U.S. FOOD & DRUG ADMINISTRATION

July 23, 2019

Siri & Glimstad LLP
200 Park Avenue
Seventeenth Floor
New York, NY 10166

In reply, refer to file: F18-6943

Dear Mr. Siri,

This is in reply to your Freedom of Information Act request dated August 22, 2018, in which you requested "A copy of the report for each clinical trial relied upon by the FDA when approving Ipol in 1990." Your request was received in the Center for Biologics Evaluation and Research on August 24, 2018.

A search of the IPOL product license application file located the enclosed documents that are responsive to your request. Please note that we have provided you with the best available copies of the records.

We have withheld portions of pages under Exemption (b)(4), 5 U.S.C. § 522(b)(4). That exemption permits the withholding of trade secrets and commercial or financial information that was obtained from a person outside the government and that is privileged or confidential. The withholding of such information is permitted if disclosure is likely to cause substantial competitive harm to the person who submitted the information.

In addition, we have withheld portions of pages under Exemption (b)(6), 5 U.S.C. § 522(b)(6). That exemption protects information from disclosure when its release would cause a clearly unwarranted invasion of personal privacy. FOIA Exemption 6 is available to protect information in personnel or medical files and similar files. This requires a balancing of the public's right to disclosure against the individual's right to privacy.

You have the right to appeal this determination. By filing an appeal, you preserve your rights under FOIA and give the agency a chance to review and reconsider your request and the agency's decision.

Your appeal must be mailed within 90 days from the date of this response to:

Deputy Agency Chief FOIA Officer
U.S. Department of Health and Human Services
Office of the Assistant Secretary for Public Affairs
Room 729H
200 Independence Avenue, S.W.
Washington, DC 20201
Email: FOIARequest@PSC.hhs.gov

Please clearly mark both the envelope and your letter or email "**FDA** Freedom of Information Act Appeal."

If you would like to discuss our response before filing an appeal to attempt to resolve your dispute without going through the appeals process, please contact:

Beth Brockner-Ryan, Branch Chief
Center for Biologics Evaluation and Research (CBER)
Access Litigation and Freedom of Information Branch
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Building 71, Room 1114
Silver Spring, MD 20993-0002
Email: beth.brocknerryan@fda.hhs.gov
Main Line 240-402-7800
FOI Line 240-402-8008

You also have the right to contact:

FDA FOIA Public Liaison
Office of the Executive Secretariat
5630 Fishers Lane
Room-1050
Rockville, MD 20857
Email: FDAFOIA@fda.hhs.gov

If you are unable to resolve your FOIA dispute through our FOIA Public Liaison, the Office of Government Information Services (OGIS), the Federal FOIA Ombudsman's office, offers mediation services to help resolve disputes between FOIA requesters and Federal agencies. The contact information for OGIS is:

Office of Government Information Services
National Archives and Records Administration
8601 Adelphi Road–OGIS
College Park, MD 20740-6001
Telephone: 202-741-5770
Toll-Free: 1-877-684-6448
E-mail: ogis@nara.gov
Fax: 202-741-5769

The following may be included in a monthly invoice:

Reproduction	1 CD @ $1.00	$1.00
TOTAL		**$1.00**

The above charges may not reflect final charges for this request. Please DO NOT send any payment until you receive an invoice from the Agency's Freedom of Information Staff (HFI-35).

If you have any questions or if we can be of further assistance, please let us know by referencing the above file number. You can contact Mechelle Bray by phone at 240-402-8024 or by e-mail at Mechelle.Bray@fda.hhs.gov.

Sincerely,

Beth A. Brockner Ryan -S

Digitally signed by Beth A. Brockner Ryan -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300052489, cn=Beth A. Brockner Ryan -S
Date: 2019.07.23 12:19:33 -04'00'

Beth Brockner Ryan
Chief, Access Litigation and Freedom of Information Branch

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

MERIEUX INSTITUTE, INC.

April 28, 1983

John C. Petricciani, M.D.
Director
Office of Biologics HFN-800
National Center for Drugs & Biologics
8800 Rockville Pike
Bethesda, Maryland 20205

REFERENCE: 83-087

Dear Dr. Petricciani:

Enclosed is a report from Dr. A. Marshall McBean and co-investigators on a comparison of oral and Merieux killed polio vaccine.

The Merieux vaccine was produced from primary monkey kidney cells, however, it was made by the same basic methods used to produce the current polio vaccine from VERO cells.

This data was recently presented at the International Polio Symposium held at PAHO, Washington, D.C., March 14-17, 1983.

Because of the similarity of the final products, which differ only in cell substrate, this data on potency and efficacy is submitted in support of this application under Item 26.d.

Sincerely,

Pinya Cohen

Pinya Cohen, Ph.D.
Vice President
Quality Control
and Regulatory Affairs
FOR C. CHARBONNIER
PC/(b) (6)
83282

Attachments

1200 N.W. 78th Avenue, Suite 109 / Miami, Florida 33126 / Telephone (305) 593-9577 / Telex: 807387

A Comparison of the Serologic Response to Oral and Injectable Trivalent Polio Vaccine

Authors: A. M. McBean, M.D., M.Sc.; M. L. Thoms, R.N., Dr.P.H.; R. H. Johnson, M.D., M.P.H.; B. R. Gadless, M.H.S.; B. MacDonald, B.S.; L. Nerhood, R.N.; P. Cummins, B.S.N.; J. Hughes, B.S.N.; J. Kinnear, B.S.N., M.H.S.; C. Watts, B.S.N.; M. Kraft, M.D.; P. Albrecht, M.D.; E. J. Boone; R. Bernier, Ph.D.

Institutions: Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD; Prince George's County Health Department, Prince George's County, MD; Bureau of Biologics, F.D.A., Bethesda, MD; Centers for Disease Control, Atlanta, GA.

Running Head: Serologic Response to IPV and OPV

1. The authors gratefully acknowledge the assistance of the nursing and medical staff of the pediatric clinics of the cooperating agencies. In particular we thank Dr. Helen McAllister of the Prince George's County Health Department; Dr. Lindsey Grossman and Dr. John Neff of the Baltimore City Hospitals; Dr. John Krager of the Baltimore County Health Department, Dr. Venita Thweat of the Baltimore City Health Department; and Dr. Ruth Steerman of the Prince George's County General Hospital.

2. This research is supported by contract #200-80-0512(P) of the Centers for Disease Control, United States Department of Health and Human Services.

3. Informed consent was obtained from the parents of children in the study and guidelines for human experimentation of the United States Department of Health and Human Services and the Johns Hopkins University School of Hygiene and Public Health were followed in the conduct of the clinical research.

4. Please address requests for reprints to Dr. A. Marshall McBean, Johns Hopkins University School of Hygiene and Public Health, 615 North Wolfe Street, Baltimore, Maryland 21205

ABSTRACT

American children two months of age were randomly assigned to two groups which received either the commercially available oral trivelant polio vaccine (OPV) or an injectable trivalent polio vaccine (IPV) with a confirmed minimum D-antigen content of 27, 3.5 and 29 units for polio virus type I, II and III respectively. Vaccine was given at 2, 4, and 18 months of age. Sera was obtained at 2, 4, 6 months of age on 439 children and on 85 children at 18 and 20 months of age and examined for neutralizing antibodies.

The percent of children with detectable antibodies and the reciprocal geometric mean titers (GMTs) were similar for both groups at two months of age for all three polio types. At twenty months of age, all children but one had detectable antibodies to all three polio types. Significantly higher GMTs against types I and III were noted at twenty months for the IPV group.

I. Introduction

Protection of the United States population against poliomyelitis has been greatly facilitated by the availability of two very effective and safe types of vaccine: inactivated poliovirus vaccine (IPV) and live attenuated oral poliovirus vaccine (OPV). During the period from 1955 to 1961, immunization efforts using IPV were successful in reducing the number of reported paralytic polio cases from 13,850 (7.9/100,000 population) in 1955 to 820 (0.7/100,000) in 1961 [1]. In spite of this tremendous achievement, "The Cutter Incident" [2] in which the virus in the IPV was not inactivated, and the contamination of monkey kidney cells in which the IPV virus was grown by SV-40 virus which is oncogenic in hamsters, helped create an environment in which the use of IPV was rapidly discontinued after OPV became available in 1962. The decision to use OPV was also based on its ease of administration and acceptance; expected long lasting (perhaps life-long) immunity; rapid production of bowel immunity which could interrupt wild virus transmission, even in epidemic situations; and the spread of OPV virus to unvaccinated persons which could induce immunity in these people [3,4]. The continued reduction in the number of cases of paralytic disease in the era of OPV use has been reported annually by the Center for Disease Control (CDC), Atlanta, Georgia, U.S.A. By 1972, the number of cases has been reduced to 29 per year (0.01/100,000). During the years 1973-79, 82 cases of paralytic polio have been reported to CDC, an average of 12 cases per year.

Thus, the efficacy of both the IPV and OPV in inducing immunity and protecting recipients is well documented. However, there are reports of areas where children were given IPV and antibody levels were detectable in only 65 to 74% of the children who had received multiple doses of IPV [5]. For IPV, the seroconversion rates, post-immunization titers and the duration of immunity have been proportional to the potency of the vaccine; i.e., are dose-dependent

[6]. Vaccine production methods reported by (b) (6) of the Rijks Instituut Voor de Volksgezondheid, Bilthoven, The Netherlands, allow for higher concentrations of vaccine antigens than were attainable in previous IPV.

This study will compare the immunologic response in American infants given three doses of IPV made by the new production techniques with three doses of commercially available OPV. Data available through February, 1983 will be presented.

II. Materials and Methods

Participants: Children attending Well-child Clinics in Maryland were enrolled in the study and randomly assigned to receive either the OPV or the IPV. Children entered the study when they were between 6 and 13 weeks ("2 months") of age, and either OPV or IPV was administered at that time. Sixty days later, when the child was "4 months" of age, a second dose of the same vaccine was given. A third dose of the same polio vaccine was given at "18 months" of age. Diphtheria, Tetanus, Pertussis vaccine (DTP) and either an oral or injectable polio placebo were administered at the same time as the polio vaccines. As shown in Table 1, blood specimens were taken at 2, 4, 6, 18 and 20 months of age.

Vaccines: The OPV used was the commercially licensed available vaccine manufactured by Lederle Laboratories (Wayne, New Jersey, U.S.A.). It contained 800,000 $TCID_{50}$ of type I, 100,000 $TCID_{50}$ of type II, and 500,000 $TCID_{50}$ of type III per 0.5cc dose. The IPV was manufactured by the Merieux Institute (Lyon, France). It had a minimum potency of 27 D-antigen units of type I, 3.5 D-antigen units of type II, and 29 D-antigen units of type III per 0.5cc dose. The DTP contained (b) (4) Lf of diphtheria toxoid, 5 Lf of tetanus toxoid and 4 Units of pertussis per 0.5cc dose. The potency of the IPV, as measured by D-antigen content, was confirmed every three months at the Rijks Instituut.

Blood Specimen Handling: After collection, blood specimens were allowed

to clot, and the serum was drawn off. Specimens were then refrigerated and frozen within 4 to 8 hours. They were stored at -20°C until examined in the laboratory. Specimens were coded prior to being sent to the laboratory to insure unbiased laboratory analysis.

Laboratory Testing: Serum polio neutralizing antibodies were measured at the Bureau of Biologics, FDA, DHHS, Bethesda, Maryland (U.S.A.) by a virus cytopathic effect (CPE) neutralization test in microtiter trays (96 well, flat-bottomed, Microtest II, Falcon, Oxnard, CA). Each day a known serum prepared by the Rijks Instituut for each polio type was tested with the experimental sera. A conversion factor was then calculated to convert the observed reciprocal of the serum dilution which neutralized CPR in 50% of the wells to International Units (IU).

III. Results

Of the 558 children enrolled in the study to date, serum specimens from 484 have been analyzed for neutralizing antibodies. Of the 119 children not included in the analysis, 103 have been lost to follow-up, and sixteen were deleted because of lost specimens, broken collection tubes, or insufficient data. Therefore, 439 children comprise the study population, of which 196 received OPV, and 243 received IPV. All of these children have completed their 6-month visit, and 85 have completed their twenty-month visit.

As a confirmation of the randomization process, the sex distribution, the number of siblings living with the participants, and the number of siblings who received oral polio vaccine during the time of the study were similar for the two study groups. In addition, the percentage of children with detectable antibodies and the reciprocal geometric mean titers (GMTs) to the three polio virus types were the same for the children in each vaccine group at two months of age (Tables 2 and 3).

Comparing the two vaccine groups at each age for each virus type, there is

no difference in the percent of children in each group with detectable antibodies. Approximately 25% of all children do not have antibodies against type III at 2 months of age, but this decreases to 17% at 4 months of age and 5% or less, from 6 months on. At 6 months of age (2 months after the second dose of vaccine), a minimum of 93% of the children have antibodies against two polio types, I and II. The percent is unchanged between 6 and 18 months. At 20 months (2 months after the third dose of vaccine), all but one child has demonstrable antibodies.

At four months of age, the GMTs in the OPV group are significantly higher for type II and type III virus, compared with themselves at 2 months of age and with the IPV group at 4 months of age. The GMT against type I is similar for both vaccine groups and shows no change from 2 months of age. At six months of age, the GMT against type I poliovirus is significantly higher in the IPV group, and the GMT against type II is significantly higher in the OPV group. The GMTs against type III are similar in both groups.

The results from the analysis of the eighty-five children who have completed the 18 and 20-month visits reveal that, at eighteen months, the GMT in the OPV group remains significantly higher than the IPV group for type II polio virus. At twenty months, the GMTs against type II have become similar for both vaccine groups, while the GMTs against types I and III are now significantly greater for the IPV group.

IV. Discussion

An ideal study of the serologic response to polio vaccines would involve the administration of vaccine to children without antibodies to any of the polio virus types (triple negative children). Enrolling children into this study when they are 2 months of age precludes that possibility. In fact, only 12 of the 439 children were triple negative upon entry into this study, and three others were triple negative at 4 months of age. Thus, discussion of our results will

focus on the ability of the two vaccines to stimulate antibody production and protect the entire group of children given each vaccine.

If we take the presence of detectable serum neutralizing antibodies to indicate protection against polio, then both vaccines as well as residual maternal antibodies protect a similar percent of children during their first six months of life even though at 4 months of age the antibody level, as measured by the GMT, is lower in the IPV group to types I and II. The equivalency of the two vaccines in stimulating demonstrable antibodies is verified by the results at 18 and 20 months of age.

Although the percent of children with detectable antibodies at 4 months is not significantly greater than at 2 months in either group, the immunizing effect on the children receiving the first dose of OPV can be seen for types II and III by the increases in the GMTs. For the IPV and the type I oral vaccine, the GMTs decrease or remain the same after 1 dose of vaccine. The lower response to the IPV at 4 months of age is probably due to the presence of maternal antibodies in the children who received IPV at 2 months of age. On the other hand, the first dose of OPV, particularly types II and III, is able to multiply in the intestine, and stimulate the production of measurable serum antibodies at 4 months of age.

The ability of antibodies to type III to reach the same level for both OPV and IPV and a higher level for IPV to type I after the administration of the second dose of IPV may reflect either a significant primary response due to the high potency of the vaccine in the presence of declining maternal antibodies at the time of this dose, or the presence of an unmeasurable response to the first dose of IPV which is then boosted by the dose given at 4 months of age. The booster effect of the third dose of IPV is clearly seen by the great increase in GMTs to all three types between 18 and 20 months. The duration of protection cannot be estimated. However, it is likely that the higher the level of antibodies the more long lasting they will be.

Currently the Advisory Committee on Immunization Practice recommends three doses of the previously available IPV in the first year of life with a booster at 18 months. The preliminary data from this study indicates that 2 doses in the first year of life will probably be sufficient. This schedule is effective even when begun at 2 months of age when maternal antibodies are high.

REFERENCES

1. Schonberger, L. B., McGowan, J. E. Jr. Vaccine associated poliomyelitis in the United States, 1961-1972. Am. J. Epi. 104: 202-211, 1976.
2. Nathanson, M., Langmuir, A.D. The Cutter incident. Am. J. Hyg. 78: 16-81, 1963.
3. Nightingale, E.O. Recommendations for a national policy on poliomyelitis vaccination. N. Eng. J. Med. 297: 249-253, 1977.
4. Melnick, J. L. Advantages and disadvantages of killed and live poliomyelitis vaccines. Bull. WHO 56: 21-38, 1978.
5. MacLeod, D. R. E., Ing, W. K., Belcourt, R. J-P., Pearson, E. W., Bell, J. S. Antibody status to poliomyelitis, measles, rubella, diphtheria and tetanus, Ontario 1969-1970: deficiencies discovered and remedies required. Can. Med. Assn. J. 113: 619-623, 1975.
6. Salk, J., Salk, D. Control of influenza and poliomyelitis with killed virus vaccines. Science 195: 834-847, 1977.

TABLE I

Schedule of immunizations and blood collection

Immunizations	2 Months	4 Months	6 Months	18 Months	20 Months
Dose of either OPV or IPV	1	2	-	3	-
Dose of DTP	1	2	3	4	-
Blood Collection	yes	yes	yes	yes	yes

Table 2

A Comparison of the Serologic Response to Oral and Injectable Trivalent Polio Vaccine

Number and Percent of Children 2, 4, 6, 18 and 20 Months of Age with Detectable Antibodies to the Three Types of Wild Polio Virus

	Polio Virus Type I			Polio Virus Type II			Polio Virus Type III		
	Number of children with antibodies	Number of children receiving vaccine	Percent of children with antibodies	Number of children with antibodies	Number of children receiving vaccine	Percent of children with antibodies	Number of children with antibodies	Number of children receiving vaccine	Percent of children with antibodies
2 MONTHS OF AGE									
Oral Vaccine	162	183	88.5	173	186	93.0	133	174	76.4
Injectable Vaccine	203	224	90.6	224	233	96.1	161	214	75.2
4 MONTHS OF AGE									
Oral Vaccine	159	187	85.0	189	194	97.4	158	190	83.2
Injectable Vaccine	210	228	92.1	218	228	95.6	186	225	82.7
6 MONTHS OF AGE									
Oral Vaccine	175	189	92.6	191	192	99.5	181	191	94.8
Injectable Vaccine	234	237	98.7	235	238	98.7	232	235	98.7
18 MONTHS OF AGE									
Oral Vaccine	41	45	91.1	46	46	100.0	45	46	97.8
Injectable Vaccine	39	40	97.5	41	42	97.6	41	42	97.6
20 MONTHS OF AGE									
Oral Vaccine	43	44	97.7	45	45	100.0	45	45	100.0
Injectable Vaccine	41	41	100.0	41	41	100.0	41	41	100.0

None of the differences between the oral and injectable vaccine groups is significant

Table 3

A Comparison of the Serologic Response to Oral and Injectable Trivalent Polio Vaccine

Reciprocal Geometric Mean Titers (in International Units) to Three Types of Wild Polio Virus In Children 2, 4, 6, 18&20 Months of Age

	Polio Virus Type I	Polio Virus Type II	Polio Virus Type III
		2 MONTHS OF AGE	
Oral Vaccine	0.42	1.03	0.31
Injectable Vaccine	0.43	1.13	0.27
		4 MONTHS OF AGE	
Oral Vaccine	0.43	7.90 *	1.87 *
Injectable Vaccine	0.30	0.66	0.34
		6 MONTHS OF AGE	
Oral Vaccine	1.10 *	16.93 *	4.22
Injectable Vaccine	1.90	3.54	4.71
		18 MONTHS OF AGE	
Oral Vaccine	2.31	16.30 *	2.91
Injectable Vaccine	1.53	6.04	2.65
		20 MONTHS OF AGE	
Oral Vaccine	4.74 *	20.35	4.38 *
Injectable Vaccine	11.36	20.40	18.75

* Difference in Reciprocal Geometric meanTiter between Oral and injectable Vaccine Groups significant at $p < 0.01$

MERIEUX INSTITUTE, INC.

7855 n.w. 12th street, suite #114, miami, florida 33126-1818
p.o. box 52-3980, miami, florida 33152-3980
phone (305) 593-9577 / telex: 807387

October 9, 1987

Elaine C. Esber, M.D., Director
Office of Biologics Research & Review
ATT: Division of Product Certification,
HFN-825
Room 9B-05, Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

REFERENCE NO. 83-087

Dear Dr. Esber:

Enclosed is a progress report on the study of P. Ogra and H. Faden, SUNY, Buffalo.

This report covers data currently available on the results of two primary doses of Merieux IPV. Data from Johns Hopkins are not as advanced and are not included in this report.

Sincerely yours,

Pinya Cohen

Pinya Cohen, Ph.D.
Vice President
Quality Control and
Regulatory Affairs

PC (b) (6)
87507

Attachments

CLINICAL STUDIES OF MERIEUX IPV AT SUNY/CHILDRENS HOSPITAL, BUFFALO

PROGRESS REPORT

SUMMARY

Two doses of Merieux IPV at 2 and 4 months of age gave excellent neutralizing antibody responses at 5 months to three types of poliovirus. IPV and OPV alone produced similar levels of neutralizing antibody and IgA in the nasopharyngeal secretions. A combined schedule of IPV and OPV resulted in a strong priming effect by IPV on mucosal immune response of OPV for neutralizing antibody and IgA in the nasopharyngeal secretions and for IgA in the stool. Merieux IPV induced comparable responses in premature and full term infants. Single and two dose boosters in adults showed high anamestic responses in all recipients and that a second dose of IPV did not increase the GMT compared to only one dose.

Introduction

The Merieux Inactivated Polio Vaccine (M-IPV) produced from continuous cell lines of Vero cells using micro-carrier culture has been extensively tested in Finland, Israel, India, Brazil, Indonesia, Mali, France, and the United States. This highly purified more potent vaccine has been shown to be safe, highly immunogenic and efficacious when used in a two-dose schedule for primary immunization followed by a booster dose.

A clinical trial at Johns Hopkins comparing M-IPV to the oral polio vaccine

currently used in the United States showed that approximately 99% of children had neutralizing antibodies to all three types of polio virus after receiving M-IPV at 2 and 4 months of age and that a significant boost in titers occurred after the third dose at 18 months of age. The titers to M-IPV for Types I and III poliovirus were superior to OPV, but equivalent for Type II when given in the same 3 dose schedule. This vaccine was made exactly as the Vero cell vaccine intended for license except the cell substrate for the Johns Hopkins trial was primary monkey kidney cells.

