Billing Code: 4165-15

DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 110

RIN: 0906-AA79

Countermeasures Injury Compensation Program: Pandemic Influenza Countermeasures Injury Table

AGENCY: Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS).

ACTION: Final rule.

SUMMARY: HHS is establishing the Pandemic Influenza Countermeasures Injury Table as authorized by the Public Readiness and Emergency Preparedness Act (PREP Act). Through this final rule, the Secretary of the U.S. Department of Health and Human Services (Secretary) adds regulations for the purpose of creating Covered Countermeasures Injury Tables. The pandemic influenza countermeasures are identified in Secretarial declarations relating to pandemic influenza, including influenza caused by the 2009 H1N1 pandemic influenza virus (hereafter referred to as the 2009 H1N1 virus) and other potential pandemic strains, such as H5N1 avian influenza.

DATES: This rule is effective **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**.

FOR FURTHER INFORMATION CONTACT: Dr. Avril M. Houston, Director, Division of Injury Compensation Programs, Healthcare Systems Bureau, HRSA, Parklawn Building, Room

11C-26, 5600 Fishers Lane, Rockville, MD 20857, or by telephone (855) 266-2427. This is a toll-free number.

SUPPLEMENTARY INFORMATION: On March 30, 2014, HHS published the Notice of Proposed Rulemaking (NPRM) in the Federal Register to amend the Countermeasures Injury Compensation Program's (CICP or Program) implementing regulation and establish a table of injuries resulting from the administration or use of covered pandemic influenza countermeasures. The NPRM provided a 60-day comment period resulting in HHS receipt of five sets of comments -- one set from a physicians' organization and four sets from individuals. HHS carefully considered these comments when developing this final rule. In "Section III, Comments and Responses" of this final rule, the comments are summarized and HHS provides responses to them.

I. Background

The Public Readiness and Emergency Preparedness Act of 2005 (PREP Act) directs the Secretary to establish, through regulation, a Covered Countermeasures Injury Table (Table) identifying serious physical injuries that are presumed to be directly caused by the administration or use of covered countermeasures identified in PREP Act declarations issued by the Secretary.

The Secretary may only add to a Table injuries that are directly caused by the administration or use of the covered countermeasure based on "compelling, reliable, valid, medical and scientific evidence."[1] This Table informs the public about serious physical injuries known to be directly caused by covered countermeasures through support by compelling, reliable, valid, medical and scientific evidence. In addition, this Table creates a rebuttable

[1] 42 U.S.C. 247d-6e (b)(5)(A).

presumption of causation for eligible individuals whose injuries are listed on a Table and meet the requirements of a Table.

The PREP Act authorizes both liability protections and compensation based on the terms of the PREP Act declarations, but this final rule concerns only the compensation program, not the liability protections set forth therein.

The Secretary published the interim final rule implementing the Program on October 15, 2010.[2] The final rule, which was published on October 7, 2011, explains the Program's policies, procedures, and requirements. Title 42 of the Code of Federal Regulations (CFR) §110.20(a) states that individuals must establish that a covered injury occurred in order to be eligible for benefits under the Program. A covered injury is death or a serious injury determined by the Secretary to be: (1) an injury meeting the requirements of a Table, which is presumed to be the direct result of the administration or use of a covered countermeasure unless the Secretary determines there is another more likely cause; or (2) an injury (or its health complications) that is the direct result of the administration or use of a covered countermeasure. This includes a covered countermeasure causing a serious aggravation of a pre-existing condition.[3] In general, only injuries that warranted hospitalization (whether or not the person was actually hospitalized), or injuries that led to a significant loss of function or disability are considered serious injuries.[4]

Individuals with injuries not meeting the requirements listed on the Table may still pursue their claims as non-Table injuries under the Program. In this instance, the requester does not receive the presumption of causation for a Table injury and must demonstrate that the use or administration of the covered countermeasure directly caused the injury. Proof of a causal

[2] 42 CFR part 110.
[3] 42 CFR 110.3(g)(2).
[4] 42 CFR 110.3(z).

association for the non-Table injury must be based on compelling, reliable, valid, medical and scientific evidence.

II. Summary of the Final Rule

Through this final rule, the Secretary will be adding subpart K to 42 CFR part 110, which had been reserved for the purpose of creating a Covered Countermeasures Injury Table. The Table established in this final rule is limited to pandemic influenza covered countermeasures. These countermeasures are identified in Secretarial declarations relating to pandemic influenza, including influenza caused by the 2009 H1N1 virus, and other potential pandemic strains, such as H5N1 avian influenza. The Secretary may create and publish Tables in the Federal Register through separate amendments to 42 CFR part 110 in the future. Tables may be created for other countermeasures in accordance with the PREP Act. To date, declarations have been issued with respect to countermeasures against pandemic influenza A viruses, anthrax, botulism, smallpox, acute radiation syndrome, and the Ebola virus.

