January 15, 1991

Professor Giuliano DaVilla
Via Generale Orsini, 42
Napoli, Italy

Dear Professor DaVilla,

My cousin, Dr. Albert Sabin sent me a copy of your paper entitled "A Pilot Model of Vaccination Against HBV. In an Area Hyperendemic for Viral Hepatitis B In the Compania Territory - The Town of Afragola."

The results of your study are very impressive. You have achieved a significant decrease in the incidence of hepatitis B and the HBsAg-positive carrier rates during the course of your project.

I believe that your manuscript will be improved if you can clarify the following questions and comments:

Page 4, line 1: The statement "vaccination of all older children" should specify their ages.

Page 5, 3rd paragraph: The recommended dose of Engerix B (SKF) is 10 mcg (see enclosed recommendations). Why did you use 20 mcg?

Page 6, line 1: Same as page 5, 3rd paragraph.

Page 7, 2nd paragraph: The estimate that 50% of reported cases of hepatitis B may be valid for adults but not for children. Most cases of hepatitis B in infants and children are anicteric or inapparent.

Pages 9 and 10: As indicated by Dr. Sabin it would be helpful if you reported your results by more definitive age groups. I suggest the following: 1-4 years, 5-10 years, 11-19 years, 20-40 years and > 40 years. It is well known that the anti-HBs response is excellent in infants, children and adults under the age of 40 and that the numbers of non-responders increase after that age.
Tables 1-4. As indicated previously the data would be more meaningful if the results were presented by the proposed age groups: 1-4, 5-10, 11-19, 20-40 and > 40 years.

Figures 1 and 2. The age ranges of "older children" and "adults" should be indicated.

Figure 5. The caption and title should indicate that these results include infants and children up to 10 years of age.

Congratulations to you and your colleagues for carrying out an outstanding study and for your contribution to the community in Afragola.

With best wishes for the New Year,

Sincerely,

Saul Krugman, M.D.
Professor

SK:ch
Encl.
cc Dr. Sabin
Field trials of the vaccines licensed in the United States have shown 80%-95% efficacy in preventing infection or clinical hepatitis among susceptible persons \((31,35)\). Protection against illness is virtually complete for persons who develop an adequate antibody response after vaccination. The duration of protection and need for booster doses are not yet fully defined. Between 30% and 50% of persons who develop adequate antibody after three doses of vaccine will lose detectable antibody within 7 years, but protection against viremic infection and clinical disease appears to persist \((36-38)\). Immunogenicity and efficacy of the licensed vaccines for hemodialysis patients are much lower than in normal adults. Protection in this group may last only as long as adequate antibody levels persist \((33)\).

**Vaccine Usage**

Primary vaccination comprises three intramuscular doses of vaccine, with the second and third doses given 1 and 6 months, respectively, after the first. Adults and older children should be given a full 1.0 ml/dose, while children <11 years of age should usually receive half (0.5 ml) this dose. See Table 3 for complete information on age-specific dosages of currently available vaccines. An alternative schedule of four doses of vaccine given at 0, 1, 2, and 12 months has been approved for one vaccine for postexposure prophylaxis or for more rapid induction of immunity. However, there is no clear evidence that this regimen provides greater protection than the standard three-dose series. Hepatitis B vaccine should be given only in the deltoid muscle for adults and children or in the anterolateral thigh muscle for infants and neonates.

For patients undergoing hemodialysis and for other immunosuppressed patients, higher vaccine doses or increased numbers of doses are required. A special formul-

**TABLE 3. Recommended doses and schedules of currently licensed HB vaccines**

<table>
<thead>
<tr>
<th>Group</th>
<th>Heptavax-B*;†</th>
<th>Recombivax HB*</th>
<th>Engerix-B*§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants of HBV-carrier mothers</td>
<td>10 (0.5)</td>
<td>5 (0.5)</td>
<td>10 (0.5)</td>
</tr>
<tr>
<td>Other infants and children &lt;11 years</td>
<td>10 (0.5)</td>
<td>2.5 (0.25)</td>
<td>10 (0.5)</td>
</tr>
<tr>
<td>Children and adolescents 11-19 years</td>
<td>20 (1.0)</td>
<td>5 (0.5)</td>
<td>20 (1.0)</td>
</tr>
<tr>
<td>Adults &gt;19 years</td>
<td>20 (1.0)</td>
<td>10 (1.0)</td>
<td>20 (1.0)</td>
</tr>
<tr>
<td>Dialysis patients and other immunocompromised persons</td>
<td>40 (2.0)††</td>
<td>40 (1.0)**</td>
<td>40 (2.0)§††</td>
</tr>
</tbody>
</table>

*Usual schedule: three doses at 0, 1, 6 months.
†Available only for hemodialysis and other immunocompromised patients and for persons with known allergy to yeast.
‡Alternative schedule: four doses at 0, 1, 2, 12 months.
§Two 1.0-ml doses given at different sites.
**Special formulation for dialysis patients.
††Four-dose schedule recommended at 0, 1, 2, 6 months.