The Office of Biologics requested, December 1985, that 75-100 children and 25-30 adults be immunized according to the United States schedule. In response to this request clinical studies on children and adults were carried out at Childrens Hospital/State University of New York, Buffalo by Drs. H. Faden and P. Ogra. Supplemental studies on groups of children using only IPV or a combined schedule were also initiated at Johns Hopkins by Drs. McBean and Modlin at a later date.

To meet the FDA request for M-IPV licensure, data are now presented on sufficient children and adults only from Buffalo. The studies are still in progress at Buffalo and Baltimore and will be completed in late 1988.

METHODS

Details of the methods used are outlined in the protocols already submitted under IND. Merieux IPV Lots Z1102, Z1103 and A0304 were used. The general approach was to compare immunogenicity of two primary doses of M-IPV. OPV or a combined schedule in children 2 months old. Originally, a minimum of 15-20 children were to be recruited in Groups A, C, and D and 50-60 were to be recruited in Group B.

At this time, 114 children are available for analysis. The groups and vaccines are shown below:

IMMUNIZATION PLAN FOR CHILDREN

GROUP	2 MONTHS	4 MONTHS	12 MONTHS
A	OPV	OPV	OPV
B	IPV	IPV	IPV
C	IPV	OPV	OPV
D	IPV	IPV	OPV

Blood samples for antibody determinations were collected at 2 and 4 months of age just prior to administration of vaccine and one month after the second and third doses of vaccine. There are insufficient data on the booster dose given at 12 months for presentation at this time. A detectable antibody titer was considered $\geq$ 1:10. GMT's were computed and also expressed in international units based on the FDA reference serum results.

Groups B and D are identical for the first two doses of vaccine, therefore, their data have been combined for this report.

The numbers of subjects in the OPV control (Group A) was small at the time of this report.

For the adult studies, 30 individuals were immunized and available for the analysis. Half received one dose (Group F1) and half received a second dose 4 weeks later (Group F2). Serum antibody titers were done prior to immunization

and 4 weeks after each dose of vaccine.

RESULTS IN CHILDREN

M-IPV induced detectable neutralizing antibodies after two doses of vaccine in 97.6% (Type I), 100% (Type II) and 97.6% (Type III) of the children (Table 1). Two doses of OPV gave 100% response for all types of poliovirus and a mixed schedule of IPV + OPV induced nearly 95% response for Types I and III and 100% response for Type II.

The GMT (Table I) was the same in all groups for Type I. For Type II two doses of IPV gave lower GMT's than OPV or a mixed schedule. The GMT obtained for Type III with a mixed schedule was significantly lower than in the other two groups.

Table 2 shows that two doses of M-IPV produced neutralizing antibodies in the nasopharyngeal secretions (NPS) to Type I polovirus in 34%, to Type II in 53% and to Type III in 42% of the children. OPV produced neutralizing antibodies to Type I in 50%, to Type II in 70%, and to Type III in 50% of the children. The mixed schedule resulted in NPS neutralizing antibody in 47, 90 and 42% of the children, respectively. The GMT for Type II antibody in the mixed schedule was significantly higher than schedules of only IPV or only OPV indicating a priming effect by IPV on Type II OPV induced antibody.

The percentage of children with IgA antibodies in the NPS (Table 3) were generally at similar levels for M-IPV and OPV for all types of poliovirus, but were highest in children receiving the mixed schedule. The GMT of IgA was

highest in the mixed schedule suggesting IPV exerts a priming effect on a subsequent dose of OPV. The GMT for all OPV or all IPV recipients was similar for types I and II but OPV was higher for type III.

The percentage of children with detectable neutralizing antibody in the stool (Table 4) was generally 5 to 33% regardless of schedule except for Type II poliovirus with OPV (56%) and the mixed schedule (42%). The percentage of children with detectable stool neutralizing antibody for Types I & II poliovirus was low in those receiving OPV, however the number of children analyzed was small. The GMT's for OPV, IPV and mixed schedules
were similar.

The percent detectable IgA levels in the stool ranged from 5 to 20% for IPV, 11 to 33% for OPV and 15 to 36% for the mixed schedule (Table 5). The mixed schedule resulted in the highest GMT's for Types II and III antibodies. IPV induced a moderate priming effect for OPV for Type II antibody.

Tables 6 and 7 summarize results of serum neutralizing antibodies in children 6 to 13 weeks of age at the time of entry into the study compared to those over 13 weeks. The percentage with detectable neutralizing antibody was the same for the two groups, however, those over 13 weeks of age had higher GMT values.

The NPS neutralizing antibody data for the two age groups (Tables 8 and 9) showed that OPV, IPV or a mixed schedule induced detectable antibody to any type of poliovirus in approximately 60% to 93% of recipients. In 6-13 week old children, combined use of IPV and OPV produced detectable Type I and II antibody in nearly

twice the number of vaccinees compared to IPV only and in nearly 50% more recipients of OPV only. The GMT for Type II was 6 times higher in children immunized with a mixed schedule than in children receiving only IPV and twice the level of children receiving only OPV. Similar NPS data was obtained for children over 13 weeks who received a combined schedule. The data from both age groups suggest a strong priming effect exerted by IPV on a subsequent dose of OPV.

Tables 10 and 11 show that neutralizing antibody in the stool specimens was highest with OPV only, intermediate with a mixed schedule and lowest with IPV only.

Detectable IgA in the NPS ranging from 50 to 100% was observed in children 6-13 weeks old and those over 13 weeks regardless of the vaccines used and virus types (Tables 12 & 13). The combined schedule of IPV and OPV gave GMT's for IgA two to nearly 10 times greater than schedules of OPV or IPV alone.

Overall 50% or less of recipients for either age group or for any vaccine schedule had detectable stool IgA antibody. The combined schedule gave percentages of detectable stool IgA twice those observed for IPV alone and GMT's approximately 50% higher (Tables 14 & 15).

Premature and full term infants developed detectable serum neutralizing antibody levels with equal frequency to two doses of M-IPV and had comparable GMT's (Table 16).

Children who had potential contact with an OPV recipient had significantly higher

GMT's for serum neutralizing antibody (Tables 17 & 18), NPS neutralizing antibody (Tables 19 & 20) and NPS IgA (Tables 21 & 22). This difference was not seen in stool neutralizing antibody levels of children who had contact with OPV compared to those whom were not exposed to OPV (Tables 23 & 24) or in stool IgA levels of the same children (Tables 25 & 26), however, this analysis is based on small numbers of children with
OPV contacts.

RESULTS IN ADULTS

Nearly all adults had detectable neutralizing antibodies at the time of entry into the study so that a single dose of M-IPV ensured a 100% response (Table 27).

A single dose of M-IPV induced increases in GMT of nearly 30 fold for Type I, 50 fold for Type II and 125 fold for Type III. A second dose of IPV did not significantly increase the GMT compared to only a single dose (Table 27).

The results of neutralizing antibodies in the NPS (Table 28) show that the percent of subjects with detectable antibody was the same with one or two doses and suggests that a greater increase over base titer and higher GMT is obtained in individuals who had a lower antibody titer upon entry.

In contrast, both the percent of individuals with stool neutralizing antibody and the GMT were higher in adults receiving two doses of M-IPV compared to only one dose (Table 29).

The IgA antibody levels in the NPS and stool were similar for one or two doses although there was a higher percentage of detectable antibody in NPS of recipients of two doses compared to one dose of M-IPV (Tables 30 & 31).

There were no major differences in antibody responses whether this was exposure or nonexposure to OPV (Tables 32 & 33).

DISCUSSION

The interim results of this study have demonstrated that two doses of M-IPV given at 2 and 4 months of age produce excellent neutralizing antibody responses to all three types of poliovirus one month after the second dose. The percentage of children at 5 months of age with detectable antibody to the Vero cell vaccine is similar to and the GMT's higher than results obtained with children 6 months old in the earlier Johns Hopkins/CDC/FDA study with M-IPV produced in primary monkey kidney cells.

Two children (b) (6) immunized at the same private clinic with two doses of M-IPV formed good neutralizing antibody titers to Type II but not the Types I and III poliovirus. The Type II preimmunization titer and titer one month post 12 month booster was 320 for both children. The Types I and III titers at baseline and post booster were for (b) (6) 10 and 10 and 40 and 20, respectively, and for (b) (6) 10 and 10 and 10 and 20 respectively. Both children had normal IgG at 5 months of age and measurable tetanus antibody levels at 13 months of age. The children are apparently immunocompetent but the reasons for poor Types I and III response are unclear.

This study has shown that children given two doses of only OPV or only IPV produce similar levels of neutralizing antibodies and IgA in the NPS, however, of particular interest was the finding that a dose of IPV followed by a dose of OPV produced significantly higher levels of neutralizing antibody and IgA in the NPS than two doses of OPV or two doses of IPV. This clearly shows that the M-IPV has a strong priming effect on the mucosal antibody induced by OPV and that it is greater than the priming effect of OPV alone. This finding confirms the observation of Ogra etal with less potent, killed poliovirus vaccine. However, in the earlier studies of Ogra, priming was seen using three doses of IPV followed by an OPV booster whereas in his current study priming was seen with only a single dose of the new M-IPV. These data clearly show that IPV stimulates local immunity when used alone or in combination with OPV.

Based on stool antibody data "gut immunity" appears to be a concept applicable to both M-IPV and OPV. Both vaccines used alone or in combination gave detectable neutralizing antibody in the stool with similar GMT's. Furthermore both IPV and OPV, alone or in combination, induced stool IgA. The GMT Type II IgA was the same for IPV or OPV alone and lower for Types I and III when IPV was used alone. Of particular interest is that the highest GMT for Types II and III IgA antibodies was obtained with a combined schedule, again demonstrating that a single dose of IPV can prime a subsequent dose of OPV producing a GMT of IgA higher than either vaccine alone.

The relatively low percentage of children (approximately 50%) with detectable

stool neutralizing antibodies and detectable IgA antibodies (30%) is surprising in view of the "gut immunity" usually attributed to OPV. In fact, the GMT's for IPV and OPV were similar for Types I & III neutralizing antibody and for Type II IgA antibody.

Because nearly 30% of the infants receiving two doses of IPV were premature births it was possible to compare responses to full term infants. Although full term infants had higher maternal antibody levels, as expected, both premature and full term infants had similar percentages of responders and comparable GMT's after two doses of IPV.

The studies in adults showed that a single dose of M-IPV produced booster responses of very high titers of neutralizing antibodies and that a second dose is unnecessary. However, stool neutralizing antibody levels were higher in adults receiving a second dose of IPV.

TABLE 1

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months		4 Months		5 Months	
I	PLAN A	9/10	(90.0)	7/10	(70.0)	10/10	(100.0)
	PLAN BD	66/85	(77.6)	53/84	(63.1)	81/83	(97.6)
	PLAN C	15/19	(78.9)	16/19	(84.2)	18/19	(94.7)
II	PLAN A	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
	PLAN BD	72/85	(84.7)	80/84	(95.2)	83/83	(100.0)
	PLAN C	18/19	(94.7)	19/19	(100.0)	19/19	(100.0)
III	PLAN A	9/10	(90.0)	10/10	(100.0)	10/10	(100.0)
	PLAN BD	62/85	(72.9)	68/84	(81.0)	81/83	(97.6)
	PLAN C	14/19	(73.7)	15/19	(78.9)	18/19	(94.7)
ANY	PLAN A	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
	PLAN BD	83/85	(97.6)	84/85	(98.8)	83/85	(97.6)
	PLAN C	18/19	(94.7)	19/19	(100.0)	19/19	(100.0)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN A	10	25.81	10	28.35	10	259.92
	PLAN BD	85	17.11	84	7.94	83	251.92
	PLAN C	19	19.08	19	12.46	19	263.53
II	PLAN A	10	60.63	10	519.84	10	3151.73
	PLAN BD	85	33.11	84	33.01	83	857.28
	PLAN C	19	79.07	19	38.57	19	2212.41
III	PLAN A	10	27.66	10	52.78	10	735.17
	PLAN BD	85	13.37	84	17.65	83	889.04
	PLAN C	19	10.14	19	17.74	19	131.77

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN A	10	0.30	10	0.33	10	3.03
	PLAN BD	85	0.20	84	0.09	83	2.94
	PLAN C	19	0.22	19	0.15	19	3.08
II	PLAN A	10	0.34	10	2.94	10	17.81
	PLAN BD	85	0.19	84	0.19	83	4.84
	PLAN C	19	0.45	19	0.22	19	12.50
III	PLAN A	10	0.28	10	0.53	10	7.35
	PLAN BD	85	0.13	84	0.18	83	8.89
	PLAN C	19	0.10	19	0.18	19	1.32

TABLE 2

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	PLAN A	0/ . (0.0)	3/ 9 (33.3)	5/10 (50.0)
	PLAN BD	0/ . (0.0)	1/82 (1.2)	27/79 (34.2)
	PLAN C	0/ . (0.0)	0/18 (0.0)	9/19 (47.4)
II	PLAN A	0/ . (0.0)	7/ 9 (77.8)	7/10 (70.0)
	PLAN BD	0/ . (0.0)	1/82 (1.2)	42/79 (53.2)
	PLAN C	0/ . (0.0)	2/18 (11.1)	17/19 (89.5)
III	PLAN A	0/ . (0.0)	2/ 9 (22.2)	5/10 (50.0)
	PLAN BD	0/ . (0.0)	2/82 (2.4)	33/79 (41.8)
	PLAN C	0/ . (0.0)	1/18 (5.6)	8/19 (42.1)
ANY	PLAN A	0/ . (0.0)	7/10 (70.0)	7/10 (70.0)
	PLAN BD	0/ . (0.0)	3/85 (3.5)	49/85 (57.6)
	PLAN C	0/ . (0.0)	3/19 (15.8)	17/19 (89.5)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN A	0	.	9	1.71	10	3.03
	PLAN BD	6	1.00	82	1.02	79	1.90
	PLAN C	0	.	18	0.00	19	3.10
II	PLAN A	0	.	9	8.00	10	9.19
	PLAN BD	6	1.00	82	1.03	79	3.30
	PLAN C	0	.	18	1.17	19	19.20
III	PLAN A	0	.	9	2.00	10	5.28
	PLAN BD	6	1.00	82	1.03	79	2.82
	PLAN C	0	.	18	1.08	19	2.40

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN A	0	.	9	0.02	10	0.04
	PLAN BD	6	0.01	82	0.01	79	0.02
	PLAN C	0	.	18	0.00	19	0.04
II	PLAN A	0	.	9	0.05	10	0.05
	PLAN BD	6	0.01	82	0.01	79	0.02
	PLAN C	0	.	18	0.01	19	0.11
III	PLAN A	0	.	9	0.02	10	0.05
	PLAN BD	6	0.01	82	0.01	79	0.03
	PLAN C	0	.	18	0.01	19	0.02

Polio Protocol 01

TABLE 3

NASOPHARYNGEAL SECRETIONS (b) (4) IgA ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	PLAN A	0/ . (0.0)	7/ 9 (77.8)	6/10 (60.0)
	PLAN BD	0/ . (0.0)	33/82 (40.2)	45/80 (56.3)
	PLAN C	0/ . (0.0)	9/18 (50.0)	15/19 (78.9)
II	PLAN A	0/ . (0.0)	7/ 9 (77.8)	6/10 (60.0)
	PLAN BD	0/ . (0.0)	33/82 (40.2)	49/80 (61.3)
	PLAN C	0/ . (0.0)	9/18 (50.0)	16/19 (84.2)
III	PLAN A	0/ . (0.0)	7/ 9 (77.8)	8/10 (80.0)
	PLAN BD	0/ . (0.0)	34/82 (41.5)	49/80 (61.3)
	PLAN C	0/ . (0.0)	10/18 (55.6)	17/19 (89.5)
ANY	PLAN A	0/ . (0.0)	7/10 (70.0)	8/10 (80.0)
	PLAN BD	0/ . (0.0)	39/85 (45.9)	53/85 (62.4)
	PLAN C	0/ . (0.0)	10/19 (52.6)	17/19 (89.5)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	PLAN A	0	.	9	8.63	10	7.46
	PLAN BD	6	0.00	82	3.13	80	5.81
	PLAN C	0	.	18	4.50	19	14.87
II	PLAN A	0	.	9	8.00	10	7.46
	PLAN BD	6	0.00	82	3.29	80	6.01
	PLAN C	0	.	18	4.16	19	16.59
III	PLAN A	0	.	9	9.33	10	13.93
	PLAN BD	6	0.00	82	3.32	80	6.39
	PLAN C	0	.	18	5.66	19	21.42

TABLE 4

Polio Protocol 01

STOOL SPECIMENS NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	PLAN A	0/ . (0.0)	1/10 (10.0)	1/ 9 (11.1)
	PLAN BD	0/ . (0.0)	0/75 (0.0)	4/78 (5.1)
	PLAN C	0/ . (0.0)	0/18 (0.0)	3/19 (15.8)
II	PLAN A	0/ . (0.0)	4/10 (40.0)	5/ 9 (55.6)
	PLAN BD	0/ . (0.0)	3/75 (4.0)	9/78 (11.5)
	PLAN C	0/ . (0.0)	0/18 (0.0)	8/19 (42.1)
III	PLAN A	0/ . (0.0)	1/10 (10.0)	3/ 9 (33.3)
	PLAN BD	0/ . (0.0)	2/75 (2.7)	6/78 (7.7)
	PLAN C	0/ . (0.0)	0/18 (0.0)	2/19 (10.5)
ANY	PLAN A	0/ . (0.0)	4/10 (40.0)	5/10 (50.0)
	PLAN BD	0/ . (0.0)	4/85 (4.7)	16/85 (18.8)
	PLAN C	0/ . (0.0)	0/18 (0.0)	8/19 (42.1)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN A	0	.	10	1.15	9	1.17
	PLAN BD	5	0.00	75	0.00	78	1.10
	PLAN C	0	.	18	0.00	19	1.44
II	PLAN A	0	.	10	3.73	9	5.04
	PLAN BD	5	0.00	75	1.08	78	1.22
	PLAN C	0	.	18	0.00	19	2.49
III	PLAN A	0	.	10	1.15	9	1.59
	PLAN BD	5	0.00	75	1.06	78	1.16
	PLAN C	0	.	18	0.00	19	1.29

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN A	0	.	10	0.01	9	0.01
	PLAN BD	5	0.00	75	0.00	78	0.01
	PLAN C	0	.	18	0.00	19	0.02
II	PLAN A	0	.	10	0.02	9	0.03
	PLAN BD	5	0.00	75	0.01	78	0.01
	PLAN C	0	.	18	0.00	19	0.01
III	PLAN A	0	.	10	0.01	9	0.02
	PLAN BD	5	0.00	75	0.01	78	0.01
	PLAN C	0	.	18	0.00	19	0.01

Polio Protocol 01

TABLE 5

STOOL SPECIMENS (b) (4) IgA ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	PLAN A	0/ . (0.0)	2/10 (20.0)	3/ 9 (33.3)
	PLAN BD	0/ . (0.0)	5/74 (6.8)	4/77 (5.2)
	PLAN C	0/ . (0.0)	1/18 (5.6)	3/19 (15.8)
II	PLAN A	0/ . (0.0)	1/10 (10.0)	1/ 9 (11.1)
	PLAN BD	0/ . (0.0)	9/74 (12.2)	8/77 (10.4)
	PLAN C	0/ . (0.0)	3/18 (16.7)	7/19 (36.8)
III	PLAN A	0/ . (0.0)	3/10 (30.0)	3/ 9 (33.3)
	PLAN BD	0/ . (0.0)	8/74 (10.8)	15/77 (19.5)
	PLAN C	0/ . (0.0)	3/18 (16.7)	7/19 (36.8)
ANY	PLAN A	0/ . (0.0)	3/10 (30.0)	3/10 (30.0)
	PLAN BD	0/ . (0.0)	13/85 (15.3)	16/85 (18.8)
	PLAN C	0/ . (0.0)	4/19 (21.1)	7/19 (36.8)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	PLAN A	0	.	10	1.52	9	2.00
	PLAN BD	6	0.00	74	1.17	77	1.12
	PLAN C	0	.	18	1.13	19	1.39
II	PLAN A	0	.	10	1.23	9	1.36
	PLAN BD	6	0.00	74	1.35	77	1.29
	PLAN C	0	.	18	1.47	19	2.23
III	PLAN A	0	.	10	1.87	9	2.33
	PLAN BD	6	0.00	74	1.30	77	1.55
	PLAN C	0	.	18	1.53	19	2.49

TABLE 6

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
AGE 6 - 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months		4 Months		5 Months	
I	Plan A	9/10	(90.0)	7/10	(70.0)	10/10	(100.0)
	Plan BD	58/70	(82.9)	43/69	(62.3)	66/68	(97.1)
	Plan C	13/15	(86.7)	12/15	(80.0)	14/15	(93.3)
II	Plan A	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
	Plan BD	64/70	(91.4)	66/69	(95.7)	68/68	(100.0)
	Plan C	14/15	(93.3)	15/15	(100.0)	15/15	(100.0)
III	Plan A	9/10	(90.0)	10/10	(100.0)	10/10	(100.0)
	Plan BD	53/70	(75.7)	55/69	(79.7)	66/68	(97.1)
	Plan C	11/15	(73.3)	12/15	(80.0)	14/15	(93.3)
ANY	Plan A	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
	Plan BD	70/70	(100.0)	69/70	(98.6)	68/70	(97.1)
	Plan C	14/15	(93.3)	15/15	(100.0)	15/15	(100.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	10	25.81	10	28.35	10	259.92
	Plan BD	70	22.55	69	7.75	68	213.62
	Plan C	15	22.30	15	9.56	15	228.14
II	Plan A	10	60.63	10	519.84	10	3151.73
	Plan BD	70	48.79	69	31.44	68	666.63
	Plan C	15	94.82	15	40.00	15	2228.61
III	Plan A	10	27.66	10	52.78	10	735.17
	Plan BD	70	14.94	69	16.77	68	748.45
	Plan C	15	9.87	15	15.90	15	78.82

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	10	0.30	10	0.33	10	3.03
	Plan BD	70	0.26	69	0.09	68	2.49
	Plan C	15	0.26	15	0.11	15	2.66
II	Plan A	10	0.34	10	2.94	10	17.81
	Plan BD	70	0.28	69	0.18	68	3.77
	Plan C	15	0.54	15	0.23	15	12.59
III	Plan A	10	0.28	10	0.53	10	7.35
	Plan BD	70	0.15	69	0.17	68	7.48
	Plan C	15	0.10	15	0.16	15	0.79