Through the Pandemic Influenza Countermeasures Injury Table Final Rule, the Secretary provides, as authorized by statute, a Table for several covered countermeasures listing serious physical injuries. The serious physical injuries included on the Table are injuries that are supported by compelling, reliable, valid, medical and scientific evidence showing that the administration or use of the covered countermeasures directly causes such injuries. The Table lists the serious injuries directly caused by a specific countermeasure, the time interval within which the first symptom or manifestation of onset of injury must appear, and the definition of the injury. Table definitions are included to further explain each covered injury and the level of severity necessary to qualify as a Table injury.

The injuries, time intervals, definitions, and requirements reflect the Secretary's efforts to identify those serious physical injuries causally related to the covered countermeasures. The causal linkages between the covered countermeasures and these associated injuries are based on compelling, reliable, valid, medical and scientific evidence. The Secretary will stay informed of updates in the scientific and medical field concerning new information about causal associations between injuries and covered countermeasures.

In this final rule, the Secretary has made the following changes to the Qualifications and Aids to Interpretation (QAI) of the Table for purposes of clarity.

a. Changed section (b)(4)(i) by adding an accent over the "e" in Guillain-Barre Syndrome (GBS). The revised section term reads, "Guillain-Barré Syndrome." In the first sentence, added "currently is known to encompass" after "that" and delete "encompasses." The revised sentence states, "GBS is an acute monophasic peripheral neuropathy that currently is known to encompass a spectrum of four clinicopathological subtypes described below." In the fourth sentence, changed "nine" to "9." The revised sentence states, "Treatment related fluctuations in all subtypes of GBS can occur within 9 weeks of GBS symptom onset and recurrence of symptoms after this time frame would not be consistent with GBS."

b. Changed section (b)(4)(iv) by adding "The results of both…" to the beginning of the second sentence. The revised sentence states, "The results of both CSF and electrophysiologic studies are frequently normal in the first week of illness in otherwise typical cases of GBS."

c. Deleted section (b)(4)(v) which states, "For all types of GBS, the onset of symptoms less than three days (72 hours) after exposure to the influenza vaccine excludes vaccine exposure as a cause" because timeframes for serious physical injuries to be Table injuries are listed in the Table, not in the QAI.

d. Changed section (b)(4)(vi) to (b)(4)(v) since (b)(4)(v) has been deleted as stated above and added to the beginning of the first sentence of section (b)(4)(v), "For GBS to qualify as a Table injury." The revised sentence states, "For GBS to qualify as a Table injury, there must not be a more likely alternative diagnosis for the weakness."

e. Changed section (b)(5)(i)(A) by adding "or" after "tube;". The revised statement states, "(A) trauma or necrosis from an endotracheal tube; or."

f. Changed section (b)(6)(i) by deleting "Definition -" before "VAP" at the beginning of the first sentence. In the fourth sentence, changed the phrase "radiographic infiltrate in the lungs that is consistent with pneumonia" to "radiographic infiltrate that is in the lungs and consistent with pneumonia."

g. Changed section (b)(7) by adding "To qualify as Table injuries," before "these" to the beginning of the last sentence. The revised sentence states, "To qualify as Table injuries, these manifestations must occur in patients who are being mechanically ventilated at the time of initial manifestation of the VILI." VILI is Ventilator-Induced Lung Injury.

h. Changed section (b)(8) by adding "who are" after "patients" and before "under" to the first sentence. The revised sentence states, "Bleeding events are defined as excessive or abnormal bleeding in patients who are under the pharmacologic effects of anticoagulant therapy provided for extracorporeal membrane oxygenation (ECMO) treatment."

III. Comments and Responses

The NPRM set forth a 60-day public comment period, which ended on May 30, 2014. During this comment period, HHS received five sets of comments -- one set from a physicians' organization and four sets from individuals. Below is a summary of the comments and HHS's responses.

1. Anaphylaxis

COMMENT: A commenter suggested expanding to 12 hours the time frame within which the first symptom or manifestation of anaphylaxis must appear, stating that some cases of anaphylaxis may exhibit a late phase response up to 8 – 12 hours after exposure, and thus the 0 – 4 hour time frame is not long enough.

RESPONSE: HHS respectfully disagrees with this comment. There is no consensus within the medical and scientific community about the time frame in which the late phase response starts. As stated in the NPRM, anaphylaxis after immunization is serious, but it occurs rarely. After initial treatment and clinical improvement, some patients with allergic reactions may develop a late phase or "biphasic" reaction, which may be more severe than the initial presentation. Little is known of the pathophysiology of biphasic reactions. The variations and the subjective nature of definitions used for determining the incidence of biphasic reactions in various studies are likely a major contributor to differing results, ranging from a 0.5 percent to 20 percent incidence rate. This makes comparisons of data across studies problematic. Previous guidelines have advocated the monitoring of patients post-anaphylaxis, with recommended durations varying between 4 and 24 hours. This is likely a testament to the uncertainty in the literature. Hence there is no compelling, reliable, valid, medical and scientific evidence upon which to base a Table time frame for biphasic anaphylactic reactions. HHS recognizes the occurrence of biphasic anaphylactic reactions in a minority of cases. Therefore, the Program will consider a claim for anaphylaxis occurring after the 4-hour time frame leading to a serious injury or death on a case-by-case basis as a non-Table claim.

