8 March 1977

TO: Elena O. Nightingale, Project Director
   Committee for the Study of Poliomyelitis Vaccines

FROM: Jonas Salk

SUBJ: Summary Statement on Poliomyelitis Vaccination

This statement contains a summary of background material submitted separately on the question of killed and live poliovirus vaccines. It focuses on the following points of particular interest to the Committee, as outlined in your letter of 17 February.

1. The comparative safety of each type of vaccine.

2. The comparative efficacy and effectiveness of each type of vaccine (with special reference to the question of duration of immunity).

3. The proper use and administration of informed consent documents for poliomyelitis vaccination when employing either type of vaccine, the need for appropriate information on alternative vaccines, and the hazards of remaining unvaccinated as well as the possible hazards of being vaccinated.
Data and discussion relative to safety and effectiveness are contained in a recent article, "Control of Influenza and Poliomyelitis with Killed Virus Vaccines" (SCIENCE 195:834-847, 4 March 1977), a copy of which is appended (Appendix I). Additional relevant data accompany this statement which also contains my views on vaccination policy and on informed consent.

COMPARATIVE SAFETY

Between 1955, following the Cutter incident caused by improperly prepared vaccine, and 1968 (when manufacture in the United States of killed poliovirus vaccine [KPV] was discontinued) more than 452 million doses of KPV were distributed without evidence of risk of vaccine-induced paralytic poliomyelitis. Between 1961 and 1976, the number of doses of live poliovirus vaccine (LPV) distributed in the United States was of a similar order of magnitude; during that period 148 cases of paralytic poliomyelitis, attributed to its use, occurred in vaccinees and contacts (Appendix I, Table 8).

The degree of risk of vaccine-induced paralytic poliomyelitis associated with the use of either vaccine is most often expressed as cases per number of doses distributed or as cases per number of individuals vaccinated; another measure compares the number of cases of vaccine-induced disease versus the number of naturally acquired cases. In this regard, in the period January 1973 to September 1976,
30 domestically arising cases of paralytic poliomyelitis occurred in the United States, 29 of which were associated with the use of the attenuated live virus vaccine; only one was not vaccine-associated (Appendix I, Table 9).

COMPARATIVE EFFECTIVENESS

Both LPV and KPV have been shown to be effective in inducing protection against paralytic poliomyelitis. Issues about differences between the two have been mainly in regard to (1) effectiveness in inducing a "herd effect," (2) relative acceptability of an injected versus an orally administered preparation, and (3) relative duration of induced immunity. The following data are relevant to each of the foregoing issues and show the equivalence of both types of vaccine in these respects:

1. Appendix II, Chart 1, shows that in the United States herd immunity was induced by the killed virus vaccine. The risk to unvaccinated individuals of encountering naturally occurring poliovirus in 1961 was markedly reduced as compared to the six-year period prior to introduction of the KPV in 1955. In other countries which have continued to use only KPV up to the present time, domestically arising cases of wild-type virus have been eradicated (Appendix I, Table 2 and Figure 4).
Appendix II, Chart 2, shows that the decline in incidence of poliomyelitis in the United States, following the introduction of the LPV, continued at the same rate as when KPV was the only vaccine in use. Chart 3 shows the extent to which the population was under the influence of KPV and LPV during this period of time. From the epidemiologic data in Appendix II and in Appendix I, Table 2, and Figures 3 and 4, it would appear that the LPV effect was simply additive and that "intestinal immunity," induced more efficiently by LPV than by KPV, is not an essential requirement for blocking virus dissemination. It is clear that this is also accomplished by use of the KPV.

2. Appendix II, Chart 4, indicates the relatively high proportion of the population to which three or more doses of KPV were administered prior to 1961. Contrary to expectation, Appendix I, Table 7, shows a lower rate of administration of three or more doses of LPV given by mouth, as compared with three or more doses of DTP given by injection, indicating that acceptability of injectable vaccines is well established in the United States, even in inner city areas. It also suggests the value of combining DTP and KPV for simplicity and for economy in administration costs.
3. In regard to duration of immunity induced by a KPV:

a. Data presented in Appendix III suggest that durable immunity to paralytic poliomyelitis is related to the length of its incubation period and to the persistence of immunologic memory.

b. Data presented in Appendix IV show that maximum antibody levels evident early after primary or booster stimulation decline within a year to a relatively stable plateau level. This has been observed for six years after the last primary or booster dose; serum samples collected approximately 10 years after the last dose are available for test. The data suggest that KPV induces enduring immunologic memory with characteristics (in terms of antibody persistence and secondary-type responsiveness) which are associated with life-long immunity. The data also suggest that for maintaining immunity to paralytic poliomyelitis repeated booster doses are not necessary.

