net present value.[89]

To compute the upper-bound costs, the Administrator assumed that cases of uterine cancer in the WTC Health Program will continue to increase at the WTC Health Program incidence rate derived from self-reported uterine cancer diagnoses. He further assumed that 243 cases of uterine cancer in 2023 will be considered ''new'' and certified by the WTC Health Program for treatment and monitoring and that every new case in 2023 will incur first-year costs (*see* Table A) because no information is available about the stage of treatment for each Program member who has reported a uterine cancer diagnosis. For treatment costs in future years, the Administrator applied the same formula as above for the lower-bound estimate and assumed that 11 percent of uterine cancer certification requests will not be granted.

The sum of the annual costs in the table for the years 2023 through 2026 represents the estimated treatment costs to the WTC Health Program for coverage of uterine cancer for the 12 percent of approximately 84,000 WTC responders who are female and the 50 percent of approximately 34,000 WTC survivors who are female.

Summary of Costs

Because HHS lacks data to account for recoupment from workers' compensation insurance or primary payment by either private health insurance or Medicare/Medicaid payments specific to uterine cancer, the estimates offered here are reflective of estimated WTC Health Program costs only and assume the Program is the primary payer. This analysis offers assumptions about the number of

[84] The 23-year survival limit is imposed based on the analytic time horizon.

[85] *See supra* note 73.

[86] *See* WTC Health Program [Feb 2015], *Policy and Procedures for Certification of Physician Determinations for Aerodigestive and Cancer Health Conditions, https://www.cdc.gov/wtc/pdfs/policies/WTCHPPPCertPhysDetFINAL20Feb2015-508.pdf.*

[87] The minimum latency requirement for all solid cancers, including uterine cancer, is 4 years after first 9/11 exposure. *See* WTC Health Program [Jan 2015], *Minimum Latency & Types or Categories of Cancer, https://www.cdc.gov/wtc/pdfs/policies/WTCHP-Minimum-Cancer-Latency-PP-01062015-508.pdf.*

[88] The 89 percent certification approval rate is based on historic WTC Health Program data.

[89] *See* OMB Circular A–94, *Guidelines and Discount Rates for Benefit-Cost Analysis of Federal Programs, https://obamawhitehouse.archives.gov/sites/default/files/omb/assets/a94/a094.pdf.*

current and future WTC Health Program members who are and will likely be diagnosed with uterine cancer and have their certification requests granted, to provide a conservative estimate of treatment costs to the WTC Health Program. The U.S. population average uterine cancer rate is used to identify a baseline number of expected cases among WTC Health Program members for the lower bound; an upper-bound estimate was based on a review of the number of WTC Health Program members who self-reported uterine cancer diagnoses in questionnaires completed from January 2013 to November 2022. This analysis does not include administrative costs associated with certifying additional WTC-related uterine cancers that might result from this action.

Since the implementation of provisions of the Patient Protection and Affordable Care Act on January 1, 2014, all members and future members are assumed to have or have access to medical insurance coverage other than through the WTC Health Program.[90] Therefore, all treatment costs to be paid by the WTC Health Program from 2023 through 2026 are considered transfers.

TABLE D—MEDICAL TREATMENT COSTS FOR CERTIFIED UTERINE CANCER CASES DURING 2023–2026, 2022 DOLLARS

	2023 Costs, undiscounted		2024–2026 Costs,* 7% discount rate	2024–2026 Costs, 3% discount rate
	Cancer rate		Cancer rate	
	U.S. average	WTCHP average	U.S. average	WTCHP average
Total	$1,785,423	$9,508,626	$5,040,394	$5,712,066

* Since this table summarizes the lowest and highest cost estimates for treatment of uterine cancer, values representing 2024–2026 costs at the 7% discount rate and at the increased cancer rate and 2024–2026 costs at the 3% discount rate and at the U.S. population average rate were not included.

The Administrator found the total cost estimate range—$1,706,454 to $3,805,173 annually—by adding the low estimate for 2023, $1,785,423 (U.S. cancer rate average), and the low 2024–2026 estimate in Table D, $5,040,394 (7 percent discount rate, U.S. cancer rate average, 89 percent certification rate), and dividing the sum by four to find the annual low-cost estimate (*i.e.,* $1,706,454). The same calculation was done for the annual high-cost estimates, adding the high estimate for 2023, $9,508,626.20 (WTC Health Program average uterine cancer rate), to the high 2024 through 2026 estimate, $5,712,066 (3 percent discount rate, WTC Health Program average uterine cancer rate, 89 percent certification rate), and dividing the sum by four (*i.e.,* $3,805,173).