2. Pandemic Influenza Intranasal Vaccines

COMMENT: A commenter asked if a child would be eligible to receive compensation if he/she is injured from the intranasal vaccine, which was administered because the child was advised by his/her doctor to have the intranasal vaccine, even if perhaps, the child would have been more suited for the vaccine injection.

RESPONSE: Under the CICP, any person who meets the appropriate declaration's definition of covered population, is administered or used a covered countermeasure in accordance with the terms of that declaration (or in good faith belief of such), and is seriously injured as a direct result of the countermeasure, may be eligible for CICP benefits.

3. Antiviral Usage in Individuals Younger than 2 Years of Age

COMMENT: A commenter was concerned that the guidelines for administration of Tamiflu (oseltamivir), Relenza (zanamivir), and peramivir for infants are not uniform. The commenter stated that the Food and Drug Administration has approved Tamiflu for children as young as 2 weeks of age but that the Centers for Disease Control and Prevention (CDC) recommends Tamiflu, through its safety profile, for treatment of both term and preterm infants from birth, as benefits for therapy are likely to outweigh possible risks of treatment. The commenter suggested that this rule establish the minimum age for administration of these countermeasures to children so that children are not denied compensation because of conflicting policy recommendations about the appropriate administration of these antiviral medications.

RESPONSE: The CICP is not authorized to establish age ranges for the administration of any drug, and therefore, cannot do so through this rule, as suggested by the commenter. The Program can only provide benefits to the population of individuals set forth in the applicable Secretarial declaration.

4. Incorporation of Children and Infants in Overall Guidelines

COMMENT: A commenter made the statement that his organization "firmly believes that the Table should better incorporate the needs of children." The commenter wants HHS and HRSA to ensure that children are being considered in all aspects of the proposed countermeasures, as well as in this Table.

RESPONSE: As indicated above, Secretarial declarations describe the covered countermeasures and the covered population. Under the CICP, any person who meets the definition of the covered population in the relevant declaration, who receives or uses a covered countermeasure in accordance with the terms of that declaration (or in good faith belief of such), and is seriously injured as a direct result of the countermeasure may be eligible for CICP benefits.

5. Guillain-Barré Syndrome

COMMENT: One commenter was concerned that the description of Guillain-Barré Syndrome (GBS) is incomplete because it does not address the fact that GBS affects the peripheral nervous system.

RESPONSE: HHS respectfully disagrees with this comment. The description of GBS as stated in the NPRM and final rule is complete and explicitly addresses that GBS affects the peripheral nervous system. It is an acute monophasic peripheral neuropathy that currently is known to encompass a spectrum of four clinicopathological subtypes described in the Qualifications and Aids to Interpretation section of the Table. GBS may manifest with weakness, abnormal sensations, and/or abnormality in the autonomic (involuntary) nervous system.

COMMENT: A commenter was concerned that this allegedly incomplete description of GBS may make it difficult for requesters to prove injuries such as Miller-Fisher Syndrome or other variants of GBS that include attacks that lead to organ damage. Another commenter noted that the variants of GBS should be considered.

RESPONSE: HHS respectfully disagrees with the comments that the variants of GBS were not considered. The Table, including its Qualifications and Aids to Interpretation, explicitly addresses how variants of GBS, including Miller-Fisher Syndrome, can meet the Table requirements. GBS may present as one of a spectrum of four clinicopathological subtypes or variants. The most common type in North America and Europe, comprising more than 90 percent of cases, is acute inflammatory demyelinating polyneuropathy (AIDP), which has the pathologic and electrodiagnostic features of focal demyelination of motor and sensory peripheral nerves and roots.

Another subtype called acute motor axonal neuropathy (AMAN) is generally seen in other parts of the world and is predominated by axonal damage that primarily affects motor nerves. AMAN lacks features of demyelination. The axon is a portion of the nerve cell that transmits nerve impulses away from the nerve cell body. Another less common subtype of GBS includes acute motor and sensory neuropathy (AMSAN), which is an axonal form of GBS that is similar to AMAN, but also affects the axons of sensory nerves and roots.

According to the Brighton Collaboration, Fisher Syndrome (FS), also known as Miller-Fisher Syndrome, is a subtype of GBS characterized by ataxia, areflexia, and ophthalmoplegia, and overlap between FS and GBS may be seen with limb weakness.

GBS is proposed for inclusion on the Table because it is a serious physical injury, and the fact that it may be directly caused by the use of the monovalent 2009 H1N1 influenza vaccine (hereafter 2009 H1N1 vaccine) is supported by compelling, reliable, valid, medical and scientific evidence. Further, GBS is characterized by various degrees of weakness, sensory abnormality and autonomic dysfunction due to damage to peripheral nerves and nerve roots. These variants or subtypes of GBS were addressed fully in the NPRM and are adopted in the final rule.

Furthermore, as explained above, the description of GBS as stated in the NPRM, and adopted in this final rule, is complete. To the extent that one comment suggested that organ damage should be included as a Table injury, HHS respectfully disagrees. Although demyelination of peripheral nerves or axonal damage can lead to disruption of organ function, they do not lead directly to organ damage. At this time, there is no compelling, reliable, valid, medical and scientific evidence to support including organ damage on the Table.

