Dear Dr. Sabin:

Thank you very much for sending me your very important last papers concerning live poliovaccine including manuscript "Present position of immunization against poliomyelitis with live virus vaccine" which is most stimulating for our laboratory.

All your advices in further study of live vaccine in the field trials we accept as obligatory for our program. From the July of 1958 we have included for production and testing of living vaccine in Leningrad your type I /L Sc, 2ab/. Now all strains corresponds to your large lots of the 3 types that you prepared in USA. Our official Ministry of Health USSR/ instruction on production of live vaccine demands the introduction of only yours original selected strains.

Let me to inform you about the recent progress of this work in my laboratory.

After we studied to the 1 October 1958 in Leningrad nearly 2100 vaccinated children of preschool age I couldn't start immediately with proposed great field trial /100,-200,000/ because the official permission was given in November for 20,000 only. Now this stage of work is going to the end under very careful clinical survey which stated the complete safety of your method. 8,000 were vaccinated with your original vaccine and 12,000 with our Leningrad production. Serological survey was organised in accordance with your quantitative desires and now the collected sera from 1200 children are under examination /after I and 2 month/. The method of immunization with both preparations was different:

I. (50%) I, 3, 2 type (I month interval)
II. (50%) I type and after I month 2+3 types together

We have sufficient evidence that II method is very practical, convenient, effective and stimulates very regular and distinct rise of antibodies as method I.

So I have vaccinated to the present time 22,000 children +30% of internal nonvaccinated control (contact groups), or nearly 30,000. All they were under very strong clinical control of most experienced neurologists, pediatrician and infectious doctors. They stated complete absence in vaccinated and control groups of any complications or specific clinical neurological or other reactions, connected with the introduction of vaccine. About 8,000 of children were vaccinated with living vaccine primary and 14,000 received previously (in 1957-1958) 2 or 3 injections of Salk vaccine.
I am busy now to receive permission for vaccination of further 500,000 children to accomplish the control of epidemiological efficiency of living vaccine in 1-2 large cities. In August - October Dr Chumakov and myself met pretty strong opposition against immediate mass immunisation but I hope that now after I have finished the second stage of work on 20,000 children it will be more simple. I will use this future trial all your vaccine batch (300 cc of the I type I have sent recently to Prague to Dr Jabek for the first immunisation in Chechoslovakia, I hope to receive this amount back from you or from Jabek).

Let me answer now your questions to my paper which will be published in WHO Bulletin:

1.) I would be very glad if you find it necessary to use our work and my recent information for any citation you desire;

2.) We used M. rhesus monkeys repeatedly very rare and only for preliminary examinations, of undiluted original passaged strains. All data in my paper were obtained on fresh monkey only, infected with 3 - 4 dilutions i/cer and i/spinally. Our method of i/spinal titration is in strong correlation with your methodical indications made in your last unpublished article.

3.) Additional 5 monkeys for histological examinations (to 7 paralyzed monkeys in Table I) were obtained in the process of examination of passaged strains through the intestinal tract of healthy children and also of repeated titrations of our samples of vaccine during its storage in 1957-1958.

4.) "Sabin's vaccine strains" in Table I represents your original data published in one of your papers, which I submitted now with appropriate citation in my manuscript.

5.) Our college Dr Sviatuhina, responsible for histopathology of inoculated monkeys, found that animals inoculated intracerebrally or i/spinaly and not exhibited clinical signs gives only traumatic nonspecific changes without specific polio morphological changes. Possibly the amount of our monkeys is too small for generalization of this statement, what I have corrected in my paper.

6.) The values given in fig. I represents the amount of virus in I gram of feces,

7.) Most extensive spread to contacts of type I was observed under conditions in which it was one of three viruses disseminated simultaneously at the same time to 14 unvaccinated children. In repeated tests with one virus examined separately on various groups type 3 was spread very extensively too.

8.) The degree of increase in neutralizing antibodies did not depend on the order of administering the various types of virus. This statement is based on groups of 35-40 youenings children, vaccinated primarily with 1, 2 or 3 types and after 2,5 and
3.5 month with additional 3, 2; 1, 3; 1, 2 correspondingly. The intervals were strictly equal for all 3 groups: 2,5 month (summer time) between first and second and 1 month between second and third application. The multiplication of all types were the best during the first application and some less after the second and third vaccination. The time of antibody responses was very distinct in all groups after 3 weeks and 2 month and later. We didn't observed any distinct influence of seasonal factor on immunological response and multiplication of different types of vaccination was made in spring of automne.

9.) Up to now 12 strains of viruses of different types excreted after the presumed A-5 natural passages through contacts were titrated on monkeys in original concentration (with nearly 7.0 lg 10 concentration), 1:10 and 1:100 dilutions of cultural medium i/cerebral and 1/spinal with the results very close to that by artificial passages.

10.) The intracerebral tests with all 3 types of attenuated viruses studied during the process of prolonged 8 intestinal passages are entirely favourable as it is shown on the final text of our data up to now in my published paper. Very rare cases of positive intracerebral tests on monkeys still exists including type I.

II.) Additional attenuation of your strains was connected with prolonged (25-30) times) passages of all original strains in tubes with monolayer monkey kidney inoculated with 5 cc each of original liquid from infected bottles containing maximal concentration of viruses. Incubation period for virus reproduction didn't exceed 3 days and passages through tubes included every time one additional passage in Povitsky bottle. We didn't found any evidence that we succeeded in further attenuation and eradication of end neurotropism of original strains for CNS of monkeys but possibly we have obtained more fixed strains in neurotropic stability for intestinal tract of human beings. Thus I tried to repeat in this trial one more time your very new and perspective system of virus attenuation in monkeys kidney (mass inoculation after short period). Passaged strains didn't became more neurotropic during further passages for monkeys in different pure lines according to your final process of its selection.

Nevertheless I am shure that we shall use now only your original strains for maximum standartisation of different field trials not provided with your original vaccine and I have introduced this important point in official minimum requirement accepted in my country in production of living vaccine.

I am very interested to see you in Leningrad or Moscow during March. End of March 1959 I go to Cairo for 2 months through Prague-Geneve. In this connection I can meet you also in Prague or Geneve if your visit to our country will be more late

With warmest greetings
Sincerely yours

Anatol A. Smorodintsev