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