DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

42 CFR Part 100

RIN 0905–AD64

National Vaccine Injury Compensation Program Revision of the Vaccine Injury Table

AGENCY: Health Resources and Services Administration, PHS, HHS.

ACTION: Final rule.

SUMMARY: This final rule amends the existing regulations governing the National Vaccine Injury Compensation Program (VICP) by adding a new section regarding the Vaccine Injury Table (Table) to the regulations, pursuant to section 312 of the National Childhood Vaccine Injury Act of 1986 and section 2114(c) of the Public Health Service Act (the Act). The VICP provides a system of no-fault compensation for certain individuals who have been injured by specific childhood vaccines. The Vaccine Injury Table included in the Act establishes presumptions about causation of certain illnesses and conditions, which are used by the Court to adjudicate petitions. The amendments to the Vaccine Injury Table will affect only those petitions filed for compensation under the VICP after the effective date of this rule.

EFFECTIVE DATE: This regulation is effective March 10, 1995.

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SUPPLEMENTARY INFORMATION:

Introduction and Procedural History

On August 14, 1992, the Assistant Secretary for Health, with the approval of the Secretary of Health and Human Services (the Secretary), published in the **Federal Register** (57 FR 36878) a Notice of Proposed Rulemaking (NPRM) to amend the Vaccine Injury Table (the Table). (A correction notice to the NPRM was also published on September 11, 1992, 57 FR 41809). The NPRM was issued pursuant to section 2114(c) of the Act, which authorizes the Secretary to promulgate regulations to modify the Table.

As stated in the preamble to the proposed rule, under section 312 of the National Childhood Vaccine Injury Act of 1986 (Pub. L. 99–660), Congress mandated that the Secretary review the scientific literature and other information on specific adverse consequences of pertussis and rubella vaccines. The Secretary entered into a contract with the Institute of Medicine (IOM), as recommended by Congress, to perform this review. The IOM published a report of its review entitled, ''Adverse Effects of Pertussis and Rubella Vaccines,'' on August 27, 1991 (hereinafter ''IOM Report''). The Public Health Service Task Force on the VICP evaluated the IOM report and made the initial recommendations regarding possible revision of the Table.

These recommendations were reviewed by a special subcommittee of the National Vaccine Advisory Committee (NVAC) (a committee authorized under section 2105 of the Act). The subcommittee overwhelmingly endorsed all of the proposed revisions except for the addition of chronic arthritis to the Table. The full NVAC endorsed the subcommittee's recommendations for revising the Table.

The Advisory Commission on Childhood Vaccines (ACCV), whose membership by statutory directive reflects a variety of views relating to childhood immunizations (authorized under section 2119 of the Act), considered the NVAC report as well as the PHS Task Force recommendations. The ACCV deliberations included public policy considerations, whereas the NVAC charge was to consider only the scientific issues raised by the existing Table, the recent IOM report, and other scientific information. The ACCV voted approval of all of the PHS Task Force recommendations except for the removal of the condition of Encephalopathy. The ACCV voted unanimously to retain Encephalopathy on the Table provided the existing definition in the Aids to Interpretation was clarified. The Secretary proposed changes to the Table after reviewing the recommendations of these three entities.

As provided by section 2114(c) of the Act, the Department provided for a 6-month comment period, which closed on February 11, 1993. On December 3, 1992, the Department held a public hearing for the purpose of receiving oral testimony on the proposed rule.

During the process of analyzing the comments received in response to the NPRM, the Agency became aware of the imminent publication of a 10-year follow-up study to the National Childhood Encephalopathy Study (NCES) (Madge N., Diamond J., Miller D., Ross E., McManus C., Wadsworth J., Yule W. The National Childhood Encephalopathy Study: A 10-year follow-up. A report of the medical, social, behavioural and educational outcomes after serious, acute, neurologic illness in early childhood. Developmental Medicine and Child Neurology 1993; Supplement No. 68;35(7):1–118; Miller D.L., Madge N., Diamond J., Wadsworth J., Ross E. Pertussis immunization and serious acute neurological illness in children. British Medical Journal 1993; 307:1171–1176, hereinafter ''Miller study.''). Because the Miller study looked specifically at the relationship between vaccine administration and subsequent neurological damage, the Department determined that it should not proceed with publication of the final rule until there had been a sufficient opportunity to consider the conclusions of the new Miller study. Accordingly, the Department asked the IOM to convene a Committee for purposes of evaluating the Miller study in light of the conclusions of its initial report. On March 2, 1994, the Institute of Medicine issued a report entitled ''DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis.'' On March 24, 1994, the Department published a notice in the **Federal Register** affording members of the public and additional 30 days to comment on the Miller study and the IOM report. See **Federal Register** March 24, 1994, (59 FR 13916).

The Agency also asked a subcommittee of the NVAC to review the IOM's conclusions regarding the implications of the Miller study. On March 15, the NVAC subcommittee met to review (among other things) the Miller study. The subcommittee was composed of members of the NVAC, and received input from outside experts from the fields of epidemiology, pediatric infectious disease, and pediatric neurology. The views of the NVAC are discussed below where relevant.

The ACCV reviewed the IOM report on the Miller study at its meetings in March and June, 1994. In addition, the ACCV was asked to provide comments during the additional public comment period. Comments received from two individual Commission members will be discussed below. At the June meeting, the Commission discussed in detail the Miller study and the IOM report. The consensus of the Commission was that the original table in the statute requires modification to make it consistent with current medical and scientific knowledge regarding adverse events associated with certain vaccines. The Commission was split, however, on the appropriate frame of reference for modifying the Table. Some

Commission members expressed the view that the starting point for revisions to the Table should be the original Table in the statute. The other commissioners agreed that the Secretary should further refine the Table, but that the starting point for additional revisions should be the modified Table as published in the NPRM on August 14, 1992.

The Department has listened carefully to the Commissioners' concerns. After weighing all the varied opinions expressed at the June meeting, as well as the written comments received from two commission members, the Department has decided that a final rule which is a revised and refined version of the proposed rule published in 1992 will reflect best the scientific evidence. However, in drafting the final rule, the Department made many of the changes suggested by members of the Commission. These changes will be explained below. In this regard, the Department recognizes that one of the objectives of the National Vaccine Plan, which was released recently by the National Vaccine Program Office/OASH, is to ensure that the Vaccine Injury Table is updated periodicall to reflect the latest scientific knowledge. The final rule is consistent with this goal, as well as the statutory directive that the Secretary revise the Table.

Although by law the regulation will only affect those petitions filed after the effective date specified above, the Department encourages the Special Masters of the U.S. Court of Federal Claims to apply the scientific findings which form the basis of the revised Table where appropriate. For instance, in cases where petitioners are intending to prove causation in fact, the IOM's conclusions regarding causation may be relevant for consideration by the Special Master. In addition, the Special Master could find, based on the conclusions of the IOM, that a particular injury was due to a factor unrelated to vaccine administration. Prior to promulgation of this rule, several Special Masters viewed the IOM report as instructive regarding certain illnesses and conditions and their relationship to vaccine administration. The Department hopes that the use of the IOM report continues, and that the findings and conclusions made by the Secretary in promulgating this rule will be applied by the Masters where the facts of the case make it appropriate to do so. In some cases, as explained below, the Secretary's findings as set forth in the NPRM at 57 FR 36879 were not incorporated into the final rule. This decision does not affect the Secretary's findings and should not deter the Special Masters from applying the findings where appropriate.

The Department received 41 written comments and five oral comments on the NPRM, and five comments in response to the **Federal Register** Notice to Extend the Public Comment Period (March 24, 1994). Comments were received from health professional organizations, parent organizations, medical professionals, attorneys, and the general public. All comments were carefully considered. The Department's responses to the comments are discussed below in two separate sections. Section I discusses the comments addressing legal issues, and Section II discusses those comments addressing medical issues. The discussion does not address comments that either generally supported or generally criticized the proposed Table changes without making a specific point. In preparing this final rule, the Department also made a number of changes, both editorial and substantive in nature. The substantive changes are discussed where appropriate as follows:

I. Legal Issues

The Secretary's Authority To Promulgate the Regulation

Several commenters suggested that the Department had exceeded its authority in promulgating the regulation. First, commenters argued that this is a function which belongs to the legislative branch and which cannot be delegated to the Department based on the Separation of Powers doctrine. The Department disagrees with this legal argument for several reasons. In enacting a particular statutory scheme, Congress will often leave particular gaps with instructions to the Department charged with executing the statute to promulgate regulations to fill the gaps and interpret the statutory language. *See Chevron* v. *Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). In promulgating regulations, the Department is limited to the authority delegated by Congress, and is obligated to act consistent with Congressional intent. *See Bowen* v. *Georgetown University Hospital*, 488 U.S. 204 (1988). Pursuant to these basic principles of administrative law, the Secretary is promulgating this regulation to amend the Vaccine Injury Table.

The statute explicitly authorizes the Secretary in section 2114(c) of the Act to modify the Table and states that the ''Secretary may promulgate regulations to modify * * * the Vaccine Injury Table.'' See 42 U.S.C. 300aa–14(c)(1). The statute further provides that ''a modification of the Vaccine Injury Table under paragraph (1) may add to, or delete from, the list of injuries, disabilities, illnesses, conditions, and deaths for which compensation may be provided, or may change the time periods for the first symptom or manifestation of the onset of the significant aggravation of any such injury, disability, illness, condition, or death.'' See 42 U.S.C. 300aa–14(c)(3). Under section 312 of Pub. L. 99–660, Congress mandated that the Secretary review the scientific literature and other information on specific adverse consequences of pertussis and rubella vaccines. As mandated by the statute, after completion of this study (undertaken by the Institute of Medicine), and the consultation required by section 2114(c) of the Act, the Department proposed the revisions to the Table. In so doing, the Department was acting exactly within the authority delegated to it by the Congress.

Further, as stated in the preamble to the Notice of Proposed Rulemaking, the legislative history explains that Congress intended the Secretary to modify the Table. The Conference Report states as follows:

> The Committee recognizes that there is public debate over the incidence of illnesses that coincidentally occur within a short time of vaccination. The Committee further recognizes that the deeming of vaccine-relatedness adopted here may provide compensation to some children whose illness is not, in fact, vaccine-related. The Committee anticipates that the research on vaccine injury and vaccine safety now ongoing and mandated by this legislation will soon provide more definitive information about the incidence of vaccine injury and that, when such information is available, the Secretary or the Advisory Commission on Childhood Vaccines * * * may propose to revise the Table, as provided below in section 2114 [Initial Table]. Until such time, however, the Committee has chosen to provide compensation to all persons whose injuries meet the requirements of the petition and the Table and whose injuries cannot be demonstrated to be caused by other factors.

See H.R. Rept. 99–908, Part 1, September 26, 1986, page 18 (reprinted in 1986 U.S. Code Cong. and Admin. News, Vol. 6, page 6359). This passage indicates that the Department is acting consistent with Congressional intent.

At least two commenters argued that the Department exceeded its authority in modifying the ''Qualifications and Aids to Interpretation'' (Qualifications) found in section 2114(b) of the Act. This argument, too, is misplaced. First, section 312 requires that the Secretary make findings regarding which illnesses

and conditions can reasonably be determined to be caused by certain vaccines. It further requires the Secretary to make findings regarding ''the circumstances under which such causation or aggravation can reasonably be determined to occur.'' 42 U.S.C. 300aa–1 note. The purpose of the Qualifications and Aids to Interpretation is to describe those circumstances under which certain conditions occur. Congress stated that the Qualifications provide ''various descriptions and definitions that the Committee intends be used in interpreting the meaning of the Table.'' See H.R. Rept. 99–908, Part 1, September 26, 1986, page 19 (reprinted in 1986 U.S. Code Cong. and Admin. News, Vol. 6, page 6360). Given that Congress required the Secretary to make findings regarding the circumstances under which causation can occur, and that she was then required to promulgate regulations as a result of such findings, she could not have fulfilled her obligations under section 312 without modifying the Qualifications as well as the Table itself.

Moreover, the statutory language and the legislative history quoted above indicate that the Qualifications must be viewed as part of the Table. The statute states that ''the following qualifications and aids to interpretation shall apply to the Vaccine Injury Table in subsection (a).'' See 42 U.S.C. 300aa–14(b). Thus, Congress intended the Table and the Qualifications to be viewed as one unit because the Qualifications explain and clarify the terms of the Table. It stands to reason, therefore, that if the Table is changed, the Qualifications must be changed accordingly.