COMMENT: A commenter was concerned that the 3- to 42-day window of GBS onset is unreasonable because some cases of GBS have been reported to have an onset outside of this interval. The commenter cited the article, "Chart-Confirmed Guillain-Barré Syndrome After 2009 H1N1 Influenza Vaccination Among the Medicare Population, 2009-2010, American Journal of Epidemiology, (2014), 179 (5): 660."

RESPONSE: HHS respectfully disagrees with this comment. The study that was cited by the commenter and published in the American Journal of Epidemiology looked at the risk of GBS development within 119 days of vaccination. The researchers found a slightly increased statistically significant risk of GBS only within the 6-week period after 2009 H1N1 vaccination when compared with the post-vaccination control period.

As stated in the NPRM, multiple studies performed to monitor the safety of 2009 H1N1 vaccine provide evidence that demonstrates a small statistically significant increased risk of GBS in the 6 weeks following administration of the 2009 H1N1 vaccine.[5] Additionally, a meta-analysis was performed of the Emerging Infections Program, the Vaccine Safety Datalink, and

[5] Lawrence B. Schonberger, et al., "Guillain-Barrè Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976-1977, American Journal of Epidemiology, 25 Apr. 1979, 118; IOM, "Immunization Safety Review: Influenza Vaccines and Neurological Complications," (Washington, D.C.: The National Academies Press, 2004) 25; Sharon K. Greene, et al., "Risk of Confirmed Guillain-Barrè Syndrome Following Receipt of Monovalent Inactivated Influenza A (H1N1) and Seasonal Influenza Vaccines in the Vaccine Safety Datalink Project, 2009-2010; and American Journal of Epidemiology, Jun. 1, 2012, 1100.

the Post-Licensure Rapid Immunization Safety Monitoring System data, together with additional data from safety surveillance studies performed by the Centers for Medicare & Medicaid Services, the Department of Defense, and the Department of Veterans Affairs, which analyzed data from 23 million vaccinated people. The meta-analysis found that the 2009 H1N1 inactivated vaccine was associated with a small increased risk of GBS within 6 weeks of vaccination.

The symptoms of GBS do not develop immediately after exposure to the causative agent. The immune system requires a specified time to complete the steps leading to nerve injury and dysfunction and the early symptoms of GBS. A minimum of 3 days would be necessary from the time of exposure and immune system stimulation to the first symptoms of GBS. Therefore, onset of GBS within less than 72 hours or 3 days of immunization would be strong evidence that the vaccine is not the causative agent.[6]

HHS believes that the American Journal of Epidemiology study cited by the commenter is consistent with the other studies referenced above in indicating that the window of onset for GBS on the Table is appropriate based on current compelling, reliable, valid medical and scientific evidence.

6. Comparison of CICP Table Injuries to the VICP Table Injuries

COMMENT: A commenter compared the CICP Table injuries with the National Vaccine Injury Compensation Program (VICP) Table injuries because the 2009 H1N1 strain has been included in the seasonal influenza vaccine since 2010 and questioned why the Tables are different.

RESPONSE: The VICP and CICP are different programs authorized by two distinct federal statutes. The VICP covers certain vaccines that are recommended by the CDC for routine

[6] Peripheral Neuropathy, 4th edition, 2005; Dyck & Thomas, eds. 626.

administration to children and are subject to an excise tax, whereas the CICP covers certain countermeasures, including pandemic influenza vaccines, as identified in Secretarial declarations. Accordingly, the VICP covers seasonal influenza vaccines, such as the quadravalent influenza vaccine, and the CICP covers pandemic vaccines, such as the 2009 monovalent H1N1 vaccine. Presently, the VICP's Table does not include any associated injuries for seasonal influenza vaccines.

7. West Nile Virus (WNV)

COMMENT: A commenter stated "I strongly believe it is beneficial to have an injury compensation program implemented for those who have been extremely touched by West Nile and other harmful influenzas..." HHS' understanding is that the commenter wants a compensation program established that would cover the adverse effects of the underlying pandemic or epidemic condition itself.

RESPONSE: Injuries from the WNV or any influenza infection are not covered by the CICP. As stated in the NPRM, only serious injuries directly caused by the administration or use of the covered countermeasure – not injuries that result from the disease (or health condition or threat to health) itself – are covered injuries. For more information, see 42 CFR 110.20(d).

8. Notification to Individuals Who Have Been Deemed Ineligible for Compensation

COMMENT: A commenter suggested that HHS inform all individuals who have previously applied but were deemed ineligible for compensation that they can reapply for compensation.

RESPONSE: HHS agrees with the commenter. Previous requesters, who were deemed ineligible for compensation, will be notified of the new Table by its publication in the Federal Register. The published final rule also will be posted on the CICP Website at www.hrsa.gov/cicp. Such requesters may have an additional 1-year filing deadline from the

effective date of the Table amendment or publication. This additional filing deadline will apply only if the new or amended Table enables a requester, who could not establish a Table injury before the new or amended Table, to establish a covered injury.[7]

IV. Regulatory Impact Analysis

HHS has examined the impact of this rulemaking as required by Executive Order 12866 on Regulatory Planning and Review, Executive Order 13563 on Improving Regulation and Regulatory Review, the Congressional Review Act (5 U.S.C. 804(2)), the Regulatory Flexibility Act (RFA), section 202 of the Unfunded Mandates Reform Act of 1995, section 654(c) of the Treasury and General Government Appropriations Act of 1999, and Executive Order 13132 on Federalism.

