Dr. Aims C. McGuinness, Chairman
Committee on Immunization and
Therapeutic Procedures for
Acute Infectious Diseases
Graduate School of Medicine
University of Pennsylvania

Dear Doctor McGuinness:

I am attaching for your information and for transmission to the other members of the Committee on Immunization of the American Academy of Pediatrics certain facts relating to the forthcoming poliomyelitis mass vaccination trials planned by the National Foundation for Infantile Paralysis to begin in February 1954.

You will recall that the National Foundation in recent press releases has stated that it is planned to vaccinate between 500,000 and 1,000,000 children, mostly second graders, with formalin-inactivated vaccine developed by Dr. Jonas Salk. You may recall, too, that the Academy of Pediatrics at the meeting in Florida passed a resolution which stated that the Academy of Pediatrics will cooperate with the National Foundation for Infantile Paralysis in the forthcoming poliomyelitis vaccination trials.

It is my earnest conviction that the Academy was in error in promising such cooperation and that the implied endorsement of the vaccination plans may conceivably do the Academy of Pediatrics some disservice in the future. It must be noted that other organizations, such as the American Public Health Association, have failed to pass resolutions on these matters.

It is the purpose of the attached material to put forth information on the nature of the formalin-inactivated vaccine to the Committee on Immunization of the American Academy of Pediatrics. Based on these data, it is my personal conviction, as well as that of other virologists, that the formalin-inactivated vaccine is insufficiently tested for mass trial, potentially unsafe, of undetermined potency, and of undetermined stability.
I do not anticipate that the data here presented will in any way stem the tide or defer the proposed mass injections. It seems remarkable that there appears to be a general unwillingness on the part of virologists to go on record in public against the plans of the National Foundation for Infantile Paralysis. I believe this is in the hope that all will yet be well, that our fears are unfounded, and finally because it is unpopular to appear to be against rapid progress in the field of immunization against poliomyelitis. On the contrary, it is my view that these facts should be publicized among people competent to judge and in order to get a fair, honest appraisal for the problems involved.

Thank you for affording me an opportunity to make these views available to the Committee.

Very sincerely yours,

C. Henry Kempe, M.D.
Assistant Professor
Department of Pediatrics
1. Preparation of formalin-inactivated trivalent poliomyelitis virus to be used by the National Foundation mass vaccination campaign:

The three antigenic strains of poliomyelitis virus are grown in tissue culture utilizing monkey kidney. The material is then 'inactivated' in a 1:8000 dilution of formalin. The material is incubated for an unspecified time at a specific pH. It is then removed to an ice box and tested for safety by inoculation into tissue culture. If a cytopathogenic effect (suggesting the presence of live virus) is demonstrated in the test, the vaccine-formalin mixture is again incubated for an unspecified time; then again removed and retested, and so on—until no cytopathogenic effect can be obtained. Final safety testing consists of inoculation of samples from each batch of vaccine into tissue cultures and into 10 monkeys, intracerebrally. Four weeks after inoculation, these monkeys are sacrificed and the central nervous system examined for specific lesions. The material is being prepared in large amounts in the Connaught Laboratories in Toronto, Canada and then shipped to Dr. Salk for formalin-inactivation. The Foundation plans to have each lot, manufactured either in Toronto or by manufacturers such as Parke, Davis & Company, finally approved by Dr. Salk's own testing before release.

2. Almost all data presented by Dr. Salk in the Miami meetings related to adjuvant-type vaccine, because of his findings of better antigenic stimulation in terms of antibody response by adjuvant vaccines. Presumably the Academy's approval was based on that serologic evidence presented at the meetings. Since then, however, the Foundation has decided to substitute three injections of aqueous vaccine for the adjuvant vaccine, because of the significantly high incidence of sterile abscesses and fibrotic nodules from adjuvant type of vaccines. I believe Dr. Sabin had some influence in bringing about this change. Serologic evidence on the efficacy of aqueous vaccine given intramuscularly is meager.

