icddr,b	**RRC APPLICATION FORM**

RESEARCH PROTOCOL **Number: 20060** **Version No. 1.06** **Version date: 03-Dec-2020**	**FOR OFFICE USE ONLY**		
	RRC Approval:	☒ Yes ☐ No	Date:17.07.2020
	ERC Approval:	☒ Yes ☐ No	Date: 22.08.2020
	AEEC Approval:	☐ Yes ☐ No	Date:
	External IRB Approval	☐ Yes ☐ No	Date:
	Name of External IRB: _____		

Protocol Title:* (maximum 250 characters including space**)** Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

Short Title: (maximum **100** characters including space)
nOPV2 with and without bOPV

Key Words:* nOPV2, bOPV, immunogenicity, Bangladesh

Name of the Research Division Hosting the Protocol:*

- ☐ Health Systems and Population Studies Division (HSPSD)
- ☐ Nutrition and Clinical Services Division (NCSD)
- ☒ Infectious Diseases Division (IDD)
- ☐ Maternal and Child Health Division (MCHD)
- ☐ Laboratory Sciences and Services Division (LSSD)
- ☐ Other (specify) _____

Has the Protocol been Derived from an Activity:* ☒ No ☐ Yes (please provide following information):

Activity No. :
Activity Title:
PI:
Grant No.: Budget Code: Start Date: End Date:

icddr,b Strategic Priority/ Initiative (SP 2015-8):* (check all that apply**)**

- ☐ Reducing maternal and neonatal mortality
- ☒ Controlling enteric and respiratory infections
- ☐ Preventing and treating maternal and childhood malnutrition
- ☐ Detecting and controlling emerging and re-emerging infections
- ☐ Achieving universal health coverage
- ☐ Examining the health consequences of climate change
- ☐ Preventing and treating non-communicable diseases
- ☐ Others (specify) _____

Research Phase (4 Ds):* (check all that apply**)**

- ☐ Discovery
- ☒ Development
- ☒ Delivery
- ☐ Evaluation of Delivery

Anticipated Impact of Research:* (check all that apply and please provide details below**)**

- ☒ Knowledge Production
- ☐ Capacity Building
- ☒ Informing Policy
- ☐ Health and Health Sector Benefits
- ☐ Economic Benefits

Please provide details here:

The results will guide Global Polio Eradication Initiative (GPEI), including WHO, in making policy for responding to polio outbreaks with the goal of eradication of polio.

Which of the Sustainable Development Goal This Protocol Relates to?:* (check all that apply**)**

- ☐ 1. End poverty in all its forms everywhere
- ☐ 2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture
- ☒ 3. Ensure healthy lives and promote well-being for all at all ages
- ☐ 4. Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all
- ☐ 5. Achieve gender equality and empower all women and girls
- ☐ 6. Ensure availability and sustainable management of water and sanitation for all
- ☐ 7. Ensure access to affordable, reliable, sustainable and modern energy for all
- ☐ 8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all
- ☐ 9. Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation
- ☐ 10. Reduce inequality within and among countries
- ☐ 11. Make cities and human settlements inclusive, safe, resilient and sustainable
- ☐ 12. Ensure sustainable consumption and production patterns
- ☐ 13. Take urgent action to combat climate change and its impacts
- ☐ 14. Conserve and sustainably use the oceans, seas and marine resources for sustainable development
- ☐ 15. Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss
- ☐ 16. Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels
- ☐ 17. Strengthen the means of implementation and revitalize the global partnership for sustainable development

Does this Protocol Use the Gender Framework:* (Please visit: http://www.icddrb.net.bd/jahia/Jahia/pid/684 for Gender Alanysis Tool with instructions)	☐ Yes (please complete Gender Analysis Tool) ☒ No
If 'no' is the response, its reason(s) in brief: Nothing known about gender issues in polio vaccination	
Will this Research Specifically Benefit the Disadvantaged (economically, socially and/or otherwise**):**	☐ Yes ☒ No
Does this Protocol use Behaviour Change Communication:	☐ Yes ☒ No

Principal Investigator (Should be icddr,b staff):* Sex ☐ Female ☒ Male **K. Zaman, Senior Scientist and Epidemiologist** **kzaman@icddrb.org Exg: 3806** Cell phone: 01713047100, Do you have ethics certification? ☐ No ☒ Yes (please attach in your CV below) Do you have RBM training certification? ☐ No ☒ Yes (please attach the certificate with CV below)	Primary Scientific Division of the PI IDD
Co-Principal Investigator(s) Internal: Sex ☐ Female ☒ Male **Md. Yunus, myunus@icddrb.org** Signature or written consent of Co-PI: _____ (electronic signature or email or any sort of written consent) [if more than one, please copy and paste this row for additional Co-PIs] Do you have ethics certification? ☐ No ☒ Yes (please attach in your CV below) Do you have RBM training certification? ☐ No ☒ Yes (please attach the certificate with CV below)	Primary Scientific Division/ Programme of the Co-PI E-mail approval Page 107 HSPSD _____ Approval of the Respective Senior Director/ Programme Head (Signature)

Co-Investigator(s) - Internal: Sex ☒ Female ☐ Male **Dr. Asma Binte Aziz** (Position, phone no, extension no, cell, and email address **):** Research Investigator, asma.aziz@icddrb.org Signature or written consent of Co-I: _____ (electronic signature or email or any sort of written consent) [if more than one, please copy and paste this row for additional Co-Is Do you have ethics certification? ☐ No ☒ Yes (please attach in your CV below) Do you have RBM training certification? ☐ No ☒ Yes (please attach the certificate with CV below)	Primary Scientific Division of the Co-I IDD E-mail approval Page 107 _____ Approval of the Respective Senior Director/ Programme Head (Signature)
Co-Investigator(s) - Internal: Sex ☒ Female ☐ Male **Dr. Masuma Hoque** (Position, phone no, extension no, cell, and email address **):** Senior Research Investigator, masuma.hoque@icddrb.org Signature or written consent of Co-I: _____ (electronic signature or email or any sort of written consent) [if more than one, please copy and paste this row for additional Co-Is Do you have ethics certification? ☐ No ☒ Yes (please attach in your CV below) Do you have RBM training certification? ☐ No ☒ Yes (please attach the certificate with CV below)	Primary Scientific Division of the Co-I IDD E-mail approval Page 108 _____ Approval of the Respective Senior Director/ Programme Head (Signature)
Co-Principal Investigator(s) - External: Sex ☒ Female ☐ Male Amanda L. Wilkinson Global Immunization Division US Centers for Disease Control and Prevention 1600 Clifton Road NE Atlanta, GA, USA lxq6@cdc.gov Signature or written consent of Co-PI: _____ (electronic signature or email or any sort of written consent) E-mail approval Page 122	
Co-Investigator(s) - External: Sex ☐ Female ☒ Male Abhijeet Anand Global Immunization Division US Centers for Disease Control and Prevention 1600 Clifton Road NE Atlanta, GA, USA aanand@cdc.gov office: +1-404-639-1970 Blackberry: +1-404-797-9074 Signature or written consent of Co-I: _____ (electronic signature or email or any sort of written consent) E-mail approval Page 122	

Co-Investigator(s) - External: Sex ☒ Female ☐ Male
Cindi Snider
Global Immunization Division
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
csnider@cdc.gov
Office: +1-404-718-6328
Blackberry: +1-404-431-4626

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 123

Co-Investigator(s) – External: Sex ☒ Female ☐ Male
Concepcion F. Estivariz
Global Immunization Division
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
cge3@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 124

Co-Investigator(s) – External: Sex ☒ Female ☐ Male
Qian An
Global Immunization Division
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
fei8@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 125

Co-Investigator(s) – External: Sex ☐ Female ☒ Male
Mark Pallansch
National Center for Immunization and Respiratory DiseasesUS Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
map1@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 125

Co-Investigator(s) – External: Sex ☐ Female ☒ Male
Steven Wassilak
Global Immunization Division
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
sgw1@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 126

Co-Investigator(s) – External: Sex ☐ Female ☒ Male
Steve Oberste
Division of Viral Diseases
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
mbo2@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 127

Co-Investigator(s) - External: Sex ☒ Female ☐ Male
Jacquelyn S. Lickness
Global Immunization Division
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
wxx3@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 127

Co-Investigator(s) - External: Sex ☐ Female ☒ Male
Jaymin Patel
Global Immunization Division
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
isr0@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 128

Co-Investigator(s) - External: Sex ☒ Female ☐ Male
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Division of Viral Diseases
US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
yrq1@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 129

Co-Investigator(s) - External: Sex ☒ Female ☐ Male
Cara Burns
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US Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA, USA
zqd1@cdc.gov

Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 130

Technical Advisor(s) HOUSEHOLD TRANSMISSION ADD-ON COMPONENT ONLY

Ananda S. Bandyopadhyay
Bill and Melinda Gates Foundation
500 5th Avenue N
Seattle, WA, USA
Ananda.Bandyopadhyay@gatesfoundation.org
Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 130

Jillian Gauld
Institute for Disease Modeling
139th Avenue SE
Bellvue, WA, USA
jgauld@idmod.org
Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 130

Mike Famulare
Institute for Disease Modeling
139th Avenue SE
Bellvue, WA, USA
mfamulare@idmod.org
Signature or written consent of Co-I: _____
(electronic signature or email or any sort of written consent) E-mail approval Page 130

Collaborating Institute(s): Please provide full official address

Institution # 1

Country	USA
Contact person	Abhijeet Anand
Department (including Division, Centre, Unit)	Global Immunization Division
Institution (with official address)	US Centers for Disease Control and Prevention 1600 Clifton Road NE Atlanta, GA, 30329
Directorate (in case of GoB i.e. DGHS)	
Ministry (in case of GoB)	

Institution # 2

Country	Bangladesh
Contact person	Dr. Md. Shamsul Haque
Department (including Division, Centre, Unit)	DGHS
Institution (with official address)	Line Director, MNC & AH
Directorate (in case of GoB i.e. DGHS)	
Ministry (in case of GoB)	

Note: If less than or more than three collaborating institutions, please delete or insert blocks as needed.

Contribution by the Members of the Scientific Team:

Members' Name	Contribution								
	Research idea/ concept	Study design	Protocol writing	Respond to external reviewers' comments	Defending at IRB	Developing data collection Tool(s)	Data Collection	Data analysis/ interpretation of results	Manuscript writing
K. Zaman	☒	☒	☒	☒	☒	☒	☒	☒	☒
Md. Yunus	☒	☒	☒	☒	☒	☒	☒	☒	☒
Amanda Wilkinson	☒	☒	☒	☒	☐	☒	☐	☒	☒
Abhijeet Anand	☒	☒	☒	☒	☐	☒	☐	☒	☒
Cindi Snider	☒	☒	☒	☒	☐	☒	☐	☒	☒
Concepcion Estivariz	☒	☒	☒	☒	☐	☒	☐	☒	☒
Qian An	☐	☒	☒	☒	☐	☒	☐	☒	☒
Steven Wassilak	☒	☒	☒	☒	☐	☒	☐	☒	☒
Mark Pallansch	☒	☒	☒	☒	☐	☒	☐	☒	☒
Steve Oberste	☒	☒	☒	☒	☐	☒	☐	☒	☒
Jacquelyn S. Lickness	☐	☒	☒	☒	☐	☒	☐	☒	☒
Asma Aziz	☐	☐	☒	☒	☒	☒	☒	☒	☒
Masuma Hoque	☐	☐	☒	☒	☒	☒	☒	☒	☒
Jaymin Patel	☐	☒	☒	☐	☐	☒	☐	☒	☒
Jennifer Anstadt	☐	☒	☒	☐	☐	☒	☐	☒	☒
Cara Burns	☐	☒	☒	☐	☐	☒	☐	☒	☒
Ananda S. Bandyopadhyay	☐	☒	☒	☐	☐	☒	☐	☒	☒
Jillian Gauld	☐	☒	☒	☐	☐	☒	☐	☒	☒
Mike Famulare	☐	☒	☒	☐	☐	☒	☐	☒	☒

Study Population: Sex, Age, Special Group and Ethnicity

Research Subject:
- ☒ Human
- ☐ Animal
- ☐ Microorganism
- ☐ Other (specify): _____

Sex:
- ☒ Male
- ☒ Female
- ☐ Transgender

Age:
- ☒ 0 – 4 years
- ☒ 5 – 10 years
- ☐ 11 – 17 years
- ☐ 18 – 64 years
- ☐ 65 +

Special Group:
- ☐ Pregnant Women
- ☐ Fetuses
- ☐ Prisoners
- ☐ Destitutes
- ☐ Service Providers
- ☐ Cognitively Impaired
- ☐ CSW
- ☐ Expatriates
- ☐ Immigrants
- ☐ Refugee
- ☐ Others (specify): _____

Ethnicity:
- ☒ No ethnic selection (Bangladeshi)
- ☐ Bangalee
- ☐ Tribal group
- ☐ Other (specify): _____

NOTE: It is icddr.b's policy to include men, women, children and transgender in its research projects involving participation of humans, unless there is strong justification(s) for their exclusion.

Consent Process: (Check all that apply**)**

☒ Written
☐ Oral
☐ Audio
☐ Video
☐ None

Language:

☒ Bangla
☐ English
☐ Other (specify: _____

Project/Study Site: (Check all that apply**)**

☐ Chakaria
☐ Bandarban
☐ Dhaka Hospital
☐ Kamalapur Field Site/HDSS
☒ Mirpur (Dhaka)
☐ Matlab DSS Area
☐ Matlab non-DSS Area
☐ Matlab Hospital
☐ Mirzapur
☐ Bianibazar (Sylhet)
☐ Kanaighat (Sylhet)
☐ Jakigonj (Sylhet)
☒ Other community in Dhaka
Name: CTU, Mohakhali_____
☐ Other sites in Bangladesh
Name: _____
☐ Multi-national Study
Name of the country_____

Project/Study Type: (Check all that apply)

☐ Case Control Study
☒ Clinical Trial (Hospital/Clinic/Field)*
☐ Community-based Trial/Intervention
☐ Cross Sectional Survey
☐ Family Follow-up Study
☐ Longitudinal Study (cohort or follow-up)
☐ Meta-analysis
☐ Programme Evaluation
☐ Programme (Umbrella Project)
☐ Prophylactic Trial
☐ Record Review
☐ Secondary Data Analysis
Protocol No. of Data Source: _____
☐ Surveillance/Monitoring
☐ Systematic Review
☐ Other (specify): _____

***Note**: International Committee of Medical Journal Editors (ICMJE) defines Clinical Trial as "*Any research project that prospectively assigns human participants to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome*".

PI of the RRC- and ERC-approved Clinical Trials should provide necessary information to IRB Secretariat (Research Administration) for registration and uploading into relevant websites (usually at the https://register.clinicaltrials.gov/). They should also provide relevant information to the IRB Secretariat in the event of amendment/modification after their approval by RRC and ERC.

Biological Specimen:

a) Will the biological specimen be stored for future use?	☒ Yes ☐ No ☐ Not applicable
b) If the response is 'yes', how long the specimens will be preserved?	_____5_____ years
c) What types of tests will be carried out with the preserved specimens?	Studies involving polio and/or other vaccine preventable diseases may request preserved serum and/or stool specimens. No DNA or genetic testing of blood specimens will be permitted. Proposals to test stored specimens will need to be reviewed and approved by icddr,b's research and ethical review committees as well as the institution requesting preserved specimens.
d) Will the consent be obtained from the study participants for use of the preserved specimen for other initiative(s) unrelated to this study, without their re-consent?	☐ Yes ☒ No ☐ Not applicable
e) Will the specimens be shipped to other country/ countries? If yes, name of institution(s) and country/countries.	☒ Yes ☐ No ☐ Not applicable Name Centers for Disease Control and Prevention, Atlanta, USA_____

f) If shipped to another country, will the surplus/unused specimen be returned to icddr,b? If the response is 'no', then the surplus/unused specimen must be destroyed.	☐ Yes ☒ No ☐ Not applicable
g) Who will be the custodian of the specimen at icddr,b?	Dr. K. Zaman
h) Who will be the custodian of the specimen when shipped outside Bangladesh?	Dr. Bernardo A. Mainou, CDC
i) Who will be the owner(s) of the specimens?	icddr,b
j) Has a MoU been signed with regards to collection, storage, use and ownership of specimen? If the response is 'yes', please attach a copy of the MoU. If the response is 'no', appropriate justification should be provided for not signing a MoU.	☐ Yes ☒ No ☐ Not applicable The MOU for icddr,b will be obtained prior to start of the study.

