July 9, 1953

Dr. Albert Sabin
Children's Hospital Research Foundation
Children's Hospital
Cincinnati, Ohio

Dear Albert:

I am returning the copy of your analysis which you were so kind to send me. I think it hits the nail right on the head, and no one could say it better than you do. I should like very much to be able to quote portions of it, if you are willing for me to do so. I would like to insert the quotations as editorial discussion to follow abstracts of Hammon's papers which will appear in the Year Book of Pediatrics. I enclose a copy of what I have picked from your entire report; if you prefer that I do not use it, or if you differ with the material I have selected for quotation, please don't hesitate to say so. If I may use it, will you let me know what journal is to publish the report?

With kindest regards,

Sincerely,

[Signature]

Sydney S. Gellis, M.D.
(Dr. Albert Sabin was invited by the Ohio State Medical Association to prepare a critical analysis of the available experimental and epidemiologic data on the use of human gamma globulin in the prophylaxis of poliomyelitis. Dr. Sabin has kindly permitted us to quote from this analysis:

"The final results in all 3 field tests indicated that 31 clinically diagnosed cases of poliomyelitis, regardless of severity, occurred among those inoculated with gamma globulin and 73 among those inoculated with gelatin. This would be a significant result in favor of gamma globulin if one could be certain that it was not in part due to an artificial increase in the number of cases among those receiving gelatin, and that it was repeatable with different lots of gamma globulin in different epidemics. The possibility that gelatin may have increased the incidence of the disease in the control group will have to be considered, particularly since Bodian (Bodian, D., Federation Proceedings, 1953 (March, 12, p.36.) has recently obtained suggestive evidence in monkeys that gelatin may act in such a manner.

"It seems to me that the conservative conclusion to be drawn from these field trials should have been that further studies on the use of gamma globulin are indicated and that we need much more information before we can be certain, a) whether or not it will be regularly effective in the small doses that can be used practically, and b) if it is regularly effective, how best to use a material that is of necessity in limited supply. The conclusion that the value of gamma globulin in the prophylaxis of poliomyelitis had been proved beyond doubt, has practically halted further urgently needed experimental studies in animals, has made further controlled field studies in this country most difficult, if not, for the present at least, impossible, and has led to the expenditure of millions of dollars for the purchase of large amount of gamma globulin.

"As to the actual use of the available gamma globulin, it has been suggested that certain household associates and other intimate contacts of a clinically diagnosed case of poliomyelitis receive gamma globulin. It should be remembered that there is no scientific evidence that gamma globulin in the dose used will have any effect on the incidence of the disease among those who have already been exposed. Available
evidence indicates that 80 per cent of secondary cases in a household occur within 7 days after the first clinically diagnosed case, and that is the period during which gamma globulin had no effect on the incidence of the disease in the field trials. It is quite possible that the remaining 20 per cent who develop the disease after the first 7 days were also infected prior to recognition of the first case, and there is no evidence that the small dose of gamma globulin would have any effect on these. Besides, in approximately 95 per cent or more of households there are no secondary cases of clinically recognized poliomyelitis. Even if the small doses of gamma globulin were effective in household contacts, this procedure of administering it would miss more than 90 per cent of the people who develop poliomyelitis.

"It is clear that if one accepts the suggestive evidence of the field trials, there is only one rational basis for using gamma globulin and that is to administer it to those at greatest risk in areas with a very high incidence of the paralytic disease. I stress here the paralytic disease because we neither need nor want protection against the mild nonparalytic forms of the infection. Furthermore we should remember that indiscriminate widespread use of gamma globulin, particularly in effective dosage, may interfere with the acquisition of those mild or inapparent infections which give us lifelong immunity. It is in my opinion illogical to point to certain animal experiments in which the injection or ingestion of large doses of virus can produce active immunity despite the presence of a certain amount of antibody in the blood. The fact of the matter is we don't know what small doses of virus would do under similar circumstances in animals, and we as yet have no information whatever as to what may happen in large segments of the population under natural conditions. It should be pointed out, however, that if gamma globulin could be given in a dosage that was regularly effective in the prevention of both paralysis and infection, I would still regard its use as desirable during severe epidemics, because it is better to acquire one's immunity during interepidemic periods when the risk of paralysis is low than during periods when the risk is very much higher. I would therefore like to make a plea that most of the available gamma globulin be used
only in epidemic areas and that the limited amount be assigned to the age groups at greatest risk of acquiring paralysis as well as to pregnant women. Since there will not be enough gamma globulin for everybody, particularly in epidemics in large metropolitan areas, there should be an opportunity to make further epidemiologic studies on the effectiveness of the selected dose of gamma globulin as a prophylactic agent in poliomyelitis. This would require a good deal of cooperation and concentrated work for a limited period of time on the part of the practicing physician and health departments in an epidemic area, but it would mean that gamma globulin would be used in the only way for which there is now suggestive evidence that it might have some effectiveness.---Ed.)