Executive Order 12866 requires that all regulations reflect consideration of alternatives, costs, benefits, incentives, equity, and available information. Regulations must meet certain standards, such as avoiding an unnecessary burden. Regulations that are "significant" because of cost, adverse effects on the economy, inconsistency with other agency actions, effects on the budget, or novel legal or policy issues, require special analysis. In 2011, President Obama supplemented and reaffirmed Executive Order 12866. This rulemaking is not being treated as a significant regulatory action under section 3(f) of Executive Order 12866. Accordingly, the final rule has not been reviewed by the Office of Management and Budget.

Executive Order 13563 provides that, to the extent feasible and permitted by law, the public must be given a meaningful opportunity to comment on any proposed regulations, with at least a 60-day comment period. In addition, to the extent feasible and permitted by law, agencies must provide timely on-line access to both proposed and final rules of the rulemaking docket on

[7] 42 CFR 110.42(f).

Regulations.gov, including relevant scientific and technical findings, in an open format that can be searched and downloaded. Federal agencies must consider approaches to maintain the freedom of choice and flexibility, including disclosure of relevant information to the public. Regulations must be guided by objective scientific evidence, easy to understand, consistent, and written in plain language. Furthermore, Federal agencies must attempt to coordinate, simplify, and harmonize regulations to reduce costs and promote certainty for the public.

In this final rule, the Secretary specifies a Table identifying serious physical injuries that shall be presumed to result from the administration or use of the covered countermeasures, and the time interval in which the onset of the first symptom or manifestation of each such serious physical injury must manifest in order for such presumption to apply. The Secretary is also specifying Table definitions and requirements. This final rule would have the effect of affording certain persons a presumption that particular serious physical injuries were sustained as the result of the administration or use of covered pandemic influenza countermeasures. The Table will establish a presumption of causation and relieve requesters of the burden of demonstrating causation for covered injuries listed on the Table. However, this presumption is rebuttable based on the Secretary's review of the evidence. In addition, this Table may afford some requesters a new filing deadline.

Other than showing that a serious physical injury or death directly resulted from an injury included on the Table, individuals may, in the alternative, be eligible for compensation if they otherwise meet the CICP's requirements and can show a causation-in-fact relationship between an injury or death and a covered countermeasure. This rule is based upon legal authority.

Because any resources required to implement the regulatory requirements imposed by the Program are not required by virtue of the establishment of a Table, and because the Secretary

conducted an independent analysis concerning any burdens associated with the implementation of the Program when the Secretary published the companion regulation setting forth the Program's administrative implementation,[8] the Secretary has determined that no resources are required to implement the provisions included in this final rule. Therefore, in accordance with the Regulatory Flexibility Act of 1980 (RFA) and the Small Business Regulatory Enforcement Fairness Act of 1996, which amended the RFA, the Secretary certifies that this rule will not have a significant impact on a substantial number of small entities.

The Secretary has also determined that this rule does not meet the criteria for a major rule as defined by Executive Order 12866 and would have no major effect on the economy or Federal expenditures. The Secretary has determined that this rule is not a "major rule" within the meaning of the statute providing for Congressional Review of Agency Rulemaking, 5 U.S.C. 801. Similarly, it will not have effects on State, local, and tribal governments or on the private sector such as to require consultation under the Unfunded Mandates Reform Act of 1995. This final rule comports with the 2011 supplemental requirements.

Unfunded Mandates Reform Act of 1995

The Secretary has determined that this final rule will not have effects on State, local, and tribal governments or on the private sector such as to require consultation under the Unfunded Mandates Reform Act of 1995.

Federalism Impact Statement

The Secretary has also reviewed this final rule in accordance with Executive Order 13132 regarding federalism, and has determined that it does not have "federalism implications." This final rule will not "have substantial direct effects on the States, or on the relationship between the

[8] 75 FR 64955.

national government and the States, or on the distribution of power and responsibilities among the various levels of government."

Impact on Family Well-Being

This final rule will not adversely affect the following elements of family well-being: family safety, family stability, marital commitment; parental rights in the education, nurture, and supervision of their children; family functioning, disposable income, or poverty; or the behavior and personal responsibility of youth, as determined under section 654(c) of the Treasury and General Government Appropriations Act of 1999. In fact, this rule may have a positive impact on the disposable income and poverty elements of family well-being to the extent that injured persons or their families may receive medical, lost employment income, and/or death benefits paid under this part without imposing a corresponding burden on them.

Paperwork Reduction Act of 1995, as amended

This final rule has no information collection requirements.