Proposed Sample Size:
Sub-group (Name of subgroup e.g. Men, Women) and Number

Name	Number	Name	Number
(1) A: nOPV2 @ 6, 10, and 14 weeks	265		
(2) B: nOPV2 + bOPV @ 6, 10, and 14 weeks	265		
(3) C: bOPV @ 6, 10, and 14 weeks	265		
Total sample size	795		

Determination of Risk: Does the Research Involve (Check all that apply**)**

☐ Human exposure to radioactive agents?
☐ Foetal tissue or abortus?
☐ Investigational new device?
Specify: _____
☐ Existing data available from Co-investigator?
☐ Human exposure to infectious agents?
☒ Investigational new drug/vaccine?
☐ Existing data available via public archives/sources?
☐ Pathological or diagnostic clinical specimen only?
☐ Observation of public behaviour?
☐ New treatment regime?

	Yes	No
Will the information be recorded in such a manner that study participants can be identified from the information directly or through identifiers linked to the study participants?	☒	☐
Does the research deal with sensitive aspects of the study participants' sexual behaviour, alcohol use or illegal conduct such as drug use?	☐	☒

Could information on study participants, if available to people outside of the research team:

	Yes	No
a) Place them at risk of criminal or civil liability?	☐	☒
b) Damage their financial standing, reputation or employability, or social rejection, or lead to stigma, divorce etc.?	☐	☒

Do you consider this research: (check one)

☐ Greater than minimal risk	☒ No more than minimal risk	☐ Only part of the diagnostic test

Note: Minimal Risk: The probability and the magnitude of the anticipated harm or discomfort to participants is not greater than those ordinarily encountered in daily life or during the performance of routine physical, psychological examinations or tests, e.g. the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than when the same is performed for routine management of patients.

Risk Group of Infectious Agent and Use of Recombinant DNA	
a) Will specimens containing infectious agent be collected?	☒ Yes ☐ No ☐ Not applicable
b) Will the study involve amplification by culture of infectious agents?	☒ Yes ☐ No ☐ Not applicable
c) If response to questions (a) and/or (b) is 'yes', to which Risk Group (RG) does the agent(s) belong? (Please visit http://www.icddrb.net.bd/jahia/Jahia/pid/684 to review list of microorganism by Risk Group)	☐ RG1 ☒ RG2 ☐ RG3 ☐ RG4
d) Does the study involve experiments with recombinant DNA?	☐ Yes ☒ No ☐ Not applicable

Does the study involve any biohazards materials/agents or microorganisms of risk group 2, 3, or 4 (GR2, GR-3 or GR4)?

☒ Yes ☐ No

[If the response is 'yes'] I, (print name of the PI) affirm that we will use the standard icddr,b laboratory procedures for biosafety of the hazardous materials/agents or microorganisms in the conduction of the study.

_____ _____

Signature of the Principal Investigator **Date**

Dissemination Plan: [please explicitly describe the plans for dissemination, including how the research findings would be shared with stakeholders, identifying them if known, and the mechanism to be used; anticipated type of publication (working papers, internal (institutional) publication, international publications, international conferences/seminars/workshops/ agencies. [Check all that are applicable]

Dissemination type	Response		Description (if the response is a yes)
Seminar for icddr,b scientists/ staff	☐ No	☒ Yes	The results will be shared in icddr,b internal seminars
Internal publication	☒ No	☐ Yes	
Working paper	☒ No	☐ Yes	
Sharing with GoB (e.g. DGHS/ Ministry, others)	☐ No	☒ Yes	The clinical trials results could inform government of Bangladesh immunization policy
Sharing with national NGOs	☐ No	☒ Yes	The results will be shared with national NGOs
Presentation at national workshop/ seminar	☐ No	☒ Yes	The results will be presented at a national workshop/seminar
Presentation at international workshop/ conference	☐ No	☒ Yes	The results will be shared in international conferences as these results could have global implication
Peer-reviewed publication	☐ No	☒ Yes	Multiple peer-reviewed publications are possible
Sharing with international agencies	☐ No	☒ Yes	The results will be shared with international agencies such as World Health Organization
Sharing with donors	☐ No	☒ Yes	CDC is funding agency for this clinical trial and the results will be shared with CDC
Policy brief	☒ No	☐ Yes	
Other			
Other			

Funding:

Is the protocol fully funded?	☒ Yes	☐ No
If the answer is yes, please provide sponsor(s)'s name	1. CDC through co-operative agreement.	
	2.	
Is the protocol partially funded?	☐ Yes	☐ No
If the answer is yes, please provide sponsor(s)'s name	1.	
	2.	

If fund has not been identified:

Is the proposal being submitted for funding?	☐ Yes	☐ No
If yes, name of the funding agency	1.	
	2.	

Conflict of interest:
Do any of the participating investigators and/or member(s) of their immediate families have an equity relationship (e.g. stockholder) with the sponsor of the project or manufacturer and/or owner of the test product or device to be studied or serve as a consultant to any of the above?

☒ No	☐ Yes (please submit a written statement of disclosure to the Executive Director, icddr,b)

Proposed Budget:

Dates of Proposed Period of Support

Cost Required for the Budget Period ($)

(Day, Month, Year - DD/MM/YY)

Beginning Date: September 2020

End Date: June 2021

Years	Direct Cost	Indirect Cost	Total Cost
Year-1	586,896	174,938	761,834
Year-2			
Year-3			
Year-4			
Year-5			
Total	586,896	174,938	761,834

Certification by the Principal Investigator:

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept the responsibility for the scientific conduct of the project and to provide the required progress reports including updating protocol information in the NAVISION if a grant is awarded as a result of this application.

I also certify that I have read icddr,b Data Policies and understand the PIs' responsibilities related to archival and sharing of research data, and will remain fully compliant to the Policies. (Note: The Data Policies can be found here: http://www.icddrb.org/who-we-are/data-policies)

_____ _____

Signature of PI **Date**

Approval of the Project by the Division Director of the Applicant:

The above-mentioned project has been discussed and reviewed at the Division level.

Name of the Division Director | Signature | Date of Approval

Table of Contents

☒ Check here if appendix is included

Protocol Version Control Page

Listed below is the guidance for protocol version control. The table below lists the protocol versions, date of activation of a version, the name of the study staff who finalized the said protocol version and the reason for creating the protocol version compared to a prior existing version.

1. Version number:
    a. The first draft of the document would be 1.01
    b. Subsequent drafts will have an increase of 0.01 (e.g. 1.02, 1.03, 1.04)
    c. The file name and footer of every page on the protocol will include the name of the protocol and version number. For this protocol the file name and footer will read: "nOPV2 and bOPV Study ver 1.XX"
    d. Each version of the protocol after 1.01 should have two copies: version labeled "track changes" and version labeled "clean". Track change version will highlight the changes in the named version compared to prior.
    e. A pdf file of protocol should follow the same naming convention as the protocol in word processing software
2. Date of activation
    a. Date the protocol version number went into effect as the study protocol
    b. Activation date can be skipped for development versions of the protocol, i.e. versions before sharing with co-investigators
3. Responsible study staff
    a. The study staff who is primarily responsible for creating the version and sharing with other study team
4. Summary reason for protocol version
    a. A reason for creating the version and its eventual use, e.g. version for submission to external peer review, version for submission to RRC. One does not need to list the detailed changes in the named version compared to the prior version as that can be noted by the track changes copy

Version number	**Date of Activation**	**Staff Finalizing the Version**	**Summary reason**
Ver 1.01	05-Mar-2020	Abhijeet Anand / Amanda Wilkinson	Draft protocol shared with co-investigators
Ver 1.02	17-Mar-2020	Amanda Wilkinson	Revisions based on co-investigator comments
Ver 1.03	08-Jun-2020	Amanda Wilkinson	Removed study arms with nOPV2 candidate 2, added stool collection at 8 weeks, updated study site
Ver 1.04	14-Jul-2020	Amanda Wilkinson	Revisions based on RRC comments
Ver 1.05	10-Aug-2020	Amanda Wilkinson	Revisions based on ERC comments
Ver 1.06	03-Dec-2020	Amanda Wilkinson / Jaymin Patel	Adding household transmission component

Glossary of Terms

AE	Adverse Event
bOPV	Bivalent Oral Poliovirus Vaccine
CDC	Centers for Disease Control and Prevention
CRF	Case Report Form (paper)
cVDPV	Circulating Vaccine-Derived Poliovirus
DSMB	Data Safety Monitoring Board
eCRF	Case Report Form (electronic/tablet)
EPI	Expanded Program on Immunization
ERC	Ethical Review Committee
fIPV	Fractional IPV
GPEI	Global Polio Eradication Initiative
icddr,b	International Center for Diarrhoeal Disease Research, Bangladesh
IPV	Inactivated Poliovirus Vaccine
IRB	Institutional Review Board
nOPV2	Novel monovalent oral poliovirus vaccine type 2
OPV	Oral Poliovirus Vaccine
PID	Participant Identification Number
PCR	Polymerase Chain Reaction
RRC	Research Review Committee
SAE	Serious Adverse Event
SAGE	Strategic Advisory Group of Experts on Immunization
SC	Subcutaneous
SOP	Standard operating procedure
tOPV	Trivalent Oral Poliovirus Vaccine
VAPP	Vaccine-Associated Paralytic Poliomyelitis
VDPV	Vaccine-Derived Poliovirus
WHO	World Health Organization
WPV	Wild poliovirus

Project Summary

[The summary, within a word limit of 300, should be stand alone and be fully understandable.]

Principal Investigator: Dr. K. Zaman

Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

Proposed start date: December 2020
Estimated end date: September 2021

Background:

Wild poliovirus type 2 (WPV2) was declared eradicated in 2015 and type 2 oral poliovirus vaccine (OPV2) was withdrawn globally in May 2016. Monovalent OPV2 (mOPV2) is stockpiled for responding to circulating type 2 vaccine-derived poliovirus (cVDPV2) outbreaks. However, Sabin polioviruses in OPV can revert to neurovirulence and there is evidence that mOPV2 vaccines used to control cVDPV2 outbreaks have generated new VDPV2 emergences that have led to cVDPV2 outbreaks. Novel OPV2 (nOPV2) candidates have been developed with improved genetic stability to reduce the risk of seeding new VDPVs. Findings from a phase 1 clinical trial in adults demonstrated the safety and immunogenicity of nOPV2. Preliminary results from phase 2 clinical trials in adults and children also suggest that the nOPV2 vaccines are safe and immunogenic.

As of late 2019, nOPV2 candidate 1 was selected for Emergency Use Listing submission and commercial scale manufacturing. It is expected that nOPV2 would replace mOPV2 for responding to type 2 outbreaks. Outbreak response for cVDPV2 also offers the opportunity to close immunity gaps to polioviruses types 1 and 3. Furthermore, GPEI might have to respond to two poliovirus outbreaks in the same geography. For either scenario, it would be important to get data on the immunogenicity of co-administered nOPV2 and bOPV, compared to either vaccine given alone. No study has yet assessed the immunogenicity of co-administered nOPV2 and bOPV. The proposed study further builds on the growing evidence around nOPV2 use by investigating household transmission and the potential development of intertypic vaccine-derived recombinants following the first study vaccination.

Objectives:

Primary

1. To compare type 2 immunogenicity of two doses of nOPV2 with two doses of nOPV2 co-administered with bOPV.
2. To compare type 1 and 3 immunogenicity of two doses of bOPV with two doses of bOPV co-administered with nOPV2.

Secondary

1. To compare type 2 immunogenicity of one or three doses of nOPV2 with the same number of doses of nOPV2 co-administered with bOPV.
2. To compare type 1 and 3 immunogenicity of one or three doses of bOPV with the same number of doses of bOPV co-administered with nOPV2.
3. To assess the presence of fecal viral shedding (as determined by real-time RT-PCR) over time following one dose of nOPV2, bOPV, or co-administered nOPV2 and bOPV.
4. To estimate household transmission of nOPV2 by assessing the presence of fecal viral shedding (as determined by real-time RT-PCR) among siblings of vaccine recipients.
5. To assess the occurrence and genomic characteristics of intertypic recombinants in stool specimens of vaccine recipients and siblings after one dose of nOPV2 given with or without bOPV.

Methods:

This is an open-label randomized clinical trial. Vaccine recipient participants will be enrolled and randomized at 6 weeks to one of three arms:

A: nOPV2 @ 6, 10, and 14 weeks
B: nOPV2 + bOPV @ 6, 10, and 14 weeks
C: bOPV @ 6, 10, and 14 weeks

For each vaccine recipient, a sibling below 10 years of age will be selected for participation as a sibling.

Outcome measures/variables:
Poliovirus antibody titers to types 1, 2 and 3 will be measured in sera extracted from vaccine recipient blood collected at 6, 10, 14, and 18 weeks. Antibody titers at 6 weeks of age will be the assumed starting point for the expected decline in maternal antibody assuming a half-life of 28 days. Shedding of poliovirus will be measured from stool specimens collected from vaccine recipients and one sibling each at 1, 2, and 4 weeks post-vaccination in Arm A and at 2 and 4 weeks post-vaccination in Arms B and C. Intertypic recombinants will be characterized in a subset of stool specimens collected from vaccine recipients and siblings.

Description of the Research Project

Hypothesis to be tested:

Does this research proposal involve testing of hypothesis: ☐ No ☒ Yes (describe below)

Primary hypotheses to be tested are:

1. Type 2 immune response after two doses of nOPV2 with bOPV is non-inferior to the immune response observed after two doses of nOPV2 given alone (10% non-inferiority margin).
   [Primary objective: 1]
2. Type 1 and 3 immune responses after two doses of bOPV with nOPV2 are non-inferior to the immune responses observed after two doses of bOPV given alone (10% non-inferiority margin).
   [Primary objective: 2]

Secondary hypotheses to be tested are:

1. Type 2 immune responses after one or three doses of nOPV2 with bOPV are non-inferior to the immune responses observed after the same number of doses of nOPV2 given alone (10% non-inferiority margin).
   [Secondary objective: 1]
2. Type 1 and 3 immune responses after one or three doses of bOPV with nOPV2 are non-inferior to the immune responses observed after the same number of doses of bOPV given alone (10% non-inferiority margin).
   [Secondary objective: 2]

Exploratory questions:

1. What are the shedding rates among vaccine recipients following one dose of nOPV2, bOPV, or co-administered nOPV2 and bOPV?
   [Secondary objective: 3]
2. What is the shedding rate among siblings of vaccine recipients following one dose of nOPV2?
   [Secondary objective: 4]
3. What is the estimated household transmission rate following one dose of nOPV2?
   [Secondary objective: 4]
4. What proportion of vaccine recipients and siblings have intertypic recombinants in stool following one dose of nOPV2 given with or without bOPV? What are the characteristics of the recombinants?
   [Secondary objective: 5]

Specific Objectives:

Table 1: Schematic representation of study arms.

Arms		Age of participant						Unadjusted sample size	Enrollment target*
		6 weeks	7 weeks	8 weeks	10 weeks	14 weeks	18 weeks		
A	nOPV2	• nOPV2	▲	▲	▲ • nOPV2	• nOPV2	•	238	265
B	nOPV2/bOPV	• nOPV2 + bOPV		▲	▲ • nOPV2 + bOPV	• nOPV2 + bOPV	•	238	265
C	bOPV	• bOPV		▲	▲ • bOPV	• bOPV	•	238	265
Total								714	795

• Indicates blood collection
▲ Indicates stool collection from participant and from youngest sibling household contact (<10 years of age)
Household transmission component
* Adjusted for 10% attrition

Primary objectives*

1. To compare type 2 immunogenicity of two doses of nOPV2 with two doses of nOPV2 co-administered with bOPV.
    a. nOPV2 at 6 and 10 weeks (**A**) vs. nOPV2 + bOPV at 6 and 10 weeks (**B**)
2. To compare type 1 and 3 immunogenicity of two doses of bOPV with two doses of bOPV co-administered with nOPV2.
    a. bOPV at 6 and 10 weeks (**C**) vs. nOPV2 + bOPV at 6 and 10 weeks (**B**)

Secondary objectives*

1. To compare type 2 immunogenicity of one or three doses of nOPV2 with the same number of doses of nOPV2 co-administered with bOPV.
    a. nOPV2 at 6 weeks (**A**) vs. nOPV2 + bOPV at 6 weeks (**B**)
    b. nOPV2 at 6, 10, and 14 weeks (**A**) vs. nOPV2 + bOPV at 6, 10, and 14 weeks (**B**)
2. To compare type 1 and 3 immunogenicity of one or three doses of bOPV with the same number of doses of bOPV co-administered with nOPV2.
    a. bOPV at 6 weeks (**C**) vs. nOPV2 + bOPV at 6 weeks (**B**)
    b. bOPV at 6, 10, and 14 weeks (**C**) vs. nOPV2 + bOPV at 6, 10, and 14 weeks (**B**)
3. To assess the presence of fecal viral shedding (as determined by real-time RT-PCR) over time following one dose of nOPV2, bOPV, or co-administered nOPV2 and bOPV.
4. To estimate household transmission of nOPV2 by assessing the presence of fecal viral shedding (as determined by real-time RT-PCR) among siblings of vaccine recipients.
5. To assess the occurrence and genomic characteristics of intertypic recombinants in stool specimens of vaccine recipients and their siblings after one dose of nOPV2 given with or without bOPV.