In fact, Congress anticipated that changes to the Table would require similar changes to the Qualifications and Aids to Interpretation in order to guarantee that the two sections are consistent. The statute states that ''if a provision of the table to which paragraph (1), (2), (3), or (4) [the paragraphs of the Qualifications and Aids to Interpretation] applies is revised under subsection (c) or (d), such paragraph shall not apply to such provision after the effective date of the revision unless the revision specifies that such paragraph is to continue to apply.'' (42 U.S.C. 300aa–14(b)(4)). Thus, the Qualifications contained in the original statute become null and void once that initial Table is changed, unless the Secretary specifies that they are to apply. Implicit in this authority is the authority to promulgate by regulation Qualifications applicable to the revised Table.

Two commenters stated that the regulation exceeded the Department's authority by attempting to prescribe elements of proof necessary to prevail in a petition for vaccine compensation. They argued that this function is reserved to the United States Court of Federal Claims. As explained above, the Secretary is authorized to revise the Qualifications as well as the Table. The statute states that the Secretary may ''add to, or delete from, the list of injuries, conditions, and deaths for which compensation may be provided or may change the time periods for the first symptom or manifestation of the onset or the significant aggravation of any such injury, disability, illness, condition or death.'' The original Table and Qualifications delineate those elements which must be proven in order to take advantage of a presumption of causation.

In this regard, the commenters should understand the function of the Table. The purpose is not to set forth standards of proof for establishing causation-in-fact. Rather, the purpose is to set out a standard for establishing presumed causation, which, absent a finding of a factor unrelated to the vaccine, will allow a petitioner to receive compensation without the burden of proving causation for those conditions included on the Table. Accordingly, the Qualifications properly set out standards for defining those conditions on the Table. Petitioners remain free to establish causation in fact by producing credible scientific information peculiar to their conditions.

Although the commenters assert that the Department is impermissibly creating elements of proof, the Qualifications as drafted originally contain numerous requirements that are, in essence, elements of proof. For example, the paragraph describing the requirements for a 'residual seizure disorder' states the number of seizures which must have occurred in the year after the vaccine was administered for the petitioner to be found to have suffered a residual seizure disorder. In addition, section 2114(b)(3)(A) of the Act describing the definition of encephalopathy states that ''Encephalopathy usually can be documented by slow wave activity on an electroencephalogram.'' Similarly, the revised Qualifications indicate the elements which must be proven to establish a presumption of causation for those injuries and conditions listed in the modified Table.

In objecting to this aspect of the Qualifications, the commenters assume erroneously that the revised Qualifications alter the Special Master's role in determining whether a Table Injury has been proven. The Special Master's role is to consider the information contained in the record, including oral testimony, medical records and medical opinion. The Master must weigh the evidence, examine the credibility of the witnesses, reconcile the points of disagreement between the parties and issue a final decision. The revised Qualifications do not alter this role. As did the former Qualifications, they require the petitioner to demonstrate a Table condition by proving that various events occurred. The Special Master must still analyze the evidentiary issues which arise in the context of attempting to prove a Table injury.

The Effect of the Regulation on Other Statutory Sections

One commenter stated that the Qualifications and Aids to Interpretation are inconsistent with section 2113(b) of the Act, which permits the Special Master to find that the injury occurred within the Table period even if the symptoms were not recorded or were incorrectly recorded in the medical records. The commenter specifically took issue with the section of the revised Qualifications which states that an ''an acute encephalopathy should be sufficiently severe to require health care intervention and hospitalization.'' In addition, during the June 1994 meeting of the ACCV, at least one member of the Commission objected to this requirement as being overly restrictive because hospitalization is required. The Commission member voicing this concern felt that the rule should recognize that not all parents would respond to a possible encephalopathic event by taking the child to the hospital.

The revised Qualifications and Aids to Interpretation are not inconsistent with section 2113(b) of the Act, because the Special Master may still find that a preponderance of the evidence indicates that the encephalopathy was severe enough to require medical intervention or hospitalization, but that because of error or omission the event was either not recorded or was incorrectly recorded. In addition, under the revised Qualifications, although medical records should be provided in most cases, the language ''sufficiently severe'' is meant to be consistent with section 2113(b)(2) of the Act and would permit a finding in favor of petitioner if the Special Master found that a preponderance of the evidence indicated that the injury was sufficiently severe such that medical intervention should have been sought.

In the Department's view, the original statute does not intend the Special Master to find that the injury occurred within the Table period in the absence of any records recording the injury, unless the petitioner is able to produce clear, cogent, and consistent testimony to explain the absence of records. The Court has found in favor of petitioners in the absence of corroborating medical records where the preponderance of evidence, including oral testimony, demonstrates that the adverse event occurred within the Table timeframe. The requirement contained within the revised Aids to Interpretation is meant to include only those events which are so serious that they require medical intervention (whether or not medical intervention was actually sought), and are, therefore, properly referred to as encephalopathies. The requirement is simply meant to exclude those conditions which are not serious enough to warrant medical attention. These types of minor symptoms (e.g., excessive crying, sleepiness) were specifically excluded from the definition of encephalopathy contained within the original statute, but have been alleged by some petitioners to be signs and symptoms of an encephalopathy. The revised Qualifications and Aids to Interpretation simply seek to make clear the intent of Congress.

The Department recognizes, however, that the language ''should be sufficiently severe,'' is somewhat confusing. In addition, the Department recognizes that the phase ''medical intervention and hospitalization'' is redundant, and open to various interpretations. Accordingly, the regulatory language in § 100.3(b)(2)(i) as proposed has been revised to read ''An acute encephalopathy is one that is sufficiently severe so as to require hospitalization.'' The Department is making this change in the interests of clarity, consistent with the explanation articulated above. In order to demonstrate a Table encephalopathy, the petitioner must prove that the injury was indeed serious enough to warrant hospitalization, whether or not records of such hospitalization exist. Certainly, however, contemporaneous medical records are of extreme importance in proving that a Table injury occurred.

The Sufficiency of the IOM Report as the Basis for the Changes to the Vaccine Injury Table

Several commenters stated that the Department relied on insufficient data in proposing modifications to the Table. These commenters argued that Congress intended that more definitive information be available before the Table is revised. The commenters took issue with both the conclusions of the Institute of Medicine and the Department's interpretation of those conclusions. Section 312 of Pub. L. 99–660 (42 U.S.C. 300aa–1, note) required the Secretary to complete a review of ''all relevant medical and scientific information regarding the connection between various vaccines and specified adverse events.'' The Secretary was then required to publish in the **Federal Register** findings regarding ''whether each of the illnesses or conditions set forth in subsection (a) can reasonably be determined in some circumstances to be caused or significantly aggravated by pertussis containing vaccines.'' *See* 42 U.S.C. 300aa–1, note. Simultaneously, the statute required that the Secretary propose changes to the Table as a result of the findings.

This language indicates that Congress intended that the Secretary modify the Table consistent with the conclusions of the review undertaken by the Institute of Medicine. Nowhere is there a requirement, however, that the causal connection between the administration of vaccines and certain adverse events be definite and conclusive before any changes are made. The IOM concluded that ''the evidence is insufficient to indicate a causal relation between vaccines containing pertussis'' and certain adverse events. Because the evidence was determined as ''insufficient,'' the Department concluded that it could not ''reasonably determine'' that a causal connection exists, and the Table is being revised accordingly.

The section of the legislative history cited by the commenter in support of the objection states that ''the Committee anticipates that the research on vaccine injury and vaccine safety now ongoing and mandated by this legislation will soon provide more definitive information about the incidence of vaccine injury and that, when such information is available, the Secretary or the Advisory Commission on Childhood Vaccines (discussed below in section 2119) may propose to revise the Table as provided below in section 2114.'' This statement merely indicates a recognition by Congress that the original Vaccine Injury Table was overinclusive, and that more research would yield *more* definitive information. As described in the preamble to the proposed regulation, and consistent with the statutory requirements, the findings of the Institute of Medicine represented a comprehensive review of the existing evidence as well as numerous opportunities for comment from various experts and members of the public. The systematic process undertaken by the Department to evaluate the findings of the IOM demonstrates that the Department reviewed sufficiently the findings of the IOM and their applicability to the Table. These findings clearly indicated that the original Table was out of step with the state of medical knowledge. Accordingly, the Secretary was obliged to propose revisions. Although the IOM's original conclusion was modified somewhat in the 1994 report regarding pertussis vaccine and chronic nervous system damage, the Department has determined that the major changes to the Table published in the NPRM reflect the IOM's latest conclusions regarding this difficult issue. Nevertheless, as discussed below, the final rule reflects some minor changes made to the proposed rule in light of the Miller study and comments provided to the Department in connection with this study.

Two commenters felt that the Department had ignored relevant information in revising the Table. Specifically, they believed that the Department should have viewed the claims that have either been compensated or conceded by the Department as proof that the presumptions conferred by the Table are accurate. However, the fact that a particular case has either been adjudicated compensable or conceded by HHS does not imply that a medical conclusion regarding vaccine-relatedness has been made. The process of deciding claims is based on whether the claim fits the parameters of the Table, or whether causation has been proven. Most claims have been adjudicated ''table cases,'' meaning that the petitioners were afforded the presumption of causation conferred by the statute. This determination involves an analysis of various evidentiary and other legal issues, but does not prove or disprove whether a causal relationship exists in fact between certain vaccines and adverse events. The outcome of these cases does not have any bearing on whether the Table should be revised to reflect the findings of the Institute of Medicine.

One commenter referred to a letter written by the organization Dissatisfied Parents Together on May 8, 1991, to then Secretary Sullivan regarding concerns that members of the Immunization Practices Advisory Committee (ACIP) who have advised pharmaceutical companies, or conducted research funded by such companies may have a conflict of interest which precludes their serving

on the ACIP. The Department has determined that this comment is irrelevant as far as the modification of the Table is concerned. In undertaking its review, the IOM did not rely on the views of members of the ACIP or the work-product of that Committee.

The Effect of the Proposed Changes on the Vaccine Injury Compensation Program

Two commenters suggested that the result of the proposed revisions would be an increase in the transaction costs of the Program because many petitioners will pursue their cases by attempting to prove causation-in-fact. The Department has taken this concern into consideration and has concluded that the benefits of the proposed regulation outweigh the possibility of more protracted and complex hearings. The intent of the regulation is to make the Table consistent with medical knowledge regarding the relationship between vaccines and certain adverse events. The Department notes that Congress recognized that the original Vaccine Injury Table would permit individuals whose conditions were not related to vaccine administration to be adjudicated eligible for compensation. If the Table is revised to permit compensation only in those cases where vaccine relatedness is more accurately proven, greater resources will be available to compensate those truly deserving of compensation.

In a similar vein, several commenters expressed concern that the Department was seeking to prevent children deserving of compensation from receiving assistance under the Program. In fact, exactly the opposite is true. The revised Table merely affects the presumption of causation available to certain petitioners. Petitioners will, of course, continue to have the option of proving causation by a preponderance of evidence if they are unable to prove a Table injury. Moreover, the Department recognizes that there is a desperate need for parents to obtain resources to cover the significant medical costs of caring for a sick child. However, the intent of the VICP was to compensate only those individuals whose injuries are vaccine-related. The proposed regulation is simply an attempt to come closer to realizing this goal than was possible with the language of the original Vaccine Injury Table.

Three commenters suggested that the proposed regulation would result in an increased number of civil actions filed against vaccine manufacturers and administrators. In enacting the National Childhood Vaccine Injury Act, Congress determined that one of the goals of the Act was to reduce the number of civil actions filed against vaccine administrators and manufacturers. The other major goal was to provide compensation to those individuals whose conditions were caused by vaccines. *See* H.R. Rept. 99–908, Part 1, September 26, 1986, page 6 (reprinted in 1986 U.S. Code Cong. & Admin News, Vol. 6, page 6347). The Committee recognized, however, that the Table would possibly provide compensation to some children whose illnesses are not vaccine-related, but that further research and modifications to the Table would result in a more equitable distribution of funds. In balancing these two Congressional goals, the Department has determined that the benefits of fulfilling the latter requirement outweigh the risk that an increased number of civil actions will be filed against vaccine administrators or manufacturers.

Furthermore, the Department believes that the combined effect of the IOM's review and this regulatory action may reduce the extent of tort litigation by giving the courts (and potential plaintiffs weighing the wisdom of filing suit) definitive guidance as to the state of scientific knowledge regarding vaccine-related injuries. As causation must typically be proven in tort actions, the Department believes that the findings on these issues may well reduce the amount of tort litigation and may allow easier resolution of any such claims that are litigated.

II. Medical Issues

The Department's Interpretation of the IOM Report

Six commenters suggested that the Department's findings are a misinterpretation of the IOM Report. In the Department's view, however, the proposed changes do reflect accurately the conclusions of the IOM report.