TABLE 7

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
AGE > 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months		4 Months		5 Months	
I	Plan BD	8/15	(53.3)	10/15	(66.7)	15/15	(100.0)
	Plan C	2/ 4	(50.0)	4/ 4	(100.0)	4/ 4	(100.0)
II	Plan BD	8/15	(53.3)	14/15	(93.3)	15/15	(100.0)
	Plan C	4/ 4	(100.0)	4/ 4	(100.0)	4/ 4	(100.0)
III	Plan BD	9/15	(60.0)	13/15	(86.7)	15/15	(100.0)
	Plan C	3/ 4	(75.0)	3/ 4	(75.0)	4/ 4	(100.0)
ANY	Plan BD	13/15	(86.7)	15/15	(100.0)	15/15	(100.0)
	Plan C	4/ 4	(100.0)	4/ 4	(100.0)	4/ 4	(100.0)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan BD	15	4.72	15	8.86	15	531.99
	Plan C	4	10.64	4	33.64	4	452.55
II	Plan BD	15	5.42	15	41.27	15	2681.07
	Plan C	4	40.00	4	33.64	4	2152.69
III	Plan BD	15	7.96	15	22.30	15	1940.12
	Plan C	4	11.25	4	26.75	4	905.10

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan BD	15	0.06	15	0.10	15	6.21
	Plan C	4	0.12	4	0.39	4	5.28
II	Plan BD	15	0.03	15	0.23	15	15.15
	Plan C	4	0.23	4	0.19	4	12.16
III	Plan BD	15	0.08	15	0.22	15	19.40
	Plan C	4	0.11	4	0.27	4	9.05

TABLE 8

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES
AGE 6 - 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	3/ 9 (33.3)	5/10 (50.0)
	Plan BD	0/ . (0.0)	1/67 (1.5)	23/65 (35.4)
	Plan C	0/ . (0.0)	0/67 (0.0)	8/15 (53.3)
II	Plan A	0/ . (0.0)	7/ 9 (77.8)	7/10 (70.0)
	Plan BD	0/ . (0.0)	1/67 (1.5)	34/65 (52.3)
	Plan C	0/ . (0.0)	2/14 (14.3)	14/15 (93.3)
III	Plan A	0/ . (0.0)	2/ 9 (22.2)	5/10 (50.0)
	Plan BD	0/ . (0.0)	2/67 (3.0)	29/65 (44.6)
	Plan C	0/ . (0.0)	1/14 (7.1)	6/15 (40.0)
ANY	Plan A	0/ . (0.0)	7/10 (70.0)	7/10 (70.0)
	Plan BD	0/ . (0.0)	3/70 (4.3)	41/70 (58.6)
	Plan C	0/ . (0.0)	3/15 (20.0)	14/15 (93.3)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	9	1.71	10	3.03
	Plan BD	1	1.00	67	1.02	65	1.96
	Plan C	0	1.00	14	1.00	15	3.82
II	Plan A	0	.	9	8.00	10	9.19
	Plan BD	1	1.00	67	1.03	65	3.23
	Plan C	0	1.00	14	1.22	15	18.38
III	Plan A	0	.	9	2.00	10	5.28
	Plan BD	1	1.00	67	1.04	65	3.13
	Plan C	0	1.00	14	1.10	15	2.19

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	9	0.02	10	0.04
	Plan BD	1	0.01	67	0.01	65	0.02
	Plan C	0	0.01	14	0.01	15	0.04
II	Plan A	0	.	9	0.05	10	0.05
	Plan BD	1	0.01	67	0.01	65	0.02
	Plan C	0	0.01	14	0.01	15	0.10
III	Plan A	0	.	9	0.02	10	0.05
	Plan BD	1	0.01	67	0.01	65	0.03
	Plan C	0	0.01	14	0.01	15	0.02

TABLE 9

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES
AGE) 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan BD	0/ . (0.0)	0/ . (0.0)	4/14 (28.6)
	Plan C	0/ . (0.0)	0/ . (0.0)	1/ 4 (25.0)
II	Plan BD	0/ . (0.0)	0/ . (0.0)	8/14 (57.1)
	Plan C	0/ . (0.0)	0/ . (0.0)	3/ 4 (75.0)
III	Plan BD	0/ . (0.0)	0/ . (0.0)	4/14 (28.6)
	Plan C	0/ . (0.0)	0/ . (0.0)	2/ 4 (50.0)
ANY	Plan BD	0/ . (0.0)	0/ . (0.0)	8/15 (53.3)
	Plan C	0/ . (0.0)	0/ . (0.0)	3/ 4 (75.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan BD	5	1.00	15	1.00	14	1.64
	Plan C	0	1.00	4	1.00	4	1.41
II	Plan BD	5	1.00	15	1.00	14	3.62
	Plan C	0	1.00	4	1.00	4	22.63
III	Plan BD	5	1.00	15	1.00	14	1.72
	Plan C	0	1.00	4	1.00	4	3.36

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan BD	5	0.01	15	0.01	14	0.02
	Plan C	0	0.01	4	0.01	4	0.02
II	Plan BD	5	0.01	15	0.01	14	0.02
	Plan C	0	0.01	4	0.01	4	0.13
III	Plan BD	5	0.01	15	0.01	14	0.02
	Plan C	0	0.01	4	0.01	4	0.03

TABLE 10

Polio Protocol 01

STOOL SPECIMENS NEUTRALIZING ANTIBODIES
AGE 6 - 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	1/10 (10.0)	1/ 9 (11.1)
	Plan BD	0/ . (0.0)	0/10 (0.0)	4/63 (6.3)
	Plan C	0/ . (0.0)	0/ . (0.0)	2/15 (13.3)
II	Plan A	0/ . (0.0)	4/10 (40.0)	5/ 9 (55.6)
	Plan BD	0/ . (0.0)	3/61 (4.9)	8/63 (12.7)
	Plan C	0/ . (0.0)	0/61 (0.0)	5/15 (33.3)
III	Plan A	0/ . (0.0)	1/10 (10.0)	3/ 9 (33.3)
	Plan BD	0/ . (0.0)	2/61 (3.3)	5/63 (7.9)
	Plan C	0/ . (0.0)	0/61 (0.0)	1/15 (6.7)
ANY	Plan A	0/ . (0.0)	4/10 (40.0)	5/10 (50.0)
	Plan BD	0/ . (0.0)	4/70 (5.7)	14/70 (20.0)
	Plan C	0/ . (0.0)	0/70 (0.0)	5/15 (33.3)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	10	1.15	9	1.17
	Plan BD	1	1.00	61	1.00	63	1.13
	Plan C	0	1.00	14	1.00	15	1.45
II	Plan A	0	.	10	3.73	9	5.04
	Plan BD	1	1.00	61	1.10	63	1.25
	Plan C	0	1.00	14	1.00	15	2.41
III	Plan A	0	.	10	1.15	9	1.59
	Plan BD	1	1.00	61	1.07	63	1.17
	Plan C	0	1.00	14	1.00	15	1.26

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	10	0.01	9	0.01
	Plan BD	1	0.01	61	0.01	63	0.01
	Plan C	0	0.01	14	0.01	15	0.02
II	Plan A	0	.	10	0.02	9	0.03
	Plan BD	1	0.01	61	0.01	63	0.01
	Plan C	0	0.01	14	0.01	15	0.01
III	Plan A	0	.	10	0.01	9	0.02
	Plan BD	1	0.01	61	0.01	63	0.01
	Plan C	0	0.01	14	0.01	15	0.01

TABLE 11

Polio Protocol 01

STOOL SPECIMENS NEUTRALIZING ANTIBODIES
AGE) 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan BD	0/ . (0.0)	0/ . (0.0)	0/ . (0.0)
	Plan C	0/ . (0.0)	0/ . (0.0)	1/ 4 (25.0)
II	Plan BD	0/ . (0.0)	0/ . (0.0)	1/15 (6.7)
	Plan C	0/ . (0.0)	0/ . (0.0)	3/ 4 (75.0)
III	Plan BD	0/ . (0.0)	0/ . (0.0)	1/15 (6.7)
	Plan C	0/ . (0.0)	0/ . (0.0)	1/ 4 (25.0)
ANY	Plan BD	0/ . (0.0)	0/ . (0.0)	2/15 (13.3)
	Plan C	0/ . (0.0)	0/ . (0.0)	3/ 4 (75.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan BD	4	1.00	14	1.00	15	1.00
	Plan C	0	1.00	4	1.00	4	1.41
II	Plan BD	4	1.00	14	1.00	15	1.10
	Plan C	0	1.00	4	1.00	4	2.83
III	Plan BD	4	1.00	14	1.00	15	1.15
	Plan C	0	1.00	4	1.00	4	1.41

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan BD	4	0.01	14	0.01	15	0.01
	Plan C	0	0.01	4	0.01	4	0.02
II	Plan BD	4	0.01	14	0.01	15	0.01
	Plan C	0	0.01	4	0.01	4	0.02
III	Plan BD	4	0.01	14	0.01	15	0.01
	Plan C	0	0.01	4	0.01	4	0.01

TABLE 12

Polio Protocol v1

NASOPHARYNGEAL SECRETIONS (b) (4) IgA ANTIBODIES
AGE 6 - 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	7/ 9 (77.8)	6/10 (60.0)
	Plan BD	0/ . (0.0)	30/67 (44.8)	38/66 (57.6)
	Plan C	0/ . (0.0)	8/14 (57.1)	12/15 (80.0)
II	Plan A	0/ . (0.0)	7/ 9 (77.8)	6/10 (60.0)
	Plan BD	0/ . (0.0)	31/67 (46.3)	41/66 (62.1)
	Plan C	0/ . (0.0)	8/14 (57.1)	12/15 (80.0)
III	Plan A	0/ . (0.0)	7/ 9 (77.8)	8/10 (80.0)
	Plan BD	0/ . (0.0)	31/67 (46.3)	40/66 (60.6)
	Plan C	0/ . (0.0)	9/14 (64.3)	13/15 (86.7)
ANY	Plan A	0/ . (0.0)	7/10 (70.0)	8/10 (80.0)
	Plan BD	0/ . (0.0)	36/70 (51.4)	44/70 (62.9)
	Plan C	0/ . (0.0)	9/15 (60.0)	13/15 (86.7)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	9	0.00	10	7.46
	Plan BD	1	1.00	67	3.46	66	6.09
	Plan C	0	1.00	14	0.00	15	14.59
II	Plan A	0	.	9	8.00	10	7.46
	Plan BD	1	1.00	67	3.96	66	6.48
	Plan C	0	1.00	14	5.38	15	13.30
III	Plan A	0	.	9	9.33	10	13.93
	Plan BD	1	1.00	67	3.88	66	6.69
	Plan C	0	1.00	14	7.61	15	19.25

TABLE 13

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS (b)(4) IgA ANTIBODIES
AGE) 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan BD	0/ . (0.0)	3/15 (20.0)	7/14 (50.0)
	Plan C	0/ . (0.0)	1/ 4 (25.0)	3/ 4 (75.0)
II	Plan BD	0/ . (0.0)	2/15 (13.3)	8/14 (57.1)
	Plan C	0/ . (0.0)	1/ 4 (25.0)	4/ 4 (100.0)
III	Plan BD	0/ . (0.0)	3/15 (20.0)	9/14 (64.3)
	Plan C	0/ . (0.0)	1/ 4 (25.0)	4/ 4 (100.0)
ANY	Plan BD	0/ . (0.0)	3/15 (20.0)	9/15 (60.0)
	Plan C	0/ . (0.0)	1/ 4 (25.0)	4/ 4 (100.0)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan BD	5	1.00	15	2.00	14	4.64
	Plan C	0	1.00	4	0.00	4	16.00
II	Plan BD	5	1.00	15	1.45	14	4.20
	Plan C	0	1.00	4	1.68	4	38.05
III	Plan BD	5	1.00	15	1.66	14	5.12
	Plan C	0	1.00	4	2.00	4	32.00

TABLE 14

Polio Protocol 01

STOOL SPECIMENS (b) (4) IgA ANTIBODIES
AGE 6 - 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	2/10 (20.0)	3/ 9 (33.3)
	Plan BD	0/ . (0.0)	4/60 (6.7)	4/63 (6.3)
	Plan C	0/ . (0.0)	1/14 (7.1)	2/15 (13.3)
II	Plan A	0/ . (0.0)	1/10 (10.0)	1/ 9 (11.1)
	Plan BD	0/ . (0.0)	6/60 (10.0)	7/63 (11.1)
	Plan C	0/ . (0.0)	3/14 (21.4)	5/15 (33.3)
III	Plan A	0/ . (0.0)	3/10 (30.0)	3/ 9 (33.3)
	Plan BD	0/ . (0.0)	5/60 (8.3)	11/63 (17.5)
	Plan C	0/ . (0.0)	3/14 (21.4)	5/15 (33.3)
ANY	Plan A	0/ . (0.0)	3/10 (30.0)	3/10 (30.0)
	Plan BD	0/ . (0.0)	9/70 (12.9)	12/70 (17.1)
	Plan C	0/ . (0.0)	4/15 (26.7)	5/15 (33.3)

GEOMETRIC MEAN TITERS

TYPE		2 Months		4 Months		5 Months	
		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	10	0.00	9	2.00
	Plan BD	2	1.00	60	1.18	63	1.15
	Plan C	0	1.00	14	0.00	15	1.32
II	Plan A	0	.	10	1.23	9	1.36
	Plan BD	2	1.00	60	1.27	63	1.30
	Plan C	0	1.00	14	1.64	15	2.09
III	Plan A	0	.	10	1.87	9	2.33
	Plan BD	2	1.00	60	1.22	63	1.50
	Plan C	0	1.00	14	1.72	15	2.30

TABLE 15

Polio Protocol 01

STOOL SPECIMENS (b) (4) IgA ANTIBODIES
AGE) 13 WEEKS

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan BD	0/ . (0.0)	1/14 (7.1)	0/ . (0.0)
	Plan C	0/ . (0.0)	0/14 (0.0)	1/ 4 (25.0)
II	Plan BD	0/ . (0.0)	3/14 (21.4)	1/14 (7.1)
	Plan C	0/ . (0.0)	0/14 (0.0)	2/ 4 (50.0)
III	Plan BD	0/ . (0.0)	3/14 (21.4)	4/14 (28.6)
	Plan C	0/ . (0.0)	0/14 (0.0)	2/ 4 (50.0)
ANY	Plan BD	0/ . (0.0)	4/15 (26.7)	4/15 (26.7)
	Plan C	0/ . (0.0)	0/15 (0.0)	2/ 4 (50.0)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan BD	4	1.00	14	1.16	14	1.00
	Plan C	0	1.00	4	0.00	4	1.68
II	Plan BD	4	1.00	14	1.72	14	1.22
	Plan C	0	1.00	4	1.00	4	2.83
III	Plan BD	4	1.00	14	1.72	14	1.81
	Plan C	0	1.00	4	1.00	4	3.36

TABLE 16

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
PLAN BD

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months		4 Months		5 Months	
I	PREME	12/19	(63.2)	8/19	(42.1)	19/19	(100.0)
	TERM	54/66	(81.8)	45/65	(69.2)	62/64	(96.9)
II	PREME	16/19	(84.2)	16/19	(84.2)	19/19	(100.0)
	TERM	56/66	(84.8)	64/65	(98.5)	64/64	(100.0)
III	PREME	15/19	(78.9)	14/19	(73.7)	19/19	(100.0)
	TERM	47/66	(71.2)	54/65	(83.1)	62/64	(96.9)
ANY	PREME	18/19	(94.7)	19/19	(100.0)	19/19	(100.0)
	TERM	65/66	(98.5)	65/66	(98.5)	64/66	(97.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	PREME	19	6.88	19	4.39	19	308.54
	TERM	66	22.25	65	9.44	64	237.21
II	PREME	19	20.02	19	24.92	19	1147.31
	TERM	66	38.27	65	35.83	64	786.23
III	PREME	19	14.78	19	15.15	19	888.74
	TERM	66	12.99	65	18.45	64	889.13

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	PREME	19	0.08	19	0.05	19	3.60
	TERM	66	0.26	65	0.11	64	2.77
II	PREME	19	0.11	19	0.14	19	6.48
	TERM	66	0.22	65	0.20	64	4.44
III	PREME	19	0.15	19	0.15	19	8.89
	TERM	66	0.13	65	0.18	64	8.89

TABLE 17

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months		4 Months		5 Months	
I	Plan A	2/ 2	(100.0)	2/ 2	(100.0)	2/ 2	(100.0)
	Plan BD	14/19	(73.7)	10/18	(55.6)	18/18	(100.0)
	Plan C	2/ 3	(66.7)	3/ 3	(100.0)	3/ 3	(100.0)
II	Plan A	2/ 2	(100.0)	2/ 2	(100.0)	2/ 2	(100.0)
	Plan BD	16/19	(84.2)	17/18	(94.4)	18/18	(100.0)
	Plan C	3/ 3	(100.0)	3/ 3	(100.0)	3/ 3	(100.0)
III	Plan A	1/ 2	(50.0)	2/ 2	(100.0)	2/ 2	(100.0)
	Plan BD	12/19	(63.2)	13/18	(72.2)	18/18	(100.0)
	Plan C	2/ 3	(66.7)	2/ 3	(66.7)	3/ 3	(100.0)
ANY	Plan A	2/ 2	(100.0)	2/ 2	(100.0)	2/ 2	(100.0)
	Plan BD	19/19	(100.0)	18/19	(94.7)	18/19	(94.7)
	Plan C	3/ 3	(100.0)	3/ 3	(100.0)	3/ 3	(100.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	2	28.28	2	80.00	2	640.00
	Plan BD	19	13.09	18	4.89	18	570.18
	Plan C	3	11.70	3	20.00	3	806.35
II	Plan A	2	40.00	2	452.55	2	14481.55
	Plan BD	19	22.34	18	32.59	18	1810.19
	Plan C	3	50.40	3	25.20	3	1612.70
III	Plan A	2	6.32	2	160.00	2	2560.00
	Plan BD	19	8.56	18	13.29	18	1185.12
	Plan C	3	5.85	3	7.37	3	507.97

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	2	0.33	2	0.93	2	7.47
	Plan BD	19	0.15	18	0.06	18	6.65
	Plan C	3	0.14	3	0.23	3	9.41
II	Plan A	2	0.23	2	2.56	2	81.82
	Plan BD	19	0.13	18	0.18	18	10.23
	Plan C	3	0.28	3	0.14	3	9.11
III	Plan A	2	0.06	2	1.60	2	25.60
	Plan BD	19	0.09	18	0.13	18	11.85
	Plan C	3	0.06	3	0.07	3	5.08

TABLE 18

SERUM NEUTRALIZING ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months		4 Months		5 Months	
I	Plan A	7/ 8	(87.5)	5/ 8	(62.5)	8/ 8	(100.0)
	Plan BD	52/66	(78.8)	43/66	(65.2)	63/65	(96.9)
	Plan C	13/16	(81.3)	13/16	(81.3)	15/16	(93.8)
II	Plan A	8/ 8	(100.0)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan BD	56/66	(84.8)	63/66	(95.5)	65/65	(100.0)
	Plan C	15/16	(93.8)	16/16	(100.0)	16/16	(100.0)
III	Plan A	8/ 8	(100.0)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan BD	50/66	(75.8)	55/66	(83.3)	63/65	(96.9)
	Plan C	12/16	(75.0)	13/16	(81.3)	15/16	(93.8)
ANY	Plan A	8/ 8	(100.0)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan BD	64/66	(97.0)	66/66	(100.0)	65/66	(98.5)
	Plan C	15/16	(93.8)	16/16	(100.0)	16/16	(100.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	8	25.22	8	21.87	8	207.49
	Plan BD	66	18.48	66	9.06	65	200.92
	Plan C	16	20.92	16	11.40	16	213.68
II	Plan A	8	67.27	8	538.17	8	2152.69
	Plan BD	66	37.08	66	33.12	65	697.00
	Plan C	16	86.03	16	41.77	16	2347.53
III	Plan A	8	40.00	8	40.00	8	538.17
	Plan BD	66	15.20	66	19.07	65	821.01
	Plan C	16	11.25	16	20.92	16	102.31

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	8	0.29	8	0.26	8	2.42
	Plan BD	66	0.22	66	0.11	65	2.34
	Plan C	16	0.24	16	0.13	16	2.49
II	Plan A	8	0.38	8	3.04	8	12.16
	Plan BD	66	0.21	66	0.19	65	3.94
	Plan C	16	0.49	16	0.24	16	13.26
III	Plan A	8	0.40	8	0.40	8	5.38
	Plan BD	66	0.15	66	0.19	65	8.21
	Plan C	16	0.11	16	0.21	16	1.02

TABLE 19

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	1/ 2 (50.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	0/ 2 (0.0)	9/18 (50.0)
	Plan C	0/ . (0.0)	0/ . (0.0)	2/ 3 (66.7)
II	Plan A	0/ . (0.0)	2/ 2 (100.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	0/ 2 (0.0)	14/18 (77.8)
	Plan C	0/ . (0.0)	0/ . (0.0)	3/ 3 (100.0)
III	Plan A	0/ . (0.0)	1/ 2 (50.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	1/19 (5.3)	11/18 (61.1)
	Plan C	0/ . (0.0)	0/19 (0.0)	2/ 3 (66.7)
ANY	Plan A	0/ . (0.0)	2/ 2 (100.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	1/19 (5.3)	16/19 (84.2)
	Plan C	0/ . (0.0)	0/19 (0.0)	3/ 3 (100.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	2	2.00	2	8.00
	Plan BD	0	.	19	1.00	18	3.05
	Plan C	0	.	3	1.00	3	4.00
II	Plan A	0	.	2	11.31	2	11.31
	Plan BD	0	.	19	1.00	18	6.86
	Plan C	0	.	3	1.00	3	20.16
III	Plan A	0	.	2	11.31	2	11.31
	Plan BD	0	.	19	1.08	18	5.88
	Plan C	0	.	3	1.00	3	6.35

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	2	0.02	2	0.09
	Plan BD	0	.	19	0.01	18	0.04
	Plan C	0	.	3	0.01	3	0.05
II	Plan A	0	.	2	0.06	2	0.06
	Plan BD	0	.	19	0.01	18	0.04
	Plan C	0	.	3	0.01	3	0.11
III	Plan A	0	.	2	0.11	2	0.11
	Plan BD	0	.	19	0.01	18	0.06
	Plan C	0	.	3	0.01	3	0.06