*Note: For all objectives, timepoints refer to the timing of vaccine administration.

Background of the Project including Preliminary Observations:

Polioviruses are a member of family Picornaviridae in the enterovirus subgroup, and poliomyelitis is an acute infection caused by polioviruses. Polioviruses are transmitted from person to person either faeco-orally or through pharyngeal secretions. There is minimal cross-immunity between the three distinct serotypes of polioviruses (types 1, 2 and 3). After entering the body through the mouth, polioviruses replicate in the gastrointestinal tract for several days or weeks. In the majority of cases, they cause no apparent illness or mild illness including diarrhea, fever, and/or vomiting. In approximately one out of 200 infections, however, polioviruses invade the cells of the spinal cord leading to paralysis of limb(s) or invade brain stem cells affecting the respiratory muscles. Of those individuals with paralytic poliomyelitis, an estimated 5-10% die because of breathing failure. The remaining suffer from lifelong paralysis of one or more limbs. Before the availability of vaccines, poliomyelitis was the leading cause of permanent disability worldwide [1, 2].

Poliovirus Vaccines

Inactivated poliovirus vaccine (IPV) was licensed in 1955 in the United States and was the first licensed poliovirus vaccine. Subsequently, three type-specific, live, attenuated oral poliovirus vaccines were licensed in 1961–62. These monovalent oral poliovirus vaccines (mOPV) were quickly followed by licensure of trivalent OPV (tOPV) in 1963, which protects against all three poliovirus serotypes. Because of its low cost, ease of administration, induction of mucosal immunity, and ability to indirectly vaccinate susceptible contacts, tOPV largely replaced IPV as the vaccine of choice for polio vaccination in most countries [2-4].

Despite their many advantages, there are important disadvantages with OPV use. Because Sabin viruses are live attenuated viruses, they can mutate during replication and revert to a neurovirulent form leading to vaccine-associated paralytic polio (VAPP). It is estimated a VAPP case occurs for every 1.2–1.5 million OPV doses administered [2]. In addition, Sabin viruses can circulate in areas with inadequate polio vaccination coverage. Prolonged person-to-person transmission facilitates mutations and the emergence of virus variants called circulating vaccine-derived polioviruses (cVDPVs) which have re-acquired the neurovirulence and transmissibility of wild poliovirus (WPV) [5]. Therefore, polio eradication will require eventual cessation of all traditional Sabin OPVs [6, 7].

Immunological response after poliovirus vaccines is determined by measuring type-specific poliovirus antibodies using neutralization assays. After the first exposure to poliovirus antigens, which could be wild or vaccine-derived, a rapid rise in IgM titers is observed. This is followed by a slower rise in IgG titers, which typically peaks in four weeks [8].

OPV Cessation

Wild poliovirus type 2 (WPV2) was declared eradicated in September 2015 [9, 10]. Since then, paralysis associated with type 2 poliovirus has continued mainly due to VDPVs from type 2 OPV. Due to the continued threat of paralysis from a mutated, neurovirulent and vaccine-derived type 2 poliovirus, the Strategic Advisory Group of Experts on Immunization (SAGE), a global advisory committee on immunization, recommended a phased cessation of OPV starting with type 2 oral poliovirus vaccine (OPV2) [11].

Subsequently, OPV2 was withdrawn globally, including the replacement of tOPV with bivalent OPV (bOPV), containing poliovirus types 1 and 3, in May 2016. Since then, monovalent type 2 OPV (mOPV2) has been used for responding to circulating type 2 vaccine-derived poliovirus (cVDPV2) outbreaks. Since 2016, over 300 million doses of mOPV2 have been used to respond to cVDPV2 outbreaks and some of these responses have led to emergence of new cVDPV2s, likely from the mOPV2 used during the

outbreak response. Therefore, novel OPV2 (nOPV2) candidates have been developed with improved genetic stability, thereby reducing the possibility of generating new VDPVs and cVDPV outbreaks [12, 13].

nOPV2 Candidates and Clinical Trials

GPEI has been pursuing two candidate nOPV2 vaccines. To develop the current nOPV2 candidates, the existing OPV type 2 was modified to improve its genetic stability (additional details provided in the "Description of Study Vaccines" section of the protocol) [12-14]. For both nOPV2 candidates, clinical trials lots underwent standard monkey neurovirulence testing and the vaccine formulation testing used by Bio Farma for Sabin-based OPV products.

Human clinical trials of nOPV2 began in 2017. As of June 2020, three human trials of nOPV2 have been conducted.

The first human study was a double-blind, phase 1 trial conducted under biological containment in Belgium by the University of Antwerp. Thirty IPV-primed adults were randomized to receive one dose of either nOPV2 vaccine candidate. Both candidates were well tolerated; reversion to neurovirulence was low in shed virus when tested in transgenic mice, and >80% of participants demonstrated a type 2 immune response [14].

Phase 2 studies were implemented in Belgium and Panama to evaluate the safety and immunogenicity of both nOPV2 candidates. The University of Antwerp conducted a double-blinded, randomized, placebo-controlled trial without containment that was completed in Q2 2019. The study enrolled 200 healthy OPV-primed adults and 50 healthy IPV-only-primed adults and adolescents [15]. Preliminary results from the Belgium phase 2 trial suggest that both nOPV2 candidates (dose = 10^6 $CCID_{50}$) are immunogenic. One-dose seroconversion rates were ~75% for candidate 1 and ~51% for candidate 2, and both higher than the historical Sabin 2 control at a lower dose (29%; dose = 10^5 $CCID_{50}$) (University of Antwerp, unpublished).

In Panama, a phase 2 trial was implemented using an age de-escalation scheme. Participants were 100 children aged 1–5 years with prior IPV and/or OPV vaccination in the first year of life, and 648 healthy infants who received bOPV (3 doses) and IPV (1 dose) prior to vaccination with nOPV2 at 18–22 weeks of age [16] . The infant component of the trial included both high-dose (10^6 $CCID_{50}$) and low-dose (10^5 $CCID_{50}$) nOPV2 formulations. The main study activities were completed in Q3 2019, except for the longer-term safety follow up, which ended in early 2020. Early results from the phase 2 trials in Belgium and Panama were reviewed by an independent data safety monitoring board, which supported age group progression from adults to toddlers and infants based on the available safety information.

Toddlers in the Panama trial all received high-dose nOPV2; based on preliminary findings, one-dose seroconversion rates were high (~95%) for both candidates and exceed that of 10^5 $CCID_{50}$ Sabin 2 (~63%). Among infants, immunogenicity non-inferiority to mOPV2 was achieved for both high- and low-dose candidate 1, but only for high-dose candidate 2 (A. Bandyopadhyay, unpublished). Both candidates were shown to replicate in the gut. Based on preliminary neurovirulence results, both candidates appear to be more phenotypically stable than Sabin 2; however, candidate 1 performed better than candidate 2, i.e. had significantly lower rates of paralysis in the mouse model. There was no evidence of viral recombination in the sequencing results (A. Bandyopadhyay, unpublished).

Overall, trial results to date suggest that nOPV2 is safe, immunogenic, and more genetically stable than Sabin 2 [16]. As of late 2019, nOPV2 candidate 1 was selected for Emergency Use Listing submission and commercial scale manufacturing.

Two upcoming trials of nOPV2 candidate 1 are planned. In Bangladesh, icddr,b will implement a phase 2 study on the safety and immunogenicity of nOPV2 in OPV-naïve newborns. A phase 3 trial will be conducted in The Gambia to assess expanded safety and lot-to-lot consistency of nOPV2.

Intertypic Recombination

Enteroviruses, such as poliovirus, have a large degree of genetic variability and evolve through mutation and recombination. Recombination can occur between different Sabin vaccine strains, or Sabin virus can recombine with wild polio strains or non-polio enteroviruses [17]. For recombination to occur, a cell needs to be simultaneously infected with two different viral strains. Recombination is a common event among OPV recipients and can occur soon after vaccination; it rarely results in negative outcomes such as VAPP [18-22]. Intertypic recombination is thought to contribute to VDPV emergence as even a single recombination event can lead to replacement and reversion of attenuating elements. The nOPV2 candidates were designed to be more genetically stable than mOPV2; however, their recombination behaviour in settings with high prevalence of enterovirus infection or other OPV strains is still unknown.

Justification for this Study

It is expected that nOPV2 would replace mOPV2 for responding to type 2 outbreaks when authorized by Emergency Use Listing and/or licensed and available for use. Vaccination campaigns as part of outbreak response for cVDPV2 also offers the opportunity to close immunity gaps to polioviruses types 1 and 3 through co-administration of bOPV. Furthermore, GPEI might have to respond to two poliovirus outbreaks in the same geography such as WPV1 and cVDPV2 in Nigeria, Pakistan in 2016, and Afghanistan and Pakistan in 2019–2020; cVDPV2 and cVDPV3 in Somalia in 2018; and cVDPV2 and cVDPV1 in the Philippines and Malaysia in 2019/2020. It would be important to get data on coadministration of nOPV2 and bOPV, particularly to note if there is any inhibitory effect on the immunogenicity of either vaccine.

No study has assessed co-administration of nOPV2 and bOPV; therefore, the study we have proposed compares the type-specific immunogenicity of co-administered nOPV2 and bOPV with each vaccine given alone. This clinical trial will build on existing evidence for nOPV2 immunogenicity and generate data to inform global poliovirus outbreak response strategies.

Although nOPV2 was designed to be more genetically stable than mOPV2, there is a lack of real-world evidence on its recombination behaviours. Therefore, in the current study, we will assess recombinants at two timepoints for all arms (8 and 10 weeks; two and four weeks post-vaccination, respectively). Timepoints for stool collection were selected based on when shedding would be expected to be high in children without pre-existing mucosal immunity.

While phase I and II trials have measured shedding post-vaccination among nOPV2 vaccine recipients, these were among individuals with previous poliovirus vaccination [14, 16]. There is also currently a lack of data to estimate potential secondary transmission of the vaccine virus to close contacts of vaccine recipients. The household transmission component of the study will be descriptive of not include a Sabin 2 comparison group; nevertheless, it is important to assess the transmissibility of nOPV2 in order to better anticipate risks.

Overall, these data will be programmatically valuable and can inform future decision making around nOPV2 use, particularly for outbreak response.

Research Design and Methods

Study Area

Mirpur is one of the 14 Thanas of Dhaka city with a population of about two million in an area of 59 square kilometers. Mirpur Thana of Dhaka city is divided into 14 sections. The area is densely populated and is about eight kilometers from icddr,b's Dhaka Hospital. The population is stable with low socioeconomic conditions. The average income in the slum areas of Mirpur is Tk.4200 (about US $55) per month per family. Only 25% of fathers and 15% of mothers have more than five years of formal education. The study will be conducted in sections 1- 2, 6-7 and 10-13 of Mirpur, which has a population of about 500,000. icddr,b and CDC have collaborated on multiple polio vaccine trials that were conducted in the study clinic in Mirpur [23, 24].

If feasible based on guidelines/recommendations related to the COVID-19 pandemic (e.g., physical distancing), the study will also be conducted at the clinical trial unit (CTU), Dhaka. The study area includes the adjoining slum and non-slum areas of icddr,b Mohakahli, Dhaka - Kunipra, Arjat Para, Nakhalpara, Korail, Begunbari, Chairman bari and Badda. Participants will attend CTU, which is about one kilometer from the areas. The population is approximately 300,000 and literacy is ~50%. It is stable with low socio-economic conditions. The population is mainly engaged in industrial labour, garment factory, small businesses and rickshaw pullers.

Study staff will identify infants eligible to be vaccine recipients through house-to-house visits at the two proposed sites of Mirpur and Mohakahli.

Study Design

This is an open-label, non-inferiority, balanced three arm randomized clinical trial assessing immunogenicity of poliovirus vaccines. Vaccine recipients will be identified through active surveillance of new births in the community and parents will be requested to participate through home visits by local field workers. Vaccine recipients will be enrolled at 6 weeks of age, randomly assigned to one of the three arms and followed to 18 weeks of age.

Inclusion Criteria

Criteria for both vaccine recipient and sibling must be met for enrolment in the trial.

Vaccine Recipient

1. Healthy infants 6 weeks of age (range: 42–48 days).
2. Parents that consent for participation in the full length of the study.
3. Parents that can understand and comply with planned study procedures.
4. Infant has at least one sibling aged <10 years living in the same household that is eligible for participation in the study and can be enrolled at the same time as the vaccine recipient.

Sibling

1. Healthy child aged <10 years.
2. Sibling of the vaccine recipient and resides in the same household.
3. Parents that consent for participation in the study until and including the Clinic Visit at 10 weeks (age of vaccine recipient).
4. Parents that can understand and comply with planned study procedures

Exclusion Criteria

If either vaccine recipient or sibling meets the exclusion criteria, then neither can be enrolled in the trial.

Vaccine Recipient

1. Parents, infants, and siblings who are unable to participate in the full length of the study (e.g., plan to move away from the study area during the study period).
2. A diagnosis or suspicion of immunodeficiency disorder either in the infant or in an immediate family member.
3. A diagnosis or suspicion of bleeding disorder that would contraindicate administration of bOPV or nOPV2 or collection of blood by venipuncture.
4. Acute diarrhoea, infection or illness at the time of enrolment (6 weeks of age) that would require infant's admission to a hospital.
5. Acute vomiting and intolerance to liquids within 24 hours before the enrolment visit (6 weeks of age).
6. Evidence of a chronic medical condition identified by a study medical officer during physical exam.
7. Receipt of any polio vaccine (OPV or IPV) before enrolment based upon documentation or parental recall.
8. Known allergy/sensitivity or reaction to polio vaccine, or its contents.
9. Infants from multiple births. Infants from multiple births will be excluded because the infant(s) who is/are not enrolled would likely receive OPV through routine immunization and transmit vaccine poliovirus to the enrolled infant. Even if all births from a multiple birth could be enrolled in the study, we will exclude multiple births as discontinuation of one may lead to discontinuation of multiple vaccine recipients.
10. Infants from premature births (<37 weeks of gestation).

Sibling

1. Participant in a previous poliovirus vaccine clinical trial.
2. Unable to participate in the study until and including the Clinic Visit at 10 weeks (age of vaccine recipient).
3. A diagnosis or suspicion of immunodeficiency disorder either in the sibling or in an immediate family member.
4. Acute diarrhoea, infection or illness at the time of enrolment that would require sibling's admission to a hospital.
5. Evidence of a chronic medical condition identified by a study medical officer during physical exam.

<u>Discontinuation Criteria</u>

Vaccine Recipient

1. Withdrawal of consent for participation for any reason.
2. Request by parents of vaccine recipient to terminate all study procedures.
3. Identification of immunodeficiency disorder, bleeding disorder or another medical condition for which continued participation, in the opinion of the principal investigator, would pose a risk to the vaccine recipient to continue in the study.
4. Receipt of immunosuppressive medications.
5. Receipt of any polio (OPV or IPV) vaccine outside of study after enrolment (as per parent's report). Vaccine recipients who received polio vaccines outside of the study, including any polio vaccine administered in polio campaigns, would be excluded from further study procedures.
6. Temporary discontinuation may occur when there has been a temporary suspension of study activities. Study enrolment will be suspended from 12 weeks before the start of polio campaigns in the study areas to 6 weeks after the completion of polio campaigns in the study areas. This measure is to prevent potential interference from polio vaccine administered during polio campaigns in the study areas. If vaccine recipients receive vaccine during polio campaigns, they would be discontinued from further study procedures.