List of Subjects in 42 CFR part 110

Anaphylaxis, Anticoagulation, Antiviral, Avian, Benefits, Biologics, Bleeding, Bursitis, Compensation, Countermeasure, Declaration, Deltoid, Diagnostics, Device, Eligibility, Extra-Corporeal Membrane Oxygenation (ECMO), Fisher Syndrome, Guillain-Barré Syndrome, 2009 H1N1, Influenza, Injury Table, Immunization, Oseltamivir, Pandemic, Peramivir, Public Readiness and Emergency Preparedness Act (PREP Act), Radiation Syndrome, Respiratory Protection, Relenza, Respirator, Respirator Support, Tamiflu, Tracheal Stenosis, Vaccine, Vasovagal Syncope, Ventilator, Ventilator-Associated Pneumonia and Tracheobronchitis, Ventilator-Induced Lung Injury, Zanamivir.

Dated: July 24, 2015.

_____

James Macrae,

Acting Administrator,

Health Resources and Services Administration.

Approved: July 30, 2015.

_____

Sylvia M. Burwell,

Secretary.

Therefore, for the reasons stated, the Department of Health and Human Services amends 42 CFR part 110 as follows:

PART 110—COUNTERMEASURES INJURY COMPENSATION PROGRAM

1. The authority citation for part 110 continues to read as follows:

   Authority: 42 U.S.C. 247d-6e.

2. Add § 110.100 to subpart K to read as follows:

§110.100 Injury Tables

(a) Pandemic influenza countermeasures injury table.

Covered countermeasures under Secretarial declarations	Serious physical injury (illness, disability, injury, or condition)[1]	Time interval (for first symptom or manifestation of onset of injury after administration or use of covered countermeasure, unless otherwise specified)
I. Pandemic influenza vaccines administered by needle into or through the skin.	A. Anaphylaxis B. Deltoid Bursitis C. Vasovagal Syncope	A. 0-4 hours. B. 0-48 hours. C. 0-1 hour.
II. Pandemic influenza intranasal vaccines.	A. Anaphylaxis	A. 0–4 hours.
III. Pandemic influenza 2009 H1N1 vaccine.	A. Guillain-Barrè Syndrome	A. 3-42 days (not less than 72 hours and not more than 42 days).
IV. Oseltamivir Phosphate (Tamiflu) when administered or used for pandemic influenza.	A. Anaphylaxis	A. 0-4 hours.
V. Zanamivir (Relenza) when administered or used for pandemic influenza.	A. Anaphylaxis	A. 0-4 hours.

[1] Serious physical injury as defined in 42 CFR 110.3(z). Only injuries that warranted hospitalization (whether or not the person was actually hospitalized) or injuries that led to a significant loss of function or disability will be considered serious physical injuries.

VI. Peramivir when administered or used for 2009 H1N1 influenza.	A. Anaphylaxis	A. 0-4 hours.
VII. Pandemic influenza personal respiratory protection devices.	A. No condition covered[2]	A. Not applicable.
VIII. Pandemic influenza respiratory support devices.	A. Postintubation Tracheal Stenosis	A. 2-42 days (not less than 48 hours and not more than 42 days) after extubation (removal of a tracheostomy or endotracheal tube).
	B. Ventilator-Associated Pneumonia and Ventilator-Associated Tracheobronchitis	B. More than 48 hours after intubation (placement of an endotracheal or tracheostomy tube) and up to 48 hours after extubation (removal of the tube).
	C. Ventilator-Induced Lung Injury	C. Throughout the time of intubation (breathing through an endotracheal or tracheostomy tube) and up to 48 hours after extubation (removal of the tube).
IX. Pandemic influenza respiratory support device: extra-corporeal membrane oxygenation (ECMO).	A. Bleeding Events	A. Throughout the time of anticoagulation treatment for ECMO therapy, including the time needed to clear the effect of the anti-coagulant treatment from the body.
X. Pandemic influenza diagnostic testing devices.	A. No condition covered	A. Not applicable.

[2] The use of ''No condition covered'' in the Table reflects that the Secretary at this time does not find compelling, reliable, valid, medical and scientific evidence to support that any serious injury is presumed to be caused by the associated covered countermeasure. For injuries alleged to be due to covered countermeasures for which there is no associated Table injury, requesters must demonstrate that the injury occurred as the direct result of the administration or use of the covered countermeasure. *See* 42 CFR 110.20(b), (c).

(b) Qualifications and aids to interpretation (table definitions and requirements). The following definitions and requirements shall apply to the Table set forth in this subpart and only apply for purposes of this subpart.

(1) Anaphylaxis. Anaphylaxis is an acute, severe, and potentially lethal systemic reaction that occurs as a single discrete event with simultaneous involvement of two or more organ systems. Most cases resolve without *sequelae*. Signs and symptoms begin minutes to a few hours after exposure. Death, if it occurs, usually results from airway obstruction caused by laryngeal edema or bronchospasm and may be associated with cardiovascular collapse. Other significant clinical signs and symptoms may include the following: cyanosis, hypotension, bradycardia, tachycardia, arrhythmia, edema of the pharynx and/or trachea and/or larynx with stridor and dyspnea. There are no specific pathological findings to confirm a diagnosis of anaphylaxis.

