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