Both the NPRM and the final rule (with some revisions are discussed below), reflect most closely the package of recommendations as developed by the PHS Task Force, reviewed by the NVAC, and endorsed by the ACCV. The proposed changes are in accordance with the scientific findings of the IOM Committee. In instances where the IOM found information suggesting a causal relation *and* continued effects, the Department acted to ensure coverage under the Program (e.g., adding chronic arthritis to the Table). However, where the IOM found that the evidence did not support a causal relation and continued effects, the Department removed the legal presumption of causation by removing or redefining the current injury listed on the Table. The fact that the proposed revisions received overwhelming approval from three independent science and health policy committees, and the endorsement of two national health professionals associations (American Academy of Pediatrics and American Medical Association), confirms the basic soundness of the initial proposed revisions.

One of the commenters addressing the Miller study suggested that in light of the 1994 IOM Report, the Department should rescind certain findings made after release of the 1991 Report and published in the preamble to the NPRM. In the NPRM, published on August 14, 1992, the Department made certain findings as required by section 312(b) of Pub. L. 99–660 (42 U.S.C. 300aa–1 note). The Department has reviewed these findings again in light of the commenter's concerns, and has determined that the findings remain valid. In fact, the conclusions of the IOM and the NVAC subcommittee (discussed below) with respect to pertussis vaccine and chronic neurological damage confirm the soundness of findings three and four as listed in the NPRM. These findings read, in pertinent part, as follows:

> 3. The evidence is insufficient to indicate a causal relation between vaccines containing pertussis and: Epilepsy * * * chronic neurologic damage, * * * learning disabilities and attention-deficient disorder, * * * or permanent neurologic damage or death following hypotonic-hyporesponsive episodes.
>
> 4. The evidence is consistent with a causal relation between vaccines containing pertussis and? Acute encephalopathy and shock and ''unusual shock-like state.''

The recent IOM report was confined to a review of the Miller study, and is, therefore, limited to the circumstances of that particular study. Given the conclusions articulated by the IOM and the accompanying caveats, and the discussion and conclusions of the NVAC subcommittee, the Department concludes that the findings published with the NPRM reflect best the state of scientific knowledge. It should be noted again that in drafting the revised Qualifications and Aids to Interpretation, the Department decided not to eliminate the presumption of causation for encephalopathy despite the conclusions of the 1991 IOM study. Rather, consistent with the recommendation of the ACCV, the Department included a presumption of vaccine causation for those individuals who experience an acute encephalopathy within 3 days after vaccination, who go on to suffer 6

months of residual effects, and who experience chronic neurological dysfunction. This presumption is consistent with the IOM's conclusions articulated in its 1994 report.

Four commenters suggested that the IOM's causation category of ''insufficient evidence'' should not be interpreted to mean that DTP vaccine does not cause the condition. Furthermore, they suggest that both the IOM and the Department present no data which support the proposition that acute encephalopathy, subsequent to the receipt of a pertussis vaccine, has a more benign neurological outcome than acute encephalopathies from other agents. The Department has considered these comments but maintains that the IOM report provides a foundational basis for the proposed changes.

The 1991 IOM report concluded the evidence was insufficient to indicate a causal relationship between vaccines containing pertussis and chronic neurological damage for a variety of conditions including encephalopthy, shock collapse or Hypotonic-Hyporesponsive Episode (HHE), epilepsy, and other neurologic and non-neurologic disorders. Comments that expressed concern over this classification focused for the most part on acute encephalopathy and chronic neurologic damage, while a few discussed shock-collapse (HHE) or recurrent seizures (epilepsy). The issue of encephalopathy following pertussis vaccination is a difficult one. On one hand, in its 1991 Report, the TOM found evidence ''consistent with a familiar evidence ''consistent with a causal relation'' for acute encephalopathy, yet on the other hand, it decided there was ''insufficient evidence'' regarding *chronic* nuerologic damage. Due to limitations in the data, the IOM could not conclude with any certainty whether there is any causal relationship between pertussis vaccine and shock-collapse (HHE), epilepsy, or any of the other disorders under this classification category. In its 1994 report addressing the Miller study, the IOM concluded that ''evidence is insufficient to indicate whether or not DTP increases the overall risk in shildren of chronic nervous system dysfunction.'' They concluded further, that the ''balance of evidence is consistent with a causal relation between DTP and the forms of chronic nervous system dysfunction described in the NCES in those children who experienced a serious acute neurological illness within 7 days after vaccine administration.'' The IOM also concluded, however, that ''the evidence remains insufficient to indicate the presence or absence of a causal relation between DTP and chronic nervous system dysfunction under any other circumstances.'' *See* 1994 IOM Report, Executive Summary.

Because section 2111(c) of the Act requires that a Petitioner must show 6 months of residentual effects of a Table injury, a finding of a relation pertussis-containing vaccines and acute, but not chronically, does not justify the presumption of causation for long-term neurologic damage. However, should the evidence show that abnormal neurologic signs continued beyond the acute state, and therefore the injured indidivual never returned to a ''normal neurological state,'' than title may be granted. This conclusion is consistent with the 1994 IOM report.

The language of section 312 of Pub. L. 99–660 (42 U.S.C. 300aa–1, note) also supports the Department's conclusion. The IOM determined in its 1991 report that the evidence is insufficient to support a conclusion that a causal relationship between DTP vaccine and chronic neurologic damage exists. The 1994 IOM finding was limited to the conditions described in the NCES and to those children who experienced an acute event following vaccination. Therefore, the Department concluded that it could not ''reasonably determine'' that as a general rule a causal relationship exists, and the Table is being modified accordingly. Because section 312 requires such a determination in order to sustain the presumption of causation, the Department was obligated to revise the Table consistent with the conclusions of the IOM.

The removal of the legal presumption of causation has been applied to other conditions in the ''insufficient evidence'' category (i.e., HHE and residual seizure disorder). The Department notes, however, that the removal of a condition from the Table, or the inclusion of a revised definition thereof, will not necessarily result in compensation being denied where it would have previously been awarded. Petitioners may still prevail by providing proof that the vaccine actually caused the specific injury alleged to have occurred.

Three commenters suggested that the IOM's burden of proof standard was too high. They suggested that the IOM should develop a confidence level that is more lenient than 95 percent, particularly when it is applied to the ''preponderance of the evidence'' burden of proof standards present in the VICP. After consideration of the process used by the IOM in developing its report, it is the Department's view that the IOM's standard was appropriate.

Congress mandated that the IOM review the scientific literature and other information on specific adverse consequences of pertussis and rubella vaccines. The Committee was composed entirely of physicians and scientists, whose task it was to evaluate the literature on adverse events following these vaccines. Any ''burden of proof'' standard had to be consistent with the standard applied throughout the science of epidemiology, policy considerations notwithstanding. It is the Secretary's responsibility under section 312 of Pub. L. 99–660 (42 U.S.C. 300aa–1, note) to utilize the IOM's conclusions to provide a better scientific rationale for any presumptions of vaccine causation under the Program.

Moreover, although the statute requires merely a ''preponderance of the evidence'' standard in evaluating compensation claims, there is no requirement that anything other than the standard commonly used among scientific and medical professionals be applied in re-defining those conditions which will receive a presumption of causation by use of the Table. The preponderance of evidence standard is only relevant when a Master is evaluating a particular case.

One commenter suggested that the IOM conclusions were incorrect regarding DTP's pathological effects in animals or children. The commenter stated that the IOM erred in diminishing the importance of, or incorrectly judged, the conclusions of controlled epidemiologic studies. Furthermore, the commenter suggested that the IOM Committee was remiss in its examination of the evidence concerning long-term sequelae for HHE. Finally, two commenters criticized the IOM because no original research was done in putting together its conclusions. As stated above, the Department has considered these comments, but has determined that the process used by the IOM was appropriate.

The 1991 IOM Committee was made up of 11 experts in infectious disease, pediatrics, internal medicine, neurology, epidemiology, biostatistics, decision analysis, immunology and public health. During the 20 months of their work, approximately 1,400 citations were reviewed and 5 public meetings were held. No new research was conducted. Committee members considered new or controversial data and various points of view and sought to identify gaps in knowledge. The IOM cited many gaps and limitations of knowledge. Its conclusions were reached, however, after an exhaustive analysis of the best epidemiologic data available, and other information.

Congress did not mandate any specific research, but rather, an extensive review of all the available information on adverse events.

One commenter suggested the IOM incorrectly judged the conclusions of the British National Childhood Encephalopathy Study (NCES). Another commenter stated that the NCES is the only ''suitable'' study that has been done, and that it concluded that there was a causal relationship between the DTP vaccine and permanent neurologic injuries. One commenter also suggested that the NCES proved the onset of a neurologic disorder, including seizures, within 7 days of a DTP vaccination is vaccine-related. The Department has reviewed the conclusions of the NCES in light of these comments, but disagrees for the following reasons.

The 1991 IOM Report considered carefully the results of the NCES, which concluded there is an increased risk of acute neurologic illness (encephalopathy and seizures) within 7 days following DTP immunization, and that in some instances, this may lead to permanent neurologic illness. The methods and results of the NCES have been thoroughly analyzed since publication of the study, which has led to continued controversy about the study's findings and a reassessment of the role of pertussis vaccine as a cause of permanent neurologic damage. (IOM Report, page 99–107)

In its 1991 report, the IOM described potential areas of error and bias regarding the study's conclusions on acute neurologic illness and chronic neurologic damage. Regarding acute neurologic illness, the Committee cited three areas of potential study weakness: case ascertainment, determination of the onset of illness, and the lack of control for potential confounding factors. Despite these limiting factors, the IOM believed that the NCES demonstrated statistical significance for acute neurologic illness where onset is within 7 days of DTP vaccination. Their conclusion was based on the fact that only controlled epidemiological studies can address the relationship between neurologic illness and vaccine causation. Of the four controlled studies reviewed (including the NCES), only the NCES demonstrated a statistically significant risk following DTP vaccine. However, the IOM noted that the ''total number of cases reported in the other three studies was consistent with attributable risk found in the NCES,'' and on this basis concluded *the evidence was consistent* with a causal relation between DTP vaccine and acute encephalopathy. (IOM Report, page 117)

The NCES' conclusion regarding permanent neurologic damage was viewed differently by the 1991 IOM Committee. The Committee described concerns over (1) the number and composition of cases on which the estimates were based and (2) the nature of the relationship between an episode of acute neurologic illness and subsequent demonstration of neurologic or developmental abnormalities. Both concerns cast doubt upon the NCES' conclusion that DTP vaccine causes residual neurologic injury.

The conclusion regarding permanent injury was based on seven children who were found to have residual neurologic illness on follow-up. Since the NCES was published, some of these seven children have been diagnosed with non-vaccine related conditions. Thus, the risk estimates are ''very fragile'' at best, since the number of children with new unexplained neurologic illness was very small. (IOM Report, page 106).

Similarly, the NCES' conclusions on residual effects begs the central question of causation. All seven children found to have ''permanent neurologic illness'' on follow-up were presumed to be normal prior to vaccination. However, no baseline neurologic examination was performed on any of these children. Additionally, two of the seven had seizures as their manifestation of acute neurologic illness within 7 days of DTP vaccination. As the IOM noted, many experts question whether seizures alone cause neurologic illness, or rather are the ''markers'' of those children with pre-existing neurologic disease. (IOM Report, page 107).

As explained above, a follow-up study to the NCES was published by Miller, et al. in the fall of 1993. The Department asked the IOM to look at the Miller study's conclusions regarding DTP vaccine and subsequent neurological damage. The Department then asked a subcommittee of the National Vaccine Advisory Committee (NVAC) to review this later IOM report, as well as the Miller study. The NVAC Subcommittee acknowledged the original NCES (and Miller follow-up) as the most comprehensive long-term study on this subject to date, yet noted there are limitations in the data. These include the lack of neuropathologic studies on case children, the fact that young infants with pre-existing neurologic disorders (damage) can be normal on physical examination at the time of immunization, the failure to exclude alternative etiologic diagnoses, and the non-specific range of disorders classified by NCES authors under the rubric ''chronic nervous system dysfunction.'' The subcommittee noted also that the working definition of ''acute neurologic illness'' used in the NCES is not consistent with the current medical understanding of acute encephalopathy as an acute, generalized disorder of the brain. Children were placed in the NCES case definition who experienced only febrile seizures, a benign condition known to be triggered by DTP vaccine, yet never proven to have lasting effects, absent signs of acute encephalopathy. These limitations disallow definitive causal conclusions that would necessitate changes to the Secretary's definition of encephalopathy in the NPRM.

In reviewing the Miller study, the IOM Committee reached three conclusions:

(a) The evidence is insufficient to indicate whether or not DTP increases the overall risk in children of chronic nervous system dysfunction.

(b) The balance of evidence is consistent with a causal relation between DTP and the forms of chronic nervous system dysfunction described in the NCES in those children who experienced a serious acute neurologic illness within 7 days after vaccine.