3. The following questions arise in connection with the above stated plans:

A. The vaccine contains three unmodified polio strains, the inactivation of which depends wholly on formalin-inactivation by one or more incubations. The method of repeated incubation of 1:8000 formalin-vaccine is admittedly very crude.

1. Does antigenic capacity drop with each repeated additional incubation?

2. Since a critical pH is involved in the 1:8000 formalin-incubation, would the accidental change in pH by some small margin change the safety of the vaccine and allow some virus particles to survive? Could not a pH change or temperature change during storage result in reactivation of 'inactivated' virus?

3. Would it not be possible to demonstrate live virus particles by concentrating the finished product instead of using it in the test described as it comes from the bottle?
4. Is it not true that a number of virologists have failed to reproduce the inactivation results of Dr. Salk's at 1:8000 dilution of formalin, even when his method was scrupulously followed?

B. While it would be possible to remove well over 93% of the foreign protein nitrogen of monkey kidney tissue without impairing the antigenic capacity of a tissue culture vaccine, this has not been done. Rather, the material as is now contemplated for use in children contains over 93% of foreign protein nitrogen of monkey kidney tissue.

1. Is it not possible that three sensitizing doses of monkey kidney tissue might result in a nephrotoxic effect in young children?

2. Have antigenic studies been done to demonstrate the possible presence of anti-renal substances in the serum of children injected experimentally?

C. Stability of the vaccine in terms of formalin-inactivated virus particles and in terms of antigenic capacity remains undetermined at this time.

D. I believe that no potency tests are employed to compare one batch of vaccine to the next. We do not know if potency tests will be applied to these lots before they are released for public use, or what these potency tests will be.

E. A large bulk of the presently available data is an adjuvant type vaccine. Other data bears on intradermal vaccine. There is very little actual information on the antibody response of children with three intramuscular injections of aqueous vaccine, especially as it relates to children who do not have any antibodies against poliomyelitis before vaccination. Needless to say, pediatricians are less interested in a booster response in children already having had the experience with one or more strains of poliomyelitis virus than in primary immunization of children who have failed to have had such experience yet. The mass vaccination trial about to be initiated will not give data on this point, since no paired blood specimens will be available and the trial, as advertised, will be geared to clinical observations of incidence of poliomyelitis in second grade vaccinated children as compared to first and third grade unvaccinated children.
SUMMARY:

1. Considering the present high state of biologic controls on immunizing products exercised by the National Institute of Health, as well as by the manufacturer, it appears that the poliomyelitis vaccine about to be administered to between 500,000 and 1,000,000 second grade children has not given the guarantees of safety, foreign protein purity, stability, and known antigenic potency. I, therefore, feel the mass trial is premature and that the American Academy of Pediatrics should reverse its announced plan of cooperation with the National Foundation for Infantile Paralysis for the mass inoculations to be initiated on February 8, 1954.

2. The data here supplied are, to my best knowledge, accurate. It is possible that I am misinformed on one or more points. If that is the case, it would be understandable, because of the extreme degree of secrecy which has surrounded this entire matter except on the newspaper side. This material has not been available for testing to virologists outside the group immediately concerned.

3. I would respectfully suggest that the comments of leading virologists might be sought on the Committee on Immunization of the American Academy of Pediatrics at an early date to ascertain whether they personally would favor the mass use of formalin-inactivated trivalent monkey kidney tissue vaccine at this time. It might be of interest to inquire also if they are planning to use the material on their own children or relatives who might qualify by being in the proper age.

Without question, you as Chairman and the other members of the Committee will think of additional scientists but, with your permission, I would suggest a few who might give information on these points. The majority of these are within the folds of the Academy. They are: Doctors Blattner, Curnen, Enders, Hodes, Melnik, Robbins, Sabin and Weller.

Very sincerely yours,

C. Henry Kempe, M.D.
Assistant Professor
Department of Pediatrics