7. Unable to collect or obtain blood at enrolment (Clinic Visit at 6 Weeks of Age).
8. Allergic reaction to a prior dose of polio vaccine, or its contents.
9. Premature termination of the study.

Sibling

1. Vaccine recipient is discontinued from the study.
2. Withdrawal of consent for participation for any reason.
3. Receipt of any polio (OPV or IPV) vaccine after enrolment (as per parent's report). Siblings who receive polio vaccines during their participation in the study, including any polio vaccine administered in polio campaigns, would be excluded from further study procedures.

Description of Study Vaccines

Two polio vaccines will be used in the study: bOPV and nOPV2

1. **Bivalent oral polio vaccine (bOPV)**
   a. Manufacturer: Bio Farma
   b. Presentation: the vaccine will be available in multi-dose vials
   c. Formulation: Each dose (2 drops = 0.1 ml).
   d. Administration: one vaccine vial will be used per participant.
   e. Previous use at icddr,b: bOPV is part of the routine immunization schedule in Bangladesh.

2. **Candidate 1 novel monovalent oral poliovirus vaccine type 2 (nOPV2)**
   a. Manufacturer: Bio Farma
   b. Description: nOPV2 candidate 1 (S2/cre5/S15domV/rec1/hifi3) is a live-attenuated serotype-2 poliovirus that was derived from a modified Sabin type-2 infectious cDNA clone and propagated in Vero cells. To improve genetic stability, nucleotide sequence modifications were made in the major determinant for attenuation in the Sabin 5'-untranslated region. Additionally, two modifications in the polymerase 3D were made to further improve stability of the attenuation, and a key replication element from the 2C coding region was relocated to the 5′-untranslated region to inhibit recombination [14].
   c. Manufacturer: Bio Farma
   d. Presentation: the vaccine will be available in multi-dose vials.
   e. Formulation: approximately 10^5 CCID50/dose, dose = 2 drops
   f. Administration: one vaccine vial will be used per participant.
   g. Previous use at icddr,b: Prior to the start of the current study, icddr,b will implement a naïve infants trial that includes nOPV2 (PR-20001).

Disposal of Used Study Vaccines

At the end of each day, the used study vaccine vials will be returned from the study clinics to icddr,b where they will be stored. After using all doses in the vial or after having passed the usage duration recommended by the manufacturer, the vaccine vials will be stored for the duration of the study but not used for administration to participants. This will be done to ensure availability of the used vaccine vials should a need arise, such as an investigation of adverse events. The used vaccine vials will be stored at least three months after the completion of data analysis for the study. Four weeks prior to the planned disposal of the used vaccine vials, the PI will notify the Data Safety and Monitoring Board (DSMB) of the intent to destroy the used vaccine vials by a specific date; this may be delayed at the request of DSMB. Unless the DSMB requests the PI to delay disposal of the used vaccine vials, the used vaccine vials will be destroyed per icddr,b's standard procedures for biohazardous materials.

Study Procedures

Field workers will inform parents about the study and briefly explain the study procedures, including stool sampling from both the vaccine recipient and the sibling. If interested in participating, parents will be asked to visit the study clinic when the vaccine recipient is 6 weeks of age to obtain comprehensive information on the study and to complete enrolment procedures; both the vaccine recipient and sibling will need to be present at this visit. Parents will be provided transport costs for all study visits to/from the clinic.

The below description summarizes the study clinic and home visits over the course of the study. Vaccine recipients may additionally visit the study clinic for routine childhood vaccinations or for management of adverse events. Although non-study vaccines included in the routine immunization schedule in Bangladesh will be available and vaccination will be encouraged, parents will have the final decision to vaccinate their infant. Injectable non-polio, routine immunization vaccines will be administered at the recommended body site per the national guidelines of Government of Bangladesh. If a study visit involves collection of blood as well as administration of study vaccines, then blood collection will precede study vaccine administration. For Arm B, concomitant administration will be defined as nOPV2 provided first, followed by bOPV on the same day in rapid succession with a target of ≤5 minutes apart.

Enrolment visit – 6 weeks of age (acceptable range 42–48 days) [All arms; sibling must also be present at this clinic visit, but not subsequent clinic visits]

During this visit, the following procedures will be conducted:

1. The medical officer will confirm that the vaccine recipient and sibling are eligible to participate. If the vaccine recipient and sibling are eligible, all study procedures will be explained to the parents. The parents will be requested to provide informed consent; consent will be documented per study procedures.
2. The vaccine recipient will be assigned a participant identification number (PID) and to a study arm according to a pre-determined randomization scheme. Further details of the randomization scheme are described in the "Data Analysis" section.
3. Vaccination record of the sibling will be obtained and recorded by the medical officer.
4. Socio-demographic and clinical information will be recorded on the corresponding electronic case report form (eCRF).
5. One blood specimen (1 ml) will be collected from the vaccine recipient by venipuncture.
6. The first dose of study vaccines will be administered to the vaccine recipient, as directed by study arm.
7. The vaccine recipient will be observed for 30 minutes to monitor for any adverse reactions from the blood collection or administration of study vaccines.
8. The vaccine recipient will receive the recommended routine childhood vaccinations, except polio vaccination. Routine polio vaccines will be replaced by the study vaccine.
9. Clinical information will be collected about the sibling. The sibling must be present at this visit so that he/she may be examined by a medical officer but does not need to be present for any subsequent clinic visits.
10. Schedule the household visit(s) and the next clinic visit.

Phone call or home Visit (24–48 hours after the first study vaccination) [All arms]

1. A study staff will contact the parents of the vaccine recipient to inquire and record any potential adverse events after the first study vaccination.
2. This phone call or visit will be conducted 24–48 hours after the first study vaccination visit.

Home Visit – 7 weeks of age [Arm A only]

Home Visit #1 (two days prior to 7 weeks of age)

1. The study field worker will visit the vaccine recipient's home and provide two plastic screw-cap stool containers to the mother. She will review the stool collection procedures with the mother, including sibling sampling.
2. The study field worker will complete the top portion of the study questionnaire.

Home Visit #2 (7 weeks of age)

1. Mother will collect stool specimens from the vaccine recipient and sibling. If possible, mother will collect fresh stool from each child's diaper or have the child defecate into a clean plastic pot. Mother will be asked to collect stool about the size of one adult thumb (8 grams). She will place the containers with the collected stool specimens immediately into the freezer (if available) or in a cool place in the home. The same procedures will be used for collecting stool specimens from the sibling. Mother will immediately notify the study field worker after each stool collection.
2. Within two hours of notification, the study field worker will go to the vaccine recipient's home with ice packs, two stool containers, and a stool carrier bag. If necessary, she will transfer stool from the original stool container to a new stool container. Otherwise, the study field worker will place the stool containers in the stool carrier bag, between the two ice packs.
3. The study field worker will complete the rest of the study questionnaire.
4. The study field worker will transport the stool samples to the study clinic within 30 minutes of pick up and store the stool containers at 2-8^{o}C.
5. The study field worker will provide the completed study questionnaire to the data entry staff.
6. Data entry staff will enter the completed study questionnaire into REDCap (eCRF).

Home Visit – 8 weeks of age [All arms]

Home Visit #1 (two days prior to 8 weeks of age)

1. The study field worker will visit the vaccine recipient's home and provide two plastic screw-cap stool containers to the mother. She will review the stool collection procedures with the mother, including sibling sampling.
2. The study field worker will complete the top portion of the study questionnaire.

Home Visit #2 (8 weeks of age)

1. Mother will collect stool specimens from the vaccine recipient and sibling. If possible, mother will collect fresh stool from each child's diaper or have the child defecate into a clean plastic pot. Mother will be asked to collect stool about the size of one adult thumb (8 grams).
   She will place the containers with the collected stool specimens immediately into the freezer (if available) or in a cool place in the home. The same procedures will be used for collecting stool specimens from the sibling. Mother will immediately notify the study field worker after each stool collection.
2. Within two hours of notification, the study field worker will go to the vaccine recipient's home with ice packs, two stool containers, and a stool carrier bag. If necessary, she will transfer stool from an original stool container to a new stool container. Otherwise, the study field worker will place the stool containers in the stool carrier bag, between the two ice packs.
3. The study field worker will complete the rest of the study questionnaire.
4. The study field worker will transport the stool samples to the study clinic within 30 minutes of pick up and store the stool containers at 2-8^{o}C.
5. The study field worker will provide the completed study questionnaire to the data entry staff.
6. Data entry staff will enter the completed study questionnaire into REDCap (eCRF).

Home Visit – 10 weeks of age [All arms]

Home Visit #1 (two days prior to 10 weeks of age)

1. The study field worker will visit the vaccine recipient's home and provide two plastic screw-cap stool containers to the mother. She will review the stool collection procedures with the mother, including sibling sampling.
2. The study field worker will complete the top portion of the study questionnaire.

Home Visit #2 (10 weeks of age)

1. Mother will collect stool specimens from the vaccine recipient and sibling. If possible, mother will collect fresh stool from each child's diaper or have the child defecate into a clean plastic pot. Mother will be asked to collect stool about the size of one adult thumb (8 grams).
   She will place the containers with the collected stool specimens immediately into the freezer (if available) or in a cool place in the home. The same procedures will be used for collecting stool specimens from the sibling. Mother will immediately notify the study field worker after each stool collection.
2. Within two hours of notification, the study field worker will go to the vaccine recipient's home with ice packs, two stool containers, and a stool carrier bag. If necessary, she will transfer stool from an original stool container to a new stool container. Otherwise, the study field worker will place the stool containers in the stool carrier bag, between the two ice packs.
3. The study field worker will complete the rest of the study questionnaire.
4. The study field worker will transport the stool samples to the study clinic within 30 minutes of pick up and store the stool containers at 2-8^{o}C.
5. The study field worker will provide the completed study questionnaire to the data entry staff.
6. Data entry staff will enter the completed study questionnaire into REDCap (eCRF).

Study Clinic Visit – 10 weeks of age [All arms]

During this visit, the following procedures will be conducted:

1. The medical officer will complete the eCRF and examine the vaccine recipient.
2. One blood specimen (1 ml) will be collected by venipuncture.
3. Study vaccines will be administered, as directed by study arm.
4. The vaccine recipient will be observed for 30 minutes to monitor for any adverse reactions to the study vaccine.
5. The vaccine recipient will receive the recommended routine childhood vaccinations, except polio vaccination. Routine polio vaccines will be replaced by the study vaccine.
6. Schedule the next visit.

Study Clinic Visit – 14 weeks of age [All arms]

During this visit, the following procedures will be conducted:

1. The medical officer will complete the eCRF and examine the vaccine recipient.
2. One blood specimen (1 ml) will be collected by venipuncture.
3. Study vaccines will be administered, as directed by study arm.
4. The vaccine recipient will be observed for 30 minutes to monitor for any adverse reactions to the study vaccine.
5. The vaccine recipient will receive the recommended routine childhood vaccinations, except polio vaccination. Routine polio vaccines will be replaced by the study vaccine.
6. Schedule the next visit.

Study Clinic Visit – 18 weeks of age [All arms]

During this visit, the following procedures will be conducted:

1. The medical officer will complete the eCRF and examine the vaccine recipient.
2. One blood specimen (1 ml) will be collected by venipuncture.
3. Completion of study activities.
4. Vaccine recipients in Arms A and B will be given the first of three bOPV doses. Note: Arm B will be given three doses of bOPV to account for possible immunologic interference during co-administration of bOPV with nOPV2. All vaccine recipients will be given the first of two fIPV doses.

Timing of Evaluations

Entry/eligibility evaluations

- Entry evaluations will be completed at 6 weeks of age.
- Blood collection and study vaccine administration are planned during the study entry evaluation at 6 weeks of age. Blood will be collected before administration of any study vaccines. On the date of enrolment, study vaccines will be administered only if adequate blood specimen has been collected. If blood cannot be collected on the day of enrolment, study vaccine recipients will be discontinued from the study.
- The window for entry evaluation including collection of blood and administration of vaccine is 42–48 days of age.

Post-entry evaluations and follow-up

- After the first enrolment visit (6 weeks of age, range 42–48 days), the window for study visits is +/- 3 days.
- Blood will be collected before any study or EPI vaccines are administered.
- Stool collection from vaccine recipients and one sibling each will take place at 8 and 10 weeks of age for all Arms, and additionally at 7 weeks for Arm A only.

Concomitant Medications and Vaccines

There will be no restrictions on the use of medications or treatments for concomitant diseases. If the vaccine recipient needs to receive medications that cause immunosuppression, the vaccine recipient will be discontinued from the study.

If the vaccine recipient receives a dose of either polio vaccines (OPV or IPV) outside of the study during the study period, the vaccine recipient will be discontinued from the study. Parents will be encouraged and offered an opportunity to have their child vaccinated with routine childhood immunizations during study clinic visits, in accordance with Bangladesh EPI's vaccination schedule. Other non-routine immunizations will not be prohibited if they do not contain polio vaccines.

Specimen Collection, Handling and Testing

Sera: Table 2 summarizes the blood samples that will be collected for serological testing. All study visits requiring blood collection will collect 1 ml of blood. Blood will be stored temporarily in the study clinic and transported from the clinic to the icddr,b virology laboratory at 2–8 degrees Celsius within 6 to 8 hours of collection. Then sera will be separated by centrifugation in icddr,b virology lab within one hour. Tubes with haemolysed blood will be discarded following standard biohazard waste disposal protocol. After sera have been aliquoted separately for testing of poliovirus (0.2 mL), the remaining sera will be stored at icddr,b in cryovials with CDC provided labels that include vaccine recipient identification number (PID) and study protocol number. At all visits, only one aliquot (0.2 mL) will be prepared for shipment for Atlanta. The samples stored at icddr,b are reserve samples that may need to be shipped to CDC in the event that samples in the initial shipment were adversely affected, resulting in

the inability to perform testing or uninterpretable results. Cryovial tubes that will be sent to CDC for testing will be stored in a -20 degree Celsius freezer. The rest of the aliquoted sera will be stored at -70 degree Celsius at icddr,b.

Table 2. Summary of sera samples for serological testing

Age of vaccine recipient	Blood collected from arms	Volume of blood collection	Sera available	Sera for poliovirus testing	Sera stored at icddr,b
6 weeks	All arms	1 ml	0.4 ml	0.2 ml	0.2 ml
10 weeks	All arms	1 ml	0.4 ml	0.2 ml	0.2 ml
14 weeks	All arms	1 ml	0.4 ml	0.2 ml	0.2 ml
18 weeks	All arms	1 ml	0.4 ml	0.2 ml	0.2 ml

Stool: For the follow-ups at 7 (Arm A only), 8, and 10 weeks of age, parents of enrolled participants will be requested to collect about 8 grams (about the size of one adult thumb) of stool from vaccine recipients and from one sibling each. After collection, specimens will be kept at a temperature of 2–8 degrees Celsius at the study clinic and transferred to icddr,b within the same day. Upon arrival at icddr,b, samples will be aliquoted and stored at -20 degrees Celsius. Two aliquots will be prepared for each stool sample; 4 g will be aliquoted for shipment and testing and a second aliquot will be stored at icddr,b. Aliquots will be labelled with CDC-provided labels that include PID, indication of whether the sample corresponds to a vaccine recipient or sibling, and date of collection.