(c) The evidence remains insufficient to indicate the presence or absence of a causal relation between DTP and chronic nervous system dysfunction under any other circumstances.

After extensive review and discussion, the NVAC subcommittee agreed with the IOM's conclusion that children who experience serious, acute neurological events after DTP vaccination can go on to exhibit ''chronic nervous system dysfunction.'' The NVAC subcommittee concluded that despite the conclusions of the Miller study, the information remains insufficient to accept or reject whether DTP administration prior to the acute, serious neurologic event influenced the likelihood of neurologic dysfunction. In order to avoid any confusion on this point, the Subcommittee approved the following summary statement:

> Children immunized with whole-cell DTP vaccines rarely experience acute, serious neurologic events that require hospitalization. An important question pertains to the long-term complications of these events. Among all children hospitalized with serious neurologic events, irrespective of their etiology or relationship to DTP, there is a potential for the presence of neurologic dysfunction when they are evaluated 10 years later. However, the data are insufficient to accept or reject whether DTP administration prior to the acute, serious neurologic event influenced the potential for neurologic dysfunction. *See* National Vaccine Advisory Committee (NVAC), Report of the Ad Hoc Subcommittee on Childhood Vaccines, p.7.

The Agency has reviewed carefully the IOM's conclusions and the NVAC subcommittee's evaluation of the IOM report, recognizing that questions will continue regarding DTP vaccine and chronic nervous system dysfunction. In addition, the Agency has considered comments provided by three individuals in response to the March 24, 1994 **Federal Register** Notice. These commenters suggested that the Department should retract some of the changes to the Vaccine Injury Table proposed in 1992, arguing that those changes are not inconsistent with the 1994 IOM report. The Agency has determined that despite the uncertainty regarding causation, the final rule is consistent with both the IOM report and the NVAC subcommittee's conclusions regarding the Miller study. The final rule permits an individual to receive a presumption of causation if the DTP vaccine recipient ''manifests, within the applicable period, an injury meeting the description * * * of an acute encephalopathy, and then a chronic encephalopathy persists in such person for more than six months beyond the date of vaccination.'' *See* § 100.3(b)(2). Thus, the final rule is consistent with the IOM's conclusion that some children have been shown to have experienced an acute encephalopathy following vaccine administration and then have gone on to develop chronic neurologic dysfunction. *See* 1994 IOM Report, Executive Summary.

The only circumstances under which a presumption of causation would not be available to an individual with chronic neurological dysfunction would be (1) where the child had not experienced an acute encephalopathy within several days after DTP vaccination, or (2) where the child experienced an acute encephalopathy within several days of DTP vaccination, but returned to a normal neurological state, and did not suffer 6 months of residual effects after the administration of the vaccine.

The denial of a presumption of causation for the former is consistent with the IOM's conclusions as articulated in both its 1991 and 1994 reports. The IOM did not conclude that chronic neurological dysfunction should be presumed to be caused by DTP vaccine in the absence of an acute encephalopathy that occurs within several days following vaccination. See 1994 IOM Report at page 10. The IOM stated the following:

> The evidence remains insufficient to indicate the presence or absence of a causal relation between DTP and chronic nervous system dysfunction under any other circumstances. That is, because the NCES is the only systematic study of chronic nervous system dysfunctions after DTP, the committee can only comment on the causal relation between DPT and those chronic nervous system dysfunctions under the conditions studied by the NCES. In particular, it should be noted that the chronic nervous system dysfunctions associated with DTP followed a serious acute neurologic illness that occurred in children within 7 days after receiving DPT. 1994 IOM Report at page 11.

Neither the IOM report nor the Miller study addressed the scenario where a child would experience an acute encephalopathy within several days following vaccine administration, would return to a normal neurological state, but at some point in the future would exhibit signs of chronic neurological dysfunction. The most recent report by the IOM does not present any information which warrants a modification of the presumptions in the final rule. Therefore, the final rule is consistent with the IOM's conclusions and the NVAC subcommittee's assessment of those conclusions.

The NVAC subcommittee was also asked to look at whether the evidence as described in the IOM report would support a conclusion that the time period in the vaccine injury table for acute encephalopathy following DTP vaccine should be changed from 3 to 7 days. The subcommittee concluded that there is presently insufficient information to justify such a change. The Department has reviewed the conclusions of the IOM report as well as those of the NVAC subcommittee and has determined that the rule should not be modified. In this regard, the Department recognizes that it is accepting the analysis of the NVAC subcommittee, rather than acting solely on the basis of this particular statement from the 1994 IOM report. However, it is important to note that the 1991 IOM report, which included a review of numerous scientific studies and other medical literature, did not draw any conclusions regarding the appropriate time period.

In preparing the latest report, the IOM confined its analysis to the Miller study, which was a follow-up to the original NCES. Given the limitations of the IOM's conclusions, including the lack of primary data analysis, as well as the methodologic limitations that have been noted with regard to the NCES, the NVAC subcommittee determined that the conclusions of the Miller study with respect to the appropriate timeframe could not be extended beyond the parameters of this one particular study. After careful consideration, and recognizing the extensive expertise of the NVAC subcommittee, the Department has decided to accept the conclusions of the NVAC subcommittee. Accordingly, the 3 day timeframe, as originally determined by Congress, will not be changed. Petitioners may seek to prove causation in fact for conditions arising between 3 and 7 days after vaccination and may, of course, introduce the Miller study and the IOM report as evidence bearing on such an argument.

One commenter suggested that the 1991 IOM report contradicts an earlier 1985 IOM report which gave risk estimates for reactions following whole cell pertussis vaccination, and stated that pertussis vaccine causes permanent neurologic damage.

The 1985 IOM Report focused on building a model to help evaluate the risks and benefits for existing and new vaccines to allow informed judgments on priorities for developing new vaccines. In drafting their conclusions, the 1985 group used informed judgments on vaccine risks, and the financial benefits of reducing disease. Because of the larger number of vaccines studied in the 1985 report, the review of the scientific literature on specific adverse events in this report was far less extensive than that in the 1991 report.

Analysis of Other Data

Before any changes should be made to the Table, four commenters suggested that the Vaccine Adverse Events Reporting System (VAERS) data and/or Vaccine Injury Compensation Program records should be examined and analyzed. VAERS is a passive reporting system which relies in large part on reports of events temporally related to vaccine administration. Therefore, no reliable conclusions about causation could be drawn from the reported VAERS data without its undergoing substantial analysis. While the Department recognizes the importance of VAERS, it is unwilling to overstate its importance by using temporal relationships to define a new Table.

Further, the IOM's section 312 study involved a thorough review of scientific and medical information contained in peer reviewed journals. However, information based on anecdotal reports (e.g., VAERS), or a series of case reports, such as claims filed under the VICP, has less certain scientific reliability, and therefore should also not be used as a basis for revising the Table. Because of the limitations of these types of evidence, the Department does not concur with this suggested approach.

The ACCV's Scientific Review Subcommittee reviews cumulative data

collected through the VAERS system at each quarterly meeting. In December 1992, the Subcommittee wrote the following concerning: ''VAERS as a means of surveillance of temporally-related adverse events, has definite limitations and does not allow the evaluation of possible causal relationships between vaccine administration and adverse events.'' VAERS's data potentially serve as a ''signal'' of possible causal relationships, which can then be investigated through what are termed Large Linked Data Bases (LLDB's). The Subcommittee encouraged increased utilization of LLDB data because of its potential for surveillance of adverse events and their possible causal relationship to vaccine administration.

The Department will monitor future analysis of VAERS and LLDB data. Should information suggest modifications to the Table, the Department will publish a new NPRM reflecting this new information with proposals for change.

One commenter suggested that the Department ignored cases in the medical literature (and VICP case files) that show a pattern of increasingly severe reactions after succeeding DTP shots in the same child. The commenter argued that the IOM Report indicated it would tend to support the hypothesis of a causal link between pertussis vaccine and permanent neurologic damage if case histories show such a pattern.

In its analysis, the IOM reviewed case reports and case series along with controlled epidemiologic studies. It is true that the IOM suggested that the increasing severity of a reaction following immunization in the same individual *might* indicate a causal link to the vaccine. The Department did not view this hypothesis as strong enough to warrant a presumption of causation. The results of the 1994 IOM Report have not changed this conclusion. However, any petitioner who can demonstrate evidence of progressive or repetitive adverse effects following vaccination may be eligible for compensation by proving causation in fact.

Three commenters suggested there should be no changes to the Table before the section 313 study (of other vaccine risks) is completed. One commenter suggested specifically that changes to the timeframe under Residual Seizure Disorder are not appropriate before results of the section 313 study have been published.

In publishing the final rule, the Department has considered the effect of the section 313 study. Section 313 of The National Childhood Vaccine Injury Act of 1986, Pub. L. 99–660, mandated that the Secretary arrange with the IOM for an additional broad study of the risks associated with each vaccine set forth in the Table, other than the vaccines (pertussis and rubella) previously identified in the section 312 study discussed above. The IOM section 313 study, entitled ''Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality,'' was released on September 14, 1993. The study covers adverse events following these commonly-administered vaccines: measles, mumps, diphtheria, tetanus, polio, Hemophilus influenza type b, and Hepatitis B.

On March 15, 1994, a subcommittee of the NVAC met to consider the section 313 report. The subcommittee was composed of members of the NVAC and received testimony from outside experts in the fields of epidemiology, pediatric infectious disease, and pediatric neurology. The Department determined that the conclusions of the subcommittee regarding the section 313 report do not provide a basis for changing the final rule at this time. However, the Department is presently reviewing the conclusions of the NVAC subcommittee regarding the section 313 report. It is likely that after this review the Department will initiate further rulemaking proceedings. The Department has concluded, however, that there are no compelling reasons which would justify delaying the promulgation of the final rule pending completion of that review.

Anaphylaxis

One commenter suggested that the examples of anaphylaxis given by the IOM do not provide a basis for the proposed revisions.

The IOM examined case reports and epidemiologic studies concerning anaphylaxis and anaphylactic shock. There was considerable variability in the onset and clinical signs of what was defined as ''anaphylaxis.'' One ''suspected association'' with pertussis vaccine was a case report of twins from 1946, both of whom died within 24 hours of pertussis vaccination (IOM Report, page 146). Forensic examination confirmed tissue evidence of anaphylaxis. However, both exhibited clinical signs within 4 hours of vaccination. Other than the 1946 case reports, none of the other examples of ''anaphylaxis'' cited by the IOM, that began after 4 hours of vaccination, was associated with permanent injury. Again, Petitioners may receive compensation under the Program if they prove their injury was caused by the vaccination, even if the onset was after the 4 hours specified in the Table.

One commenter noted that the IOM Committee did not address the timeframe within which to expect anaphylaxis. The commenter suggested further that the Department should have taken into account the fact that infants react differently than children and adults.

Although it is true that infants may react differently to illness or medications, the pediatric literature is clear in stating that severe anaphylactic reactions occur immediately with antigen exposure and rarely show their first manifestation after 4 hours.

One commenter suggested that the proposed revision for DTP, MMR and Polio fail to allow for delayed hypersensitivity.

The medical literature supports the conclusion that the more severe anaphylactic reactions occur closer in time to the antigen exposure. An anaphylactic reaction that shows its first manifestation greater than 4 hours after antigen exposure is likely to be a mild reaction and thus very unlikely to lead to any permanent injury or sequelae. If a petitioner is injured by a delayed hypersensitivity reaction, compensation still can be awarded if causation in fact is proven.

One commenter suggested that the changes do not allow for hypoxia, ischemia, or hypoxia/ischemia, which are common complications of anaphylaxis and anaphylactoid shock. However, the proposed Table allows for any sequela whose first sign or clinical manifestation falls within Table guidelines, as long as the sequela is caused by the Table injury.

Encephalopathy

Much of the discussion of comments related to ''encephalopathy'' is set forth above under the heading ''The Department's Interpretation of the IOM Report.'' Set forth below are the remaining issues regarding encephalopathy.

One commenter suggested that the initial sentence under the definition of ''encephalopathy'' which states, ''[t]he term encephalopathy means any acute or chronic significant acquired abnormality of, or injury to, or impairment of function of the brain,'' is too vague and seems to contradict the more specific definitions which follow the proposed subparagraphs (i) and (ii).

The Department had proposed to retain the language of the original Aids to Interpretation to serve as an introduction to the definition of encephalopathy. The Department agrees that it is imprecise, and that it tends to differ from the guidance provided in the definitions for acute and chronic

encephalopathy which immediately follow. Accordingly, the proposed language in § 100.3(b)(2) has been revised to clarify the definitions for acute and chronic encephalopathy.