Examination of Benefits (Health Impact)

This section qualitatively describes the potential benefits of this rulemaking to add uterine cancer to the List in terms of the expected improvements in the health and health-related quality of life of potential uterine cancer patients treated through the WTC Health Program, compared to not conducting the rulemaking.

The Administrator does not have information on the health of the population that may have experienced 9/11 exposures and is not currently enrolled in the WTC Health Program. In addition, the Administrator has only limited information about health insurance and healthcare services available for cases of uterine cancer potentially caused by 9/11 exposures and suffered by any population of responders and survivors, among responders and survivors both currently enrolled in the WTC Health Program and those who are not enrolled. For the purposes of this analysis, the Administrator assumed that all unenrolled responders and survivors are now covered by health insurance due to access provided by the Patient Protection and Affordable Care Act and may be receiving treatment outside the WTC Health Program.

Although the Administrator cannot quantify the benefits associated with the WTC Health Program, members with certified WTC-related uterine cancer are expected to experience better treatment outcomes with WTC Health Program physicians as compared to receiving care outside of the WTC Health Program. A recent study found that ''WTC-exposed responder cancer patients enrolled in the Fire Department of the city of New York Clinical Center of Excellence or in the General Responder Cohort had higher survival rates compared with those not so enrolled.'' [91] Moreover, under other insurance plans, patients would likely have deductibles and copays, which impact access to care and, particularly, its timeliness.[92] WTC Health Program members have first-dollar coverage and hence are likely to seek care sooner, when indicated, resulting in improved treatment outcomes.

Finally, during public meetings, WTC Health Program members have expressed that the lack of social and clinical support, and lack of recognition that their diagnosed uterine cancer is a WTC-related health condition, have had a significant negative impact on their morale and quality of life.

Limitations

The analysis presented here was limited by the dearth of verifiable data on the uterine cancer status of responders and survivors who have yet to apply for enrollment in the WTC Health Program. Because of the limited data, the Administrator is not able to estimate benefits in terms of averted healthcare costs; nor is the Administrator able to estimate administrative costs, or indirect costs, such as averted absenteeism, short- and long-term disability, and productivity losses averted due to premature mortality.

B. Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA), 5 U.S.C. 601 *et seq.,* requires each agency to consider the potential impact of its regulations on small entities, including small businesses, small governmental units, and small not-for-

[90] Sec. 3331(c)(3) of the PHS Act requires WTC Health Program members to maintain minimum essential insurance coverage.

[91] Goldfarb D.G., Zeig-Owens R., Kristjansson D., Li J., Brackbill R.M., Farfel M.R., Cone J.E., Kahn A.R., Qiao B., Schymura M.J., Webber M.P., Dasaro C.R., Lucchini R.G., Todd A.C., Prezant D.J., Hall C.B., Boffetta P. [2021], *Cancer Survival among World Trade Center Rescue and Recovery Workers: A Collaborative Cohort Study,* Am J Ind Med 64(10):815–826.

[92] Wharam J.F., Galbraith A.A., Kleinman K.P., Soumerai S.B., Ross-Degnan D., Landon B.E. [2008], *Cancer Screening before and after Switching to a High-Deductible Health Plan,* Ann Intern Med 148(9):647–655.

profit organizations. The Administrator certifies that this final rule has ''no significant economic impact upon a substantial number of small entities'' within the meaning of the RFA.

C. Paperwork Reduction Act

The Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.,* requires an agency to invite public comment on, and to obtain OMB approval of, any regulation that requires 10 or more people to report information to the agency or to keep certain records. The Administrator has determined that this rulemaking does not contain any new information collection requirements or recordkeeping requirements; thus, the PRA does not apply to this rulemaking. Data collection and recordkeeping requirements for the WTC Health Program are approved by OMB under ''World Trade Center Health Program Enrollment, Appeals & Reimbursement'' (OMB Control No. 0920–0891, exp. September 30, 2025).

D. Small Business Regulatory Enforcement Fairness Act

As required by Congress under the Small Business Regulatory Enforcement Fairness Act of 1996, 5 U.S.C. 801 *et seq.,* HHS will report the promulgation of this rule to Congress prior to its effective date.