Table 3. Summary of stool samples for testing

Age of vaccine recipient	Stool collected from arms	Volume of stool collection	Stool for testing	Stool stored at icddr,b
7 weeks	Vaccine recipient: Arm A only	Approximately 8 g	4 g	Remaining stool quantity (no more than 4 grams)
	Sibling: One sibling from Arm A only	Approximately 8 g	4 g	Remaining stool quantity (no more than 4 grams)
8 weeks	Vaccine recipient: All arms	Approximately 8 g	4 g	Remaining stool quantity (no more than 4 grams)
	Sibling: One sibling from all arms	Approximately 8 g	4 g	Remaining stool quantity (no more than 4 grams)
10 weeks	Vaccine recipient: All arms	Approximately 8 g	4 g	Remaining stool quantity (no more than 4 grams)
	Sibling: One sibling from all arms	Approximately 8 g	4 g	Remaining stool quantity (no more than 4 grams)

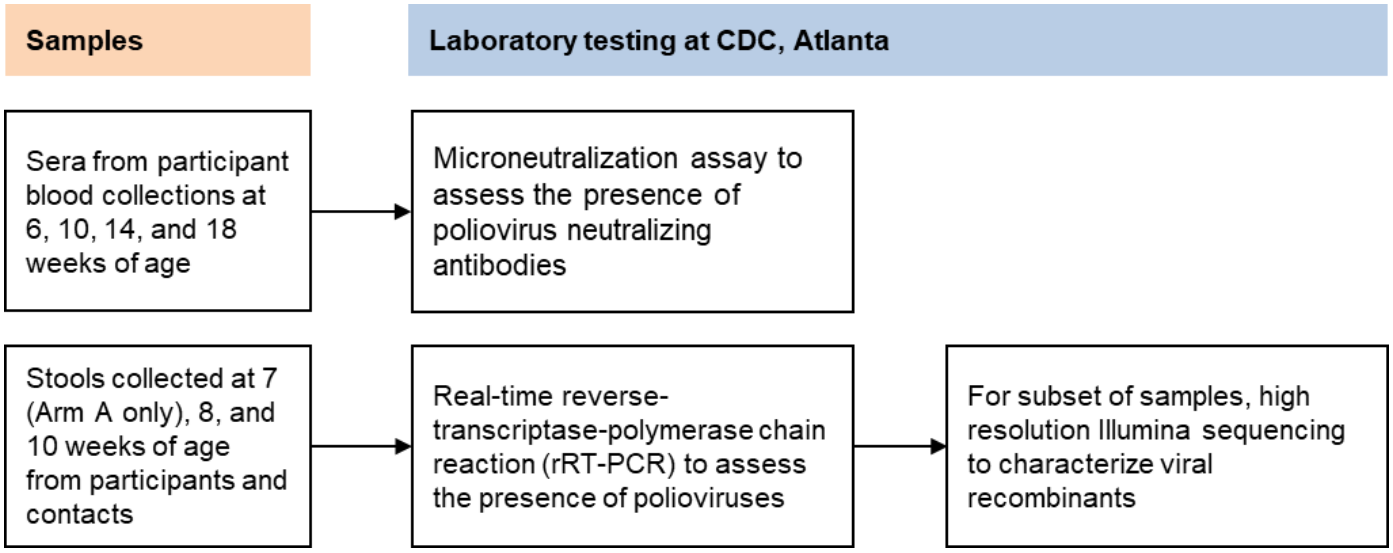
Sera and stool specimens will be sent to the Polio and Picornavirus Laboratory Branch of the Division of Viral Diseases, CDC, Atlanta for testing. Sera will be shipped to Atlanta after the completion of the

18 weeks visits. Stool samples will be shipped to Atlanta in multiple batches. CDC laboratory staff will be blinded to the randomization assignment.

Presence of poliovirus neutralizing antibodies to all three poliovirus types will be assessed using microneutralization assay (Appendix B). Antibody titers below 1:8 will be considered negative for presence of protective levels of poliovirus antibodies. The highest detectable titer will be ≥1:1448. The antibody titers at six weeks of age will be the assumed starting point for the expected decline in maternal antibody assuming a half-life of 28 days.

Real-time reverse-transcriptase polymerase chain reaction will be used to detect the presence of type-specific poliovirus shed in stool samples. For a subset of stool samples, viral recombinants will be characterized using high resolution Illumina sequencing (Appendix C). Sequencing reads will be mapped against all three Sabin vaccine reference sequences to generate coverage plots.

The figure below provides an overview of specimens that will be collected and tested as part of this trial.



Long-term Specimen Storage

Vaccine recipients will be requested to permit storage of blood and stool specimens for no more than five years for potential future use in studies. Prior to testing of the stored specimens for any additional objective(s) not specified in the approved protocol, human subject approval would be requested from the ethical review committees of icddr,b. Parents of study vaccine recipients will not be contacted, and no genetic testing will be performed on blood specimens. All specimens will be destroyed after five years from the end date of the study (the date of last clinic visit among study vaccine recipients). Specimens will be destroyed per the laboratory's standard procedures for destruction of biohazardous waste.

Sample Size Calculation and Outcome Variables

Sample size

Sample size calculations are based on an assumption of 10% attrition and the study is powered to address the two primary objectives.

For *primary objectives 1 and 2*, immune responses to two doses of co-administered nOPV2 and bOPV will be assessed for non-inferiority in comparison with two doses of nOPV2 or bOPV given alone. Based on unpublished phase 2 data from Panama, we assume that after two doses of nOPV2, 90% of vaccine recipients will demonstrate a type 2 immune response. After two doses of bOPV, approximately 85% of vaccine recipients are expected to demonstrate a type 3 immune response and at least 85% are expected to demonstrate a type 1 immune response [24, 25].

A sample size of 238 per group is required to achieve 90% power with α of 0.05 to detect a non-inferiority margin of 10% in seroconversion proportions between the groups of nOPV2 to nOPV2 with bOPV, and bOPV to bOPV with nOPV2. After adjustment for attrition, the enrolment target is 265 per group.

Note: For a non-inferiority comparison with a 10% margin, the minimum sample size required for type-2 response of assumed 90% seroconversion is smaller than that for type-1 and type-3 response of assumed 85% seroconversion. As this is a balanced trial, minimum sample size is determined by the larger sample size requirement.

To assess transmissibility of nOPV2 among infants receiving one dose of nOPV2 vaccine and their siblings, two power calculations were computed to: 1) detect at least one transmission event and 2) estimate transmission rate. Both power calculations were based on the established sample size for the primary objectives and expected shedding rate. Shedding rates were estimated using mOPV2 shedding rates from the mOPV2 transmission study in Bangladesh [26] as a comparator and using a simulation model which includes shedding duration and decline in type 2 immunity. All power calculations for the simulation are based on the expected shedding at day 14 post-vaccination. As there are two additional follow-up points and opportunities to observe transmission, the reported power calculations are likely a lower-bound.

Based on the expected recruitment size of 265 vaccine recipients in the nOPV-2 only Arm (Arm A) and 265 next youngest siblings, many of which are expected to be under the age of 5 years, there is evidence of sufficient power to detect transmission events, as well as to estimate a reasonable confidence interval for shedding prevalence. Using sample sizes for the primary objectives, the probability of detecting at least one household transmission event is close to 1. Using our nOPV2 simulation model, we estimate prevalence and 95% CI of shedding to be 53% among vaccine recipients (46.4 – 59.5%) and 23% (17.8 – 28.8%) among siblings under the age of 5 years.

Table 4: Sample size of study arms

Arms		Unadjusted sample size	Enrolment target*
A	nOPV2	238	265
B	nOPV2/bOPV	238	265
C	bOPV	238	265
Total		714	795
* Adjusted for 10% attrition			

Outcome variables

Poliovirus antibody titers to types 1, 2 and 3 will be measured in sera extracted from blood collected at 6, 10, 14, and 18 weeks of age. Seropositivity is defined as reciprocal polio neutralizing antibody titers of at least 1:8. Immune response will be defined as either seronegative vaccine recipients (<1:8 titers)

who become seropositive (≥1:8) (seroconversion) or vaccine recipients who demonstrate at least a four-fold increase in titer (boosting). Baseline maternal antibody titer will be determined at 6 weeks of age and the estimated maternal antibody level at each blood collection will be calculated assuming an exponential decline with a half-life of 28 days. Vaccine recipients and siblings will be categorized for shedding poliovirus through results from multiple real-time PCR (rRT-PCR) assay designed to detect poliovirus. Household transmission will be defined as present if siblings test positive for nOPV2 vaccine virus at either 1, 2, or 4 weeks following the vaccine recipient's vaccination at 6 weeks of age. nOPV2 vaccine virus in stool specimens from vaccine recipients and siblings will be further characterized through high-resolution Illumina RNA sequencing. Intertypic vaccine-derived recombinants will be characterized in stool collected from study vaccine recipients and siblings.

Randomization

Vaccine recipients will be randomized to one of three arms using a block randomization scheme. The randomization algorithm will be generated by CDC staff and executed in REDCap. The randomization algorithm will not be known to study staff in icddr,b. Randomization assignment will be revealed after completing enrolment procedures, when study staff "click" on randomization button on the study tablets. Therefore, study staff enrolling and managing vaccine recipients will not have *a priori* knowledge of randomization scheme. As this is an open-label trial, the arm assignment of vaccine recipients will be known to study staff and the vaccine recipient's parents after randomization. Laboratory staff processing blood samples in Bangladesh will not have *a priori* knowledge of randomization scheme but will know the arm assignment after randomization. However, CDC laboratory staff testing for poliovirus antibody titers will remain blinded throughout the study.

Timeline of activities

Activities	**Year 1 (months)**					
	2	**4**	**6**	**8**	**10**	**12**
Protocol development/IRB approval, Staff training/site preparation	■	■				
Enrolment		■	■			
Start and completion of vaccination		■	■	■		
Follow up of vaccine recipients		■	■	■		
Lab testing				■	■	
Dissemination/Publications					■	■

Data Analysis

General Issues

This is an open-label, non-inferiority, randomized clinical trial that will compare immune response to types 1, 2 and 3 polioviruses of nOPV2 and bOPV when co-administered compared to nOPV2 and bOPV given alone. The study will recruit 795 vaccine recipients in three arms. Vaccine recipients will be enrolled at 6 weeks of age and followed until 18 weeks of age, for 12 weeks of follow-up. For each vaccine recipient enrolled, one sibling will be enrolled at the same time and followed for 4 weeks .

General Analytical Issues

The data will be analysed by study investigators that include epidemiologists and statisticians. Statistical packages that will be used for the analysis include R, SAS and STATA.

For assessing immunity to polio, seropositivity is defined as reciprocal polio neutralizing antibody titers

of at least 1:8. Immune response will be defined as either seronegative vaccine recipients (<1:8 titers) who become seropositive (≥1:8) [seroconversion] or vaccine recipients who demonstrate a four-fold

increase in titer (boosting). Baseline maternal antibody titers will be determined at 6 weeks of age and the estimated maternal antibody level at each blood collection will be calculated assuming an exponential decline with a half-life of 28 days.

For assessing fecal viral shedding, detection of nOPV2 or bOPV vaccine virus in stool specimens from vaccine recipient or sibling at either 1, 2, or 4 weeks post-vaccination of the vaccine recipient at 6 weeks of age will be defined as positive for viral shedding. For assessing the detection of household transmission, presence of transmission will be defined as the sibling of the vaccine recipient testing positive for nOPV2 vaccine virus at either 1, 2, or 4 weeks post-vaccination of the vaccine recipient at 6 weeks of age.

To characterize the intertypic recombinants in a subset of stool specimens of vaccine recipients and siblings after one dose of nOPV2 given with or without bOPV, amplicon sequences from long-read sequencing methods will be used to confirm genome structure. Amplicon sequences will also be mapped against all three Sabin vaccine reference sequences to generate coverage plots.

Primary Analytical Approach

The primary analytical approach will be intention-to-treat. To evaluate the primary objectives, the intention-to-treat analysis will be restricted to vaccine recipients who:

- Have not withdrawn consent for receipt of vaccines and follow-up evaluations since enrolment.
- Have adequate blood specimen for serological analysis from the enrolment visit at 6 weeks of age.
- Have adequate blood specimen for serological analysis from the follow-up visit as mentioned by arm by primary objective in Table 5.

For secondary objectives 1 and 2, the intention-to-treat analysis will be restricted to vaccine recipients who:

- Have not withdrawn consent for receipt of vaccines and follow-up evaluations since enrolment.
- Have adequate blood specimen for serological analysis from the enrolment visit.
- Have adequate blood specimen for serological analysis from the follow-up visit as mentioned by arm by secondary objective in Table 5.

For secondary objectives 3-5, the intention-to-treat analysis will be restricted to vaccine recipients and siblings who:

- Have not withdrawn consent for receipt of vaccines and follow-up evaluations since enrolment.
- Have adequate stool specimens to examine vaccine-virus particles.

Secondary Analytical Approach

In addition to an intention-to-treat analysis, we will also perform per protocol analysis. To evaluate the primary objectives, per protocol analysis will be limited to vaccine recipients with the same restrictions as that outlined in primary analytical approach for primary objectives with additional restrictions of:

- Adequate blood specimen for serological analysis within 3 days of the scheduled visit date. This applies to enrolment visit blood specimen as well as follow-up visit blood collection.
- Received all scheduled study vaccines within 3 days of scheduled visit date.

For secondary objectives 1 and 2, the per protocol analysis will be limited to vaccine recipients with the same restrictions as those outlined in the primary analytical approach for secondary objectives 1 and 2 with additional restrictions of:

- Adequate blood specimen for serological analysis within 3 days of the scheduled visit date. This applies to enrolment visit blood specimen as well as follow-up visit blood collection.
- Received all scheduled study vaccines within 3 days of scheduled visit date.

For secondary objectives 3-5, the per protocol analysis will be limited to vaccine recipients or siblings with the same restrictions as those outlined in the primary analytical approach for secondary objectives 3-5 with additional restrictions of:

- Adequate stool specimen to examine vaccine-virus particles within 3 days of the scheduled visit date.
- Vaccine recipient received the scheduled study vaccination at 6 weeks of age.

Table 5: Study arms comparison, study endpoints, and results by objective

Study Objective	Study Arms Comparison	Endpoint (vaccine recipient age)	Results Included in Analysis
Primary			
1. To compare type 2 immunogenicity of two doses of nOPV2 with two doses of nOPV2 co-administered with bOPV.	A vs. B	14 weeks	Serology: 6, 10, 14 weeks
2. To compare type 1 and 3 immunogenicity of two doses of bOPV with two doses of bOPV co-administered with nOPV2.	C vs. B	14 weeks	Serology: 6, 10, 14 weeks
Secondary			
1. To compare type 2 immunogenicity of one or three doses of nOPV2 with the same number of doses of nOPV2 co-administered with bOPV.	A vs. B	10 weeks	Serology: 6, 10 weeks
		18 weeks	Serology: 6, 10, 14, 18 weeks
2. To compare type 1 and 3 immunogenicity of one or three doses of bOPV with the same number of doses of bOPV co-administered with nOPV2.	C vs. B	10 weeks	Serology: 6, 10 weeks
		18 weeks	Serology: 6, 10, 14, 18 weeks
3. To assess the presence of fecal viral shedding (as determined by real-time RT-PCR) over time following one dose of nOPV2, bOPV, or co-administered nOPV2 and bOPV.	Descriptive with comparisons of A vs. B and B vs. C	10 weeks (i.e. 4 weeks post-vaccination)	Stool: 7 (Arm A only), 8, 10 weeks from vaccine recipient
4. To estimate household transmission of nOPV2 by assessing the presence of fecal viral shedding (as determined by real-time RT-PCR) among siblings of vaccine recipients.	Descriptive	10 weeks (i.e. 4 weeks post-vaccination)	Stool: 7 (Arm A only), 8, 10 weeks from sibling
5. To assess the occurrence and genomic characteristics of intertypic recombinants in stool specimens of vaccine recipients and siblings after one dose of nOPV2 given with or without bOPV.	Descriptive with comparison of A vs. B	10 weeks (i.e. 4 weeks post-vaccination)	Stool: 8, 10 weeks from vaccine recipient and sibling

Adverse Events (AEs)

Safety will be assessed by:

- Incidence rate of solicited systemic AEs 24–48 hours after the first study vaccination.
- Incidence rate of unsolicited AEs during entire study period.
- Incidence rate of serious AEs during entire study period.

Data Safety Monitoring Plan (DSMP)

Records to be kept

The study will use a mix of paper- and electronic-based records. Participant data from clinic visits (for vaccine recipients and from siblings, who will attend the first clinic visit only) will be collected and recorded electronically on tablets through REDCap, an electronic data entry system. The Informed Consent Form and Screening Form will be paper-based exclusively. Eligibility Criteria, which is assessed at the beginning of study form Clinic Visit at 6 weeks will be exclusively paper-based for participants who are not eligible or those who are eligible but did not consent. For those who are eligible and have provided consent for participating in the study, the Eligibility Criteria component of study form Clinic Visit at 6 weeks will be paper- and web- based. Female field workers will use paper-based forms for the home visits; these will be entered by data entry staff into REDCap. All other study information for participants will be exclusively web-based. As a back-up, there will be paper-based CRFs available to collect participant data in case of any problems that arise with the web-based system. Paper-based data collection will be used as back-up in the case of power failure or malfunctioning WiFi or tablets during study procedures. In case there is complete failure of tablet-based system, the study will switch to paper-based CRF.