TABLE 20

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	2/ 7 (28.6)	4/ 8 (50.0)
	Plan BD	0/ . (0.0)	1/63 (1.6)	18/61 (29.5)
	Plan C	0/ . (0.0)	0/63 (0.0)	7/16 (43.8)
II	Plan A	0/ . (0.0)	5/ 7 (71.4)	6/ 8 (75.0)
	Plan BD	0/ . (0.0)	1/63 (1.6)	28/61 (45.9)
	Plan C	0/ . (0.0)	2/15 (13.3)	14/16 (87.5)
III	Plan A	0/ . (0.0)	1/ 7 (14.3)	4/ 8 (50.0)
	Plan BD	0/ . (0.0)	1/63 (1.6)	22/61 (36.1)
	Plan C	0/ . (0.0)	1/15 (6.7)	6/16 (37.5)
ANY	Plan A	0/ . (0.0)	5/ 8 (62.5)	6/ 8 (75.0)
	Plan BD	0/ . (0.0)	2/66 (3.0)	33/66 (50.0)
	Plan C	0/ . (0.0)	3/16 (18.8)	14/16 (87.5)

GEOMETRIC MEAN TITERS

TYPE		2 Months		4 Months		5 Months	
		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	7	1.64	8	2.38
	Plan BD	6	1.00	63	1.02	61	1.65
	Plan C	0	1.00	15	1.00	16	2.95
II	Plan A	0	.	7	7.25	8	8.72
	Plan BD	6	1.00	63	1.03	61	2.66
	Plan C	0	1.00	15	1.20	16	19.03
III	Plan A	0	.	7	1.22	8	4.36
	Plan BD	6	1.00	63	1.02	61	2.27
	Plan C	0	1.00	15	1.10	16	2.00

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months		4 Months		5 Months	
		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	7	0.02	8	0.03
	Plan BD	6	0.01	63	0.01	61	0.02
	Plan C	0	0.01	15	0.01	16	0.03
II	Plan A	0	.	7	0.04	8	0.05
	Plan BD	6	0.01	63	0.01	61	0.02
	Plan C	0	0.01	15	0.01	16	0.11
III	Plan A	0	.	7	0.01	8	0.04
	Plan BD	6	0.01	63	0.01	61	0.02
	Plan C	0	0.01	15	0.01	16	0.02

TABLE 21

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS (b)(4) IgA ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	1/ 2 (50.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	9/19 (47.4)	14/18 (77.8)
	Plan C	0/ . (0.0)	1/ 3 (33.3)	2/ 3 (66.7)
II	Plan A	0/ . (0.0)	1/ 2 (50.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	9/19 (47.4)	15/18 (83.3)
	Plan C	0/ . (0.0)	1/ 3 (33.3)	3/ 3 (100.0)
III	Plan A	0/ . (0.0)	1/ 2 (50.0)	2/ 2 (100.0)
	Plan BD	0/ . (0.0)	9/19 (47.4)	15/18 (83.3)
	Plan C	0/ . (0.0)	1/ 3 (33.3)	3/ 3 (100.0)
ANY	Plan A	0/ . (0.0)	1/ 2 (50.0)	2/ 2 (100.0)
	Plan BD	0/ . (0.0)	9/19 (47.4)	15/19 (78.9)
	Plan C	0/ . (0.0)	1/ 3 (33.3)	3/ 3 (100.0)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	2	0.00	2	4.00
	Plan BD	0	.	19	0.00	18	13.72
	Plan C	0	.	3	0.00	3	20.16
II	Plan A	0	.	2	5.66	2	4.00
	Plan BD	0	.	19	4.80	18	14.81
	Plan C	0	.	3	2.52	3	25.40
III	Plan A	0	.	2	4.00	2	16.00
	Plan BD	0	.	19	4.63	18	16.00
	Plan C	0	.	3	2.52	3	40.32

Polio Protocol 01

TABLE 22

NASOPHARYNGEAL SECRETIONS (b) (4) IgA ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	6/ 7 (85.7)	5/ 8 (62.5)
	Plan BD	0/ . (0.0)	24/63 (38.1)	31/62 (50.0)
	Plan C	0/ . (0.0)	8/15 (53.3)	13/16 (81.3)
II	Plan A	0/ . (0.0)	6/ 7 (85.7)	5/ 8 (62.5)
	Plan BD	0/ . (0.0)	24/63 (38.1)	34/62 (54.8)
	Plan C	0/ . (0.0)	8/15 (53.3)	13/16 (81.3)
III	Plan A	0/ . (0.0)	6/ 7 (85.7)	6/ 8 (75.0)
	Plan BD	0/ . (0.0)	25/63 (39.7)	34/62 (54.8)
	Plan C	0/ . (0.0)	9/15 (60.0)	14/16 (87.5)
ANY	Plan A	0/ . (0.0)	6/ 8 (75.0)	6/ 8 (75.0)
	Plan BD	0/ . (0.0)	30/66 (45.5)	38/66 (57.6)
	Plan C	0/ . (0.0)	9/16 (56.3)	14/16 (87.5)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	7	0.00	8	8.72
	Plan BD	6	1.00	63	2.75	62	4.52
	Plan C	0	1.00	15	0.00	16	14.05
II	Plan A	0	.	7	8.83	8	8.72
	Plan BD	6	1.00	63	2.94	62	4.63
	Plan C	0	1.00	15	4.59	16	15.32
III	Plan A	0	.	7	11.89	8	13.45
	Plan BD	6	1.00	63	3.00	62	4.89
	Plan C	0	1.00	15	6.65	16	19.03

TABLE 23

Polio Protocol 01

STOOL SPECIMENS NEUTRALIZING ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	1/ 2 (50.0)	0/ . (0.0)
	Plan BD	0/ . (0.0)	0/ 2 (0.0)	2/17 (11.8)
	Plan C	0/ . (0.0)	0/ . (0.0)	1/ 3 (33.3)
II	Plan A	0/ . (0.0)	1/ 2 (50.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	0/ 2 (0.0)	2/17 (11.8)
	Plan C	0/ . (0.0)	0/ . (0.0)	2/ 3 (66.7)
III	Plan A	0/ . (0.0)	1/ 2 (50.0)	0/ . (0.0)
	Plan BD	0/ . (0.0)	1/18 (5.6)	2/17 (11.8)
	Plan C	0/ . (0.0)	0/18 (0.0)	1/ 3 (33.3)
ANY	Plan A	0/ . (0.0)	1/ 2 (50.0)	1/ 2 (50.0)
	Plan BD	0/ . (0.0)	1/19 (5.3)	5/19 (26.3)
	Plan C	0/ . (0.0)	0/19 (0.0)	2/ 3 (66.7)

GEOMETRIC MEAN TITERS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	2	2.00	2	1.00
	Plan BD	0	.	18	1.00	17	1.33
	Plan C	0	.	3	1.00	3	1.59
II	Plan A	0	.	2	5.66	2	2.83
	Plan BD	0	.	18	1.00	17	1.18
	Plan C	0	.	3	1.00	3	2.52
III	Plan A	0	.	2	2.00	2	1.00
	Plan BD	0	.	18	1.08	17	1.18
	Plan C	0	.	3	1.00	3	1.59

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		2 Months		4 Months		5 Months	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	2	0.02	2	0.01
	Plan BD	0	.	18	0.01	17	0.02
	Plan C	0	.	3	0.01	3	0.02
II	Plan A	0	.	2	0.03	2	0.02
	Plan BD	0	.	18	0.01	17	0.01
	Plan C	0	.	3	0.01	3	0.01
III	Plan A	0	.	2	0.02	2	0.01
	Plan BD	0	.	18	0.01	17	0.01
	Plan C	0	.	3	0.01	3	0.02

Polio Protocol 01

TABLE 24

STOOL SPECIMENS NEUTRALIZING ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	0/ . (0.0)	1/ 7 (14.3)
	Plan BD	0/ . (0.0)	0/ . (0.0)	2/61 (3.3)
	Plan C	0/ . (0.0)	0/ . (0.0)	2/16 (12.5)
II	Plan A	0/ . (0.0)	3/ 8 (37.5)	4/ 7 (57.1)
	Plan BD	0/ . (0.0)	3/57 (5.3)	7/61 (11.5)
	Plan C	0/ . (0.0)	0/57 (0.0)	6/16 (37.5)
III	Plan A	0/ . (0.0)	0/ . (0.0)	3/ 7 (42.9)
	Plan BD	0/ . (0.0)	1/57 (1.8)	4/61 (6.6)
	Plan C	0/ . (0.0)	0/57 (0.0)	1/16 (6.3)
ANY	Plan A	0/ . (0.0)	3/ 8 (37.5)	4/ 8 (50.0)
	Plan BD	0/ . (0.0)	3/66 (4.5)	11/66 (16.7)
	Plan C	0/ . (0.0)	0/66 (0.0)	6/16 (37.5)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	8	1.00	7	1.22
	Plan BD	5	1.00	57	1.00	61	1.05
	Plan C	0	1.00	15	1.00	16	1.41
II	Plan A	0	.	8	3.36	7	5.94
	Plan BD	5	1.00	57	1.11	61	1.23
	Plan C	0	1.00	15	1.00	16	2.48
III	Plan A	0	.	8	1.00	7	1.81
	Plan BD	5	1.00	57	1.05	61	1.16
	Plan C	0	1.00	15	1.00	16	1.24

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	8	0.01	7	0.01
	Plan BD	5	0.01	57	0.01	61	0.01
	Plan C	0	0.01	15	0.01	16	0.02
II	Plan A	0	.	8	0.02	7	0.03
	Plan BD	5	0.01	57	0.01	61	0.01
	Plan C	0	0.01	15	0.01	16	0.01
III	Plan A	0	.	8	0.01	7	0.02
	Plan BD	5	0.01	57	0.01	61	0.01
	Plan C	0	0.01	15	0.01	16	0.01

TABLE 25

Polio Protocol 01

STOOL SPECIMENS (b) (4) IgA ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	1/ 2 (50.0)	0/ . (0.0)
	Plan BD	0/ . (0.0)	1/18 (5.6)	0/ . (0.0)
	Plan C	0/ . (0.0)	0/18 (0.0)	1/ 3 (33.3)
II	Plan A	0/ . (0.0)	0/ . (0.0)	0/ . (0.0)
	Plan BD	0/ . (0.0)	2/18 (11.1)	1/17 (5.9)
	Plan C	0/ . (0.0)	0/18 (0.0)	1/ 3 (33.3)
III	Plan A	0/ . (0.0)	1/ 2 (50.0)	0/ . (0.0)
	Plan BD	0/ . (0.0)	0/ 2 (0.0)	1/17 (5.9)
	Plan C	0/ . (0.0)	0/ . (0.0)	1/ 3 (33.3)
ANY	Plan A	0/ . (0.0)	1/ 2 (50.0)	0/ . (0.0)
	Plan BD	0/ . (0.0)	3/19 (15.8)	1/19 (5.3)
	Plan C	0/ . (0.0)	0/19 (0.0)	1/ 3 (33.3)

GEOMETRIC MEAN TITERS

TYPE		2 Months N	2 Months GMT	4 Months N	4 Months GMT	5 Months N	5 Months GMT
I	Plan A	0	.	2	0.00	2	1.00
	Plan BD	0	.	18	0.00	17	1.00
	Plan C	0	.	3	0.00	3	2.00
II	Plan A	0	.	2	1.00	2	1.00
	Plan BD	0	.	18	1.31	17	1.13
	Plan C	0	.	3	1.00	3	2.00
III	Plan A	0	.	2	2.83	2	1.00
	Plan BD	0	.	18	1.00	17	1.13
	Plan C	0	.	3	1.00	3	2.52

Polio Protocol 01

STOOL SPECIMENS (b) (4) IgA ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		2 Months	4 Months	5 Months
I	Plan A	0/ . (0.0)	1/ 8 (12.5)	3/ 7 (42.9)
	Plan BD	0/ . (0.0)	4/56 (7.1)	4/60 (6.7)
	Plan C	0/ . (0.0)	1/15 (6.7)	2/16 (12.5)
II	Plan A	0/ . (0.0)	1/ 8 (12.5)	1/ 7 (14.3)
	Plan BD	0/ . (0.0)	7/56 (12.5)	7/60 (11.7)
	Plan C	0/ . (0.0)	3/15 (20.0)	6/16 (37.5)
III	Plan A	0/ . (0.0)	2/ 8 (25.0)	3/ 7 (42.9)
	Plan BD	0/ . (0.0)	8/56 (14.3)	14/60 (23.3)
	Plan C	0/ . (0.0)	3/15 (20.0)	6/16 (37.5)
ANY	Plan A	0/ . (0.0)	2/ 8 (25.0)	3/ 8 (37.5)
	Plan BD	0/ . (0.0)	10/66 (15.2)	15/66 (22.7)
	Plan C	0/ . (0.0)	4/16 (25.0)	6/16 (37.5)

GEOMETRIC MEAN TITERS

TYPE		2 Months		4 Months		5 Months	
		N	GMT	N	GMT	N	GMT
I	Plan A	0	.	8	0.00	7	2.44
	Plan BD	6	1.00	56	1.19	60	1.16
	Plan C	0	1.00	15	0.00	16	1.30
II	Plan A	0	.	8	1.30	7	1.49
	Plan BD	6	1.00	56	1.36	60	1.33
	Plan C	0	1.00	15	1.59	16	2.28
III	Plan A	0	.	8	1.68	7	2.97
	Plan BD	6	1.00	56	1.41	60	1.70
	Plan C	0	1.00	15	1.66	16	2.48

TABLE 27

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1		Visit 2		Visit 3	
I	PLAN F1	14/15	(93.3)	14/15	(93.3)	15/15	(100.0)
	PLAN F2	15/15	(100.0)	15/15	(100.0)	15/15	(100.0)
II	PLAN F1	14/15	(93.3)	15/15	(100.0)	15/15	(100.0)
	PLAN F2	15/15	(100.0)	15/15	(100.0)	15/15	(100.0)
III	PLAN F1	14/15	(93.3)	15/15	(100.0)	15/15	(100.0)
	PLAN F2	14/15	(93.3)	15/15	(100.0)	15/15	(100.0)
ANY	PLAN F1	14/15	(93.3)	15/15	(100.0)	15/15	(100.0)
	PLAN F2	15/15	(100.0)	15/15	(100.0)	15/15	(100.0)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	172.90	15	4816.60	15	4888.79
	PLAN F2	15	335.13	15	4003.74	15	5615.74
II	PLAN F1	15	250.23	15	7760.48	15	12319.00
	PLAN F2	15	531.99	15	17828.90	15	17828.88
III	PLAN F1	15	143.72	15	13511.81	15	17828.90
	PLAN F2	15	345.80	15	14150.80	15	19555.19

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	2.02	15	56.21	15	57.05
	PLAN F2	15	3.91	15	46.72	15	65.54
II	PLAN F1	15	1.41	15	43.85	15	69.60
	PLAN F2	15	3.01	15	100.73	15	100.73
III	PLAN F1	15	1.44	15	135.12	15	178.29
	PLAN F2	15	3.46	15	141.51	15	195.55

TABLE 28

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	0/15 (0.0)	11/15 (73.3)	8/15 (53.3)
	PLAN F2	4/15 (26.7)	9/15 (60.0)	10/15 (66.7)
II	PLAN F1	2/15 (13.3)	12/15 (80.0)	10/15 (66.7)
	PLAN F2	1/15 (6.7)	12/15 (80.0)	10/15 (66.7)
III	PLAN F1	4/15 (26.7)	13/15 (86.7)	14/15 (93.3)
	PLAN F2	6/15 (40.0)	12/15 (80.0)	11/15 (73.3)
ANY	PLAN F1	5/15 (33.3)	14/15 (93.3)	14/15 (93.3)
	PLAN F2	8/15 (53.3)	14/15 (93.3)	14/15 (93.3)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	6.35	15	6.65
	PLAN F2	15	1.45	15	3.17	15	5.79
II	PLAN F1	15	1.45	15	7.29	15	9.62
	PLAN F2	15	1.15	15	9.19	15	7.64
III	PLAN F1	15	1.74	15	12.70	15	20.16
	PLAN F2	15	2.19	15	10.56	15	11.58

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	0.07	15	0.08
	PLAN F2	15	0.02	15	0.04	15	0.07
II	PLAN F1	15	0.01	15	0.04	15	0.05
	PLAN F2	15	0.01	15	0.05	15	0.04
III	PLAN F1	15	0.02	15	0.13	15	0.20
	PLAN F2	15	0.02	15	0.11	15	0.12

Polio Protocol 01

TABLE 29

STOOL SPECIMENS NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	0/15 (0.0)	3/15 (20.0)	1/15 (6.7)
	PLAN F2	2/15 (13.3)	2/14 (14.3)	2/15 (13.3)
II	PLAN F1	0/15 (0.0)	2/15 (13.3)	1/15 (6.7)
	PLAN F2	2/15 (13.3)	2/14 (14.3)	7/15 (46.7)
III	PLAN F1	0/15 (0.0)	3/15 (20.0)	5/15 (33.3)
	PLAN F2	1/15 (6.7)	7/14 (50.0)	7/15 (46.7)
ANY	PLAN F1	0/15 (0.0)	6/15 (40.0)	5/15 (33.3)
	PLAN F2	3/15 (20.0)	8/15 (53.3)	8/15 (53.3)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	1.32	15	1.20
	PLAN F2	15	1.26	14	1.28	15	1.45
II	PLAN F1	15	0.00	15	1.32	15	1.32
	PLAN F2	15	1.32	14	1.49	15	3.48
III	PLAN F1	15	0.00	15	1.59	15	2.19
	PLAN F2	15	1.15	14	2.97	15	3.48

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	0.02	15	0.01
	PLAN F2	15	0.01	14	0.01	15	0.02
II	PLAN F1	15	0.00	15	0.01	15	0.01
	PLAN F2	15	0.01	14	0.01	15	0.02
III	PLAN F1	15	0.00	15	0.02	15	0.02
	PLAN F2	15	0.01	14	0.03	15	0.03

TABLE 30

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS (b)(4) IgA ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1		Visit 2		Visit 3	
	PLAN F1	8/14	(57.1)	11/15	(73.3)	10/15	(66.7)
I	PLAN F2	10/15	(66.7)	10/15	(66.7)	12/15	(80.0)
	PLAN F1	10/14	(71.4)	10/15	(66.7)	10/15	(66.7)
II	PLAN F2	10/15	(66.7)	10/15	(66.7)	13/15	(86.7)
	PLAN F1	10/14	(71.4)	12/15	(80.0)	11/15	(73.3)
III	PLAN F2	11/15	(73.3)	10/15	(66.7)	14/15	(93.3)
	PLAN F1	10/15	(66.7)	12/15	(80.0)	11/15	(73.3)
ANY	PLAN F2	11/15	(73.3)	10/15	(66.7)	14/15	(93.3)

GEOMETRIC MEAN TITERS

TYPE		Visit 1		Visit 2		Visit 3	
		N	GMT	N	GMT	N	GMT
	PLAN F1	14	8.41	15	8.77	15	13.93
I	PLAN F2	15	12.13	15	6.96	15	10.56
	PLAN F1	14	9.28	15	8.77	15	12.70
II	PLAN F2	15	8.00	15	7.29	15	14.59
	PLAN F1	14	13.79	15	13.30	15	19.25
III	PLAN F2	15	10.56	15	10.08	15	20.16

TABLE 31

Polio Protocol 01

STOOL SPECIMENS (b) (4) IgA ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	3/15 (20.0)	2/15 (13.3)	5/15 (33.3)
	PLAN F2	3/15 (20.0)	1/15 (6.7)	3/15 (20.0)
II	PLAN F1	3/15 (20.0)	4/15 (26.7)	6/15 (40.0)
	PLAN F2	4/15 (26.7)	6/15 (40.0)	5/15 (33.3)
III	PLAN F1	3/15 (20.0)	5/15 (33.3)	6/15 (40.0)
	PLAN F2	3/15 (20.0)	5/15 (33.3)	4/15 (26.7)
ANY	PLAN F1	3/15 (20.0)	5/15 (33.3)	7/15 (46.7)
	PLAN F2	4/15 (26.7)	8/15 (53.3)	6/15 (40.0)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	1.82	15	1.32	15	2.19
	PLAN F2	15	1.82	15	1.15	15	1.59
II	PLAN F1	15	1.66	15	1.82	15	2.52
	PLAN F2	15	1.91	15	2.30	15	2.19
III	PLAN F1	15	1.82	15	2.19	15	2.52
	PLAN F2	15	1.59	15	2.19	15	2.00

TABLE 32

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)
II	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)
III	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)
ANY	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan F1	7	215.34	7	8400.23	7	7608.30
	Plan F2	5	422.24	5	2940.67	5	5881.34
II	Plan F1	7	430.69	7	6891.02	7	12482.72
	Plan F2	5	211.12	5	8914.46	5	8914.44
III	Plan F1	7	118.88	7	10240.02	7	16800.50
	Plan F2	5	557.15	5	17828.92	5	23525.40

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan F1	7	2.51	7	98.03	7	88.79
	Plan F2	5	4.93	5	34.32	5	68.64
II	Plan F1	7	2.43	7	38.93	7	70.53
	Plan F2	5	1.19	5	50.37	5	50.37
III	Plan F1	7	1.19	7	102.40	7	168.00
	Plan F2	5	5.57	5	178.29	5	235.25

TABLE 33

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1		Visit 2		Visit 3	
I	Plan F1	7/ 8	(87.5)	7/ 8	(87.5)	8/ 8	(100.0)
	Plan F2	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
II	Plan F1	7/ 8	(87.5)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan F2	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
III	Plan F1	7/ 8	(87.5)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan F2	9/10	(90.0)	10/10	(100.0)	10/10	(100.0)
ANY	Plan F1	7/ 8	(87.5)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan F2	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)

GEOMETRIC MEAN TITERS

TYPE		Visit 1		Visit 2		Visit 3	
		N	GMT	N	GMT	N	GMT
I	Plan F1	8	142.68	8	2960.63	8	3319.91
	Plan F2	10	298.57	10	4671.71	10	5487.48
II	Plan F1	8	155.60	8	8610.79	8	12177.50
	Plan F2	10	844.49	10	25213.87	10	25213.84
III	Plan F1	8	169.68	8	17221.64	8	18780.27
	Plan F2	10	272.43	10	12606.92	10	17828.90

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		Visit 1		Visit 2		Visit 3	
		N	GMT	N	GMT	N	GMT
I	Plan F1	8	1.67	8	34.55	8	38.74
	Plan F2	10	3.48	10	54.52	10	64.04
II	Plan F1	8	0.88	8	48.65	8	68.80
	Plan F2	10	4.77	10	142.46	10	142.46
III	Plan F1	8	1.70	8	172.22	8	187.80
	Plan F2	10	2.72	10	126.07	10	178.29

MERIEUX INSTITUTE, INC.