Comments concerning the criteria for the diagnosis of acute encephalopathy (paragraphs (b)(2)(i) (A) and (B)) were offered by three individuals. One commenter suggested that the criteria for the diagnosis in the less than 24-month-old age group were too narrow and restrictive. All three commenters felt there were clinical inconsistencies in the specific criteria. One commenter felt it was an unwarranted burden to require two out of three criteria in order to satisfy the definition of acute encephalopathy (for children 24 months of age or older). Some members of the ACCV felt that the definition of acute encephalopathy for children over 24 months implies that a seizure must last 24 hours to be within the definition. One commenter suggested the definition was unlike any other employed in medicine or science. The Department has considered carefully the concerns regarding the definition of encephalopathy and offers the following responses.

The current Qualifications and Aids to Interpretation do not reflect precisely medical knowledge of the condition ''encephalopathy.'' Many medical experts testifying in proceedings under the VICP have stated the definition is too vague and needs clarification. The term ''encephalopathy'' refers generally to a disturbance of brain function. Clinical definitions vary, as do opinions on the relationship between encephalopathy and seizures. After several pages of discussion, the IOM finally defined it as ''encephalopathy, encephalitis, or encephalomyelitis.'' Unfortunately, this definition is clinically imprecise, and in part circular. While it may serve to evaluate studies on neurologic disease, it does not impart guidance to physicians or attorneys on the specific clinical signs of a child or adult with encephalopathy.

In an effort to define encephalopathy better, the Department used the definition approved by the ACCV in 1991. The basic criteria were taken from a peer-reviewed multi-center study assessing adverse events following immunization in all age groups. (Fenichel GM., Lane DA, Livengood JR, Horwitz SJ, Menkes JH, Schwartz JF. Adverse events following immunization: Assessing probability of causation. Pediat Neurol 1989; 5:287–290) One of its authors, a pediatric neurologist and former ACCV Chairman, proposed that the Commission use the criteria as the basic framework to define encephalopathy for purposes of making changes to the Aids to Interpretation. Following its approval by the ACCV, additional clarifications were needed to define better clinical signs in the pre-verbal (less than 24-month) age group, and identify correctly infants or children who may be experiencing temporary medication effects, rather than true signs of encephalopathy. The Department appreciates that the criteria are viewed by some as overly burdensome. Any clarifications to the definition were for the sole purpose of allowing non-physicians to identify correctly infants or children with clinical signs of encephalopathy. However, the ACCV during its June 1994 meeting suggested that some modifications be made to the age criteria to reflect the fact that some children under 24 months have more advanced verbal skills. The Department agrees with this suggestion and has, therefore, changed the age marker from 24 to 18 months for purposes of distinguishing between preverbal and verbal children. § 100.3(b)(2)(i).

Additionally, the Department agrees that the term ''stupor'' is imprecise and somewhat restrictive, and has therefore decided to specify the clinical signs reflective of an acute encephalopathy and delete the terms ''stupor and coma.'' Acknowledging the difficulty of defining ''encephalopathy,'' the Department has focused on clinical criteria that clearly distinguish infants and children with brain dysfunction from those with transient ''lethargy.'' The diminished alertness and motor activity, which characterize the lethargic infant or child, are frequently observed as the physiological response to fever, infection or other acute illness. The severity and duration of the behavioral changes differentiate mere lethargy from the more serious impairment of consciousness that is the hallmark of encephalopathy (i.e., obtundation, stupor and coma). To provide the clearest guidance to petitioners' attorneys and the Court, the Department has added a new paragraph (b)(2)(i)(D) to the section to identify specific clinical signs constituting ''a significantly decreased level of consciousness.''

As to concerns articulated by members of the ACCV during the June 1–2, 1994 meeting, the Department did not intend, in listing the signs for identifying acute encephalopathy in children older than 24 months, that a ''seizure associated with loss of consciousness'' persist for 24 hours. Rather, the Department intends that in order to be experiencing an acute encephalopathy a child must experience a significantly altered mental state or decreased level of consciousness. It is the child's overall condition which must persist for 24 hours, rather than any one particular seizure.

One of the ACCV members questioned the Department's decision to use 24 hours, rather than some other period, as the appropriate time period under the definition of acute encephalopathy. The Department decided to use 24 hours because this was the marker used in the multi-center study cited above which established the criteria used by the Department in drafting the definition of encephalopathy. See Fenichel, et al. The choice of this time period is also consistent with the way in which medical professionals gauge and document clinical changes over time.

One commenter suggested there is not a clear distinction between acute and chronic encephalopathy. In response to this comment, the Department has added additional language in the final rule for clarification. For example, the Department revised the introductory language of § 100.3(b)(2) to make clear that an individual may be found to have suffered an encephalopathy only if ''such recipient manifests, within the applicable time period, an injury meeting the description below of an acute encephalopathy, and then a change in mental or neurological status persists in such person for more than 6 months beyond the date of vaccination.'' In addition, the Department added similar language to § 100.3(b)(2)(ii) to clarify the meaning of chronic encephalopathy.

Two commenters suggested that the term ''neurologically normal'' may be inappropriate because children ''who return to a normal neurological state after an acute encephalopathy,'' but later develop signs of a chronic encephalopathy, may easily be misdiagnosed as normal during this time period. Two commenters questioned whether the definition ''neurologically normal'' should be based on various testing criteria (e.g., CT or MRI scans, electroencephalogram (EEG), or lumbar puncture). The Department has considered these comments and has revised the first sentence in paragraph (b)(2)(ii) for clarification.

It is expected that any child or adult with a chronic encephalopathy as a result of a vaccine-related acute encephalopathy would show evidence of abnormalities in mental or neurological status in the days to weeks following the vaccination. In the case of an infant or child, these would be seen as a loss or slowing of developmental milestones during this time period

following the acute event. Because testing criteria and the interpretation of results may vary with age group and medical condition, no additional criteria are suggested for the diagnosis of chronic encephalopathy. The Department agrees, however, that the Aids to Interpretation should contain a clear distinction between acute and chronic encephalopathy. As explained above, additional language has been added in the final rule for clarification.

Members of the ACCV suggested the phrase ''return to a normal neurological state'' was too vague, and failed to specify the methods to be used for gauging a ''normal neurological state.'' These members also suggested that there might not be any evidence in the medical records to document this fact. The Department has considered this suggestion, but has determined that the language in the definition of chronic encephalopathy need not be changed. It is the Department's intent that if all other parts of the definition are satisfied, the presumption remains intact unless there is affirmative evidence that the child returned to a normal neurological state; such evidence could consist of documented subjective descriptions of the child's behavior and development and/or objective findings on physical examinations performed by physicians in the post-immunization period. Thus, in those cases where this issue is unclear, or not documented, the presumption would be that a child whose acute encephalopathy was followed by signs of a persistent neurologic deficit did not return to a normal neurological state.

During the June 1–2, 1994 meeting, members of the ACCV also suggested that parts of the definition of encephalopathy in the Qualifications and Aids to Interpretation as published in the NPRM were too restrictive. Specifically, they took issue with the underlined phrase of the introductory language of § 100.3(b)(2)(i)(D), which states that ''[t]he following clinical features alone, or in combination, do not qualify as evidence of an acute encephalopathy or a significant change in either mental status or level of consciousness as described above * * *.'' The Department agrees with the commenters and notes that this language did not reflect accurately the Department's intent. The point of this language as written in the NPRM was further to clarify the language as written in the NPRM was further to clarify the language in the statute, which states that certain signs and symptoms are compatible with an encephalopathy but ''in and of themselves are not conclusive evidence of encephalopathy.'' 42 U.S.C. 300aa–14(b)(3)(A). The language in the statute has been interpreted in many different ways by the Special Masters and has led to results in some cases which the Department believes are inconsistent with the medical and scientific literature on this topic. The medical evidence indicates that certain symptoms do not conclusively establish an encephalopathy, but instead are merely symptoms that are compatible with an encephalopathy. Nevertheless, in order to take account of the concerns of the ACCV, the Department has changed the underlined language above to ''do not demonstrate.''

One commenter suggested that DTP may aggravate pre-existing genetic or congenital conditions, and for that matter, other acquired conditions.

The Department is aware that, in rare instances, a vaccine may alter the clinical course of a pre-existing condition. Under section 2111(c)(1)(C) of the Act, ''significant aggravation'' of a pre-existing condition may establish eligibility for compensation provided the Petitioner is able to demonstrate that a Table injury occurred and that the prior condition was significantly aggravated during the Table timeframe, or is able to demonstrate proof of causation in fact.

In considering the comment, the Department realized that there could be confusion regarding the issue of significant aggravation of pre-existing conditions. Accordingly, the Department decided to eliminate the proposed § 100.3(b)(2)(v). Because the statute includes a definition of ''significant aggravation,'' it is unnecessary for this term to be defined in the final rule. See 42 U.S.C. 300aa–33; section 2133 of Act.

As noted above, the Department received five comments in response to the March 24, 1994, **Federal Register** notice soliciting comments regarding the 1994 IOM report. Two comments, one submitted by the American Academy of Pediatrics, and the other by a vaccine manufacturer, expressed support for the revised Vaccine Injury Table as presented in the NPRM. The commenters stated that further revisions to the proposed Vaccine Injury Table are not warranted based on the conclusions of the latest IOM review. The Academy of Pediatrics did suggest, however, that the Table should reflect the ''possibility that in some children with acute encephalopathy, chronic dysfunction may subsequently exist, but this is a rare event and the data do not allow confirmation or rejection of whether this is a direct association.''

The final rule reflects the concern articulated by the Academy. The revised Table confers a presumption of causation on those individuals who suffer an acute encephalopathy within 3 days after vaccine administration, and who then go on to exhibit 6 months of residual effects, followed by chronic neurological dysfunction.

The other three comments are discussed, where relevant, under the heading ''The Department's Interpretation of the IOM Report.''

Hypotonic-Hyporesponsive Episode (HHE)

One commenter supported the removal of hypotonic-hyporesponsive episode (HHE) from the original Table as proposed by stating that HHE has no long-term effects and does not lead to death; the remaining commenters were critical of the change. One commenter pointed out that HHE is a heterogeneous term, which includes features of HHE and anaphylaxis. It also includes a subset of children with ''unusual shock-like states'' who have a ''lot-dependent, bimodal, or other form of onset.'' It was suggested that the Department should give the benefit of doubt in terms of causation to this group. One commenter suggested features of collapse are life-threatening. The Department responds as follows.

Although HHE is not well understood, there are consistent, albeit rare, clinical signs reported to occur transiently following DTP immunization. The onset in young infants is usually within 12 hours following pertussis immunization. Clinical features include pallor, fever, and decreased activity and responsiveness. Although these infants may have a significantly decreased activity level and ''shock-like'' appearance, actual loss of consciousness and hypotension (shock) have not been demonstrated to occur. Disorders such as anaphylaxis should easily be distinguishable from shock-collapse or HHE because of the clearly defined physiologic changes known to occur with anaphylaxis, which do not occur in HHE. See 1991 IOM Report, 171–186; Cody CL, Baraff LJ, Cherry JD, March SM, Manclark CR. 1981. Nature and rates of adverse reactions associated with DTP and DT immunizations in infants and children. Pediatrics 68:650–660.

The 1991 IOM report found evidence ''consistent with a causal relation'' between the pertussis vaccine and HHE (shock collapse), but concluded there was insufficient evidence concerning chronic neurologic damage. Because there is no proven relationship between HHE and residual neurologic damage,

no purpose is served by retaining HHE on the Table. Removing HHE as a Table injury places the burden of proof on the petitioner that an HHE was caused by a vaccine and that it resulted in death or residual effects lasting at least 6 months.

Additional comments were received in response to the Notice published on March 24, 1994, requesting comments on the Miller study and 1994 IOM report. Two commenters argued that the conclusions of this IOM report are inconsistent with the Department's proposal to remove HHE from the Vaccine Injury Table. The commenters suggested that because the Qualifications and Aids to Interpretation include ''loss of consciousness'' as one of the symptoms of HHE, and because the NCES would have included a severe shock-collapse resulting in hospitalization as a serious, acute neurologic illness, it is appropriate for HHE to continue to receive the presumption of causation conferred by the Table.