Vaccine recipients will be identified by a PID, which will be provided after enrolment and randomization. The PID will be used to link information recorded in eCRFs and results from laboratory analysis of biological specimens. Personal identifiers will only be recorded on the Screening Form and the Informed Consent Form but will not be recorded on any eCRFs, biological specimens, or SAE forms. The two paper-based documents (Screening Form and Informed Consent Form) will be filed in a locked cabinet separately from the other study forms and logs. Information about the sibling and his/her stool specimens will be captured under the vaccine recipient's PID.

Data Entry, Cleaning and Storage

Paper records will be kept in a locked cabinet, in a locked room, with access restricted to select study staff and investigators. The computers and tablets will be kept in a locked room and password protected. Only select study staff and investigators will be authorized to access the digital records. Laptops/tablets will be password protected with two-levels of password protection. The first password will be device password. The second password will be to log in to the web-based data entry portal.

Information collected in the CRFs other than Screening Form will be entered into a web-based data collection system (REDCap). The web-based data collection system will include system data checks to identify and prevent data entry errors. Data collected from the web-based data collection tools will be stored in secure server accessible only after providing user ID and password. After the completion of analysis and publication of study results, the study forms and databases will be archived. The forms will be stored in a locked cabinet with access restricted to investigators. The database will be password protected.

Data Ownership and Public Release

Study data will be jointly owned by icddr,b and CDC. After completion of study activities, summary tables of study results will be available on www.clinicaltrials.gov. After study registration, clinicaltrials.gov provides unrestricted public access on study details including summary tables.

Study investigators will have access to all participant (vaccine recipient and sibling) data, without identifiers, including laboratory data. Co-investigators and technical advisors for the household transmission objectives will have access to relevant data as defined in Table 5 for the corresponding objectives.

Site Monitoring Plan

Prior to start of the study, Standard Operating Procedures (SOPs) will be developed by investigators in consultation with study staff. Study staff will receive training on the SOPs for study procedures and on Good Clinical Practices in clinical trials.

After the start of the study, monitoring will be conducted four times:

1. First monitoring visit: within 2 months after the start of the study
2. Second monitoring visit: within 2 months after the first monitoring visit
3. Third monitoring visit: within 2 months after the second monitoring visit
4. Final monitoring visit: Within two months of the last study visit by vaccine recipients

During these monitoring visits, the following study documents and procedures will be reviewed:

1. Participant records, including informed consent forms (with assistance of a medical officer)
2. eCRFs, electronic records, and other supporting data
3. Adverse event forms (with assistance of a medical officer)
4. DSMB reports
5. Laboratory specimen records
6. Vaccine and biological materials storage and records
7. Any additional medical records (with assistance of a medical officer)
8. Measures to ensure protection of study participants
9. Measures to ensure compliance with study protocol, and accuracy and completeness of records
10. Any regulatory files associated with the study will also be inspected to ensure all regulatory and reporting requirements are being followed

Site monitoring visits will be conducted by CDC staff who have not interacted with study participants. Site monitoring reports will be shared with the PI.

Safety Monitoring

CDC and icddr,b have conducted several recent polio clinical trials using OPV and IPV (i.e., tOPV, bOPV, mOPV2, fIPV, and IPV) that have included safety monitoring of participants.

Anaphylactic reactions to bOPV are very rare but possible because bOPV contains trace amounts of antibiotics, including kanamycin and erythromycin for bOPV manufactured by Bio Farma. The nOPV2 being used in this trial does not contain antibiotics. All vaccine recipients will be observed for 30 minutes after vaccination to monitor for any immediate adverse reactions to the vaccine. Properly skilled medical personnel will be immediately available in the event of an unexpected adverse reaction. Adrenaline (for anaphylactic reaction) will be available but equipment for endotracheal intubation will not be available at the site. After the 30-minute observation period, the medical officer will record the presence of any potential reaction to the vaccine on the corresponding CRF. At the end of each study visit, the physician will provide the parents with a phone number to call if they have any questions or if the vaccine recipient experiences any reactions to the vaccines. Since nOPV2 is a new vaccine, as an additional safety monitoring measure, study staff will contact the household of vaccine recipients to inquire and record any potential adverse events after the first vaccination visit; this will take place 24–48 hours after vaccination.

Should a serious illness occur while the vaccine recipient is enrolled in the study (requiring a physician's visit or hospitalization), parents will be instructed to seek medical care immediately and to notify study

staff as soon as possible. Medical care for vaccine recipients will be provided free of charge for expected minor illnesses that develop during the follow up period, such as diarrhea and respiratory infections, as well as any adverse outcomes judged to be possibly, probably or definitely related (detailed below) to study vaccines or vaccination.

Recording, Monitoring and Reporting of Adverse Events

Solicited AEs: In this study, fever, vomiting, crying abnormal, drowsiness, loss of appetite and irritability will be solicited at one timepoint 24-48 hours after the first study vaccination. This will include the definitions of mild, moderate and severe AEs, as described in Table 6, to facilitate the assessments of the level of functional impairment for each experienced AE. For fever, temperature will be recorded if available, otherwise subjective fever will be solicited.

Table 6: Intensity scales for solicited symptoms

Events	**Severity Grade**			
	0	**1**	**2**	**3**
Fever (if thermometer is available)	<37.5° C	37.5° C- 38.0 ° C	38.1° C- 39.0 ° C	>39.0 ° C
Vomiting	None	1 episode/24 hours	2-5 episodes/24 hours	≥ 6 episodes/24 hours
Abnormal Crying	None	< 1hour	1-3 hours	>3 hours
Drowsiness	None	Sleepier than usual or less interested in surroundings	Not interested in surroundings or did not wake up for a feed	Sleeping most of the time or difficult to wake up
Poor feeding	None	Eating less than normal	Missed 1 or 2 feeds completely	Refuses ≥3 feeds or refuses most feeds
Irritability	None	Easily consolable	Requiring increased attention	Inconsolable

Unsolicited AEs: The investigator will assess the incidence and maximum intensity that occurred over the duration of the event for all unsolicited AEs recorded during the study. The assessment will be based on the investigator's clinical judgment. The intensity should be assigned to one of the following categories:

1 (mild) = An AE which is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate) = An AE which is sufficiently discomforting to interfere with normal everyday activities.
3 (severe) = An AE which prevents normal, everyday activities.

During each study clinic visit, study staff will question the parents about possible AEs experienced by the vaccine recipient since the previous study visit. This information will be recorded on the corresponding

eCRF. Reported AEs will be recorded in the AE form in the eCRF. The AE form will include a description of the event, time of onset, assessment of severity, relationship to study product, and time of resolution/stabilization of the event.

Reports of AEs will be periodically discussed by the team of investigators. The study team will review the potential relationship and classify the relationship into:

- Unrelated
- Possibly related
- Probably related
- Definitely related

Interpretation of vaccine-relationship to AE will be based on the type of event, the relationship of the event to the time of vaccine administration, the known biology of the vaccine and the investigators' medical judgment. In addition, the investigation team will also report clusters of AE (at least three) to the DSMB periodically for further evaluation.

An AE will be considered a serious AE (SAE) if it meets any of the following criteria:

1. Death during the study period
2. Life threatening event
3. Hospitalization or prolongation of existing hospitalization
4. Paralysis, severe disability/incapacity, or substantial disruption of the ability to conduct normal functions
5. Anaphylaxis associated with vaccine administration

All SAEs will be notified by the principal investigator to the regulatory agencies, ethical review committees, the Data Safety Monitoring Board (DSMB), and CDC within 24 hours of information. A separate icddr,b SAE form will be completed for SAEs and submitted to the ERC for review.

Data Safety Monitoring Board (DSMB)

The study will be monitored by a DSMB constituted by icddr,b with input from the Ethical Review Committee (ERC). The DSMB will include representation outside of icddr,b. The DSMB is expected to convene once prior to the start of the study after ethical and regulatory approval of the study protocol. The DSMB will convene meetings at the middle and at study completion. The DSMB will be responsible for establishing study stopping rules. Immunogenicity data will not be available for DSMB meetings because all blood specimens will be analysed after the completion of the field activities.

Ethical Assurance for Protection of Human rights

Justification for Involving a Vulnerable Population

Vaccine recipients will be enrolled at 6 weeks of age. Enrolment at this early age is required because the study is assessing the immunogenicity of poliovirus vaccines that are routinely administered at this age. The current schedule for polio immunization in Bangladesh includes three doses of bOPV administered at 6, 10 and 14 weeks of age plus two fractional IPV (fIPV) ID doses administered at 6 and 14 weeks of age. Delaying vaccine recipient enrolment until they are older will not allow assessing the immunogenicity of alternative polio vaccines and vaccination schedules because most vaccine recipients will be immune as a result of the polio vaccines they received through routine immunization.

Potential Benefits and Compensation to Vaccine recipients

Vaccine recipients will receive all non-polio routine immunizations (BCG, Penta, PCV) as per the routine immunization schedule of Bangladesh. After completion of study activities, vaccine recipients in Arms A and B will receive three doses of bOPV. The three doses of bOPV will be given in 4-week intervals

beginning at 18 weeks of age. All vaccine recipients will also receive two doses of fIPV. The routine polio immunization schedule in Bangladesh is three doses of bOPV along with two doses of fIPV. During study visits, vaccine recipients will be examined by medical officers and their growth and development will be assessed. In addition, vaccine recipients and siblings will be offered advice on diagnosis and treatment of any other illnesses they experience during the study period at no cost.

For the larger public health community, the results of this clinical trial may be used to inform outbreak response vaccination strategies.

Risks to Vaccine recipients and Siblings

bOPV has a long safety record and is used for routine childhood immunization in Bangladesh; nOPV2 is similar to mOPV2 except that it has further attenuated type 2 poliovirus. mOPV2 has been used in a polio vaccine trial by icddr,b in 2015–2016. Compared to mOPV2 and other existing OPVs, nOPV2 has been developed to be more genetically stable and therefore less likely to revert to neurovirulence. Phase 1 clinical trials of nOPV2 in IPV-primed adults demonstrated the safety of both vaccine candidates [14]. For both, viral shedding appeared to be no greater than mOPV2, and possibly lower. Mouse neurovirulence testing of shed virus also demonstrated the stability of the shed virus and deep sequencing of the shed virus revealed no unexpected mutations or loss of key stabilizing mutations, which implies a decreased likelihood of transmission of a virus with neurovirulent phenotype, relative to Sabin 2. Preliminary results from phase 2 trials in Belgium and Panama were reviewed by an independent data safety monitoring board, which supported age group progression from adults to toddlers and infants based on the available safety information. Early trial results also suggest that both candidates are immunogenic and more genetically stable than Sabin 2 [16]. Prior to the start of the current study, icddr,b will implement an OPV-naïve infants trial in Matlab that includes nOPV2 (PR-20001).

Vaccine recipients may have less immunity to polio during the study period than similarly aged non-vaccine recipients because of the altered vaccination schedule; all vaccine recipients will receive their first dose of fIPV twelve weeks later than the EPI schedule and some vaccine recipients will receive their first dose of bOPV twelve weeks later than the EPI schedule. However, the risk of infection with WPV or cVDPV is very low in Bangladesh. The last endemic WPV case was reported in 2000, and the last imported case was reported in 2006. Furthermore, WPV type 2 and WPV type 3 have been declared globally eradicated. No cVDPV cases have ever been reported in Bangladesh thanks to the high coverage reached with routine immunization since WPV elimination.

The most significant adverse event associated with OPV is vaccine-associated paralytic poliomyelitis (VAPP); however, the risk for recipient VAPP and contact VAPP is very small as the children will be protected by maternal antibodies. The risk of VAPP is about 1 case per 1.2 to 2.4 million doses of tOPV [3]; the risk after bOPV is expected to be similar or slightly higher than tOPV for recipient VAPP as most were related to types 1 or 3 [4-6]. Because bOPV is given as part of the EPI schedule in Bangladesh, study vaccine recipients will have similar risk for developing VAPP to types 1 and 3 as infants not participating in the study. There may also be some risk of VAPP in close contacts of vaccine recipients, including the older siblings, but we assume this risk to be minimal in Bangladesh as Bangladesh has high routine immunization coverage and nOPV2 has been designed with the intent to be much less prone to reversion to neurovirulence compared to Sabin OPV.

Upon completion of study activities, vaccine recipients in the nOPV2-only arm will not have protection against types 1 and 3 and vaccine recipients in the bOPV-only arm will not have protection against type 2 until they receive their first dose of fIPV (and bOPV, depending on the arm) at 18 weeks of age.

In summary, because of protection conferred by the nOPV2 and bOPV doses provided by the study, the genetic stability of nOPV2, and the low probability of poliovirus circulation in Bangladesh during the study implementation, the risk of paralysis caused by WPV, cVDPV or OPV in study vaccine recipients, will be very low and similar or only slightly different than the risk of non-vaccine recipient infants of similar age.

Additional potential risks and discomfort to vaccine recipients stem from blood collections, adverse reactions to study vaccines, and breach of confidentiality or an unintended disclosure of confidential information. Immunogenicity to study vaccines can only be assessed from blood specimens. Four blood draws are necessary because immunogenicity is measured by determining the change in antibody titers. The subsequent blood draws 4 weeks after administration of study vaccines will assess immunogenicity of study vaccines per the study objectives. The minimal amount of blood necessary for testing (1 ml) will be collected with the most common side effect being pain at the site of collection. To minimize the discomfort and risks associated with blood draws, only qualified staff with experience in the collection of blood from infants will draw blood. Sterile equipment and technique, and alcohol swabs will be used to reduce the risk of infection from a blood draw. Pressure will be applied at the site of blood draw to minimize bleeding from the site of blood draw.

bOPV contains trace amounts of antibiotics; therefore, vaccine recipients may react to these substances although reactions are rare. To minimize the consequences of a potential anaphylactic reaction to study vaccines and/or their components, vaccine recipients will be observed for 30 minutes after vaccine administration by staff trained to respond to potential reactions. Parents of the vaccine recipient will also be contacted (either via phone call or home visit) 24–48 hours after the first vaccination. The purpose will be to inquire about and record any potential adverse events since nOPV2 is a new vaccine.

An additional risk to participants is a breach of confidentiality or an unintended disclosure of personal information. All study personnel will be trained in the protection of human subjects in research. All Case Report Forms (CRFs), laboratory specimens, and other reports including adverse events will be identified by a Participant Identification Number (PID) to maintain participant confidentiality. No identifiers will be recorded on eCRFs, other study reports and laboratory specimens. All paper records will be stored in a locked cabinet. All electronic records will be stored in a password protected database, on a password protected computer. Access to paper and electronic records will be restricted to study staff and investigators. De-identified data may be shared with vaccine manufacturers and regulatory authorities, both national and international, upon request.

Institutional Review Board (IRB) and Ethical Review

The protocol with letters of consent and other associated appendices will be reviewed and approved by the Research Review Committee (RRC) and Ethical Review Committee (ERC) and at icddr,b before any participants are enrolled. The RRC and ERC at icddr,b will be responsible for oversight of the study. Any subsequent modifications to the protocol will be submitted to the ERC and RRC at icddr,b for additional approval.

All participants will be below the legal age of consent because vaccine recipient participants will be enrolled at 6 weeks of age and siblings will be <10 years of age. Parents of potential participants will be informed that their children's participation in the study is strictly voluntary and that they are free to withdraw their children from the study at any time. Signed informed consent will be obtained from a parent of the participants, in the presence of a literate witness who is not directly related to the study. The informed consent form will describe the purpose of the study, procedures, confidentiality of information, and the risks and benefits of participation. Informed consent forms will be translated from English to Bangla, the local language. A copy of the informed consent form will be given to the parent

of the participants and noted in study records. A second copy of the signed informed consent form will be filed with study records.