(2) Deltoid bursitis. Deltoid bursitis is an inflammation of the bursa that lies beneath the deltoid muscle and between the acromion process and the rotator cuff. Subdeltoid bursitis manifests with pain in the lateral aspect of the shoulder similar to rotator cuff tendonitis. The presence of tenderness on direct palpation beneath the acromion process distinguishes this bursitis from rotator cuff tendonitis. Similar to tendonitis, isolated bursitis will have full passive range of motion. Other causes of bursitis such as trauma (other than from vaccination), metabolic disorders, and systemic diseases such as rheumatoid arthritis, dialysis, and infection will not be considered Table injuries. This list is not exhaustive. The deltoid bursitis must occur in the same shoulder that received the pandemic influenza vaccine.

(3) Vasovagal syncope. Vasovagal syncope (also sometimes called neurocardiogenic syncope) means loss of consciousness (fainting) and loss of postural tone caused by a transient decrease in blood flow to the brain occurring after the administration of an injected countermeasure. Vasovagal syncope is usually a benign condition but may result in falling and injury with significant *sequelae*. Vasovagal syncope may be preceded by symptoms such as nausea, lightheadedness, diaphoresis, and/or pallor. Vasovagal syncope may be associated with transient seizure-like activity, but recovery of orientation and consciousness generally occurs simultaneously. Loss of consciousness resulting from the following conditions will not be considered vasovagal syncope: organic heart disease; cardiac arrhythmias; transient ischemic attacks; hyperventilation; metabolic conditions; neurological conditions; psychiatric conditions; seizures; trauma; and situational as can occur with urination, defecation, or cough. This list is not complete. Episodes of recurrent syncope occurring after the applicable time period are not considered to be *sequelae* of an episode of syncope meeting the Table requirements.

(4) Guillain-Barré Syndrome (GBS). (i) GBS is an acute monophasic peripheral neuropathy that currently is known to encompass a spectrum of four clinicopathological subtypes described below. For each subtype of GBS, the interval between the first appearance of symptoms and the nadir of weakness is between 12 hours and 28 days. This is followed in all subtypes by a clinical plateau with stabilization at the nadir of symptoms, or subsequent improvement without significant relapse. Death may occur without a clinical plateau. Treatment related fluctuations in all subtypes of GBS can occur within 9 weeks of GBS symptom onset and recurrence of symptoms after this time frame would not be consistent with GBS.

(ii) The most common subtype in North America and Europe, comprising more than 90 percent of cases, is acute inflammatory demyelinating polyneuropathy (AIDP) which has the

pathologic and electrodiagnostic features of focal demyelination of motor and sensory peripheral nerves and nerve roots. Another subtype called acute motor axonal neuropathy (AMAN) is generally seen in other parts of the world and is predominated by axonal damage that primarily affects motor nerves. AMAN lacks features of demyelination. Another less common subtype of GBS includes acute motor and sensory neuropathy (AMSAN), which is an axonal form of GBS that is similar to AMAN, but also affects the sensory nerves and roots. AIDP, AMAN, and AMSAN are typically characterized by symmetric motor flaccid weakness, sensory abnormalities, and/or autonomic dysfunction caused by autoimmune damage to peripheral nerves and nerve roots. The diagnosis of AIDP, AMAN, and AMSAN requires bilateral flaccid limb weakness and decreased or absent deep tendon reflexes in weak limbs; a monophasic illness pattern; an interval between onset and nadir of weakness between 12 hours and 28 days; subsequent clinical plateau (the clinical plateau leads to either stabilization at the nadir of symptoms, or subsequent improvement without significant relapse); and, the absence of an identified more likely alternative diagnosis. Death may occur without a clinical plateau.

(iii) Fisher syndrome (FS), also known as Miller-Fisher Syndrome, is a subtype of GBS characterized by ataxia, areflexia, and ophthalmoplegia, and overlap between FS and AIDP may be seen with limb weakness. The diagnosis of FS requires bilateral ophthalmoparesis; bilateral reduced or absent tendon reflexes; ataxia; the absence of limb weakness (the presence of limb weakness suggests a diagnosis of AIDP); a monophasic illness pattern; an interval between onset and nadir of weakness between 12 hours and 28 days; subsequent clinical plateau (the clinical plateau leads to either stabilization at the nadir of symptoms, or subsequent improvement without significant relapse); no alteration in consciousness; no corticospinal track signs; and, the absence of an identified more likely alternative diagnosis. Death may occur without a clinical plateau.

(iv) Evidence that is supportive, but not required, of a diagnosis of all subtypes of GBS includes electrophysiologic findings consistent with GBS or an elevation of cerebral spinal fluid (CSF) protein with a total CSF white blood cell count below 50 cells per microliter. The results of both CSF and electrophysiologic studies are frequently normal in the first week of illness in otherwise typical cases of GBS.