It is important to understand that the Miller study did not purport to set forth a definition of ''encephalopathy'' for purposes of the VICP or the Vaccine Injury Table. Rather, it simply defined a set of conditions which fell under the rubric of ''acute neurologic illness'' that could be studied in relation to the administration of DTP vaccine. Loss of consciousness is not a recognized sign of HHE (see Cody et al.), notwithstanding its inclusion in the original statutory Qualifications and Aids to Interpretation. The Department recognizes that the 1991 IOM Report included among the symptoms of HHE a loss of consciousness. However, the Department believes that this simply reflected some of the case reports in the literature that were reviewed by the IOM. Given the IOM's statement that the cases reported may include other conditions, such as anaphylaxis, the Department does not view the IOM's discussion as a sufficient basis to expand its view of what properly constitutes HHE. *See* 1991 IOM Report, p. 171–177. Rather, children experiencing a loss of consciousness should properly be considered under the rubric of encephalopathy. Furthermore, there is no clear evidence that HHE (1) represents acute neurologic dysfunction, (2) requires medical intervention (although medical consultation is frequently sought), or (3) leads to any permanent sequelae or death. It is unlikely that nay of the cases described in the NCES were those of infants experiencing HHE. In light of these considerations, the Department concludes that there is an insufficient basis to retain HHE as a separate category on the Table.

Residual Seizure Disorder

One commenter suggested that some of the seizure classifications under Residual Seizure Disorder are out of date. They cited the example of ''grand mal'' seizures which has been dropped from the International Classification of Diseases. The commenter also questioned the use of the word ''signs'' in this section. The Department agrees with the commenter that some of the original seizure terminology has changed over time. Section 100.3(b)(4) has been revised and the word ''signs'' has been deleted from the text.

One commenter objected to proposed paragraph (b)(3)(ii) regarding the 24-hour requirement for separation of seizures under Residual Seizure Disorder. The commenter disagreed that a 24-hour separation in seizures makes the diagnosis of recurrent seizures (epilepsy) more likely, and that seizures occurring on the same day are generally regarded as part of the same event.

The Department intends that the 24-hour requirement for the separation of seizures will make it more likely that a Petitioner who qualifies under Residual Seizure Disorder has a recurring seizure disorder (epilepsy). The study cited in the NPRM, (Reference: Hauser WA. et al: Seizure recurrence after a first unprovoked seizure. NEJM 1982; 307(9):522–528), shows that seizures separated by more that 24 hours make a recurrent disorder more likely. Its importance is underscored by the fact that seizures commonly occur in clusters. For purposes of predicting recurrence of seizures, those occurring within a 24-hour period are generally viewed as a single event (with the same cause). It is likely that any petitioner who experiences a vaccine-related epileptic disorder will still qualify by having further seizures over the 12-month period specified under the statute. See section 2114(b)(2)(A) of the Act.

Recognizing the commenter's concerns, and in the interest of clarity, the Department has modified slightly the definition of a distinct seizure episode for purposes of this section. The last sentence of § 100.3(b)(3)(i) now reads, ''A distinct seizure or convulsion episode is ordinarily defined as including all seizure or convulsive activity occurring within a 24-hour period, unless competent and qualified expert neurologic testimony is presented to the contrary in a particular case.''

Two commenters did not agree with the language in paragraph (b)(4) that absence (petit mal) epilepsy is not associated with acute encephalopathy secondary to DTP immunization. Both suggested that the diagnosis be determined by requiring such a child to have an EEG with 3-per-second spike-and-wave, since it is known that children who have such minor seizures with different EEG's are often the victims of severe brain damage and should not be excluded. Finally, it was suggested that the phrase ''if properly diagnosed'' be used under these conditions. The Department's response to these comments is as follows.

There is little credible evidence to support the conclusion that absence (petit mal) epilepsy is associated with acute encephalopathy following vaccination. It is true, however, that atypical absence and other forms of spike-and-wave epilepsy may be the sequelae of an acute encephalophathy, but are not in themselves the features of such. Following acute encephalopathy, features of atypical absence seizures may develop months to years later as part of the sequelae to the acute injury. Other types of staring behavior may constitute seizure activity associated with an acute encephalopathy, such as an individual with Herpes simplex type 1 encephalitis. However, these patients typically present with other clinical signs of acute encephalopathy. (Generalized Seizures: Absence. In Dreifuss F. (ed): Pediatric Epileptology. Boston, J. Wright/PSG, 1983, p. 65–91.) It also should be noted that seizures alone do not constitute an encephalopathy. (1991 IOM Report, page 87).

Requiring EEG confirmation of 3-per-second spike-and-wave to make the diagnosis of absence (petit) epilepsy may be excessively restrictive. While patients may have these characteristic EEG findings, it is neither practical nor advisable to require that the EEG constitute the basis for diagnosis. Frequently, absence (petit mal) epilepsy is diagnosed on clinical criteria alone, (i.e., expected age group, seizure behavior, relationship to hyperventilation and/or response to ethosuximide therapy). It is therefore impractical to require EEG confirmation. Furthermore, inserting the phrase ''if properly diagnosed'' would create confusion as to whether EEG confirmation is necessary for the diagnosis of this condition.

One commenter suggested it is incorrect to state that petit mal and absence seizures are the only types of seizure activity with which staring can be associated. The Department agrees, and did not intend to imply such in the Preamble to the NPRM. Other

conditions associated with staring, such as atypical absence epilepsy, or various sequelae to central nervous system injury are noted above in the Department's response under absence (petit mal) epilepsy.

One commenter suggested that the Department has shown no evidence that pertussis-related febrile seizures have more benign outcomes than those induced by other agents. The commenter states that because the literature shows that a small percentage of children who experience febrile seizures go on to have permanent problems, the Department's findings that there is insufficient evidence are erroneous. One commenter suggested febrile seizures produce brain damage. Another commenter suggested that not every seizure which is contemporaneous with a fever is a febrile seizure. The Department agrees in part, and disagrees in part with these comments for the following reasons.

The term ''febrile seizure'' refers to seizures in infancy or childhood (between 3 months to 5 years of age) associated with fever, but without evidence of intracranial infection or other defined cause. Infants or children who have a pre-existing history of an afebrile seizure, or recurrent afebrile seizures (epilepsy) are not included in this category.

While it is true that children with a history of ''febrile seizures'' may eventually show neurologic deficits, there is no persuasive experimental or epidemiologic evidence that these deficits are a result of neurologic injury occurring at the time of the febrile seizure. Furthermore, there is no evidence that febrile seizures affect intellectual performance as judged by comparison of affected children to their siblings. (Consensus Statement. 1980. Febrile seizures: long term management of children with fever-associated seizures. Pediatrics 66:1009–1012) (Ellenberg JH, Nelson KB. Febrile seizures and later intellectual performance. Arch Neurol 1978;35:17–21)

Although the IOM concluded ''febrile seizures'' are causally related to DTP vaccine, most experts believer that febrile seizures do not cause permanent damage. The clinical courses of children experiencing febrile seizures following DTP vaccination are indistinguishable from the clinical courses of children who experience febrile seizures from other causes. (Hirtz DG, et al. Seizures following childhood immunizations. J. Pediatr. 1983;314:1085–1088)

While febrile seizures are by their very nature benign, and therefore not associated with permanent damage, not all seizures contemporaneous with fever are ''febrile seizures.'' This latter group of seizures may be the result of pre-existing neurologic disease or injury, which produces a predisposition to seizure activity with elevated temperature. Alternatively, one can have an acute encephalopathy which presents itself as fever and seizures (e.g., meningitis). In such a case, the other requisite clinical manifestations of clinical encephalopathy should be present (i.e., diminished consciousness and/or focal or generalized neurologic signs).

One commenter disagreed with the exclusion of infantile spasms. One commenter noted that the diagnosis for infantile spasms has no etiological significance. It was suggested there is no medical support to eliminate this type of seizure disorder from those potentially compensated. One commenter suggested that it is inappropriate to exclude infantile spasms, as the U.S. Court of Federal Claims has ruled that DTP causes infantile spasms. The Department has considered these comments and offers the following clarification.

The IOM concluded infantile spasms is not casually related to DTP vaccination. Therefore, there is no basis for a legal presumption of causation for this condition when it follows DTP vaccination. Petitioners have the right to prove causation in fact in instances in which infantile spasms has its onset following immunization.

The U.S. Court of Federal Claims has held that seizures diagnosed as infantile spasms can be considered a Table injury if the requisite timeframes are met. The Court has held that the respondent cannot claim that infantile spasms is a factor unrelated to vaccine administration unless the precise cause of the infantile spasms can be identified. The Court's reasoning was based on a technical interpretation of the statute, and does not purport to be an analysis of the medical issues involved. Furthermore, the Court's analysis relied, of course, on the initial Table. It cannot be viewed as relevant to the actual causation issue which is the basis for revising the Table. See Johnston v. Secretary of HHS, 22 Cl. Ct. 75 (1990).

Nevertheless, the Department has decided to remove all references to infantile spasms from the final rule. This decision was made based purely on procedural grounds. The Department concluded that this issue is more appropriately addressed in the ''factor unrelated'' section of the statute (42 U.S.C. 300aa–13(b)), rather than as part of the Vaccine Injury Table. The decision to revise the rule in this manner does not affect the Department's findings regarding infantile spasms (based on the IOM report), nor should it be viewed as inconsistent with the Department's response to the commenters' concerns. The Department continues to believe that deciding cases involving infantile spasms, the Court of Federal Claims should rely heavily on the IOM's conclusion that the evidence does not indicate a causal relationship between pertussis vaccine and infantile spasms.

One commenter claims to have concluded ''within medical certainty'' that chronic neurologic damage occurred in children who had acute afebrile seizures within the timeframes of the current Table of injuries, and as manifestations of acute encephalopathies. The commenter does not, however, provide sufficient evidence to justify a revision of the proposed language.

The IOM concluded that afebrile seizures are not causally related to DTP vaccine. They considered many studies, including one which showed that short-lived convulsions, with or without fever, have not been demonstrated to cause permanent sequelae, regardless of whether the seizures occur in association with receipt of DTP. vaccine. (IOM Report p. 118) (Hirtz DG. et al. Seizures following childhood immunizations. J. Pediatr. 1983; 102:14–18. and Ellenberg JH, Hirtz DG, Nelson KB. Do seizures in children cause intellectual deterioration? NEJM 1986; 314:1085–1088) (Ad Hoc Committee for the Child Neurology Society. Consensus Statement: Pertussis immunization and the central nervous system. Ann. of Neuro. 1991; 29 (4): 458–460).

The Department also reversed the order of § 100.3(b)(3)(i) and § 100.3(b)(3)(ii). This change was made to make the order of these two subparagraphs more logical.

In response to the March 24, 1994, **Federal Register** Notice requesting comments on the 1994 IOM Report, two commenters argued that because seizures were included in the definition of encephalopathy and chronic nervous system dysfunction used by the NCES, the Department should not remove residual seizure disorder from the Table.

The Department disagrees with the commenters on this point. As discussed above, the 1991 IOM report concluded that no causal relationship can be proven between DTP and afebrile seizures. In its 1994 report, the IOM did not retract any of its 1991 conclusions regarding DTP and seizure disorders. It merely recognized that the NCES included seizures as one of those conditions to be monitored or purposes

of tracking long-term dysfunction. This recognition does not provide any information one way or the other regarding causation.

Crucial to understanding the Department's response is the knowledge that the working definition of ''acute neurologic illness'' used in the NCES is not consistent with the current medical understanding of acute encephalopathy as an acute, generalized disorder of the brain. Children were placed in the NCES case definition who experienced only febrile seizures, a benign condition know to be triggered by DTP vaccine, yet never proven to have lasting effects absent signs of acute encephalopathy. Thus, placing seizures in the NCES case definition of encephalopathy is inconsistent with the current medical understanding of acute encephalopathy. Moreover, both the IOM and the NVAC subcommittee agreed that there is no evidence that chronic encephalopathy in the absence of acute post-immunization encephalopathy is causally related to the vaccine. Therefore, there is no basis for providing a legal presumption of vaccine causation for chronic effects based solely on the occurrence of a seizure following DTP immunization. There is simply no need for, nor is there medical evidence to support, a separate presumption for residual seizure disorder in connection with DTP vaccine.

Sudden Infant Death Syndrome

Two commenters suggested there is not a clear distinction between a death characterized as Sudden Infant Death Syndrome (SIDS) and one that is vaccine-related (paragraph (b)(2)(iii) of the NPRM).