7855 n.w. 12th street, suite #114, miami, florida 33126-1818
p.o. box 52-3980, miami, florida 33152-3980
phone (305) 593-9577 / telex: 807387

April 21, 1989

Dr. Paul Parkman
Director
Center for Biologics Evaluation
and Research
ATTN: Division of Product
Certification, ATTN: HFN-825
Parklawn Building, Room 9B-05
5600 Fishers Lane
Rockville, MD 20857

REFERENCE NO. 83-087

Dear Dr. Parkman:

Enclosed in triplicate is a final summary report of the results of clinical trials on our enhanced Poliovirus Vaccine, inactivated. The data represents the immunogenicity studies of Drs. Pearay Ogra and Howard Faden, State University of New York/Children's Hospital, Buffalo and Drs. Marshall McBean and John Modlin, Johns Hopkins University, Baltimore.

The results of these trials show that the Merieux vaccine has excellent immunogenicity and safety.

Sincerely yours,

Pinya Cohen

Pinya Cohen, Ph.D.
Vice President
Quality Control and
Regulatory Affairs

PC/(b)
89286

4-21-89

MERIEUX INACTIVATED POLIOVIRUS VACCINE

FINAL REPORT OF CLINICAL STUDIES AT

SUNY/CHILDREN'S HOSPITAL, BUFFALO, NEW YORK
JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND

SUMMARY

Two doses of Merieux Inactivated Poliovirus Vaccine (M-IPV) at 2 and 4 months of age, followed by a booster dose at 12 months of age, gave excellent neutralizing antibody responses to three types of poliovirus. IPV and OPV alone produced similar levels of neutralizing antibody and IgA in the nasopharyngeal secretions. A combined schedule of IPV and OPV resulted in a slight priming effect after primary immunization for Type II poliovirus by IPV on mucosal immune response of OPV for neutralizing antibody and IgA in the naso-nasopharyngeal secretions and for IgA in the stool. This priming effect was not seen after immunization with a booster dose.

Merieux IPV induced comparable responses in premature and full term infants.

Single and two dose boosters in adults showed high anamnestic responses in all recipients and that a second dose is unnecessary.

There were no significant adverse reactions.

INTRODUCTION

The Merieux Inactivated Polio Vaccine (M-IPV) produced from continuous cell lines of Vero cells using microcarrier culture has been extensively tested in Finland, Israel, India, Brazil, Indonesia, Mali, France and the United States. This highly purified more potent vaccine has been shown to be safe, highly immunogenic and efficacious when used in a two dose schedule for primary immunization followed by a booster dose.

A clinical trial at Johns Hopkins comparing M-IPV to the oral polio vaccine currently used in the United States, showed that approximately 99% of children had neutralizing antibodies to all three types of polio virus after receiving M-IPV at 2 and 4 months of age, and that a significant boost in titers occurred after the third dose at 18 months of age (Amer. J. Epid. 128: 615-618, 1988). The titers to M-IPV were superior to OPV given in the same 3 dose schedule. This vaccine was made exactly as the Vero cell vaccine intended for license, except the cell substrate for the Johns Hopkins trial was primary monkey kidney cells.

In December 1985, the Office of Biologics requested that 75-100 children and 25-30 adults be immunized according to the United States schedule. In response to this request, clinical studies on children and adults were carried out at

State University of New York/Children's Hospital, Buffalo by Drs. H. Faden and P. Ogra. Supplemental studies on groups of children using three of the four groups tested in Buffalo (only IPV or combined schedules) were initiated at Johns Hopkins by Drs. M. McBean and J. Modlin at a later date.

To meet the FDA request for M-IPV licensure, data are now presented on children and adults from Buffalo and on children only from Baltimore.

METHODS

Details of the methods used are outlined in the protocols already submitted under IND. Merieux IPV Lots Z1102, Z1103, A1243, A0301 and A0304 were used. The general approach was to compare immunogenicity of two primary doses of M-IPV, OPV, or a combined schedule in 2 month old children. Originally the recruitment targets were a minimum of 15-20 children each in Groups A, C and D, and 50-60 children were to be recruited in Group B. These numbers were exceeded for all groups. The groups and vaccine schedules are shown below:

IMMUNIZATION PLAN FOR CHILDREN

GROUP	2 MONTHS	4 MONTHS	12 MONTHS
A	OPV	OPV	OPV
B	IPV	IPV	IPB
C	IPV	OPV	OPV
D	IPV	IPV	OPV

Buffalo enrolled children in all groups; Johns Hopkins enrolled children in all groups except Group A.

Blood samples for antibody determinations were collected at 2 and 4 months of age just prior to administration of vaccine and one month after the second and third doses of vaccine. A detectable serum neutralizing antibody titer was considered >1:10; for neutralizing antibody in the nasopharyngeal secretions and stool >1:4 and for (b) (4) IgA in the NPS and stool >1:8. GMT's were computed and also expressed in international units based on the FDA reference serum results.

For the adult studies, 30 individuals were immunized and available for the analysis. Half received one dose (Group F1) and half received a second dose 4 weeks later (Group F2). Serum antibody titers were done prior to immunization and 4 weeks after each dose of vaccine.

RESULTS IN CHILDREN

M-IPV induced detectable neutralizing antibodies after two doses of vaccine in 97.8% to 100% (Type I), 100% (Type II), and 96.7% to 100% (Type III) of the children (Table 1). Two doses of OPV gave 100% response for all types of poliovirus and a mixed schedule of IPV and OPV induced 96.6% response for Types I and III and 100% response for Type II. The booster dose did not appreciably change the response rates.

The GMT (Table 2) rose approximately 10-fold after two doses and nearly 100-fold post-booster in all groups for Type I. For Type II, two doses of IPV gave lower GMT's than OPV or a mixed schedule, but produced overall even greater titers and fold increases pre- and post-booster than Types I or III. The GMT obtained for Type III with mixed schedules was significantly lower with a mixed regimen of IPV-OPV-OPV than IPV-IPV-OPV or the other two regimens using all IPV or all OPV.

Table 3 presents similar neutralizing antibody data expressed in international units.

Table 4 shows that two primary doses and a booster dose of M-IPV produced neutralizing antibodies in the nasopharyngeal secretions (NPS) in 64% of the children compared to 90% in all OPV recipients and 58% to 68% in recipients of mixed schedules.

After primary immunization, the GMT for Type II was slightly higher in recipients of the IPV-OPV schedule than with OPV alone indicating a priming effect by IPV on OPV-induced antibody (Table 5). The priming effect was not seen post-booster. The NPS neutralizing antibody levels for all types were highest post-booster in children who received only OPV. The data expressed as international units are shown in Table 6.

The percentage of children with IgA antibodies in the NPS (Table 7) were generally at similar levels for M-IPV,

mixed schedule, and OPV for all types of poliovirus after only two doses but were highest in children receiving the mixed schedule of IPV-OPV-OPV. This advantage disappeared post-booster in favor of the all OPV schedule. This pattern was also reflected in the GMT (Table 8).

The percentage of children receiving only IPV with detectable neutralizing antibody in the stool was less than 15% and did not show any appreciable change even after a booster (Table 9). Recipients of either of the mixed schedules or only OPV developed substantial increases in stool antibody, ranging from 23% to 57% for the three types post-booster. Both the percentage with antibody and the GMT were highest for Type II (Tables 10 and 11).

As was the case with neutralizing antibody in the stool, the percentage of children with detectable IgA levels in the stool was essentially unchanged following primary and booster doses of only IPV (Table 12). The mixed schedules resulted in approximately 35% detectable IgA for all three polio types and OPV only ranged from 35% to 55% detectable IgA. The GMT followed a similar pattern (Table 13).

Premature and full-term infants responded equally to primary and booster doses of M-IPV. The percent with detectable antibody titers was essentially 100% to all three types of poliovirus (Tables 14, 15, 16).

RESULTS IN ADULTS

Nearly all adults had detectable neutralizing antibodies at the time of entry into the study, so that a single dose of M-IPV ensured a 100% response (Table 17).

A single dose of M-IPV induced increases in GMT of nearly 30-fold for Type I, 50-fold for Type II and 125-fold for Type III. A second dose of IPV did not significantly increase the GMT compared to only a single dose.

The results of neutralizing antibodies in the NPS (Table 18) show that the percent of subjects with detectable antibody was the same with one or two doses, suggesting that a greater increase over base titer and higher GMT is obtained in individuals who had a lower antibody titer upon entry.

In contrast, both the percent of individuals with stool neutralizing antibody and the GMT were higher in adults receiving two doses of M-IPV compared to only one dose (Table 19).

The IgA antibody levels in the NPS and stool were similar for one or two doses, although there was a higher percentage of detectable antibody in NPS of recipients of two doses compared to one dose of M-IPV (Tables 20 and 21).

There were no major differences in antibody responses whether there was exposure or nonexposure to OPV (Tables 22 and 23).

ADVERSE REACTIONS

There were no serious adverse reactions reported at either Buffalo or Johns Hopkins.

The Johns Hopkins protocol was set up to include telephone follow up with the patients at 24 hours, 2 and 3 days after each polio immunization to inquire about adverse reactions. Surveillance at Buffalo was limited to an interview during each immunization visit and no adverse experiences were reported other than one adult complaining of redness at the injection site.

Johns Hopkins enrollment is shown below:

Group	No. Enrolled	No. Completing Study
B	54	44
C	16	14
D	16	16

The reactions were summarized as follows:

Immunization #	No. of Reaction Forms	No. Children with >100.6	% with Temps. >100.6
1	86	9	10
2	79	14	18
3	75	5	7

There were no serious local or systemic reactions in any of the children in this study.

Most of the children received DTP at the same time they received the IPV or OPV at 2 and 4 months of age.

One child had a temperature of 103, four children experienced temperatures of 102.

Of the 9 children who had temperatures 100.6 or greater at the time of the first polio immunization, 7 also had local reactions to DTP.

Of the 14 children who had temperatures 100.6 or greater at the time they received the second polio immunization, 9 also had local reactions to DTP. Four of these chil-dren received OPv at this time.

Of the 5 children with temperatures 100.6 or greater at the time of the third polio immunization, 2 had colds.

DISCUSSION

This study has demonstrated that two primary doses of M-IPV given at 2 and 4 months of age followed by a booster dose at 12 months of age produce excellent neutralizing antibody responses to all three types of poliovirus. The percentage of children with detectable antibody to the Vero cell vaccine was comparable to and the GMT's higher than results obtained in the earlier Johns Hopkins/CDC/FDA study with M-IPV produc-ed in primary monkey kidney cells.

Two children (b)(6), immunized at the same pri-vate clinic with two doses of M-IPV, formed good neutralizing antibody titers to Type II but not to the Types I and III poliovirus. The Type II baseline titer and titer one month post 12-month booster, was 320 for both children. The Types

I and III titers at baseline and post-booster were for (b) (6) 10 and <10 and 40 and 20, respectively; for (b) (6) 10 and <10 and <10 and 20, respectively. Both children had normal IgG at 5 months of age and measurable tetanus antibody levels at 13 months of age. It appears the children were immunocompetent, but the reason for poor Types I and III response are unclear.

This study has shown that children given two doses of only OPV or only M-IPV produce similar levels of neutralizing antibodies and IgA in the NPS. Following the booster dose, the number of children with neutralizing antibody and the neutralizing antibody level increases further but is approximately one-half that for OPV in IPV recipients. Nevertheless this level of neutralizing antibody produced by enhanced IPV in the nasopharyngeal secretions is noteworthy.

The strong priming effect of one dose of M-IPV on the mucosal antibody induced by a dose of OPV seen earlier in the primary immunization phase of the study is not maintained in the GMT following booster doses. One month after the booster dose, either of the mixed schedules induced lower GMT's than a schedule of only OPV. Nevertheless, these data clearly show that enhanced M-IPV stimulates local immunity when used alone or in a combination schedule with OPV.

Based on stool antibody data, "gut immunity" appears to be a concept applicable to both M-IPV and OPV. Both vaccines

used alone or in combination gave detectable neutralizing antibody in the stool with similar GMT's.

Because approximately 25% of the infants receiving two doses of IPV were premature births, it was possible to compare responses to full-term infants. Although full-term infants had higher maternal antibody levels, as expected, both premature and full-term infants had similar percentages of responders and comparable GMT's after two doses of IPV.

The studies in adults showed that a single dose of M-IPV produced booster responses with very high titers of neutralizing antibodies and that a second dose is unnecessary. However, stool neutralizing antibody levels were higher in adults receiving a second dose of IPV.

Serum Neutralizing Antibodies
Percent with Detectable Antibody Titer
Efficacy Patients

Type I

Mos	A	B	C	D
2	17/ 23 (73.9)	92/116 (79.3)	28/ 32 (87.5)	29/ 34 (85.3)
4	17/ 22 (77.3)	68/ 93 (73.1)	23/ 29 (79.3)	27/ 29 (93.1)
5	22/ 22 (100.0)	89/ 91 (97.8)	28/ 29 (96.6)	29/ 29 (100.0)
12	17/ 22 (77.3)	78/ 85 (91.8)	27/ 29 (93.1)	26/ 27 (96.3)
13	20/ 20 (100.0)	81/ 83 (97.6)	28/ 28 (100.0)	26/ 26 (100.0)

Type II

Mos	A	B	C	D
2	22/ 23 (95.7)	100/116 (86.2)	30/ 32 (93.8)	32/ 34 (94.1)
4	21/ 22 (95.5)	89/ 93 (95.7)	29/ 29 (100.0)	29/ 29 (100.0)
5	22/ 22 (100.0)	91/ 91 (100.0)	29/ 29 (100.0)	29/ 29 (100.0)
12	20/ 22 (90.9)	79/ 85 (92.9)	26/ 29 (89.7)	25/ 27 (92.6)
13	20/ 20 (100.0)	83/ 83 (100.0)	28/ 28 (100.0)	26/ 26 (100.0)

Type III

Mos	A	B	C	D
2	19/ 23 (82.6)	87/116 (75.0)	23/ 32 (71.9)	26/ 34 (76.5)
4	17/ 22 (77.3)	78/ 93 (83.9)	24/ 29 (82.8)	23/ 29 (79.3)
5	22/ 22 (100.0)	88/ 91 (96.7)	28/ 29 (96.6)	29/ 29 (100.0)
12	17/ 22 (77.3)	77/ 85 (90.6)	25/ 29 (86.2)	24/ 27 (88.9)
13	20/ 20 (100.0)	83/ 83 (100.0)	26/ 28 (92.9)	26/ 26 (100.0)

Type Any

Mos	A	B	C	D
2	22/ 23 (95.7)	115/116 (99.1)	31/ 32 (96.9)	33/ 34 (97.1)
4	22/ 22 (100.0)	93/ 93 (100.0)	29/ 29 (100.0)	29/ 29 (100.0)
5	22/ 22 (100.0)	91/ 91 (100.0)	29/ 29 (100.0)	29/ 29 (100.0)
12	22/ 22 (100.0)	82/ 85 (96.5)	28/ 29 (96.6)	26/ 27 (96.3)
13	20/ 20 (100.0)	83/ 83 (100.0)	28/ 28 (100.0)	26/ 26 (100.0)

Serum Neutralizing Antibodies
Reciprocal Geometric Mean Titers
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
2	23	21.29	116	20.97	32	25.78	34	30.07
4	22	35.70	93	12.16	29	10.26	29	22.90
5	22	273.36	91	208.84	29	250.04	29	354.70
12	22	67.04	85	74.19	29	157.56	27	110.77
13	20	1470.33	83	2101.29	28	1599.45	26	2629.17

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
2	23	50.41	116	36.24	32	66.34	34	56.54
4	22	492.39	93	41.52	29	41.96	29	51.17
5	22	2726.51	91	552.15	29	1442.49	29	709.40
12	22	403.46	85	128.45	29	504.35	27	203.44
13	20	3377.94	83	5120.00	28	4305.39	26	6337.16

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
2	23	17.05	116	15.40	32	11.66	34	15.05
4	22	17.85	93	21.15	29	17.08	29	15.89
5	22	351.72	91	605.15	29	72.15	29	1200.22
12	22	78.48	85	84.99	29	46.96	27	95.83
13	20	1522.19	83	4332.44	28	570.50	26	1960.92

TABLE 3

Serum Neutralizing Antibodies
Reciprocal Geometric Mean Titers in International Units
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
2	23	0.25	116	0.24	32	0.30	34	0.35
4	22	0.42	93	0.14	29	0.12	29	0.27
5	22	3.19	91	2.44	29	2.92	29	4.14
12	22	0.78	85	0.87	29	1.84	27	1.29
13	20	17.16	83	24.52	28	18.67	26	30.68

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
2	23	0.28	116	0.20	32	0.37	34	0.32
4	22	2.78	93	0.23	29	0.24	29	0.29
5	22	15.40	91	3.12	29	8.15	29	4.01
12	22	2.28	85	0.73	29	2.85	27	1.15
13	20	19.09	83	28.93	28	24.33	26	35.80

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
2	23	0.17	116	0.15	32	0.12	34	0.15
4	22	0.18	93	0.21	29	0.17	29	0.16
5	22	3.52	91	6.05	29	0.72	29	12.00
12	22	0.78	85	0.85	29	0.47	27	0.96
13	20	15.22	83	43.32	28	5.70	26	19.61

Nasopharyngeal Neutralizing Antibodies
Percent with Detectable Antibody Titer
Efficacy Patients

Type I

Mos	A	B	C	D
4	6/ 22 (27.3)	5/ 93 (5.4)	1/ 29 (3.4)	0/ 29 (0.0)
5	6/ 22 (27.3)	23/ 91 (25.3)	11/ 29 (37.9)	6/ 29 (20.7)
12	7/ 22 (31.8)	6/ 85 (7.1)	3/ 29 (10.3)	2/ 27 (7.4)
13	14/ 20 (70.0)	27/ 83 (32.5)	12/ 28 (42.9)	9/ 26 (34.6)

Type II

Mos	A	B	C	D
4	15/ 22 (68.2)	4/ 93 (4.3)	3/ 29 (10.3)	0/ 29 (0.0)
5	15/ 22 (68.2)	32/ 91 (35.2)	20/ 29 (69.0)	10/ 29 (34.5)
12	15/ 22 (68.2)	10/ 85 (11.8)	9/ 29 (31.0)	4/ 27 (14.8)
13	17/ 20 (85.0)	39/ 83 (47.0)	18/ 28 (64.3)	15/ 26 (57.7)

Type III

Mos	A	B	C	D
4	4/ 22 (18.2)	5/ 93 (5.4)	2/ 29 (6.9)	0/ 29 (0.0)
5	9/ 22 (40.9)	34/ 91 (37.4)	6/ 29 (20.7)	10/ 29 (34.5)
12	8/ 22 (36.4)	10/ 85 (11.8)	2/ 29 (6.9)	2/ 27 (7.4)
13	15/ 20 (75.0)	40/ 83 (48.2)	8/ 28 (28.6)	7/ 26 (26.9)

Type Any

Mos	A	B	C	D
4	16/ 22 (72.7)	6/ 93 (6.5)	4/ 29 (13.8)	0/ 29 (0.0)
5	16/ 22 (72.7)	43/ 91 (47.3)	21/ 29 (72.4)	13/ 29 (44.8)
12	16/ 22 (72.7)	14/ 85 (16.5)	12/ 29 (41.4)	6/ 27 (22.2)
13	18/ 20 (90.0)	53/ 83 (63.9)	19/ 28 (67.9)	15/ 26 (57.7)

Nasopharyngeal Neutralizing Antibodies
Reciprocal Geometric Mean Titers
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.86	93	1.25	29	1.17	29	0.00
5	22	1.82	91	1.88	29	2.54	29	1.43
12	22	2.31	85	1.25	29	1.24	27	1.14
13	20	5.66	83	2.17	28	2.63	26	2.05

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	7.19	93	1.22	29	1.29	29	0.00
5	22	6.83	91	2.33	29	7.81	29	2.31
12	22	7.91	85	1.38	29	2.31	27	1.40
13	20	17.15	83	3.29	28	7.25	26	6.29

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.74	93	1.24	29	1.23	29	0.00
5	22	2.92	91	2.63	29	1.50	29	2.31
12	22	3.17	85	1.41	29	1.27	27	1.11
13	20	6.50	83	3.35	28	1.95	26	2.41

Nasopharyngeal Neutralizing Antibodies
Reciprocal Geometric Mean Titers in International Units
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	0.02	93	0.01	29	0.01	29	0.01
5	22	0.02	91	0.02	29	0.03	29	0.02
12	22	0.03	85	0.01	29	0.01	27	0.01
13	20	0.07	83	0.03	28	0.03	26	0.02

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	0.04	93	0.01	29	0.01	29	0.01
5	22	0.04	91	0.01	29	0.04	29	0.01
12	22	0.04	85	0.01	29	0.01	27	0.01
13	20	0.10	83	0.02	28	0.04	26	0.04

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	0.02	93	0.01	29	0.01	29	0.01
5	22	0.03	91	0.03	29	0.02	29	0.02
12	22	0.03	85	0.01	29	0.01	27	0.01
13	20	0.06	83	0.03	28	0.02	26	0.02

Nasopharyngeal (b) (4) IgA Antibodies
Percent with Detectable Antibody Titer
Efficacy Patients

Type I

Mos	A	B	C	D
4	17/ 22 (77.3)	53/ 93 (57.0)	21/ 29 (72.4)	18/ 29 (62.1)
5	16/ 22 (72.7)	59/ 91 (64.8)	22/ 29 (75.9)	16/ 29 (55.2)
12	22/ 22 (100.0)	68/ 85 (80.0)	26/ 29 (89.7)	22/ 27 (81.5)
13	20/ 20 (100.0)	65/ 83 (78.3)	24/ 28 (85.7)	19/ 26 (73.1)

Type II

Mos	A	B	C	D
4	17/ 22 (77.3)	55/ 93 (59.1)	20/ 29 (69.0)	19/ 29 (65.5)
5	16/ 22 (72.7)	60/ 91 (65.9)	24/ 29 (82.8)	20/ 29 (69.0)
12	22/ 22 (100.0)	69/ 85 (81.2)	26/ 29 (89.7)	22/ 27 (81.5)
13	20/ 20 (100.0)	67/ 83 (80.7)	26/ 28 (92.9)	20/ 26 (76.9)

Type III

Mos	A	B	C	D
4	17/ 22 (77.3)	50/ 93 (53.8)	23/ 29 (79.3)	20/ 29 (69.0)
5	17/ 22 (77.3)	59/ 91 (64.8)	23/ 29 (79.3)	21/ 29 (72.4)
12	22/ 22 (100.0)	72/ 85 (84.7)	26/ 29 (89.7)	22/ 27 (81.5)
13	20/ 20 (100.0)	69/ 83 (83.1)	26/ 28 (92.9)	20/ 26 (76.9)