(v) For GBS to qualify as a Table injury there must not be a more likely alternative diagnosis for the weakness. Exclusionary criteria for the diagnosis of all subtypes of GBS include the ultimate diagnosis of any of the following conditions: chronic immune demyelinating polyradiculopathy ("CIDP"), carcinomatous meningitis, brain stem encephalitis (other than Bickerstaff brainstem encephalitis), myelitis, spinal cord infarct, spinal cord compression, anterior horn cell diseases such as polio or West Nile virus infection, subacute inflammatory demyelinating polyradiculoneuropathy, multiple sclerosis, cauda equina compression, metabolic conditions such as hypermagnesemia or hypophosphatemia, tick paralysis, heavy metal toxicity (such as arsenic, gold, or thallium), drug-induced neuropathy (such as vincristine, platinum compounds, or nitrofurantoin), porphyria, critical illness neuropathy, vasculitis, diphtheria, myasthenia gravis, organophosphate poisoning, botulism, critical illness myopathy, polymyositis, dermatomyositis, hypokalemia, or hyperkalemia. The above list is not exhaustive.

(5) Tracheal stenosis. (i) Postintubation tracheal stenosis means an iatrogenic (caused by medical treatment) and symptomatic stricture of the airway (narrowing of the windpipe) resulting from:

(A) Trauma or necrosis from an endotracheal tube; or

(B) Stomal injury from a tracheostomy; or

(C) A combination of the two.

(ii) Tracheal stenosis or narrowing due to tumors (malignant or benign), infections of the trachea (such as tuberculosis, fungal diseases), radiotherapy, tracheal surgery, trauma, congenital, and inflammatory or autoimmune diseases will not be considered post-intubation tracheal stenosis. Post-intubation tracheal stenosis requires either tracheostomy with placement of a tracheostomy tube or endotracheal intubation. Diagnosis requires symptoms of upper airway obstruction such as stridor (inspiratory wheeze) or exertional dyspnea (increased shortness of breath with exertion), and positive radiologic studies showing abnormal narrowing of the trachea or bronchoscopic evaluation that demonstrates abnormal narrowing.

(6) Ventilator-Associated Pneumonia (VAP) and Ventilator-Associated Tracheobronchitis (VAT). (i) VAP is defined as an iatrogenic pneumonia caused by the medical treatment of mechanical ventilation. Similarly, VAT is an iatrogenic infection of the trachea and/or bronchi caused by mechanical ventilation. The initial manifestation of VAP and VAT must occur more than 48 hours after intubation (placement of the breathing tube) and up to 48 hours after extubation (removal of the breathing tube). VAP will be considered to be present when the patient demonstrates a new or progressive radiographic infiltrate that is in the lungs and consistent with pneumonia, fever, leukocytosis (increased white blood cell count) or leucopenia (decreased white blood cell count), purulent (containing pus) tracheal secretions from a tracheal aspirate, and a positive lower respiratory tract culture. The positive lower respiratory tract culture is a diagnostic requirement only if there has not been a change in antibiotics in the 72 hours prior to collection of the culture. In addition, a tracheal aspirate that does not demonstrate bacteria or inflammatory cells in a patient without a change in antibiotics in the previous 72 hours is unlikely to be VAP and shall not be considered a condition set forth in the Table.

(ii) VAT will be considered to be present when the patient demonstrates fever, leukocytosis or leukopenia, purulent tracheal secretions, and a positive tracheal aspirate culture in the absence of a change of antibiotics within the 72 hours prior to culture. Tracheal colonization with microorganisms is common in intubated patients, but in the absence of clinical findings is not a sign of VAT.

(7) Ventilator-Induced Lung Injury (VILI). VILI results from mechanical trauma such as volutrauma leading to rupture of alveoli (air sacs in the lungs where oxygen and carbon dioxide are exchanged with the blood) with subsequent abnormal leakage of air. VILI manifests as iatrogenic pneumothorax (abnormal air from alveolar rupture in the pleural space), pneumomediastinum (abnormal air from alveolar rupture in the mediastinum (middle part of the chest between the lungs)), pulmonary interstitial emphysema (abnormal air in the lung interstitial space between the alveoli), subpleural air cysts (an extreme form of pulmonary emphysema where the abnormal air in the interstitial space has pooled into larger pockets), subcutaneous emphysema (abnormal air from alveolar rupture that has dissected into the skin), pneumopericardium (abnormal air from alveolar rupture that has traveled to the pericardium (covering of the heart)), pneumoperitoneum (abnormal air from alveolar rupture that has moved into the abdominal space), or systemic air embolism (abnormal air from alveolar rupture that has moved into the blood). To qualify as Table injuries, these manifestations must occur in patients who are being mechanically ventilated at the time of initial manifestation of the VILI.

(8) Bleeding events. Bleeding events are defined as excessive or abnormal bleeding in patients who are under the pharmacologic effects of anticoagulant therapy provided for extracorporeal membrane oxygenation (ECMO) treatment.

(c) Covered countermeasures. The Office of the Secretary publishes Secretarial declarations on the following covered countermeasures in the Federal Register:

(1) Pandemic influenza vaccines;

(2) Tamiflu;

(3) Relenza;

(4) Peramivir;

(5) Personal respiratory protection devices;

(6) Respiratory support devices;

(7) Diagnostic testing devices.

[FR Doc. 2015-19228 Filed: 8/6/2015 08:45 am; Publication Date: 8/7/2015]