E. Unfunded Mandates Reform Act of 1995

Title II of the Unfunded Mandates Reform Act of 1995, 2 U.S.C. 1531 *et seq.,* directs agencies to assess the effects of Federal regulatory actions on state, local, and tribal governments, and the private sector ''other than to the extent that such regulations incorporate requirements specifically set forth in law.'' For purposes of the Unfunded Mandates Reform Act, this final rule does not include any Federal mandate that may result in increased annual expenditures in excess of $100 million in 1995 dollars by state, local, or tribal governments in the aggregate, or by the private sector.

F. Executive Order 12988 (Civil Justice)

This final rule has been drafted and reviewed in accordance with Executive Order 12988, ''Civil Justice Reform,'' and will not unduly burden the Federal court system. This rule has been reviewed carefully to eliminate drafting errors and ambiguities.

G. Executive Order 13132 (Federalism)

The Administrator has reviewed this final rule in accordance with Executive Order 13132 regarding federalism and has determined that it does not have ''Federalism implications.'' The rule does not ''have substantial direct effects on the states, on the relationship between the national government and the states, or on the distribution of power and responsibilities among the various levels of government.''

H. Executive Order 13045 (Protection of Children From Environmental Health Risks and Safety Risks)

In accordance with Executive Order 13045, the Administrator has evaluated the environmental health and safety effects of this final rule on children. The Administrator has determined that the rule will have no environmental health and safety effect on children.

I. Executive Order 13211 (Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use)

In accordance with Executive Order 13211, the Administrator has evaluated the effects of this final rule on energy supply, distribution, or use, and has determined that the rule will not have a significant adverse effect.

J. Plain Writing Act of 2010

Under Public Law 111–274 (October 13, 2010), Executive Departments and Agencies are required to use plain language in documents that explain to the public how to comply with a requirement the Federal Government administers or enforces. The Administrator has attempted to use plain language in promulgating the final rule consistent with the Federal Plain Writing Act guidelines.

List of Subjects in 42 CFR Part 88

Aerodigestive disorders, Appeal procedures, Cancer, Healthcare, Mental health conditions, Musculoskeletal disorders, Respiratory and pulmonary diseases.

For the reasons discussed in the preamble, the Administrator and HHS Secretary amend 42 CFR part 88 as follows:

PART 88—WORLD TRADE CENTER HEALTH PROGRAM

■ 1. The authority citation for part 88 is revised to read as follows:

Authority: 42 U.S.C. 300mm to 300mm–61.

■ 2. Amend § 88.15 as follows:
■ a. Redesignate paragraphs (d)(15) through (24) as paragraphs (d)(16) through (25).
■ b. Add new paragraph (d)(15).
■ c. In newly redesignated paragraph (d)(24), remove ''*Childhood cancers:*'' and add ''Childhood cancers:'' in its place.
■ d. In newly redesignated paragraph (d)(25), remove ''*Rare cancers:*'' and add ''Rare cancers:'' in its place.

The addition reads as follows:

§ 88.15 List of WTC-Related Health Conditions.

* * * * *

(d) * * *

(15) Malignant neoplasms of corpus uteri and uterus, part unspecified.

* * * * *

John J. Howard,

Administrator, World Trade Center Health Program and Director, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Department of Health and Human Services.

Xavier Becerra,

Secretary, Department of Health and Human Services.

[FR Doc. 2023–00645 Filed 1–17–23; 8:45 am]

BILLING CODE 4163–18–P

NATIONAL TRANSPORTATION SAFETY BOARD

49 CFR Part 831

[Docket No.: NTSB–2023–0001]

RIN 3147–AA24

Civil Monetary Penalty Annual Inflation Adjustment

AGENCY: National Transportation Safety Board (NTSB).

ACTION: Final rule.

SUMMARY: Pursuant to the Federal Civil Penalties Inflation Adjustment Act Improvements Act of 2015, this final rule provides the 2023 adjustment to the civil penalties that the agency may assess for violations of certain NTSB statutes and regulations.

DATES: This final rule is effective on January 18, 2023.

ADDRESSES: A copy of this final rule, published in the **Federal Register** (FR), is available at *https://www.regulations.gov* (Docket ID Number NTSB–2023–0001).

FOR FURTHER INFORMATION CONTACT: Kathleen Silbaugh, General Counsel, (202) 314–6080 or *rulemaking@ntsb.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

The Federal Civil Penalties Inflation Adjustment Act Improvements Act of 2015 (the 2015 Act) requires, in pertinent part, agencies to make an annual adjustment for inflation by January 15th every year. OMB, M–16–06, *Implementation of the Federal Civil Penalties Inflation Adjustment Act*