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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

November 23, 1999

SUBJECT: Amendment to D259256 CARBARYL (056801) Developmental Neurotoxicity Study. Rhône-Poulenc Response to EPA Comments about Morphometric Measurements D261394

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The purpose of this memorandum is to amend our earlier review (D259256; 10/13/99) of the response of Rhône-Poulenc to a request made by HED in its review of a Developmental Neurotoxicity Study (MRID 44393701) of Carbaryl. This amendment does not affect the main conclusions in the earlier review, which were:

1. that the inability to examine the mid dose or low dose animals on morphometric measurements found statistically significantly different from control animals remained a study deficiency; and
2. despite their re-evaluation and additional statistical analyses, the decrease in female pups given 10 mg/kg in the length of the cerebellum (Line F) is still regarded as a treatment related effect.

This amendment seeks to modify the discussion of the findings related to morphometric measurements made in adult rats on day 70, specifically the width of the cerebellum, Line G.

In the original study, in adult females from the high dose group, the width of the cerebellum (Line G) was increased 19-30% for right and left cerebellum, respectively.

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The previous memo reported "In the repeat evaluation of these tissues in rats on day 70, 8-15% INCREASES in Line G were found, *the opposite of what was seen in the earlier evaluations*. It was further asserted that the original measures that showed such a large *decrease* were based on erroneous measurements and should not be considered further. The other evaluations of these tissues in other animals also support the lack of effect." (Italics added to emphasize text to be amended).

After additional review, it was recognized that in the repeat evaluation of these tissues in rats on day 70, 4-8% increases in Line G were found. These changes are much smaller than in the earlier evaluations, but in the same direction as the original study results. Further, the original measures judged on re-examination to be based on erroneous measurements were increases and not decreases. In view of their repudiation of their earlier measurements, and their re-evaluation and further statistical analyses, EPA concurs with the registrant that these changes in Line G in the 70 day old rats are not significant treatment related effects.