The IOM concluded that SIDS is not causally related to DTP vaccine. This conclusion was based on several controlled epidemiologic studies involving hundreds of thousands of vaccinations. Although the diagnosis of SIDS is one of exclusion of other causes, there are specific guidelines as to the history preceding death, findings on forensic examination, and the ruling out of other causes by death scene examination (when possible). Moreover, the possibility that DTP-related deaths are commonly misclassified as SIDS was also considered by the IOM Committee. Since there was no evidence of an increased risk of SIDS following DTP immunization, or of any observable ''pertussis death syndrome,'' the committee considered that such effects were not supported by the medical literature. In addition, those studies that examined infant deaths other than SIDS in relation to DTP vaccine also demonstrated no excess risk in the post-immunization interval. This observation argues against the possibility that DTP-related deaths were missed as a result of their being misclassified as deaths other than SIDS. (Correspondence from Christopher P. Howson, Ph.D., Project Director, Committee to Review the Adverse Consequences of Pertussis and Rubella Vaccines to Dr. George Curlin, Deputy Director, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases: 9/18/91)

Nevertheless, as with infantile spasms, the Department has decided to remove all references to Sudden Infant Death Syndrome from the final rule. This decision, too, was made based purely on procedural grounds. The Department concluded (as with infantile spasms) that this issue is more appropriately addressed in the ''factor unrelated'' section of the statute (42 U.S.C. § 300aa–13(b)), rather than as part of the Vaccine Injury Table. The decision to make this change does not affect the Department's findings regarding SIDS (based on the IOM report), nor should it be viewed as inconsistent with the above analysis regarding the Department's response to the commenters' concerns. The Department continues to believe that in deciding cases involving SIDS, the Court of Federal Claims should rely heavily on the IOM's conclusion that the evidence does not indicate a causal relationship between pertussis vaccine and SIDS.

Tuberous Sclerosis Complex

One commenter suggested that the proposed revisions do not take into account the condition of tuberous sclerosis complex (TSC), which some believe can be aggravated by DTP vaccine. Since DTP vaccine can cause fevers which trigger seizures, there remains a question whether someone with TSC would have a worse outcome as a result of a seizure following a DTP shot. One commenter suggested that infantile spasms is frequently associated with TSC and the U.S. Court of Federal Claims has found compensable infantile spasms cases that manifested after DTP vaccine. The Department provides the following clarification regarding the effect the new Table will have on individuals with TSC.

TSC is a genetic disorder manifested chiefly as mental deficiency, epilepsy and skin lesions. Seizures occur in 80–90 percent of individuals with tuberous sclerosis. This disorder frequently presents in infancy, commonly in the form of infantile spasms. Some petitioners have argued that administration of a DTP vaccine can significantly aggravate a case of TSC.

The Act provides two avenues of proof in order to establish eligibility for compensation. A petitioner is afforded a presumption of causation if he/she can establish that an injury listed in the Table occurred within the specified time period. Otherwise, the petitioner may argue that an injury occurred which is not listed in the Table, but which was nonetheless caused by the vaccine. The TSC cases presented to the Court, some petitioners who sought to establish a Table case argued that the child experienced seizures within 3 days of receipt of a vaccine and that this event significantly aggravated the pre-existing TSC. Some petitioners who were unable to establish Table cases argued that although the child did not sustain an injury listed in the Vaccine Injury Table, the vaccine nonetheless was the cause-in-fact of the aggravation of the underlying Tuberous Sclerosis. In either case, the petitioner had the burden of proving that the clinical course of the pre-existing condition had been significantly aggravated. Typically, petitioners presented expert testimony to support this theory.

The revisions to the Vaccine Injury Table do not, by and large, change the petitioner's burden of proof in TSC cases. The only difference is that there is not a presumption of causation for residual seizure disorders for DTP vaccine. As explained in the preamble to the NPRM, and reiterated here, the IOM concluded that there is no causal relation between pertussis vaccine and afebrile seizures. However, to receive a presumption of causation, petitioners may still argue that an encephalopathy (as defined in the revised Qualifications) occurred within 3 days of vaccine administration and that this encephalopathy significantly aggravated the pre-existing Tuberous Sclerosis. In addition, petitioners may continue to argue that the vaccine was the cause-in-fact of the aggravation of the TSC. As far as infantile spasms is concerned, the Department has removed all references to this condition from the final rule as explained above. Therefore, petitioners have available to them the same avenues of proof open to individuals with other types of seizures.

One commenter noted that MMR frequently triggers epilepsy in children with TSC. The same analysis as above applies. Here, the petitioner may take advantage of the presumption of causation if he or she is able to prove either a Table encephalopathy, or a Table residual seizure disorder, and that that injury significantly aggravated the underlying TSC. If the evidence does

not demonstrate that the case meets the requirements of the Table, the case will be evaluated based on a causation theory.

Diphtheria/Tetanus Vaccines (DT, TD, TT)

One commenter suggested that making changes to non-pertussis components based on studies of pertussis vaccine is inappropriate.

Although the section 312 study (''IOM Report'') did not specifically study the non-pertussis antigens of DTP vaccine (i.e., diphtheria, tetanus), most individuals receiving pertussis antigen, also were given these antigens. Therefore, some inferential data is present. Moreover, studies reveal little evidence that these antigens are causally related to the injuries currently listed in the Table under DTP, other than Anaphylaxis. In the section 313 study, the IOM concluded that the evidence favored rejection of a causal relation between DT/Td/TT and encephalopathy. After review of the section 313 Report, the Department may promulgate additional changes to the Table.

MMR Vaccines

One commenter suggested that the requirement for at least 5 days of viral replication is inappropriate. One commenter suggested that the changes for encephalopathy are wrong because there is a broad spectrum of severity. Sequelae may occur after less serious acute encephalopathy. The proposed changes would exclude all but the most severe acute encephalopathies from the Table. The Department has considered these comments, but has concluded that the medical evidence supports the proposed changes.

Since viral replication is required for a viral vaccine-associated encephalopathy, a window for the expected time of onset is appropriate. The onset of vaccine-related illness following MMR (or any of its components) is generally from 7 to 14 days, thus a time interval of 5 to 15 days would be all-inclusive. Any acute encephalopathy of unknown cause, regardless of severity or duration, that occurs during the 5 to 15 day time frame would be eligible for the Table presumption, provided the child or adult has continued evidence of ''chronic encephalopathy.'' The 1991 NVAC Subcommittee felt there was strong support in the literature to narrow the timeframe as above. Some felt Residual Seizure Disorder should be removed from the Table based on the lack of evidence for causation in the current medical literature. This was not done because it went significantly beyond the scope of changes proposed by the PHS Task Force. However, at that time, the Subcommittee recognized additional changes may be forthcoming once the section 313 study results are published and have been reviewed. Since the Subcommittee's original discussion on this issue, the IOM issued its section 313 report. The IOM concluded for both encephalopathy and residual seizure disorder that the evidence is inadequate to accept or reject a causal relation. After review of the 313 Report, the Department may promulgate additional changes to the Table based on this conclusion.

One commenter suggested that the evidence for an association between rubella vaccine and chronic arthritis is inconclusive. The section 312 IOM Committee concluded that the evidence is ''consistent with a causal relation'' between the currently used rubella vaccine (RA 27/3) and chronic arthritis in adult women, although the evidence is limited in scope and confined to reports from one institution. To establish this biologically plausible relation more firmly, the Committee expressed the need for prospective, double-blind, controlled trials in which individuals are followed for at least 12 months after vaccination with attempts to isolate and identify rubella virus. At least one medical research center is pursuing this research to try and obtain better data on causation.

Many investigators still view the evidence as inconclusive with regard to chronic arthritis. However, the IOM's finding justifies the inclusion of chronic arthritis on the Vaccine Injury Table since there is biologic plausibility of causation, and the term ''chronic arthritis'' is defined as effects lasting greater than 6 months. In this instance, the IOM is stating there is ''consistent'' evidence for both acute onset and residual effects lasting greater than 6 months. Previously described changes for Table injuries under DTP involved conditions (i.e., HHE and Residual Seizure Disorder) that the IOM did not view as having strong evidence for *both* acute and chronic effects.

Although the Department added chronic arthritis to the Table, guidelines written into the Aids to Interpretation will preclude patients with pre-existing conditions or other non-vaccine related musculoskeletal disorders from being legally presumed to have a vaccine-related injury. As information from prospective studies becomes available, modifications may be made to the Table or Aids to Interpretation based on this data.

Polio Vaccines

Two commenters suggested that Inactivated Polio Vaccine (IPV), known as the Salk vaccine, may be proven to be causally related to poliomyelitis. The IOM evaluated the relationship between polio vaccines and adverse events in its section 313 study. Except for the 1955 incident with inadequate inactivation of live polio virus in the Cutter Company supply of IPV, there have been no serious adverse events causally tied to this vaccine. Since the ''Cutter Incident,'' when manufacturing and testing difficulties were identified and corrected, the safety of released inactivated Poliovirus vaccine has been assured. (See IOM Section 313 Report at 188,; *see also* Bodian, D., et al. Interim Report, Public Health Service Technical Committee on Poliomyelitis Vaccine. JAMA:1444–7, 1955) Furthermore, no serious side effects of currently available inactivated poliovirus vaccines have been documented. (Report of the Committee on Infectious Diseases, American Academy of Pediatrics 1991:389) Because these earlier problems have been cured, and there is no current evidence bearing on a causal relationship, the section 313 study does not discuss specifically the connection between IPV and poliomyelitis. Therefore, there is no evidence of a causal relationship which would justify adding poliomyelitis to the Table for IPV.

Other Changes

At the meeting on June 1–2, 1994, members of the ACCV suggested that the definition of ''sequela'' imposes a higher burden of proof than that required by the statute. The Department disagrees that the definition affects the burden of proof, but agrees that the definition as written should be simplified. Accordingly, the definition in § 100.3(b)(5) has been modified to read as follows: ''The term sequela means a condition or event which was actually caused by a condition listed in the Vaccine Injury Table.'' This definition is consistent with current scientific understanding that in order for a subsequent event to be considered a sequela of an initial event, there must be a causal relationship between the two.

Technical Changes

First, in publishing the NPRM, the Department inadvertently misquoted the statutory introduction to the Vaccine Injury Table. Accordingly, the introductory paragraph of § 100.3(a) now reads as follows: ''In accordance with section 312(b) of the National Childhood Vaccine Injury Act of 1986,

title III of Pub. L. 99–660 (42 U.S.C. 300aa-note) and section 2114(c) of the Public Health Service Act (42 U.S.C. 300aa–14(c)), the following is a table of vaccines, the injuries, disabilities, illnesses, conditions, and deaths resulting from the administration of such vaccines, and the time period in which the first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths is to occur after vaccine administration for purposes of receiving compensation under the Program:''

Second, we are revising § 100.3(c), entitled ''Effective date provisions.'', to change the term ''United States Claims Court'' wherever it appears to read ''United States Court of Federal Claims'', in accordance with section 902(b) of title IX, Pub. L. 102–572, the Federal Courts Administration Act of 1992 (*See* 106 Stat. 4516).

In addition, the Department is making a technical change to the existing regulations (42 CFR part 100) by revising the currently codified acronym used to refer to the National Vaccine Injury Compensation Program from ''NVIC'' to ''VICP'' wherever it appears under part 100. ''VICP'' has been used for the entire history of the program to avoid confusion with the parents' advocacy group known as the National Vaccine Information Center (NVIC), Dissatisfied Parents Together (DPT).

Since these changes are of a technical nature, the Secretary has determined pursuant to 5 U.S.C. 553 and departmental policy that it is unnecessary and impractical to follow proposed rulemaking procedures.

Economic Impact

The NPRM preamble erred in not explaining that this rule will not have a significant impact on a substantial number of small businesses because it will have only small effects, and those primarily on individuals. Attorneys, while small entities within the meaning of the Act, will still be awarded costs and fees for cases they bring on a reasonable basis. The reduced number of vaccine cases brought will be negligible measured against overall business opportunities for lawyers. Therefore, SBA is incorrect in saying that a regulatory flexibility analysis is required. Therefore, the Secretary certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

Executive Order 12866 requires that all regulations reflect consideration of alternatives, of costs, of benefits, of incentives, of equity, and of available information. Regulations must meet certain standards, such as avoiding unnecessary burden. Regulations which 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.

As stated above, this final regulation modifies the Vaccine Injury Table based on legal authority, and under that authority the Court will award such fees and costs as appropriate under the law. As such, the regulation would have little direct effect on the economy or on Federal or State expenditures. For the same reasons, the Secretary has also determined that this is not a ''significant'' rule under Executive Order 12866.

Effect of the New Rule

The NPRM failed to explain the effect of the rule for individuals who were not eligible to file petitions based on the original Vaccine Injury Table, but who may be eligible to file petitions based on the revised Table. The Act permits such individuals to file a petition for such compensation not later than 2 years after the effective date of the revision if the injury or death occurred no more than 8 years before the effective date of the revision of the Table. See 42 U.S.C. 300aa–16(b). As part of the Omnibus Reconciliation Act of 1993, Congress amended this section to permit individuals to file claims within this 2-year period, even if they had already filed a claim involving a particular vaccine, but only if the Table revision will ''significantly increase the likelihood of obtaining compensation.'' See Pub. L. 103–66, sec. 13632(a)(1). (August 10, 1993). For example, this amendment would permit an individual whose claim alleging vaccine-related arthritis had been dismissed by the Claims Court to file a new claim for the same vaccine-related injury, if the individual can show that the addition of arthritis to the Table as a rubella vaccine-related condition has significantly increased the likelihood of obtaining compensation. The Department believes that the amendment would not permit someone who had had a claim for an alleged vaccine-related encephalopathy subsequent to DTP vaccine to refile a claim that had been dismissed by the Claims Court, as the changes in the Table related to DTP and encephalopathy do not appear to significantly increase the likelihood of obtaining compensation.