Type Any

Mos	A	B	C	D
4	17/ 22 (77.3)	59/ 93 (63.4)	23/ 29 (79.3)	22/ 29 (75.9)
5	18/ 22 (81.8)	65/ 91 (71.4)	25/ 29 (86.2)	22/ 29 (75.9)
12	22/ 22 (100.0)	72/ 85 (84.7)	27/ 29 (93.1)	22/ 27 (81.5)
13	20/ 20 (100.0)	71/ 83 (85.5)	26/ 28 (92.9)	20/ 26 (76.9)

Nasopharyngeal (b) (4) IgA Antibodies
Reciprocal Geometric Mean Titers
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	13.09	93	5.62	29	11.35	29	6.15
5	22	15.02	91	7.31	29	13.86	29	5.08
12	22	61.30	85	15.47	29	17.61	27	15.20
13	20	68.59	83	14.80	28	22.63	26	12.59

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	12.29	93	6.47	29	10.56	29	7.81
5	22	13.24	91	7.71	29	14.20	29	7.10
12	22	61.30	85	16.25	29	18.91	27	16.42
13	20	97.01	83	15.95	28	33.62	26	13.63

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	13.09	93	5.37	29	13.42	29	9.02
5	22	17.04	91	7.77	29	15.62	29	7.63
12	22	92.32	85	19.28	29	25.20	27	19.15
13	20	128.00	83	19.98	28	40.99	26	15.17

Stool Neutralizing Antibodies
Percent with Detectable Antibody Titer
Efficacy Patients

Type I

Mos	A	B	C	D
4	1/ 22 (4.5)	6/ 93 (6.5)	1/ 29 (3.4)	3/ 29 (10.3)
5	6/ 22 (27.3)	6/ 91 (6.6)	4/ 29 (13.8)	2/ 29 (6.9)
12	1/ 22 (4.5)	4/ 85 (4.7)	6/ 29 (20.7)	0/ 27 (0.0)
13	7/ 20 (35.0)	7/ 83 (8.4)	10/ 28 (35.7)	6/ 26 (23.1)

Type II

Mos	A	B	C	D
4	4/ 22 (18.2)	9/ 93 (9.7)	1/ 29 (3.4)	3/ 29 (10.3)
5	10/ 22 (45.5)	10/ 91 (11.0)	8/ 29 (27.6)	5/ 29 (17.2)
12	6/ 22 (27.3)	9/ 85 (10.6)	11/ 29 (37.9)	1/ 27 (3.7)
13	11/ 20 (55.0)	10/ 83 (12.0)	16/ 28 (57.1)	11/ 26 (42.3)

Type III

Mos	A	B	C	D
4	1/ 22 (4.5)	7/ 93 (7.5)	1/ 29 (3.4)	3/ 29 (10.3)
5	6/ 22 (27.3)	9/ 91 (9.9)	3/ 29 (10.3)	2/ 29 (6.9)
12	4/ 22 (18.2)	6/ 85 (7.1)	5/ 29 (17.2)	0/ 27 (0.0)
13	8/ 20 (40.0)	9/ 83 (10.8)	7/ 28 (25.0)	6/ 26 (23.1)

Type Any

Mos	A	B	C	D
4	4/ 22 (18.2)	12/ 93 (12.9)	1/ 29 (3.4)	3/ 29 (10.3)
5	13/ 22 (59.1)	17/ 91 (18.7)	8/ 29 (27.6)	6/ 29 (20.7)
12	7/ 22 (31.8)	9/ 85 (10.6)	13/ 29 (44.8)	1/ 27 (3.7)
13	12/ 20 (60.0)	12/ 83 (14.5)	16/ 28 (57.1)	11/ 26 (42.3)

Stool Neutralizing Antibodies
Reciprocal Geometric Mean Titers
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.07	93	1.26	29	1.17	29	1.61
5	22	1.74	91	1.25	29	1.49	29	1.26
12	22	1.10	85	1.17	29	1.56	27	0.00
13	20	2.92	83	1.36	28	2.24	26	1.93

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.82	93	1.34	29	1.17	29	1.61
5	22	3.83	91	1.31	29	2.13	29	1.52
12	22	2.00	85	1.31	29	2.58	27	1.05
13	20	6.94	83	1.47	28	5.33	26	4.18

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.07	93	1.30	29	1.17	29	1.61
5	22	1.74	91	1.31	29	1.42	29	1.23
12	22	1.71	85	1.20	29	1.52	27	0.00
13	20	3.47	83	1.41	28	1.89	26	2.09

TABLE 11

Stool Neutralizing Antibodies
Reciprocal Geometric Mean Titers in International Units
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	0.01	93	0.01	29	0.01	29	0.02
5	22	0.02	91	0.01	29	0.02	29	0.01
12	22	0.01	85	0.01	29	0.02	27	0.01
13	20	0.03	83	0.02	28	0.03	26	0.02

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	0.01	93	0.01	29	0.01	29	0.01
5	22	0.02	91	0.01	29	0.01	29	0.01
12	22	0.01	85	0.01	29	0.01	27	0.01
13	20	0.04	83	0.01	28	0.03	26	0.02

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	0.01	93	0.01	29	0.01	29	0.02
5	22	0.02	91	0.01	29	0.01	29	0.01
12	22	0.02	85	0.01	29	0.02	27	0.01
13	20	0.03	83	0.01	28	0.02	26	0.02

Stool (b)(4) IgA Antibodies
Percent with Detectable Antibody Titer
Efficacy Patients

Type I

Mos	A	B	C	D
4	4/ 22 (18.2)	19/ 93 (20.4)	4/ 29 (13.8)	4/ 29 (13.8)
5	4/ 22 (18.2)	16/ 91 (17.6)	4/ 29 (13.8)	3/ 29 (10.3)
12	6/ 22 (27.3)	18/ 85 (21.2)	6/ 29 (20.7)	5/ 27 (18.5)
13	7/ 20 (35.0)	15/ 83 (18.1)	6/ 28 (21.4)	10/ 26 (38.5)

Type II

Mos	A	B	C	D
4	2/ 22 (9.1)	17/ 93 (18.3)	6/ 29 (20.7)	5/ 29 (17.2)
5	3/ 22 (13.6)	16/ 91 (17.6)	8/ 29 (27.6)	3/ 29 (10.3)
12	9/ 22 (40.9)	18/ 85 (21.2)	6/ 29 (20.7)	2/ 27 (7.4)
13	11/ 20 (55.0)	17/ 83 (20.5)	10/ 28 (35.7)	9/ 26 (34.6)

Type III

Mos	A	B	C	D
4	4/ 22 (18.2)	20/ 93 (21.5)	5/ 29 (17.2)	4/ 29 (13.8)
5	4/ 22 (18.2)	20/ 91 (22.0)	8/ 29 (27.6)	6/ 29 (20.7)
12	8/ 22 (36.4)	19/ 85 (22.4)	5/ 29 (17.2)	4/ 27 (14.8)
13	10/ 20 (50.0)	17/ 83 (20.5)	10/ 28 (35.7)	10/ 26 (38.5)

Type Any

Mos	A	B	C	D
4	6/ 22 (27.3)	26/ 93 (28.0)	7/ 29 (24.1)	7/ 29 (24.1)
5	4/ 22 (18.2)	23/ 91 (25.3)	8/ 29 (27.6)	7/ 29 (24.1)
12	9/ 22 (40.9)	23/ 85 (27.1)	6/ 29 (20.7)	5/ 27 (18.5)
13	11/ 20 (55.0)	22/ 83 (26.5)	11/ 28 (39.3)	10/ 26 (38.5)

Stool (b) (4) IgA Antibodies
Reciprocal Geometric Mean Titers
Efficacy Patients

Type I

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.51	93	1.92	29	1.56	29	1.73
5	22	1.69	91	1.68	29	1.45	29	1.35
12	22	2.42	85	1.77	29	1.94	27	1.51
13	20	3.13	83	1.70	28	1.89	26	3.12

Type II

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.21	93	1.69	29	1.76	29	1.86
5	22	1.54	91	1.66	29	2.03	29	1.39
12	22	3.01	85	1.80	29	1.89	27	1.20
13	20	5.44	83	1.79	28	2.73	26	2.59

Type III

	A		B		C		D	
Mos	N	GMT	N	GMT	N	GMT	N	GMT
4	22	1.51	93	1.88	29	1.64	29	1.73
5	22	1.74	91	1.85	29	2.13	29	1.72
12	22	3.21	85	1.82	29	1.80	27	1.43
13	20	5.63	83	1.83	28	3.09	26	3.12

TABLE 14

Polio Protocol

Serum Neutralizing Antibodies
Percent with Detectable Antibody Titer
Plan B

Type I

Mos	PREMATURE	FULL TERM
2	9/ 13 (69.2)	44/ 53 (83.0)
4	3/ 11 (27.3)	32/ 46 (69.6)
5	11/ 11 (100.0)	43/ 45 (95.6)
12	9/ 9 (100.0)	39/ 44 (88.6)
13	9/ 9 (100.0)	42/ 44 (95.5)

Type II

Mos	PREMATURE	FULL TERM
2	12/ 13 (92.3)	47/ 53 (88.7)
4	9/ 11 (81.8)	44/ 46 (95.7)
5	11/ 11 (100.0)	45/ 45 (100.0)
12	9/ 9 (100.0)	42/ 44 (95.5)
13	9/ 9 (100.0)	44/ 44 (100.0)

Type III

Mos	PREMATURE	FULL TERM
2	10/ 13 (76.9)	41/ 53 (77.4)
4	7/ 11 (63.6)	38/ 46 (82.6)
5	11/ 11 (100.0)	43/ 45 (95.6)
12	9/ 9 (100.0)	40/ 44 (90.9)
13	9/ 9 (100.0)	44/ 44 (100.0)

Type Any

Mos	PREMATURE	FULL TERM
2	13/ 13 (100.0)	53/ 53 (100.0)
4	11/ 11 (100.0)	46/ 46 (100.0)
5	11/ 11 (100.0)	45/ 45 (100.0)
12	9/ 9 (100.0)	42/ 44 (95.5)
13	9/ 9 (100.0)	44/ 44 (100.0)

Serum Neutralizing Antibodies
Reciprocal Geometric Mean Titers
Plan B

Type I

	PREMATURE		FULL TERM	
Mos	N	GMT	N	GMT
2	13	9.34	53	26.81
4	11	2.57	46	9.97
5	11	150.23	45	191.49
12	9	54.43	44	63.55
13	9	2031.87	44	1938.78

Type II

	PREMATURE		FULL TERM	
Mos	N	GMT	N	GMT
2	13	37.28	53	45.81
4	11	19.20	46	38.62
5	11	438.51	45	663.16
12	9	160.00	44	131.10
13	9	6450.80	44	5716.91

Type III

	PREMATURE		FULL TERM	
Mos	N	GMT	N	GMT
2	13	18.01	53	17.19
4	11	9.22	46	19.62
5	11	320.00	45	720.19
12	9	50.40	44	118.08
13	9	4063.75	44	5453.01

Serum Neutralizing Antibodies
Reciprocal Geometric Mean Titers in International Units
Plan B

Type I

	PREMATURE		FULL TERM	
Mos	N	GMT	N	GMT
2	13	0.11	53	0.31
4	11	0.03	46	0.12
5	11	1.75	45	2.23
12	9	0.64	44	0.74
13	9	23.71	44	22.63

Type II

	PREMATURE		FULL TERM	
Mos	N	GMT	N	GMT
2	13	0.21	53	0.26
4	11	0.11	46	0.22
5	11	2.48	45	3.75
12	9	0.90	44	0.74
13	9	36.45	44	32.30

Type III

	PREMATURE		FULL TERM	
Mos	N	GMT	N	GMT
2	13	0.18	53	0.17
4	11	0.09	46	0.20
5	11	3.20	45	7.20
12	9	0.50	44	1.18
13	9	40.64	44	54.53

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	14/15 (93.3)	14/15 (93.3)	15/15 (100.0)
	PLAN F2	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)
II	PLAN F1	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)
	PLAN F2	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)
III	PLAN F1	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)
	PLAN F2	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)
ANY	PLAN F1	14/15 (93.3)	15/15 (100.0)	15/15 (100.0)
	PLAN F2	15/15 (100.0)	15/15 (100.0)	15/15 (100.0)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	172.90	15	4816.60	15	4888.79
	PLAN F2	15	335.13	15	4003.74	15	5615.74
II	PLAN F1	15	250.23	15	7760.48	15	12319.00
	PLAN F2	15	531.99	15	17828.90	15	17828.88
III	PLAN F1	15	143.72	15	13511.81	15	17828.90
	PLAN F2	15	345.80	15	14150.80	15	19555.19

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	2.02	15	56.21	15	57.05
	PLAN F2	15	3.91	15	46.72	15	65.54
II	PLAN F1	15	1.41	15	43.85	15	69.60
	PLAN F2	15	3.01	15	100.73	15	100.73
III	PLAN F1	15	1.44	15	135.12	15	178.29
	PLAN F2	15	3.46	15	141.51	15	195.55

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	0/15 (0.0)	11/15 (73.3)	8/15 (53.3)
	PLAN F2	4/15 (26.7)	9/15 (60.0)	10/15 (66.7)
II	PLAN F1	2/15 (13.3)	12/15 (80.0)	10/15 (66.7)
	PLAN F2	1/15 (6.7)	12/15 (80.0)	10/15 (66.7)
III	PLAN F1	4/15 (26.7)	13/15 (86.7)	14/15 (93.3)
	PLAN F2	6/15 (40.0)	12/15 (80.0)	11/15 (73.3)
ANY	PLAN F1	5/15 (33.3)	14/15 (93.3)	14/15 (93.3)
	PLAN F2	8/15 (53.3)	14/15 (93.3)	14/15 (93.3)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	6.35	15	6.65
	PLAN F2	15	1.45	15	3.17	15	5.79
II	PLAN F1	15	1.45	15	7.29	15	9.62
	PLAN F2	15	1.15	15	9.19	15	7.64
III	PLAN F1	15	1.74	15	12.70	15	20.16
	PLAN F2	15	2.19	15	10.56	15	11.58

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	0.07	15	0.08
	PLAN F2	15	0.02	15	0.04	15	0.07
II	PLAN F1	15	0.01	15	0.04	15	0.05
	PLAN F2	15	0.01	15	0.05	15	0.04
III	PLAN F1	15	0.02	15	0.13	15	0.20
	PLAN F2	15	0.02	15	0.11	15	0.12

TABLE 19

Polio Protocol 01

STOOL SPECIMENS NEUTRALIZING ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	0/15 (0.0)	3/15 (20.0)	1/15 (6.7)
	PLAN F2	2/15 (13.3)	2/14 (14.3)	2/15 (13.3)
II	PLAN F1	0/15 (0.0)	2/15 (13.3)	1/15 (6.7)
	PLAN F2	2/15 (13.3)	2/14 (14.3)	7/15 (46.7)
III	PLAN F1	0/15 (0.0)	3/15 (20.0)	5/15 (33.3)
	PLAN F2	1/15 (6.7)	7/14 (50.0)	7/15 (46.7)
ANY	PLAN F1	0/15 (0.0)	6/15 (40.0)	5/15 (33.3)
	PLAN F2	3/15 (20.0)	8/15 (53.3)	8/15 (53.3)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	1.32	15	1.20
	PLAN F2	15	1.26	14	1.28	15	1.45
II	PLAN F1	15	0.00	15	1.32	15	1.32
	PLAN F2	15	1.32	14	1.49	15	3.48
III	PLAN F1	15	0.00	15	1.59	15	2.19
	PLAN F2	15	1.15	14	2.97	15	3.48

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	0.00	15	0.02	15	0.01
	PLAN F2	15	0.01	14	0.01	15	0.02
II	PLAN F1	15	0.00	15	0.01	15	0.01
	PLAN F2	15	0.01	14	0.01	15	0.02
III	PLAN F1	15	0.00	15	0.02	15	0.02
	PLAN F2	15	0.01	14	0.03	15	0.03

Polio Protocol 01

NASOPHARYNGEAL SECRETIONS (b) (4) IgA ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1		Visit 2		Visit 3	
	PLAN F1	8/14	(57.1)	11/15	(73.3)	10/15	(66.7)
I	PLAN F2	10/15	(66.7)	10/15	(66.7)	12/15	(80.0)
	PLAN F1	10/14	(71.4)	10/15	(66.7)	10/15	(66.7)
II	PLAN F2	10/15	(66.7)	10/15	(66.7)	13/15	(86.7)
	PLAN F1	10/14	(71.4)	12/15	(80.0)	11/15	(73.3)
III	PLAN F2	11/15	(73.3)	10/15	(66.7)	14/15	(93.3)
	PLAN F1	10/15	(66.7)	12/15	(80.0)	11/15	(73.3)
ANY	PLAN F2	11/15	(73.3)	10/15	(66.7)	14/15	(93.3)

GEOMETRIC MEAN TITERS

TYPE		Visit 1		Visit 2		Visit 3	
		N	GMT	N	GMT	N	GMT
	PLAN F1	14	8.41	15	8.77	15	13.93
I	PLAN F2	15	12.13	15	6.96	15	10.56
	PLAN F1	14	9.28	15	8.77	15	12.70
II	PLAN F2	15	8.00	15	7.29	15	14.59
	PLAN F1	14	13.79	15	13.30	15	19.25
III	PLAN F2	15	10.56	15	10.08	15	20.16

Polio Protocol 01

STOOL SPECIMENS (b) (4) IgA ANTIBODIES

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	PLAN F1	3/15 (20.0)	2/15 (13.3)	5/15 (33.3)
	PLAN F2	3/15 (20.0)	1/15 (6.7)	3/15 (20.0)
II	PLAN F1	3/15 (20.0)	4/15 (26.7)	6/15 (40.0)
	PLAN F2	4/15 (26.7)	6/15 (40.0)	5/15 (33.3)
III	PLAN F1	3/15 (20.0)	5/15 (33.3)	6/15 (40.0)
	PLAN F2	3/15 (20.0)	5/15 (33.3)	4/15 (26.7)
ANY	PLAN F1	3/15 (20.0)	5/15 (33.3)	7/15 (46.7)
	PLAN F2	4/15 (26.7)	8/15 (53.3)	6/15 (40.0)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	PLAN F1	15	1.82	15	1.32	15	2.19
	PLAN F2	15	1.82	15	1.15	15	1.59
II	PLAN F1	15	1.66	15	1.82	15	2.52
	PLAN F2	15	1.91	15	2.30	15	2.19
III	PLAN F1	15	1.82	15	2.19	15	2.52
	PLAN F2	15	1.59	15	2.19	15	2.00

Polio Protocol 01

SERUM NEUTRALIZING ANTIBODIES
PATIENTS HAD CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1	Visit 2	Visit 3
I	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)
II	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)
III	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)
ANY	Plan F1	7/ 7 (100.0)	7/ 7 (100.0)	7/ 7 (100.0)
	Plan F2	5/ 5 (100.0)	5/ 5 (100.0)	5/ 5 (100.0)

GEOMETRIC MEAN TITERS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan F1	7	215.34	7	8400.23	7	7608.30
	Plan F2	5	422.24	5	2940.67	5	5881.34
II	Plan F1	7	430.69	7	6891.02	7	12482.72
	Plan F2	5	211.12	5	8914.46	5	8914.44
III	Plan F1	7	118.88	7	10240.02	7	16800.50
	Plan F2	5	557.15	5	17828.92	5	23525.40

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

		Visit 1		Visit 2		Visit 3	
TYPE		N	GMT	N	GMT	N	GMT
I	Plan F1	7	2.51	7	98.03	7	88.79
	Plan F2	5	4.93	5	34.32	5	68.64
II	Plan F1	7	2.43	7	38.93	7	70.53
	Plan F2	5	1.19	5	50.37	5	50.37
III	Plan F1	7	1.19	7	102.40	7	168.00
	Plan F2	5	5.57	5	178.29	5	235.25

SERUM NEUTRALIZING ANTIBODIES
PATIENTS DID NOT HAVE CONTACT WITH OPV

PERCENT WITH DETECTABLE ANTIBODY TITER

TYPE		Visit 1		Visit 2		Visit 3	
I	Plan F1	7/ 8	(87.5)	7/ 8	(87.5)	8/ 8	(100.0)
	Plan F2	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
II	Plan F1	7/ 8	(87.5)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan F2	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)
III	Plan F1	7/ 8	(87.5)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan F2	9/10	(90.0)	10/10	(100.0)	10/10	(100.0)
ANY	Plan F1	7/ 8	(87.5)	8/ 8	(100.0)	8/ 8	(100.0)
	Plan F2	10/10	(100.0)	10/10	(100.0)	10/10	(100.0)

GEOMETRIC MEAN TITERS

TYPE		Visit 1		Visit 2		Visit 3	
		N	GMT	N	GMT	N	GMT
I	Plan F1	8	142.68	8	2960.63	8	3319.91
	Plan F2	10	298.57	10	4671.71	10	5487.48
II	Plan F1	8	155.60	8	8610.79	8	12177.50
	Plan F2	10	844.49	10	25213.87	10	25213.84
III	Plan F1	8	169.68	8	17221.64	8	18780.27
	Plan F2	10	272.43	10	12606.92	10	17828.30

GEOMETRIC MEAN TITERS IN INTERNATIONAL UNITS

TYPE		Visit 1		Visit 2		Visit 3	
		N	GMT	N	GMT	N	GMT
I	Plan F1	8	1.67	8	34.55	8	38.74
	Plan F2	10	3.48	10	54.52	10	64.04
II	Plan F1	8	0.88	8	48.65	8	68.80
	Plan F2	10	4.77	10	142.46	10	142.46
III	Plan F1	8	1.70	8	172.22	8	187.80
	Plan F2	10	2.72	10	126.07	10	178.29

Attachment 2

AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 128, No. 3
Printed in U.S.A.

SEROLOGIC RESPONSE TO ORAL POLIO VACCINE AND ENHANCED-POTENCY INACTIVATED POLIO VACCINES

A. MARSHALL McBEAN,[1] MARY LOU THOMS,[1] PAUL ALBRECHT,[2]
JUDITH C. CUTHIE,[1] ROGER BERNIER,[3] AND
THE FIELD STAFF AND COORDINATING COMMITTEE[4]

McBean, A. M. (The Johns Hopkins U. School of Hygiene and Public Health, Baltimore, MD 21205), M. L. Thoms, P. Albrecht, J. C. Cuthie, R. Bernier, and the Field Staff and Coordinating Committee. The serologic response to oral polio vaccine and enhanced-potency inactivated polio vaccines. *Am J Epidemiol* 1988;128:615–28.