c. Data presented in Appendix V indicate that persistently demonstrable antibody and/or immunologic memory was induced in virtually all to whom three doses of 1955 commercially produced vaccine had been administered.
This is reflected by the presence of demonstrable levels of antibody and/or secondary-type antibody responsiveness to a fourth dose administered three years later. Böttiger (Acta Pathol. Microbiol. Scand. 81 (Sect. B): 795 [1973]) has made similar observations after an interval of seven to eight years.

d. Data in Appendix VI show a linear relationship (on a semi-log plot) between number of doses of vaccine administered and percent-effectiveness. This suggests that immunity to paralysis is induced by a single critical dose of vaccine; depending upon vaccine potency, this will be induced by the first, second, third, or fourth dose, etc. The consistency in the linear relationship between number of doses of vaccine and effectiveness over three consecutive years suggests that the critical factor for immunity to paralysis is stable. This is in keeping with the suggestion that durability of immunity to paralysis is linked to persistence of immunologic memory, whether or not antibody, once produced, persists at a demonstrable level (Appendix VII; Salk, J., Ann. N. Y. Acad. Sci. 61(4): 1023 [1955]; Salk, J., Amer. J. Med. Sci. 69: 105 [1956]).
e. Data in Appendix V (pp. 6-7) indicate that it is possible to determine the extent to which immunologic memory persists, as reflected by the presence of booster-type responsiveness (Appendix III, pp. 5-8), in those vaccinated several years previously. These data, and those in Appendix IV, indicate that immunologic memory with active recall is induced by KPV. The full duration of active recall has not yet been established, but this can readily be determined by a test for antibody on samples of serum from finger-blood (Appendix V, p. 5) drawn before and after the administration of a single dose of vaccine (Appendix V, pp. 6-7).

INFORMED CONSENT AND RESPONSIBILITY

For killed poliovirus vaccine, full and meaningful information about the risk of vaccination and of remaining unvaccinated can easily be given without its creating fear or being misleading. If live poliovirus vaccine is used, full and meaningful information should include (1) the inherent risk associated with its use, (2) the actual risk of remaining unvaccinated, and (3) the fact that an equally effective alternative exists which can be administered without risk of paralysis in vaccine recipients or contacts. As seen in Appendix VIII, the consent forms that have been in use do not provide this information.
The issue of informed consent is related to the question as to
where the ultimate responsibility lies for the occurrence of vaccine-
associated cases of paralytic poliomyelitis. In the case of a vaccine
recipient, consent can be given by the recipient or the parent to
accept personal risk. But, in the case of close contact or community
contact cases, where does the responsibility for consent lie?

If policy-making bodies recommend the continued use of LPV
when an equivalently effective vaccine exists which can be administered
without risk, and if vaccine-associated paralytic poliomyelitis con-
tinues to occur, then it would seem that the ultimate responsibility
for the occurrence of such cases rests with these policy-making bodies.

POLICY RECOMMENDATIONS

In my view, poliomyelitis immunization policy in the United
States should aim at the eradication of all paralysis-causing polio-
viruses, whether naturally occurring or arising from the live polio-
virus vaccine. Experience supports the view that this can be
accomplished by the use of a killed poliovirus preparation for routine
immunization of the susceptible population. For policy purposes, then,
the central question is what should be done now, leaving aside
decisions of the past. The reasoning in this summary statement is
that KPV should replace LPV for routine immunization because of the
incontrovertible evidence concerning safety and the prospect of eradication of polioviruses.

Therefore, I propose that:

1. KPV, rather than LPV, should be recommended for routine immunization at all ages.

2. Standard minimal potency requirements should be established for each antigenic type in killed poliovirus vaccines such that two doses a month apart will induce a serologically demonstrable response in at least 90% of vaccinees who, prior thereto, are free of maternal or infection-acquired antibody. Vaccines of such potency are readily produced and are currently in use. For this purpose a Reference Standard Vaccine should be established by a study similar to that carried out with Reference Vaccine A (Appendix VII).

3. The immunization schedule recommended should be based on the collective experience of countries in which KPV has been used effectively. In some countries primary immunization consists of two doses, given a month apart, starting beyond the age when maternal antibody is present, with a third dose given approximately 6 to 12 months later. When polio immunization is started earlier, along with or combined with DTP during the
period when maternal antibody is present, the DTP schedule has been employed.

4. The proportion of the population immunized should be maximized by administering poliovirus vaccine upon entrance into school to those who have not previously received the recommended number of doses. In order to determine whether or not to recommend, in addition, a booster dose upon school entrance for those who have previously received the recommended number of doses of vaccine, an appropriately designed study can be carried out to examine for persistence of antibody and/or booster-type responsiveness in such children (Appendix V, pp. 5-7).