Dr. Albert B. Sabin  
The Children's Hospital Research Foundation  
Elland Ave. and Bethesda  
Cincinnati, Ohio

Dear Dr. Sabin:

I have nothing further to add at present concerning  
the probable availability of the MC 858. The reason for my writing  
you at the moment is that Dr. A. F. Langlykke, Director of the  
Research and Development Laboratories, has asked me to make available  
to you a copy of the report on the trial of this drug in man during  
the 1949 polio epidemic in New York City.

You will note from this report that the use of this  
compound in patients was not unattended by toxic signs. While admit-  
tedly the dose level is probably far above what one would view as a  
prophylactic dose, the one patient showing gross hematuria and the  
one who developed generalized vesicles, conjunctivitis and stomatitis  
along with the maculo-papular rash gives us some misgivings even  
though all toxic signs promptly disappeared when the drug was with-  
drawn. We wonder what your comments concerning this might be.

Yours sincerely,

W. A. Bott, Director  
Division of Medicinal Chemistry
I. The Effect of the sodium salt of mercuric alpha-mercapto acetyl sulfathiazole (MC-858) on the Excretion of Poliomyelitis Virus in the Feces of Man.

Will MC-858, which reduces the concentration of Theiler (TO) virus in the stools of normal mice, do the same to the poliomyelitis virus in the stools of man? One hundred and sixteen patients in the first week of illness during the 1949 epidemic in New York City provided material for the test. Sixty two were treated for 7 days with the drug, while 54 served as controls. Fecal specimens were collected from all treated patients and from the controls at corresponding times as follows - (a) before drug, (b) on the 7th day of drug administration, (c) on the 1st and 7th days after drug was stopped.

Stools excreted on the 7th day of drug administration were tested first. In a group of 11 patients receiving 300 mg. daily, poliomyelitis virus was detected in the stools of 7 on the 7th day of drug administration. This dosage appears ineffective and therefore, specimens were tested from another group of 16 patients receiving 400 mg. daily. Virus was found in the stools of 5 on the 7th day of therapy. The 11 negative patients of this group were then tested for the presence of virus in the stools before drug. Seven were positive as shown in Table I.

Table I

<table>
<thead>
<tr>
<th>Dosage of MC-858</th>
<th>Before Drug</th>
<th>7th Day of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/day</td>
<td># positive</td>
<td># negative</td>
</tr>
<tr>
<td>300</td>
<td>None tested</td>
<td>-</td>
</tr>
<tr>
<td>400</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

Although the number of specimens tested to date is small, the data suggest that MC-858 used daily in a dose of 400 mg. may reduce the excretion of poliomyelitis virus. Further observations at this dosage level are required for definite conclusions.
Toxicity: Thirteen of the 46 patients receiving 300 mg. daily and 2 of the 16 on 400 mg. daily developed toxic symptoms. One of the 62 treated patients developed gross hematuria on the 4th day of drug administration. The drug was immediately discontinued and the condition improved rapidly. No mercury was found in the urine of this or any other patient treated.

Thirteen additional patients showed the following toxic symptoms in varying degrees; Nausea in 4, mild abdominal pain in 4, and a maculo-papular rash in 6. The rash was usually mild lasting only 2 days but was more severe in 2 patients where it lasted for 2 weeks. One of these patients also had generalized vesicles, conjunctivitis and stomatitis along with the maculo-papular rash. Toxic manifestations had entirely disappeared by the 18th day.

Procedure Used in Testing the Stools for Poliomyelitis Virus: Two young rhesus monkeys were used for testing each fecal specimen. One milliliter of 10% etherized suspension was inoculated intracerebrally. In addition, each monkey received 1 ml of unetherized crude 10% suspension in each nostril daily for 10 days. If no signs of poliomyelitis were evident by the 7th day, each monkey received an additional 1 ml of processed material in the contra-lateral side of the brain. Daily rectal temperatures were taken for 21 days and the animals were observed for 35 days. Histopathological studies of alternate sections of the spinal cord and medullae were made on all animals.