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