In a randomized, controlled trial carried out from November 1980 to July 1983 involving 1,114 infants in Baltimore City and in Baltimore and Prince George's counties, Maryland, the serologic response to three doses of two enhanced-potency inactivated polio vaccines was compared with the response to three doses of oral polio vaccine. The mean ages at vaccination were 2.2, 4.7, and 19.9 months, respectively, for the three doses. Seroconversion after the first dose varied from 35% to 84%, and it was higher after oral polio vaccine than after either of the enhanced-potency inactivated polio vaccines for polioviruses types 2 and 3. Approximately two and one-half and 16 months after the second dose, almost all inactivated polio vaccine recipients had antibodies against all three virus types (98–100%). Fewer oral polio vaccine recipients had detectable antibodies to type 1 (89–92%) and to type 3 (96%). After three doses of vaccine, all children had antibodies against types 2 and 3. Approximately 1% of the inactivated polio vaccine recipients and 3% of the oral polio vaccine recipients lacked antibody to type 1. One or two doses of oral polio vaccine stimulated higher reciprocal geometric mean antibody titers against type 2 poliovirus than did the inactivated polio vaccine. For the other two types, the results were mixed. The third dose of inactivated polio vaccine produced significant increases in the reciprocal geometric mean titers against each of the three poliovirus types and resulted in significantly higher reciprocal geometric mean titers after three doses of vaccine for recipients of inactivated polio vaccine than for recipients of oral polio vaccine.

poliomyelitis; poliovirus; poliovirus vaccine; serology

Since 1962, the Immunization Practices Advisory Committee (1), the Committee on Infectious Diseases of the American Academy of Pediatrics (2), and other groups (3)

Received for publication September 24, 1987, and in final form March 11, 1988.

[1] The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD.
[2] Office of Biologics Research and Review, Food and Drug Administration, Bethesda, MD.
[3] Division of Immunization, Center for Preventive Services, Centers for Disease Control, Atlanta, GA.
[4] *Field staff*: Patricia R. Cummins, Joanne M. Kinnear, Barbara MacDonald, Judith H. Nelson, Lynda J. Nerhood, Christine S. Watts, and Susan Wysor of the Johns Hopkins University School of Hygiene and Public Health. *Coordinating committee*: Dr. Venita Allen of the Baltimore City Health Department, Elizabeth J. Boone of the Office of Biologics Research and Review, Drs. John A. Frank and Melinda Moore of the Centers for Disease Control, Bonnie R. Gadless and Dr. Robert H. Johnson of the Johns Hopkins University School of Hygiene and Public Health, Drs. Lindsey K. Grossman and John M. Neff of the Francis Scott Key Medical Center, Drs. Nigel E. R. Jackman, Marcia B. Kraft, and Helen B. McAllister of the Prince George's County Health Department, Dr. John M. Krager of the Baltimore County Health Depart-

have recommended oral trivalent polio vaccine as the principal polio vaccine for use in the United States. During this time, the annual number of reported paralytic polio cases decreased from 820 cases in 1961 (0.7/100,000) to seven in 1984 (<0.01/100,000) (4), confirming the remarkable effectiveness of this vaccine.

From 1973 through 1984, a total of 138 cases of paralytic polio were reported to the Centers for Disease Control (an average of 11.5 cases per year). One hundred and five of these (76 per cent) were associated with the administration of oral polio vaccine. During the most recent three years for which reporting is complete (1982–1984), 29 cases were reported, and all but one were vaccine-associated. Estimates of the overall risk of paralysis in oral polio vaccine recipients, based on the number of cases of paralytic polio reported in the United States and the number of doses of vaccine administered from 1973 through 1984, are one case per 2.6 million doses distributed, or approximately one case per 500,000 for the first dose given and one case per 13,000,000 for subsequent doses (5).

While the United States has relied almost exclusively on oral polio vaccine for the past 24 years, other countries (Sweden, Finland, and the Netherlands) have achieved control of polio with the use of trivalent inactivated polio vaccine. Prior to the outbreak of nine cases of paralytic polio and one case of aseptic meningitis in Finland in 1984–1985 (6), the circulation of wild poliovirus had not been documented in Sweden and Finland since the early 1960s, and the few cases reported from Sweden and the Netherlands were in immigrants or in people or groups who had refused to be vaccinated (7–9).

The 1984–1985 outbreak in Finland, while raising alarm about the effectiveness of inactivated polio vaccine, was felt to be due to a combination of 1) a decrease in vaccination coverage (the vaccination coverage rate in three-year-old children dropped from 99 per cent to 78 per cent from the 1970s to 1983), 2) antigenic differences between the Finland wild virus strain and the type 3 component of the Finnish inactivated polio vaccine, and 3) low immunogenicity of the type 3 component of the inactivated polio vaccine used in Finland. Finnish authorities continue to express confidence in inactivated polio vaccine, and in 1986 Finland began administering an enhanced-potency inactivated polio vaccine similar to that described below (6).

In the past eight years, new methods have been developed by van Wezel et al. (10) at the Rijks Instituut voor de Volksgezondheid, The Netherlands, for the production of a higher-potency inactivated polio vaccine by means of the microcarrier technique and tertiary monkey kidney cells. Similar vaccines are also made by the Institut Merieux, France, and Connaught Laboratories Ltd., Canada. Salk and colleagues (11–13) have reported excellent antibody responses following one and two doses of this type of vaccine. This paper reports the results of a study that compares the serologic response in healthy American infants given three doses of enhanced-potency inactivated polio vaccine made by the new production methods with the response of children given three doses of commercially available oral polio vaccine.

Materials and Methods

Participants and study design

Children aged six through 13 weeks ("two months") attending well-child clinics in Baltimore City and Baltimore County (hereafter called Baltimore) and Prince

ment, and Dr. Ruth L. Steerman of the Prince George's County Hospital.

Reprint requests to Dr. A. Marshall McBean, Department of International Health, The Johns Hopkins University School of Hygiene and Public Health, 615 North Wolfe Street, Baltimore, MD 21205.

This research was supported by Centers for Disease Control Contract 210-80-0512 and by Connaught Laboratories Ltd., with the cooperation of the nursing and medical staff of the Baltimore City Health Department, Baltimore County Health Department, Francis Scott Key Medical Center, and Prince George's County Health Department.

George's County, Maryland, were enrolled in the study between November 1980 and July 1983. In all cases, parents or guardians were given complete information about the study, and their written informed consent was obtained. In each geographic area (Baltimore or Prince George's County), the children were randomly assigned to receive either oral polio vaccine or one of two enhanced-potency inactivated polio vaccines described below. The children were scheduled to receive additional doses of the same polio vaccine at four and 18 months of age. Diphtheria-tetanus-pertussis vaccine was administered at the same time as the polio vaccine, as was either an oral or injectable placebo corresponding to the kind of polio vaccine that the child did not receive. Blood specimens were obtained at each vaccination and two months after the dose given at four months and at 18 months, that is, at ages two, four, six, 18, and 20 months.

Vaccines

Commercially licensed oral polio vaccine manufactured by Lederle Laboratories, Inc. (Wayne, NJ) was used. It contained 800,000 $TCID_{50}$ (tissue culture infectious dose, 50 per cent infectivity) of type 1, 100,000 $TCID_{50}$ of type 2, and 500,000 $TCID_{50}$ of type 3 per 0.5 cm^3 dose. The enhanced-potency inactivated polio vaccines were manufactured by the Institut Merieux, Lyon, France (designated as inactivated polio vaccine A) and by Connaught Laboratories Ltd., Willowdale, Ontario, Canada (designated as inactivated polio vaccine B). Upon receipt of the vaccine in Baltimore and approximately every four months, samples of the enhanced-potency inactivated polio vaccines were sent to the Rijks Instituut, Bilthoven, The Netherlands, where vaccine potency, measured by D-antigen content, was determined by Dr. van Wezel. The range of potency for the Institut Merieux vaccine was 24 to 38, 3.6 to 6.5, and 28 to 36 for types 1, 2, and 3, respectively. The range of potency was 20 to 25, 7.0 to 9.2, and 26 to 30, respectively, for the Connaught vaccine. The Connaught vaccine became available 20 months after the start of the study. As a result, the initial 593 children described in this study were randomized to receive either inactivated polio vaccine A or oral polio vaccine. The last 521 children enrolled were randomized among all three vaccines, with 72 per cent of them allocated to receive inactivated polio vaccine B.

The diphtheria-tetanus-pertussis vaccine contained 12.5 Lf of diphtheria toxoid, 5 Lf of tetanus toxoid, and 4 mouse protective units of pertussis per 0.5 cm^3 dose.

Blood specimens

With Microtainer (Becton-Dickinson, Rutherford, NJ) capillary tubes, approximately 2 cm^3 of blood was obtained by a finger- or heel-stick. After collection, the blood was allowed to clot and was centrifuged. The serum was drawn off, and the serum specimens were refrigerated. They were placed in a freezer and stored at −20 C until examined in the laboratory. Unbiased laboratory analysis was ensured by coding specimens before sending them to the laboratory.

Adverse reactions

At administration of each dose of vaccine, parents were told they would be contacted for the next three days for information on possible adverse local or systemic reactions in their children. They were given a copy of the data form on which the site coordinators would record reaction information on erythema, pain, and induration at the sites of injection, as well as the systemic signs of fever, fussiness, sleepiness, spitting up, decreased eating, increased crying, or seizures. Erythema at the injection site was recorded as present or absent. Pain was rated as "none," "some" (child moved limb or responded negatively when the site was touched), or "much" (child cried when the site was touched). Parents were also instructed in how to take their children's temperatures and were

given a thermometer. When the children returned for a follow-up visit, parents were asked if any severe reactions had occurred since the previous visit.

Laboratory testing

Serum poliovirus-neutralizing antibodies were measured at the Office of Biologics Research and Review, Food and Drug Administration, Department of Health and Human Services (Bethesda, MD), by a sensitive virus cytopathic effect neutralization test in microtiter trays (14). Each day, a serum reference provided by the Rijks Instituut was tested with the experimental sera. This reference was standardized against the World Health Organization International Standard for Antipoliovirus Sera and was assigned values of 11 International Units (IU) of antibody against poliovirus type 1, 50 IU against poliovirus type 2, and 12 IU against poliovirus type 3. A conversion factor was calculated with each test for converting the observed reciprocals of the serum dilution titers to International Units. One International Unit of antibody corresponds to a serum titer of 1:110 for type 1, 1:70 for type 2, and 1:110 for type 3 poliovirus antibody.

RESULTS

Specimens were lost or collection tubes were broken for 20 of 1,134 children enrolled in the study. Of the remaining 1,114 children, 371 received enhanced-potency inactivated polio vaccine A, 366 received oral polio vaccine, and 377 received enhanced-potency inactivated polio vaccine B. In 88 instances, there was not enough serum to perform antibody determinations to all three poliovirus types starting at a dilution of 1:4. Seventy-two of these cases were in infants two months of age. When serum dilutions began at 1:8 or higher for a poliovirus type and no neutralizing activity was found, the data were omitted for that determination, but other serologic data on that child were included in the analysis.

Prevaccination

At enrollment, the percentage of children with antibodies to each of the three poliovirus types was similar for the inactivated polio vaccine A and oral polio vaccine groups (table 1 and figure 1). Approximately 90 per cent had antibodies to type 1, 95 per cent to type 2, and 78 per cent to type 3. More children in the inactivated polio vaccine B group had antibodies to type 2 poliovirus than did children in the oral polio vaccine group and to type 3 poliovirus than did children in either the inactivated polio vaccine A group or the oral polio vaccine group. However, the reciprocal geometric mean titers were similar for all three virus types for each vaccine group (table 2 and figure 2). The differences in the percentage of children with detectable antibodies were probably artifactual and were probably caused by the fact that the inactivated polio vaccine B group children were enrolled later (because enhanced-potency inactivated polio vaccine B was not available at the start of the study). After testing approximately one third of the two-, four-, and six-month blood samples from enhanced-potency inactivated polio vaccine A and oral polio vaccine recipients, we introduced a change in the virus neutralization test that increased its sensitivity approximately threefold (the serum-virus mixtures were incubated overnight at 36 C rather than at 4 C (14)). This explains the higher seropositivity rates in the inactivated polio vaccine B recipients before and after the first dose of vaccine. The change in the antibody technique had no effect, or a minimal effect, on the seropositivity rate at age six months and no effect at 18 or 20 months of age. Modifications in the performance of the neutralization test had no effect on the value of the geometric mean titers, expressed in International Units.

Post first dose

Two and one-half months after the first dose of inactivated polio vaccine, a signifi-

TABLE 1

Percentage of children with detectable antibodies to the three types of wild poliovirus at ages 2, 4, 6, 18, and 20 months, Maryland, 1980–1983

Age (months) at visit and vaccine group*	Mean age (months)	Type 1		Type 2		Type 3	
		No. of children	% with detectable antibodies	No. of children	% with detectable antibodies	No. of children	% with detectable antibodies
Two (prevaccination)							
IPV-A	2.2	331	90.9	338	96.5	318	78.3
OPV	2.2	337	89.6	343	94.2	323	78.0
IPV-B	2.2	332	93.4	351	98.9	317	89.6
Four							
IPV-A	4.6	309	93.5†	311	96.1	306	85.3
OPV	4.7	289	86.5	303	97.7	295	85.4
IPV-B	4.7	312	93.9	324	100.0	311	93.6
Six							
IPV-A	7.0	297	99.0	298	99.0	296	99.0
OPV	7.0	269	92.2	273	99.6	273	96.0
IPV-B	7.1	313	99.0	319	100.0	319	99.7
18							
IPV-A	20.2	225	98.7	229	99.6	228	97.8
OPV	19.8	187	88.8	189	100.0	189	97.4
IPV-B	20.2	245	97.6	247	99.6	247	98.4
20							
IPV-A	22.9	219	99.1	219	100.0	219	100.0
OPV	22.5	192	96.9	193	100.0	193	100.0
IPV-B	22.9	224	100.0	224	100.0	223	100.0

* IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

† Brackets indicate a difference between the two numbers that is significant at $p < 0.01$.

cant increase in the percentage of children with detectable antibodies was seen only in the inactivated polio vaccine A group and only against type 3 poliovirus, where it increased from 78 per cent to 85 per cent (table 1). Correspondingly, all of the geometric mean titers in the inactivated polio vaccine groups decreased or remained the same compared with the levels seen before vaccination was begun except the titers against type 3 poliovirus for the inactivated polio vaccine A recipients (table 2). After one dose of oral polio vaccine, there was a significant increase from 78 per cent to 85 per cent in the number of children who had detectable antibodies against type 3 poliovirus (table 1). No change was seen for types 1 and 2. Significant increases were seen in the geometric mean titers against types 2 and 3. These geometric mean titers were also statistically greater than the titers obtained after one dose of either of the enhanced-potency inactivated polio vaccines (table 2). For type 1, the geometric mean titer in the oral polio vaccine recipients did not change.

Figure 3 shows the percentage of children who demonstrated seroconversion to each of the vaccines after one dose of vaccine. (Seroconversion is defined as the presence of antibodies four or more times greater than the expected value at the second blood specimen, based on the level of maternal antibodies detected at the first vaccination and their estimated subsequent reduction.) A half-life of 28 days for the maternal antibodies was used in the calculation (15, 16). In general, this meant that children who had an antibody level at the four-month visit that equaled or exceeded the

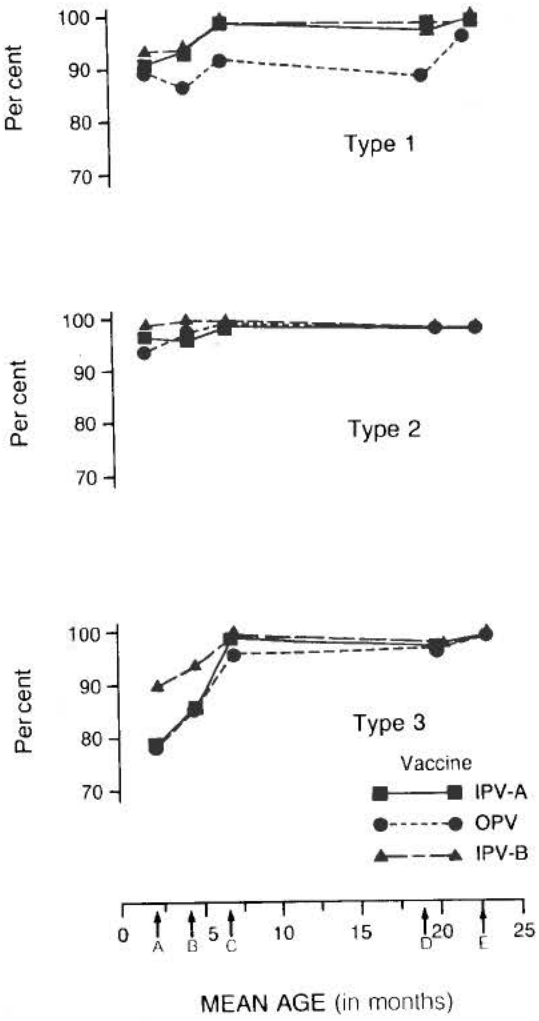

FIGURE 1. Percentage of children with detectable poliovirus-neutralizing antibodies at or after each dose of vaccine for each study group and poliovirus type: Baltimore City and Baltimore and Prince George's counties, Maryland, 1980–1983. *A*, preimmunization titer at age two months; *B*, titer two months post first dose; *C*, titer two months post second dose; *D*, titer at time of third dose; *E*, titer two months post third dose. IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

titer measured at two months of age were considered to have seroconverted. All three vaccines caused roughly the same amount of seroconversion to type 1 poliovirus (35 per cent to 42 per cent). Oral polio vaccine induced seroconversion to a greater degree than did either of the enhanced-potency inactivated polio vaccines against both type 2 and type 3 (84 per cent and 71 per cent, respectively). However, the enhanced-potency inactivated polio vaccines were able to stimulate seroconversion in a significant number of children in the presence of readily detectable maternal antibodies. For type 2, the range was between 35 per cent and 43 per cent; for type 3, it was between 54 per cent and 61 per cent.

Post second dose

Two and one-half months after receiving the second dose of vaccine, 99 per cent of the enhanced-potency inactivated polio vaccine recipients had detectable antibodies to type 1 poliovirus, while significantly fewer children (92.2 per cent) in the oral polio vaccine group had antibodies to this type. The geometric mean titers for all groups after the second dose of vaccine were significantly greater than they were after one dose. The enhanced-potency inactivated polio vaccine A stimulated the highest titers to type 1 poliovirus.

All three groups had 99 per cent or more children with detectable antibodies to type 2 poliovirus after the second dose of vaccine. The geometric mean titer for the oral polio vaccine group was significantly higher than that for either of the inactivated polio vaccine groups, and the geometric mean titer for the inactivated polio vaccine B group was significantly higher than that for the inactivated polio vaccine A group. The geometric mean titers for all groups were significantly higher than they were after one dose of vaccine.

After the second dose of vaccine, 99 per cent or more of the children in the enhanced-potency inactivated polio vaccine groups had detectable antibodies to type 3 poliovirus compared with 96 per cent for the oral polio vaccine group. The difference was significant between the inactivated polio vaccine B group and the oral polio vaccine group. The geometric mean titers for all groups were significantly greater than they were after one dose of

TABLE 2

Reciprocal geometric mean titers (GMT), in International Units, of antibody to the three types of wild poliovirus in children at ages 2, 4, 6, 18, and 20 months, Maryland, 1980–1983

Age (months) at visit and vaccine group*	Mean age (months)	Type 1		Type 2		Type 3	
		No. of children	GMT	No. of children	GMT	No. of children	GMT
Two							
IPV-A	2.2	331	0.39	338	1.07	318	0.25
OPV	2.2	337	0.38	343	0.92	323	0.25
IPV-B	2.2	332	0.36	351	0.84	317	0.20
Four							
IPV-A	4.6	309	0.28 †	311	0.64	306	0.32
OPV	4.7	289	0.39	303	7.73	295	1.94
IPV-B	4.7	312	0.17	324	0.60	311	0.20
Six							
IPV-A	7.0	297	2.10	298	3.64	296	4.98
OPV	7.0	269	1.04	273	17.01	273	4.37
IPV-B	7.1	313	1.29	319	6.77	319	3.33
18							
IPV-A	20.2	225	1.37	229	4.43	228	1.78
OPV	19.8	187	0.96	189	9.45	192	2.67
IPV-B	20.2	245	0.51	247	4.21	247	1.35
20							
IPV-A	22.9	219	12.96	219	25.44	219	16.42
OPV	22.5	192	2.69	193	19.20	193	4.41
IPV-B	22.9	224	7.98	224	28.14	223	17.75

* IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

† Brackets indicate a difference between the two numbers that is significant at $p < 0.01$.

vaccine and were not significantly different from each other.

The percentage of children with antibodies to all the poliovirus types for which their serum was tested was 97 for inactivated polio vaccine A, 90 for oral polio vaccine, and 99 for inactivated polio vaccine B. No child who received inactivated polio vaccine B was seronegative to more than one poliovirus type. One inactivated polio vaccine A recipient lacked antibodies to types 2 and 3. Five oral polio vaccine recipients lacked antibodies to types 1 and 3, and one lacked antibodies to types 2 and 3.

Pre third dose

In the 12- to 13-month interval between the third and fourth blood specimens, there was no statistically significant change in the percentage of children with detectable antibodies, and the geometric mean titers did not drop more than two dilutions.

We examined separately the results from children for whom paired serum specimens were available after the second dose and at the time the third dose of vaccine was given (table 3). The results for these children are essentially the same as those shown in table 2. During this interval, which averaged 13 months, there was less than a one-dilution decrease in the titers in the children who received oral polio vaccine. In the enhanced-potency inactivated polio vaccine groups, the decreases seen in titers were generally greater than for the oral polio vaccine group, but in no case were they more than two serial dilutions.