Possible Effect on Other Legislation

This rule will not have an effect on the Vaccines for Children Program, implemented by the Centers for Disease Control and Prevention under section 1928 of the Social Security Act, as enacted by section 13631 of the Omnibus Budget Reconciliation Act of 1993 (Pub. L. 103–66, August 10, 1993). This section provides for the establishment of a program to distribute free vaccines to all vaccine-eligible children, as defined by this section. The final rule modifies the existing Vaccine Injury Table, a mechanism by which compensation is awarded to individuals who have been found to have suffered from vaccine-related injuries. Because the two authorities are not related, the publication of this rule should not have any impact on the Vaccines for Children Program.

Paperwork Reduction Act of 1980

This final rule has no information collection requirements.

List of Subjects in 42 CFR Part 100

Biologics, Health insurance, Immunization.

Dated: November 16, 1993.

Philip R. Lee,

Assistant Secretary for Health.

Approved: November 9, 1994.

Donna E. Shalala,

Secretary.

Accordingly, 42 CFR part 100 is amended as set forth below.

PART 100—VACCINE INJURY COMPENSATION

1. The authority citation for part 100 is revised to read as follows:

Authority: Sec. 215 of the Public Health Service Act (42 U.S.C. 216); sec. 2115 of the PHS Act, 100 Stat. 3767, as amended (42 U.S.C. 300aa–15); § 100.3, the Vaccine Injury Table, issued under sec. 312 of Pub. L. 99–660, 100 Stat. 3779 (42 U.S.C. 300aa–1 note) and sec. 2114(c) of the PHS Act (42 U.S.C. 300aa–14(c)).

2. Section 100.1 is revised to read as follows:

§ 100.1 Applicability.

This part applies to the National Vaccine Injury Compensation Program (VICP) under subtitle 2 of title XXI of the Public Health Service (PHS) Act.

3. The first sentence in § 100.2 is revised to read as follows:

§ 100.2 Average cost of a health insurance policy.

For purposes of determining the amount of compensation under the VICP, section 2115(a)(3)(B) of the PHS Act, 42 U.S.C. 300aa.15(a)(3)(B), provides that certain individuals are entitled to receive an amount reflecting

lost earnings, less certain deductions.
* * *

4. Section 100.3 is added to read as follows:

§ 100.3 Vaccine injury table.

(a) In accordance with section 312(b) of the National Childhood Vaccine Injury Act of 1986, title III of Pub. L. 99–660, 100 Stat. 3779 (42 U.S.C. 300aa–1 note) and section 2114(c) of the Public Health Service Act (42 U.S.C. 300aa–14(c)), the following is a table of vaccines, the injuries, disabilities, illnesses, conditions, and deaths resulting from the administration of such vaccines, and the time period in which the first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths is to occur after vaccine administration for purposes of receiving compensation under the Program:

VACCINE INJURY TABLE

Illness, disability, injury or condition covered	Time period for first symptom or manifestation of onset or of significant aggravation after vaccine administration
I. DTP; P; DT; Td; or Tetanus Toxoid; or in any combination with Polio; or any Other Vaccine Containing Whole Cell Pertussis Bacteria, Extracted or Partial Cell Pertussis Bacteria, or Specific Pertussis Antigen(s):	
A. Anaphylaxis or anaphylactic shock	4 hours.
B. Encephalopathy (or encephalitis)	72 hours.
C. Any sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed.	Not applicable.
II. (a). Measles, mumps, rubella, or any vaccine containing any of the foregoing as a component:	
A. Anaphylaxis or anaphylactic shock	4 hours.
B. Encephalopathy (or encephalitis)	5–15 days (not less than 5 days and not more than 15 days) for measles, mumps, rubella, or any vaccine containing any of the foregoing as a component.
C. Residual seizure disorder in accordance with subsection (b)(3)	5–15 days (not less than 5 days and not more than 15 days) for measles, mumps, rubella, or any vaccine containing any of the foregoing as a component.
D. Any sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed.	Not applicable.
II. (b). In the case of measles, mumps, rubella (MMR), measles, rubella (MR) or rubella vaccines only:	
A. Chronic arthritis	42 days.
B. Any sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed.	Not applicable.
III. Polio Vaccine (other than Inactivated Polio Vaccine):	
A. Paralytic Polio	
In a non-immunodeficient recipient	30 days.
In an immunodeficient recipient	6 months.
In a vaccine associated community case	Not applicable.
B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed.	Not applicable.
IV. Inactivated Polio Vaccine:	
A. Anaphylaxis or anaphylactic shock	4 hours.
B. Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed.	Not applicable.

(b) *Qualifications and aids to interpretation.* The following qualifications and aids to interpretation shall apply to the Vaccine Injury Table in paragraph (a) of this section:

(1) *Anaphylaxis and anaphylactic shock.* For purposes of paragraph (a) of this section, Anaphylaxis and anaphylactic shock mean an acute, severe, and potentially lethal systemic allergic reaction. 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. Autopsy findings may include acute emphysema which results from lower respiratory tract obstruction, edema of the hypopharynx, epiglottis, larynx, or trchea and minimal findings of eosinophilia in the liver, spleen and lungs. When death occurs within minutes of exposure and without signs of respiratory distress, there may not be significant pathologic findings.

(2) *Encephalopathy.* For purposes of paragraph (a) of this section, a vaccine recipient shall be considered to have suffered an encephalopathy only if such recipient manifests, within the applicable period, an injury meeting the description below of an acute encephalopathy, and then a chronic encephalopathy persists in such person for more than 6 months beyond the date of vaccination.

(i) An acute encephalopathy is one that is sufficiently severe so as to require hospitalization.

(A) *For children less than 18 months of age* who present without an associated seizure event, an acute encephalopathy is indicated by a significantly decreased level of consciousness lasting for at least 24 hours. Those children less than 18 months of age who present following a seizure shall be viewed as having an acute encephalopathy if their significantly decreased level of consciousness persists beyond 24 hours and cannot be attributed to a postictal state (seizure) or medication.

(B) *For adults and children 18 months of age or older,* an acute encephalopathy is one that persists for at least 24 hours and characterized by at least two of the following:

(1) A significant change in mental status that is not medication related; specifically a confusional state, or a delirium, or a psychosis;

(*2*) A significantly decreased level of consciousness, which is independent of a seizure and cannot be attributed to the effects of medication; and

(*3*) A seizure associated with loss of consciousness.

(C) Increased intracranial pressure may be a clinical feature of acute encephalopathy in any age group.

(D) A ''significantly decreased level of consciousness'' is indicated by the presence of at least one of the following clinical signs for at least 24 hours or greater (see paragraphs (b)(2)(i)(A) and (b)(2)(i)(B) of this section for applicable timeframes):

(*1*) Decreased or absent response to environment (responds, if at all, only to loud voice or painful stimuli);

(*2*) Decreased or absent eye contact (does not fix gaze upon family members or other individuals); or

(*3*) Inconsistent or absent responses to external stimuli (does not recognize familiar people or things).

(E) The following clinical features alone, or in combination, do not demonstrate an acute encephalopathy or a significant change in either mental status or level of consciousness as described above: Sleepiness, irritability (fussiness), high-pitched and unusual screaming, persistent inconsolable crying, and bulging fontanelle. Seizures in themselves are not sufficient to constitute a diagnosis of encephalopathy. In the absence of other evidence of an acute encephalopathy, seizures shall not be viewed as the first symptom or manifestation of the onset of an acute encephalopathy.

(ii) *Chronic Encephalopathy* occurs when a change in mental or neurologic status, first manifested during the applicable time period, persists for a period of at least 6 months from the date of vaccination. Individuals who return to a normal neurologic state after the acute encephalopathy shall not be presumed to have suffered residual neurologic damage from that event; any subsequent chronic encephalopathy shall not be presumed to be a sequela of the acute encephalopathy. If a preponderance of the evidence indicates that a child's chronic encephalopathy is secondary to genetic, prenatal or perinatal factors, that chronic encephalopathy shall not be considered to be a condition set forth in the Table.

(iii) An encephalopathy shall not be considered to be a condition set forth in the Table if in a proceeding on a petition, it is shown by a preponderance of the evidence that the encephalopathy was caused by an infection, a toxin, a metabolic disturbance, a structural lesion, a genetic disorder or trauma (without regard to whether the cause of the infection, toxin, trauma, metabolic disturbance, structural lesion or genetic disorder is known). If at the time a decision is made on a petition filed under section 2111(b) of the Act for a vaccine-related injury or death, it is not possible to determine the cause by a preponderance of the evidence of an encephalopathy, the encephalopathy shall be considered to be a condition set forth in the Table.

(iv) In determining whether or not an encephalopathy is a condition set forth in the Table, the Court shall consider the entire medical record.

(3) *Residual Seizure Disorder.* (i) A petitioner may be considered to have suffered a residual seizure disorder for purposes of paragraph (a) of this section, if the first seizure or convulsion occurred 5–15 days (not less than 5 days and not more than 15 days) after administration of the vaccine and 2 or more additional distinct seizure or convulsion episodes occurred within 1 year after the administration of the vaccine which were unaccompanied by fever (defined as a rectal temperature equal to or greater than 101.0 degrees Fahrenheit or an oral temperature equal to or greater than 100.0 degrees Fahrenheit). A distinct seizure or convulsion episode is ordinarily defined as including all seizure or convulsive activity occurring within a 24-hour period, unless competent and qualified expert neurological testimony is presented to the contrary in a particular case.

(ii) For purposes of paragraph (a) of this section, a petitioner shall not be considered to have suffered a residual seizure disorder, if the petitioner suffered a seizure or convulsion unaccompanied by fever (defined as a rectal temperature equal to or greater than 101.0 degrees Fahrenheit or an oral temperature equal to or greater than 100.0 degrees Fahrenheit) before the fifth day after the administration of the vaccine involved.

(4) *Seizure and convulsion.* For purposes of paragraphs (b) (2) and (3) of this section, the terms, ''seizure'' and ''convulsion'' include myoclonic, generalized tonic-clonic (grand mal), and simple and complex partial seizures. Absence (petit mal) seizures shall not be considered to be a condition set forth in the Table. Jerking movements or staring episodes alone are not necessarily an indication of seizure activity.

(5) *Sequela.* The term ''sequela'' means a condition or event which was actually caused by a condition listed in the Vaccine Injury Table.

(6) *Chronic Arthritis.* (i) For purposes of paragraph (a) of this section, chronic arthritis may be found in a person with no prior history of arthropathy (joint disease) on the basis of:

(A) Medical documentation, recorded within 30 days after the onset, of objective signs of acute arthritis (joint swelling) that occurred within 42 days after a rubella vaccination; and

(B) Medical documentation (recorded within 3 years after the onset of acute arthritis) of the persistence of objective signs of intermittent or continuous arthritis for more than 6 months following vaccination.

(ii) For purposes of paragraph (a) of this section, the following shall not be considered as chronic arthritis: Musculoskeletal disorders such as diffuse connective tissue diseases (including but not limited to rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, mixed connective tissue disease, polymyositis/dermatomyositis, necrotizing vasculitis and vasculopathies and Sjogren's Syndrome), degenerative joint disease, infectious agents other than rubella (whether by direct invasion or as an immune reaction), metabolic and endocrine diseases, trauma, neoplasms, neuropathic disorders, bone and cartilage disorders and arthritis associated with ankylosing spondylitis, psoriasis, inflammatory bowel disease, Reiter's syndrome, or blood disorders.

(iii) Arthralgia (joint pain) or stiffness without joint swelling shall not be viewed as chronic arthritis for purposes of paragraph (a) of this section.

(c) *Effective date provisions.* The Table of Injuries set forth in paragraph

(a) of this section applies to petitions for compensation under the Program filed with the United States Court of Federal Claims on or after March 10, 1995. The Qualifications and Aids to Interpretation set forth in paragraph (b) of this section apply to petitions filed with the United States Court of Federal Claims on or after March 10, 1995. The petitions for compensation filed with the United States Court of Federal Claims before March 10, 1995 shall be governed by section 2114(a) (initial ''Table'') and section 2114(b) (initial ''Qualification and Aids to Interpretation'') of the Public Health Service Act as in effect on February 8, 1995.

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