Post third dose

Two and one-half months after receiving the third dose of vaccine, all children had measurable antibodies against poliovirus types 2 and 3. All children who received enhanced-potency inactivated polio vac-

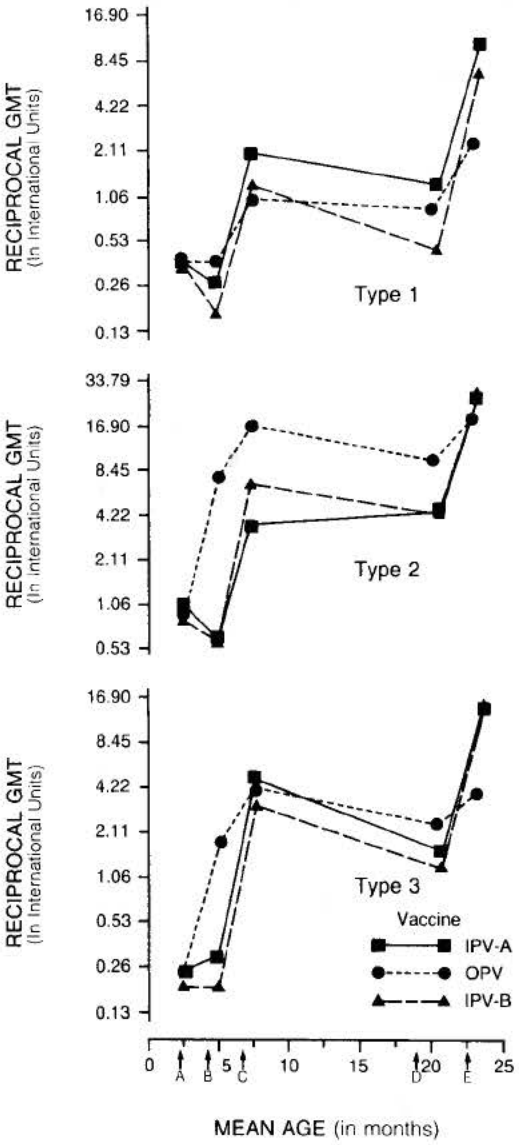

FIGURE 2. Reciprocal geometric mean titers (International Units) of poliovirus-neutralizing antibodies in children at or after each dose of vaccine for each study group and poliovirus type: Baltimore City and Baltimore and Prince George's counties, Maryland, 1980–1983. *A*, preimmunization titer at age two months; *B*, titer two months post first dose; *C*, titer two months post second dose; *D*, titer at time of third dose; *E*, titer two months post third dose. IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

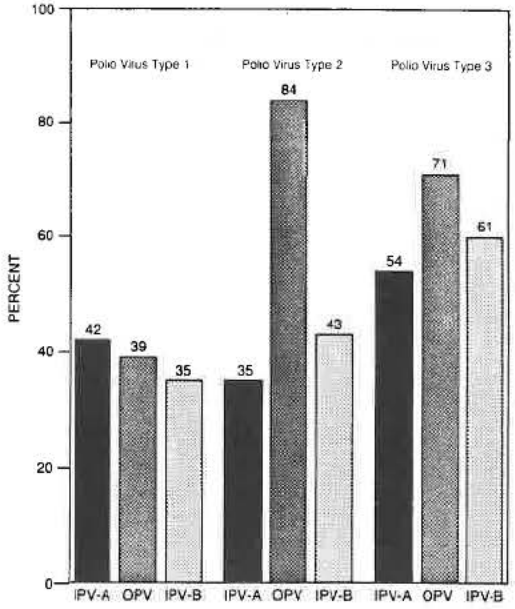

FIGURE 3. Percentage of children with seroconversion to one dose of either inactivated polio vaccine or oral polio vaccine given at two months of age: Baltimore City and Baltimore and Prince George's counties, Maryland, 1980–1983. See text for definition of seroconversion. IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

cine B were also protected against type 1. Only 1 per cent of the 219 children given three doses of enhanced-potency inactivated polio vaccine A did not produce antibodies to type 1, and only 3 per cent of the oral polio vaccine group did not have measurable antibodies to this type. At a group mean age of 22 or 23 months, the children who received the new enhanced-potency inactivated polio vaccines had significantly higher geometric mean titers to all three poliovirus types than did the children who received oral polio vaccine. The inactivated polio vaccine A group had significantly higher titers for type 1 than did the inactivated polio vaccine B group.

Adverse reactions

Table 4 presents information obtained about adverse reactions that occurred dur-

TABLE 3

Reciprocal geometric mean titers, in International Units, of poliovirus-neutralizing antibodies in children at ages 6 and 18 months for whom both specimens were taken, Maryland, 1980–1983

Poliovirus type and vaccine group*	No. of children	Geometric mean titer		p value
		Age six months	Age 18 months	
Type 1				
IPV-A	215	2.186	1.338	0.0001
OPV	175	1.068	1.027	0.7701
IPV-B	236	1.365	0.527	0.0001
Type 2				
IPV-A	215	3.724	4.416	0.1746
OPV	175	17.744	9.713	0.0001
IPV-B	236	6.855	4.133	0.0001
Type 3				
IPV-A	215	5.021	1.786	0.0001
OPV	175	4.612	2.556	0.0001
IPV-B	236	3.407	1.328	0.0001

* IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

ng the 48 hours after administration of the accines. Parents had the opportunity to provide information for the time periods of less than six, 6–23, and 24–48 hours after vaccination. Almost all parents (95.9 per cent) provided information for all three time periods. The data in table 5 represent reports following the administration of 991 first doses of polio vaccine, 893 second doses, and 544 third doses.

As mentioned above, the study groups were stratified according to geographic area, and the children were then randomized according to the polio vaccine they received. The marked difference in the adverse reaction rates according to the geographic area in which the child lived indicates the importance of the stratification. The reported adverse reaction rates recorded in children from Baltimore are higher for all but one reaction than they are for participants from the Prince George's County Health Department clinics. Interestingly, the only systemic reaction for which there is not a significant difference between the two geographic areas is a temperature ≥39 C, which is the most objective of all the observations ($p > 0.05$).

Comparison of the local reactions (erythema, pain, and induration) to inactivated polio vaccine A and to the injectable placebo given to the oral polio vaccine group for each geographic area shows no statistically significant differences. Likewise, there were no significant differences in any of the systemic reactions. Comparison of these two groups is mentioned first because it is only for these two groups that the infants were truly randomized. As was explained above, inactivated polio vaccine B was not made available for the study until 593 children (53 per cent) had been enrolled in either the inactivated polio vaccine A group or the oral polio vaccine group. Thus, rigorously speaking, the inactivated polio vaccine A and oral polio vaccine groups are historical controls for the inactivated polio vaccine B group. This fact notwithstanding, there were no significant differences between the inactivated polio vaccine B group and the two other groups in the reported rates of local reactions and for four of the six systemic reactions. A greater proportion of the children who received inactivated polio vaccine B were reported to be sleepier than usual, and in Prince George's County, a slightly greater percentage were reported to have a temperature ≥39 C.

Temperatures of >40 C were reported in 12 children. All these episodes occurred during the first 24 hours following vaccination, and they were similarly distributed in the three vaccine groups. One child who received the third dose of oral polio vaccine with the fourth dose of diphtheria-tetanus-pertussis vaccine was reported as having two convulsions within eight hours of receiving the vaccines. This child was seen by a private physician, and no neurologic sequelae were reported after 12 months of follow-up. Thus, we observed one convulsion per 834 fourth doses of diphtheria-tetanus-pertussis vaccine given, or one convulsion per 2,428 doses. No fainting or

TABLE 4

Frequency of reported local adverse reactions in vaccinated children at the site of inactivated polio vaccine or placebo injection and mild systemic reactions reported during the first 48 hours after vaccination, by geographic area and vaccine group per 100 children, Maryland, 1980–1983

	Baltimore				Prince George's County			
	IPV-A*	OPV (IPV placebo)	IPV-B	Total	IPV-A	OPV (IPV placebo)	IPV-B	Total
Number of doses	371	388	352	1,111	459	376	482	1,317
Local reaction								
Erythema	3.2	4.6	5.1	4.3	0.2	0.5	0.4	0.4
Pain								
Some	10.2	13.6	16.2	13.3	1.3	0.5	1.0	1.0
Much	2.7	1.8	1.1	1.9	0.2	0.0	0.0	0.1
Total	12.9	15.4	17.3	15.2	1.5	0.5	1.0	1.1
Induration								
<2 inches	1.1	1.3	2.8	1.7	0.2	0.0	0.0	0.1
2–4 inches	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.1
Systemic reaction								
Temperature ≥39 C	38.5	34.5	31.5	34.9	25.7	29.2	33.8 †	31.8
Sleepier than usual	40.9	36.8	59.9	54.0	5.7	6.6	12.8	8.6
Fussier than usual	63.6	64.0	69.3	63.7	18.9	21.0	26.8	23.4
Spitting up more than usual	8.9	9.2	11.1	11.7	1.3	1.5	<0.1	1.0
Eating less than usual	15.4	14.7	23.8	17.8	2.1	2.1	2.9	2.4
Crying more than usual	28.0	29.4	33.8	27.1	7.2	8.2	5.8	5.8

* IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France, OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

† Brackets indicate a difference between the vaccine groups for each geographic area that is significant at $p < 0.01$.

other neurologic events were reported for any of the children in the three days following vaccination or in the rest of the period between vaccinations.

The rates of local reactions at the site of diphtheria-tetanus-pertussis vaccinations are shown in table 5. Again, there is a marked difference in the rates for each of the two geographic areas. In no case is the rate for children who received enhanced-potency inactivated polio vaccine plus diphtheria-tetanus-pertussis vaccine significantly higher than for the children who received oral polio vaccine plus diphtheria-tetanus-pertussis vaccine.

Potentially confounding factors

Because this study was carried out in the United States, where oral polio vaccine is routinely administered, it is possible that study participants could have been exposed to vaccine virus given to a sibling or other close contact which would have stimulated the production of polio antibodies. This concern was, in part, addressed by the finding that in the 12- to 13-month interval between the third and fourth blood specimens, there was a drop in antibody titers in all three groups against all three virus serotypes except in the inactivated polio vaccine A group, which had a higher, although not statistically greater, type 2 antibody titer at the 18-month visit compared with the six-month visit (tables 2 and 3).

In addition, at each visit, parents were asked about the administration of oral polio vaccine to a sibling or other child living in the same household. Table 6 compares the

TABLE 5

Frequency of local adverse reactions in vaccinated children at the site of diphtheria-tetanus-pertussis (DTP) injection during the first 48 hours after vaccination, by geographic area and vaccine group per 100 children, Maryland, 1980–1983

	Baltimore				Prince George's County			
	IPV-A*	OPV	IPV-B	Total	IPV-A	OPV	IPV-B	Total
Number of doses	371	388	352	1,111	459	376	482	1,317
Local reaction at site of DTP injection								
Erythema	19.2	26.8	23.9	23.4	3.1	3.5	4.3	3.6
Pain								
Some	23.4	38.4	44.9 †	35.5	4.1	5.6	7.9	5.9
Much	10.8	10.3	10.5	10.5	0.2	0.0	0.2	0.2
Total	34.2	48.7	55.4	46.0	4.3	5.6	8.1	6.0
Induration								
<2 inches	22.6	22.9	28.1	24.5	1.5	2.9	4.8	3.1
2–4 inches	1.1	0.5	0.2	0.6	0.2	0.0	0.0	0.1

* IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

† Brackets indicate a difference between the vaccine groups for each geographic area that is significant at $p < 0.01$.

TABLE 6

Reciprocal geometric mean titers (GMT), in International Units, of poliovirus-neutralizing antibodies in children two months after the third dose of polio vaccine, by whether or not a sibling received oral polio vaccine during the study, Maryland, 1980–1983

Vaccine group* and poliovirus type	GMT if sibling received OPV	GMT if sibling did not receive OPV	*p* value
IPV-A	($n = 54$)†	($n = 165$)	
1	10.732	13.778	0.2508
2	24.296	25.827	0.6826
3	14.559	17.083	0.4224
OPV	($n = 37$)	($n = 156$)	
1	1.527	3.081	0.0673
2	13.136	21.015	0.0201
3	3.027	4.826	0.0394
IPV-B	($n = 60$)	($n = 164$)	
1	9.234	7.564	0.2073
2	31.146	27.120	0.1295
3	20.033	16.975	0.2351

* IPV-A, trivalent enhanced-potency inactivated polio vaccine produced by the Institut Merieux, France; OPV, trivalent oral polio vaccine; IPV-B, trivalent enhanced-potency inactivated polio vaccine produced by Connaught Laboratories Ltd., Canada.

† Number of children.

reciprocal geometric mean titers two months after the third dose of vaccine in study participants who had siblings who received oral polio vaccine during the course of the study with those who did not. If the oral polio vaccine had had a contaminating effect, one would expect to see higher titers in the children whose siblings received it. For the children who received inactivated polio vaccine A or oral polio vaccine, the data show the opposite trend. For the inactivated polio vaccine B recipients, the titers are slightly higher for children whose siblings received oral polio vaccine, but the differences are not statistically significant.

DISCUSSION

The results of this study confirm and extend the data presented by Salk (12) and Salk et al. (11) concerning the ability of the new enhanced-potency inactivated polio vaccines to stimulate antibody production in almost all children after two doses of vaccine. The initial report by Salk et al. (11) primarily involved Finnish children in

whom vaccination was begun at five months of age when the level of maternal antibodies would have waned to one eighth the level at two months of age, the age at which children were enrolled in this study. The data presented here demonstrate the ability of one dose of the new enhanced-potency inactivated polio vaccines to stimulate seroconversion in 35 per cent to 61 per cent of these younger children in spite of the higher maternal antibody levels. Although Salk (12) has argued that one dose of the enhanced-potency inactivated polio vaccine is sufficient to provide protection, the data in this study show the impact of the second and third doses of enhanced-potency inactivated polio vaccine. The second dose results in seroconversion in essentially all the enhanced-potency inactivated polio vaccine recipients and provides them with measurable protection against paralytic disease (17). As shown in table 2 and figure 2, the third dose of enhanced-potency inactivated polio vaccine causes a major rise (5.7- to 15.8-fold) in reciprocal geometric mean titers against each of the three poliovirus types. Thus, while the first two doses are important for stimulating detectable antibodies and assuring protection for all children, the third dose stimulates significantly higher antibody titers which are greater than those seen after three doses of oral polio vaccine.

This study has shown the superior ability of oral polio vaccine to induce seroconversion after one dose of vaccine in a population with high levels of maternal antibody. However, it is also clear that the second dose of oral polio vaccine is needed to bring about seroconversion in those who do not respond to the first dose and to enhance the level of antibody among all the recipients. The third dose of oral polio vaccine is important to increase the percentage of children with demonstrable antibodies against type 1 to 97 per cent and to increase the reciprocal geometric mean titer (2.5-fold) against this type. For types 2 and 3, the third dose of oral polio vaccine adds little to the reciprocal geometric mean titer. There is approximately a twofold increase bringing recipients to about the same level of antibodies they had two and one-half months after the second dose of oral polio vaccine, but it assures measurable protection in all the children (100 per cent have antibodies). Thus, we have reconfirmed the capability of oral polio vaccine to induce excellent levels of protection in almost all children who receive three doses of vaccine (18).

A US immunization program which relies on either oral polio vaccine or enhanced-potency inactivated polio vaccines should require a three-dose schedule during the first 15 to 18 months of life. Although it might be possible to give fewer doses if the first dose were withheld until children were six to seven months of age, we believe that the greatest number of children can be continuously protected by beginning polio immunization in the United States at two months of age, with a second dose at four months of age, as in this trial. Figure 1 shows the excellent situation that exists in the United States. Of those children who receive their first dose of vaccine by age two months, no more than 13.5 per cent are susceptible to type 1 poliovirus, no more than 6 per cent to type 2, and no more than 22 per cent to type 3. Because of the risk of infection with wild virus which still remains, however, susceptibility of the childhood population should not be allowed to drop below these levels by delaying the time at which polio immunization is begun.

The three-dose schedule of enhanced-potency inactivated polio vaccine is important for other elements of immunity conferred by that vaccine. It is well recognized that the lower-potency inactivated polio vaccines were not as efficient as was oral polio vaccine in protecting exposed people from incubating and shedding wild virus (19). In an epidemic in Rhode Island (19), pharyngeal shedding of virus was decreased from 75 per cent to 33 per cent in children with detectable antibody following inactivated polio vaccine administration, but shedding in the stool was decreased only ir

those children with high antibody titers (>1:128). Similar data were reported by Glezen et al. (17). They showed that in children vaccinated with inactivated polio vaccine who were given a challenge dose of type 1 oral poliovirus vaccine, the frequency of pharyngeal and fecal shedding was inversely proportional to the level of antibody present at the time of challenge. Thus, three doses of enhanced-potency inactivated polio vaccine would reduce the degree of shedding of virus and of community spread of either wild or vaccine virus to a greater extent than would two doses of enhanced-potency inactivated polio vaccine. Horstmann (20) postulates that the new enhanced-potency inactivated polio vaccines may increase the amount of secretory immune globulin A produced and thus reduce the amount of virus shed more than did the previously used inactivated polio vaccines.

The similarity in the local and systemic reaction rates presented in tables 4 and 5 ıdicates that the simultaneous adminis- ration of inactivated polio vaccine with diphtheria-tetanus-pertussis vaccine does not increase the rate of either local or systemic reactions over the simultaneous administration of oral polio vaccine with diphtheria-tetanus-pertussis vaccine. In addition, fever (temperature ≥39 C) and the mild systemic reactions reported in the oral polio vaccine group are generally similar to or lower than those reported in the literature following the administration of diphtheria-tetanus-pertussis vaccine (21, 22). Two exceptions are "crying more than usual" and "eating less than usual," which are more frequently reported in the Baltimore children in this study. However, the site coordinators asked mothers if their children were "crying more" or "eating less" than usual, not whether they were anorexic or exhibiting high-pitched, inconsolable crying, which are the signs reported in the literature. Thus, the higher rate could be expected.

The potentially confounding role of the spread of oral polio vaccine from a vaccinated sibling was addressed by the data presented in table 6. In addition, Ogra (23) and Dhar and Ogra (24), studying children in groups of six to 12, have shown that a dose of oral polio vaccine given seven months after three doses of the less potent inactivated polio vaccine given at two, three, and four months of age will result in a significantly greater booster effect than that seen with an additional dose of inactivated polio vaccine. Thus, because we did not see higher titers in the enhanced-potency inactivated polio vaccine recipients whose siblings received oral polio vaccine, it is unlikely that the very good response we have ascribed to the new enhanced-potency inactivated polio vaccines is due to contamination and unintentional immunization with oral polio vaccine shed by other children.

The presence of such high titers of antibodies following the three-dose enhanced-potency inactivated polio vaccine schedule used in this study indicates that a change could be made in the current Immunization Practices Advisory Committee recommendation to give three doses of inactivated polio vaccine at two, four, and six months of age, followed by a fourth dose one year later. For vaccines of D-antigen content comparable to those used in this study, two doses of vaccine given in the first year of life, beginning as early as two months of age, followed by a third dose at 15 to 18 months, would be appropriate.

References

1. Centers for Disease Control. Poliomyelitis prevention. Recommendation of the Immunization Practices Advisory Committee. MMWR 1982;31:22–34.
2. Committee on Infectious Diseases, American Academy of Pediatrics. Report of the Committee on Infectious Diseases, 20th ed. Elk Grove Village, IL: American Academy of Pediatrics, 1986:283–91.
3. Nightengale EO. Recommendations for a national policy on poliomyelitis vaccination. N Engl J Med 1977;297:249–53.
4. Centers for Disease Control. Poliomyelitis Surveillance Summary 1980–1981. Atlanta: Centers for Disease Control, December 1982.
5. Nkowane BM, Wassilak SCF, Orenstein WA, et al. Vaccine-associated paralytic poliomyelitis,

USA, 1973–1984. JAMA 1987;257:1335–40.
6. Centers for Disease Control. International Notes. Update: poliomyelitis outbreak—Finland, 1984–85. MMWR 1986;35:82–6.
7. Bottiger M. Long term immunity following vaccination with killed poliovirus vaccine in Sweden, a country with no circulating poliovirus. Rev Infect Dis 1984;6(suppl 2):S548–51.
8. Lapinleimu K. Elimination of poliomyelitis in Finland. Rev Infect Dis 1984;6(suppl 2):S457–60.
9. Bijkerk H. Surveillance and control of poliomyelitis in the Netherlands. Rev Infect Dis 1984; 6(suppl 2):S451–6.
10. van Wezel AL, van Steenis G, Hannik CA, et al. New approach to the production of concentrated and purified inactivated polio and rabies tissue culture vaccines. Dev Biol Stand 1978;41:159–68.
11. Salk J, van Wezel AL, Stoeckel P, et al. Theoretical and practical considerations in the application of killed poliovirus vaccine for the control of paralytic poliomyelitis. Dev Biol Stand 1981;47:181–98.
12. Salk J. One-dose immunization against paralytic poliomyelitis using a noninfectious vaccine. Rev Infect Dis 1984;6(suppl 2):S444–50.
13. Stoeckel P, Schlumberger M, Parent B, et al. Use of killed poliovirus vaccine in a routine immunization program in West Africa. Rev Infect Dis 1984;6(suppl 2):S463–6.
14. Albrecht P, Enterline JC, Boone EK, et al. Poliovirus and polio antibody assay in HEP-2 and vero cell cultures. Dev Biol Stand 1983;11:91–7.
15. Plotkin SA, Koproski H, Stokes J Jr. Clinical trials in infants of orally administered attenuated poliomyelitis viruses. Pediatrics 1959;23:1041–62.
16. Halsey N, Galazka A. The efficacy of DPT and oral poliomyelitis immunization schedules initiated from birth to 12 weeks of age. Bull WHO 1985;63:1151–69.
17. Glezen WP, McCollough RH, Lamb GA, et al. Quantitative relationship of preexisting homotypic antibodies to excretion of poliovirus types 1, 2, and 3 following the feeding of trivalent attenuated poliovirus vaccine. Am J Epidemiol 1969;90:146–56.
18. Hardy GE, Hopkins CC, Linnemann CC, et al. Trivalent oral poliovirus vaccine: a comparison of two infant immunization schedules. Pediatrics 1970;45:444–8.
19. Marine WM, Chin TDY, Gravelle CR. Limitation of fecal and pharyngeal poliovirus excretion in Salk-vaccinated children: a family study during a type 1 poliomyelitis epidemic. Am J Hyg 1962;76:173–95.
20. Horstmann DM. Control of poliomyelitis: a continuing paradox. J Infect Dis 1982;146:540–51.
21. Cody CL, Baraff LJ, Cherry JD, et al. Nature and rates of adverse reactions associated with DTP and DT immunizations in infants and children. Pediatrics 1981;68:650–60.
22. Baraff LJ, Cody CL, Cherry JD. DTP associated reactions: an analysis by injection site, prior reactions and dose. Pediatrics 1984;73:31–6.
23. Ogra PL. Mucosal immune response to poliovirus vaccines in childhood. Rev Infect Dis 1984;6(suppl 2):S361–8.
24. Dhar R, Ogra PL. Local immune responses. J Med Bull 1985;41:28–33.