Participant Confidentiality Procedures

All eCRFs, laboratory specimens, and other reports including adverse events will be identified by PID to maintain participant confidentiality. No identifiers will be recorded on eCRFs, other study reports and laboratory specimens. All paper records will be stored in a locked cabinet. All electronic records will be stored in a password protected database, on a password protected computer. Access to paper and electronic records will be restricted to study staff and investigators; CDC co-investigators will only have access to de-identified electronic records. De-identified data may be shared with vaccine manufacturers and regulatory authorities, both national and international, upon request.

Use of Animals

Not applicable

Collaborative Arrangements

This study includes two partners with the following roles in the study:

1. International Centre for Diarrhoeal Diseases Research, Bangladesh

- Design of the study and collaborate in the development of the study protocol
- Submission of protocol to icddr,b's Research and Ethical Review Committees.
- Select study site and study staff and develop a budget for study implementation.
- Work with vaccine manufacturers to secure material transfer agreements for study vaccines, if needed.
- Collaborate in the development of standard operating procedures, study forms and training material.
- Conduct training and supervise study staff.
- Carry out implementation of the study procedures and coordinate logistics for sample collection, processing, storage and shipment as well as study vaccine storage and administration.
- Record and provide treatment for potential adverse events developed during the study.
- Create and enter data from case report forms, if paper-based forms used for any participants, into a database for future analysis.
- Collaborate with CDC investigators in the analysis, interpretation and writing of study results for study reports and manuscripts to be published in peer reviewed journals.

2. Centers for Disease Control and Prevention, Atlanta, GA, USA

- Design of the study and lead in the development of the study protocol.
- Submission of the protocol for CDC ethical clearance.
- Provision of funding for study implementation.
- Provide support to icddr,b to obtain material transfer agreements for study vaccines from vaccine manufacturers, if needed.
- Collaborate in the development of standard operating procedures, study forms and training material.
- Provide support in the training of study staff.
- Plan vaccine recipient randomization assignment for vaccine recipient assignment during enrolment.
- Monitor study implementation through visits to the study site in coordination with icddr,b.
- Test serum specimens for the determination of antibodies against poliovirus and enter laboratory data into an electronic database.
- Test stool specimens for the presence of vaccine polioviruses and recombinants.
- Lead data analysis, interpretation of results and writing detailed reports and manuscripts for publication in peer reviewed journals in collaboration with icddr,b investigators.

Facilities Available

Clinical Facilities

The International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) has a large multi-disciplinary international and national scientific research staff. Existing field, hospital, laboratory and office facilities will be used for this study. icddr,b scientists have conducted a variety of vaccine studies including poliovirus.

Field Site

The study will be carried out in urban slums in Mirpur in Dhaka. CDC and icddr,b have previously collaborated on seven polio clinical trials at Mirpur.

If feasible based on guidelines/recommendations related to the COVID-19 pandemic (e.g., physical distancing), the study will also be conducted at CTU, with the adjoining slum and non-slum areas of icddr,b Mohakahli, Dhaka - Kunipra, Arjat Para, Nakhalpara, Korail, Begunbari, Chairman bari and Badda. CDC and icddr,b have previously collaborated on two polio clinical trials at Mohakahli.

Laboratory Facilities at icddr,b

Existing laboratory facilities in icddr,b will be used to store and process specimens prior to shipment to CDC, Atlanta.

Laboratory Facilities at CDC

The Polio and Picornavirus Laboratory Branch of the Division of Viral Diseases at CDC, Atlanta has the necessary staff, infrastructure and equipment to perform the laboratory testing for this study. The testing of serum and stool using the methods outlined in this protocol requires specific training and equipment that is not currently available at the laboratory of the Institute of Epidemiology, Disease Control and Research or at any other laboratory in Bangladesh.

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Budget

Name of the Project/Protocol: Immunogenicity of novel-monovalet OPV type 2 (nOPV2)
Budget Period: Sept. 30, 2020 to Sept. 29, 2021
Name of the PI: Dr. K. Zaman

Particulars	Pay level	Month Rate (S)	# of Staff	% Time	# of Month	Inflation @ 8%	Total Cost US$
Personnel:							
Dr. K. Zaman	Intl	15,625	1	15%	12	1.08	30,375
Dr. Md. Yunus	Intl	13,500	1	5%	12	1.08	8,748
Study Coordinator/Research Investigator	NOA	2,224	1	50%	12	1.08	14,412
Field Research Officer	GS5	1,010	1	100%	12	1.08	13,090
Field Research Supervisor	GS4	788	3	100%	12	1.08	30,637
Field Research Assistant	GS3	643	3	100%	12	1.08	25,000
Female Field Worker / SW / FA	UNCL	292	18	100%	12	1.08	68,118
Medical Officer	NOA	2,056	3	100%	12	1.08	79,937
Nurse	GS5	1,010	3	100%	12	1.08	39,269
Senior Scientific Officer	NOA	2,308	1	50%	12	1.08	14,956
Senior Research Officer (Lab)	GS6	1,306	1	100%	12	1.08	16,926
Research Officer (Lab)	GS5	1,010	1	100%	12	1.08	13,090
Analyst Programmer /Data Manager	NOB	2,655	1	25%	12	1.08	8,602
Data Management Assistant	GS3	666	2	50%	12	1.08	8,631
Asst. Coordination Manager	NOA	2,224	1	50%	12	1.08	14,412
Administrative Officer	GS5	1,010	1	100%	12	1.08	13,090
Assistant Programme Manager	NOA	2,224	1	50%	12	1.08	14,412
Sr. Field Attendant	GS2	553	2	100%	12	1.08	14,334
Field Attendant /FA	GS1	499	3	100%	12	1.08	19,401
Subtotal							**447,438**
Consultant		**$ Rate**		**No.**			
CCD Consultant (for Emerging infectious diseases)		24,506		1			24,506
				-			-
Subtotal							**24,506**
Travel and Perdiem		**$ Rate**		**No.**			
Local Transport including hiring vehicle	bulk	$ 10,500		1			10,500
ICDDR,B Transport		$ 14,280		1			14,280
Perdiem and Lodging		$ 3,000		1			3,000
International Travel with perdiem		$ 9,600		1			10,400
Subtotal							**38,180**
Supplies:		**$ Rate**		**No.**			
Supplies - stock/nonstock:							
Office Supplies Stock/Non Stock		$ 600		12			7,200
Specimen collection supplies - reagents							-
Supplies - Lab reagents		$ 1,200		12			14,400
PPE and other precautionary measures for Covid							15,200
Liquid Nitrogen Supplies							-
Dry ice for specimen transport							-
Office maintenance, cleaning and general supplies							-
Supplies capitals:							
Name of the items	unit	Rate	Qty.	**Total**			
Laptop/Docking Computer with all Accessories		2,200	1	2,200			
Air Condition for office		1,250	1	1,250			
Refrigerator		1,500	1	1,500			
IPS		1,000	1	1,000			
	Subtotal Capital supplies:						5,950
Subtotal							**42,750**
Others		**$ Rate**		**No.**			
Staff Development Training (Int. and local)		$ 500		1			500
Workshop / Seminar (Int. and local)		$ 500		1			500
Project implementation meeting and workshop		$ 500		1			500
Other services, Stipend / Labor charge		$ 48		12			576
Communication(Fax, Phone bill, Courier, postage etc.)		$ 209		12			2,502
Shipment and Int. Courier		$ 8,000		2			16,000
Office set up, Rent, Utilities, Repairs & Maintenance		$ 1,394		1			1,394
Lab Test Cost		$ 6,500		1			6,500
Printing and photocopy		$ 153		12			1,836
Subtotal							**30,308**
Contractual		**$ Rate**		**No.**			
To be named		3,714		1			3,714
		-		-			-
Subtotal							**3,714**
Equipment (Capital Items valued >/=US$5000)		**$ Rate**		**No.**			
Photocopy Machine		5,000		-			-
Other Capital items		-		-			-
Subtotal							**-**
Total Project cost							**586,896**
Total Project Admin and support cost (PAS):							**174,938**
PEI Admin Cost (11%)							64,559
icddr,b support cost: (19%)							110,380
Total Budget:							**761,834**

Budget Justifications

Please provide one page statement justifying the budgeted amount for each major item, including the use of human resources, major equipment, and laboratory services.

The study involves recruitment and training of staff, identification of all eligible vaccine recipients from the selected areas, vaccination, collection of blood and stool samples, and follow up of the vaccine recipients.

INVESTIGATORS AND STAFF

The amount budgeted for the investigators reflect a reasonable estimate of the minimum time required to implement the study. Dr. K. Zaman will be responsible for overall implementation of the study. Dr. Md Yunus will provide support for overall implementation as well as advice on epidemiological aspects.

- Research Investigator: Research investigator will coordinate all field research activities and will be responsible overall field management.
- Senior Scientific Officer: Will be responsible for overall lab activities of the study.
- Senior Field Research Officer: For study support and maintaining all documents.
- Field Research Officer: For supervising all field activities.
- Field Research supervisor: For supervising all field activities.
- Field Research Assistant: Informs families of the purpose and activities of the study, offer participation, complete different documents, etc.
- Female Field Worker/Surveillance Worker: Informs families of the purpose and activities of the study, offer participation, bring vaccine recipients to study clinic, complete different documents, etc.
- Medical officer: Will be responsible for examination of the vaccine recipients, take written consent, collect blood and other samples, provide necessary treatment, record and fill up of serious adverse events form and preparation of reports.
- Nurse: Assist medical officer in examining the patients, responsible for vaccination, dispensing medicines, collection of samples and filling of forms.
- Senior Research officer (Lab): For processing of samples, maintaining cold chain, and accountability of vaccines.
- Research Officer (Lab): For processing and shipping samples.
- Analyst Programmer / Senior Programmer: Overall data management and designing systems for entry and analysis of data.
- Senior Data Management Officer: Data entry and assist Senior Programmer.
- Senior Data Management assistant: Data entry and assist Senior Programmer.
- Assistant Coordination Manager: For managing all project related financial and administrative activities.
- Assistant Programme Manager: Responsible for project management and administrative activities
- Sr. Field Attendant & Field Attendant: To support study related activities

TRAVEL COSTS

- International travel - Travel costs related to attending meetings and presenting findings of the study at conferences.

- icddr,b transport - Transport costs for regular field work, monitoring data collection methods/techniques, schedule family visits, vaccine recipients transportation cost to/from the study clinic, office.
- Local transportation including hiring vehicle charges and guest house costs - Costs for land transport, vehicle hiring charges, guest house costs.

SUPPLIES AND OTHER COSTS

- Office Supplies Stock/Non Stock - This includes office and field related stock/non-stock supplies, housekeeping, janitorial, stationary, book & periodicals, food & beverage, cabinets, furniture, electronics and electric goods, mobile phone set, gasoline, petrol, diesel, fuel, CNG, tools, spares and servicing and other procurement and material item cost etc. for field activities.

Other Support

Describe sources, amount, duration, and grant number of all other research funding currently granted to PI or under consideration.

No other support will be provided for this study.

Biography of the Investigators

1. Name: K. Zaman

Present Position: Senior Scientist and Epidemiologist, icddr,b

Educational background: (last degree and diploma & training relevant to the present research proposal)

	Institution	Year
PhD	Johns Hopkins Bloomberg School of Public Health, USA	1999
MPH	Johns Hopkins Bloomberg School of Public Health, USA	1992
MBBS	Rajshahi Medical College, Bangladesh	1978
FRCP	Royal College of Physicians of Edinburgh	2020

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	PHRP	2854414	Taken on 07/13/2020

Note: If the response is "no", please get certification from CITI or NIH before study initiation and submit a copy to the Committee Coordination Secretariat

List of ongoing research protocols/ activities

Protocol/ Activity Number	Role in the protocol/ activity (PI, Co-PI, Co-I)	Starting date	End date	Percentage of time
PR 15050	PI	July 2015	Sep 2021	5
PR 16014	PI	March 2016	Dec 2019	5
PR 14059	PI	Jan 2018	Dec 2020	5
PR 18045	PI	Sep 2018	Sep 2020	20
PR 18050	PI	Sep 2018	Sep 2020	10
PR 18062	PI	Sep 2018	April 2020	20

Publications

Types of publications	Numbers
a. Original scientific papers in peer-review journals	201
b. Peer reviewed articles and book chapters	3
c. Papers in conference proceedings	135
d. Letters, editorials, annotations, and abstracts in peer-reviewed journals	4
e. Working papers	
f. Monographs	

Five recent publications including publications relevant to the present research protocol

1. **Zaman K**, Anand A. Sequential inactivated and oral polio vaccine schedules: a balancing act. **Lancet ID 2020 (in press).**

2. **Zaman K**, Kingma R, Yunus M, van Straaten I, Mekkes D, Bouwstra X, Gunale B, Kulkarni PS. Safety, immunogenicity and lot-to-lot consistency of a new Bivalent Oral Polio Vaccine (bOPV) in healthy Infants: Results of a Phase III, observer blind, randomized, controlled clinical study. **Vaccine 2019 Jun 22. doi:10.1016/j. vaccine.2019.06.048 [Epub ahead of print].**

3. **Zaman K**, Anand A. Complex tasks to estimate immune responses to various poliovirus vaccines and vaccination schedules. **Lancet ID 2019 Jul 23. pii: S1473-3099(19)30322-6. doi: 10.1016/S1473-3099(19)30322-6. [Epub ahead of print].**

4. **Zaman K**, Estívariz CF, Morales M, Yunus M, Snider CJ, Gary HE Jr, Weldon WC, Oberste MS, Wassilak SG, Pallansch MA, Anand A. Immunogenicity of type 2 monovalent oral and inactivated Poliovirus vaccines for type 2 poliovirus outbreak response: An open - level randomized controlled trial. **Lancet ID 2018 Jun;18(6):657-665.**

5. **Zaman K**, Anh DD, Victor JC, Shin S, Yunus M, Dallas MJ, Podder G, Thiem VD, Mai LP, Luby SP, Coia ML, Lewis K, Rivers SJ, Sack DA, Clemens JD, Scodel F, Steele AD, Neuzil KM, Ciarlet M. Efficacy of the pentavalent rotavirus vaccine against sever rotavirus among infants in developing countries in Asia: A randomized, double-blind placebo-controlled trial. **Lancet 2010 Aug 21;376(9741): 615-23. Epub 2010 Aug 6**.

CERTIFICATE

OF COMPLETION

PHRP Online Training, Inc. certifies that

K Zaman

has successfully completed the web-based course "Protecting Human Research Participants Online Training."

Date Completed: 2020-07-13 Certification Number: 2854414

PHRP
Protecting Human Research Participants
Online Training

Name: Md. Yunus

Present Position: Emeritus Scientist

Educational background: (last degree and diploma & training relevant to the present research proposal)

	Institution	Year
Degree MBBS	Dhaka Medical College, Dhaka University	1968
Degree MSc. CHDC	London School of Hygiene & Tropical Medicine, London	1982
Diploma		
Training		
Training		

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	NIH	2361583	29/03/2017 (date of completion)

Note: If the response is "no", please get certification from CITI or NIH before study initiation and submit a copy to the Committee Coordination Secretariat

List of ongoing research protocols/ activities

Protocol/ Activity Number	Role in the protocol/ activity (PI, Co-PI, Co-I)	Starting date	End date	Percentage of time
PR # 17034	Co-I	Oct 2017	Dec 2018	20
PR # 15016	Co-I	Jan 2017	Jan 2019	5
PR # 16077	Co-I	Dec 2016	Dec 2018	10
PR # 16014	Co-I	Apr 2016	Mar 2020	5
PR # 15111	PI	Feb 2016	Aug 2020	20
PR# 15050	Co-I	Jul 2015	Jul 2018	3
PR # 15007	Co-PI	Feb 2015	Jan 2018	10
RRC PR#16014	15/03/16	31/12/19	5 %	5

Publications

Types of publications	Numbers
Original scientific papers in peer-review journals	238
Peer reviewed articles and book chapters	8
Papers in conference proceedings	101
Letters, editorials, annotations, and abstracts in peer-reviewed journals	15
Working papers	6
Monographs	0

Five recent publications including publications relevant to the present research protocol

1. Schwartz, L. M., Zaman, K., Yunus, M., Basunia, A. H., Faruque, A. S. G., Ahmed, T., . . . Victor, J. C. (2019). Impact of rotavirus vaccine introduction in children less than 2 years of age presenting for medical care with diarrhea in rural Matlab, Bangladesh. *Clin Infect Dis*. doi: 10.1093/cid/ciz133
2. Rahman, M., Sohel, N., Yunus, F. M., Alam, N., Nahar, Q., Streatfield, P. K., & Yunus, M. (2019). Arsenic exposure and young adult's mortality risk: A 13-year follow-up study in Matlab, Bangladesh. *Environ Int, 123*, 358-367. doi: 10.1016/j.envint.2018.12.006
3. Zman K, Estivariz CF.,Morales M, **Yunus M**, Snider CJ, Gary Jr HE, Weldon WC, Oberste MS, Wassilak SG, Pallansch M A & Anand A. 2018a. Immunogenicity of type 2 monovalent oral and inactivated poliovirus vaccines for type 2 poliovirus outbreak response: an open-label, randomised controlled trial. *Lancet Infect Dis,* 18**,** 657-665
4. Anand A, Zaman K, Estívariz CF, **Yunus M**, Gary HE, Weldon WC, Bari TI, Steven Oberste M, Wassilak SG, Luby SP, Heffelfinger JD, Pallansch MA.Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial.Vaccine. 2015 Nov 27;33(48):6816-22. doi: 10.1016/j.vaccine.2015.09.039.PMID:26476367
5. **Yunus M**, Sohel N, Hore SK, Rahman M.Arsenic exposure and adverse health effects: a review of recent findings from arsenic and health studies in Matlab, Bangladesh.Kaohsiung J Med Sci. 2011 Sep;27(9):371-6. Epub 2011 Jul 6.

Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that **Mohammad Yunus** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 03/29/2017.

Certification Number: 2361583.

Name: Abhijeet Anand
Present position: Epidemiologist, Polio Eradication Branch, Global Immunization Division, CDC
Education background:

	Institution	Year
MBBS	Byramjee Jeejeebuoy Medical College, Pune, India	2001
MPH (Epidemiology)	Epidemiology, Johns Hopkins University Bloomberg School of Public Health	2003
Epidemic Intelligence Service (EIS)	US Centers for Disease Control and Prevention	2005

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	277837334	20 Dec 2021

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	13
Letters, editorials in peer-reviewed journals	8

Recent publications including publications relevant to the present research protocol:

1. **Anand A**, Luman ET, O'Connor P. Building on Success – Potential to improve coverage of multiple health interventions in Africa through integrated delivery with routine childhood vaccination. (Accepted: The Journal of Infectious Diseases)
2. Wiesen E, Wannemuehler K, Goodson JL, **Anand A**, Mach O, Thapa A, O'Connor P, Linayage J, Diorditsa S, Hasan AS, Uzzaman S, JalilMondal MD. Stability of the age distribution of measles cases over time during outbreaks in Bangladesh, 2004-2006. J Infect Dis. 2011 Jul;204Suppl 1:S414-20.
3. Upreti SR, Thapa K, Pradhan YV, Shakya G, Sapkota YD, **Anand A**, Taylor T, Mach O, Reef S, Pattamadilok S, Liyanage J, O'Connor P, Sedai T, Bhandary SR, Partridge J, Schluter W. Developing rubella vaccination policy in Nepal--results from rubella surveillance and seroprevalence and congenital rubella syndrome studies. J Infect Dis. 2011 Jul;204Suppl 1:S433-8.
4. O'Connor PM, Liyanage JB, Mach O, **Anand A**, Ramamurty N, Balakrishnan MR, Singh S. South-East Asia Regional update on measles mortality reduction and elimination, 2003-2008. J Infect Dis. 2011 Jul;204 Suppl 1:S396-402.
5. **Anand A**, Shiraishi RW, Bunnell RE, Jacobs K, Solehdin N, Abdul-Quader AS, Marum LH, Muttunga JN, Kamoto K, Aberle-Grasse JM, Diaz T. Knowledge of HIV status, sexual risk behaviors and contraceptive need among people living with HIV in Kenya and Malawi. AIDS. Jul 31 2009;23(12):1565-1573.

Name: Cindi Snider
Present position: Epidemiologist, Polio Eradication Branch, Global Immunization Division, CDC
Education background:

	Institution	Year
BSPH	University of North Carolina at Chapel Hill	1997
MHS (Epidemiology)	Johns Hopkins University Bloomberg School of Public Health	2001
PhD (Epidemiology)	University of North Carolina at Chapel Hill	2011

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	227211624	25- Nov-2021

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	11
Book chapters and review articles	2

Recent publications including publications relevant to the present research protocol:

1. **Snider CJ**, Zaman K, Estivariz CF, Yunus M, Weldon WC, Wannemuehler KA, Oberste MS, Pallansch MA, Wassilak SG, Bari TIA, Anand A. Immunogenicity of full and fractional dose of inactivated poliovirus vaccine for use in routine immunisation and outbreak response: an open-label, randomised controlled trial. Lancet. 2019 Jun 29;393(10191):2624-2634. doi: 10.1016/S0140-6736(19)30503-3. Epub 2019 May 16.
2. Farag NH, Mansour Z, Torossian L, Said R, **Snider CJ**, Ehrhardt D. Feasibility of jet injector use during inactivated poliovirus vaccine house-to-house vaccination campaigns. Vaccine. 2018 Aug 6;36(32 Pt B):4935-4938. doi: 10.1016/j.vaccine.2018.06.011.
3. Zaman K, Estívariz CF, Morales M, Yunus M, **Snider CJ**, Gary HE Jr, Weldon WC, Oberste MS, Wassilak SG, Pallansch MA, Anand A. Immunogenicity of type 2 monovalent oral and inactivated poliovirus vaccines for type 2 poliovirus outbreak response: an open-label, randomised controlled trial. Lancet Infect Dis. 2018 Jun;18(6):657-665. doi: 10.1016/S1473-3099(18)30113-0. Epub 2018 Mar 20.
4. Estivariz CF, **Snider CJ**, Anand A, Hampton LM, Bari TI, Billah MM, Chai SJ, Wassilak SG, Heffelfinger JD, Zaman K. Lessons Learned From the Introduction of Inactivated Poliovirus Vaccine in Bangladesh. J Infect Dis. 2017 Jul 1;216(suppl_1):S122-S129
5. Billah MM, Zaman K, Estivariz CF, **Snider CJ**, Anand A, Hampton LM, Bari TIA, Russell KL, Chai SJ. Cold-Chain Adaptability During Introduction of Inactivated Polio Vaccine in Bangladesh, 2015. J Infect Dis. 2017 Jul 1;216(suppl_1):S114-S121

Name: Concepcion F. Estivariz
Present position: Epidemiologist, Polio Eradication Branch, Global Immunization Division, CDC
Education background:

	Institution	Year
MD	Universidad Autonoma, Faculty of Medicine, Madrid, Spain	1990
Physician Specialist	Physician Specialist in Endocrinology and Nutrition, Ministry of Health, Spain	1995
Epidemic Intelligence Service (EIS)	US Centers for Disease Control and Prevention	2003

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	29524155	26- Nov-2021

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	38
Book chapters and review articles	7
Abstracts in scientific meetings	32

Recent publications including publications relevant to the present research protocol:

1. **Estivariz CF**, Snider CJ, Anand A, et al. Lessons Learned From the Introduction of Inactivated Poliovirus Vaccine in Bangladesh. J Infect Dis 2017;216:S122-s129
2. Anand, A., K. Zaman, **Estivariz CF**, Yunus M, Gary HG, Weldon WC, Oberste MS, Wassilak SG, Luby SP, Heffelfinger JD, Pallansch MA. "Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial." *Vaccine* 2016, **33**: 6816-6822.
3. Cardemil CV, **Estivariz C**, Shrestha C, Sherchand JB, Sharma A, Gary HE, Oberste MSJr, Weldon WC 3rd, Bowen MD, Vinje J, Schluter WW, Anand A, Mach O,Chu SY. "The effect of diarrheal disease on bivalent oral polio vaccine (bOPV) immune response in infants in Nepal." *Vaccine* 2016, **34**(22): 2519-2526.
4. Emperador, D. M., Velasquez DE, **Estivariz CF**, Lopman B, Jiang B, Parashar U, Anand A., Zaman K. "Interference of Monovalent, Bivalent, and Trivalent Oral Poliovirus Vaccines on Monovalent Rotavirus Vaccine Immunogenicity in Rural Bangladesh." *Clinical Infectious Diseases* 2016, **62**(2): 150-156.
5. **Estívariz CF**, Anand A, Gary HE Jr, Rahman M, Islam J, Bari TI, Wassilak SGF, Chu SY, Weldon WC, Pallansch MA, Heffelfinger JD, Luby SP, Zaman K. Immunogenicity of three doses of bivalent, trivalent, or type-1 monovalent oral poliovirus vaccines with a 2 week interval between doses in Bangladesh: an open-label, noninferiority, randomised, controlled trial. *Lancet ID, 2015,* **5**(8): 898-904.

Name: Amanda L. Wilkinson
Present position: Epidemiologist, Polio Eradication Branch, Global Immunization Division, CDC
Education background:

	Institution	Year
BS	Pennsylvania State University	2010
PhD (Nutritional Sciences, Epidemiology concentration)	Cornell University	2015
Epidemic Intelligence Service (EIS)	US Centers for Disease Control and Prevention	2018

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	20370998	26-Jun-2021

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	7
Book chapters and review articles	2
Abstracts in scientific meetings	12

Recent publications including publications relevant to the present research protocol:

1. Kalkowska DA, Pallansch MA, **Wilkinson AL**, Bandyopadhyay AS, Konopka-Anstadt JL, Burns CC, Oberste MS, Wassilak SGF, Badizadegan K, Thompson KM. Updated Characterization of Outbreak Response Strategies for 2019–2029: Impacts of Using a Novel Type 2 Oral Poliovirus Vaccine Strain. Risk Analysis. 2020. https://doi.org/10.1111/risa.13622.
2. Cunningham SA, Shaikh NI, Nhacolo A, Raghunathan PL, Kotloff K, Naser AM, Mengesha MM, Adedini SA, Misore T, Onuwchekwa UU, Worrell MC, El Arifeen S, Assefa N, Chowdhury A, Kaiser R, Madhi S, Mehta A, Obor D, Sacoor C, Sow A, Tapia M, **Wilkinson A**, Breiman R, Child Health and Mortality Prevention Surveillance (CHAMPS) Methods Consortium. Health and Demographic Surveillance Systems Within the Child Health and Mortality Prevention Surveillance Network. Clinical Infectious Diseases. 2019 Oct 9;69(Supplement_4):S274-9. Cited by 6.
3. **Wilkinson AL**, Pedersen SH, Urassa M, Michael D, Andreasen A, Todd J, Kinung'hi SM, Changalucha J, McDermid JM. Maternal systemic or cord blood inflammation is associated with birth anthropometry in a Tanzanian prospective cohort. Tropical Medicine & International Health, 2017; 22(1):52-62. Cited by 13.
4. Pedersen SH, **Wilkinson AL**, Andreasen A, Warhurst DC, Kinunghi S, Urassa M, Mkwashapi D, Todd J, Changalucha J, McDermid JM. Longitudinal analysis of mature breast milk and serum immune composition among mixed HIV-status mothers and their infants. Clinical Nutrition, 2016; 35(4):871-9. Cited by 18.
5. **Wilkinson AL**, Pedersen SH, Urassa M, Mkwashapi D, Kinunghi S, Todd J, Changalucha J, McDermid JM. Associations between gestational anthropometry, maternal HIV, and fetal and early infancy growth in a prospective rural/semi-rural Tanzanian cohort, 2012–13. BMC Pregnancy and Childbirth, 2015;15(1):277. Cited by 15.

Name: Qian An

Present position: Mathematical Statistician, Strategic Information and Workforce Development Branch, Global Immunization Division, CDC

Education background:

	Institution	Year
BE	Beijing Jiaotong University, Beijing, China	1999
MS (Biostatistics)	University of Minnesota, Twin Cities	2005
PhD (Biostatistics)	Emory University	2014

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	29726253	18- Dec-2021

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	37
Abstracts in scientific meetings	14

Recent publications including publications relevant to the present research protocol:

1. **An Q**, Song R, Sionean C, Finlayson T, Wejnert C. An Innovative Approach to Assess Similarity Between Sex Partners. *AIDS and Behavior* (2018). https://doi.org/10.1007/s10461-018-2285-0.
2. **An Q**, Wejnert C, Bernstein K, Paz-Bailey G. Syphilis Screening and Diagnosis Among Men Who Have Sex With Men, 2008-2014, 20 U.S. Cities. JAIDS *Journal of Acquired Immune Deficiency Syndromes* 2017. 75(S3):363–369. DOI: 10.1097/QAI.0000000000001412.
3. **An Q**, Song R, Finlayson TJ, Wejnert C, Paz-Bailey G. Estimated HIV Inter-test Interval Among Persons at High Risk for HIV Infection In the U.S. *Am J Prev Med*. 2017; 53(3):355–362.
4. **An Q**, Kang J, Song R, Hall HI. A Bayesian Hierarchical model with novel prior specifications for estimating HIV testing rates. *Statistics in Medicine*. 2016; 35(9): 1471-1487. DOI: 10.1002/sim.6795.
5. **An Q**, Chronister K, Song R, Yang B, Pearson M, Chan S and etc. Agreement of self-report and medical records review data on HIV testing behavior. *Annals of Epidemiology*. 2016; 26(4): 255-260.

Name: Steven Wassilak

Present position: Senior Epidemiologist, Polio Eradication Branch, Global Immunization Division, CDC

Education background:

	Institution	Year
BA (Biology)	University of Missouri-St. Louis	1973
MD	St Louis University School of Medicine	1977
Epidemic Intelligence Service (EIS)	US Centers for Disease Control and Prevention	1980

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	19789	

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	45
Book chapters and review articles	14
Letters, editorials in peer-reviewed journals	18

Recent publications including publications relevant to the present research protocol:

1. **Wassilak S**, Pate MA, Wannemuehler K, et al. Outbreak of type 2 vaccine-derived poliovirus in Nigeria: emergence and widespread circulation in an underimmunized population. J Infect Dis 2011;203:898-909.
2. Kidd S. Goodson JL. Aramburu J. Morais A. Gaye A. Wannemuehler K. Buffington J. Gerber S. **Wassilak S**. Uzicanin A. Poliomyelitis outbreaks in Angola genetically linked to India: risk factors and implications for prevention of outbreaks due to wild poliovirus importations. Vaccine. 29(21):3760-6, 2011 May 12.
3. Economic analysis of the global polio eradication initiative. DuintjerTebbens RJ. Pallansch MA. Cochi SL. **Wassilak SG**. Linkins J. Sutter RW. Aylward RB. Thompson KM. Vaccine. 29(2):334-43, 2010 Dec 16.
4. Challenges faced by the global polio eradication initiative. **Wassilak S**. Orenstein W. Expert Review of Vaccines. 9(5):447-9, 2010 May.
5. Kojouharova M, Zuber PL, Gyurova S, Fiore L, Buttinelli G, Kunchev A, Vladimirova N, Korsun N, Filipova R, Boneva R, Gavrilin E, Deshpande JM, Oblapenko G, **Wassilak SG**: Importation and circulation of poliovirus in Bulgaria in 2001. Bull World Health Organ 2003;81(7):476-81.

Name: Mark A. Pallansch
Present position: Director, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Education background:

	Institution	Year
BS (Biochemistry)	Virginia Tech Blacksburg, VA	1976
PhD (Biochemistry)	University of Wisconsin – Madison , WI	1982
Virology	Rockefeller University New York, NY	1984

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	7660	

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	264
Book chapters and review articles	36
Abstracts in scientific meetings	133

Recent publications including publications relevant to the present research protocol:

1. Snider CJ, Zaman K, Estivariz CF, Yunus M, Weldon WC, Wannemuehler KA, Oberste MS, **Pallansch MA**, Wassilak SGF, Bari TIA, Anand A. Immunogenicity of full and fractional dose of inactivated poliovirus vaccine for use in routine immunisation and outbreak response: an open-label, randomised controlled trial. Lancet. 2019 Jun 29;393(10191):2624-2634.
2. Zaman K, Estívariz CF, Morales M, Yunus M, Snider CJ, Gary HE Jr, Weldon WC, Oberste MS, Wassilak SG, **Pallansch MA**, Anand A. Immunogenicity of type 2 monovalent oral and inactivated poliovirus vaccines for type 2 poliovirus outbreak response: an open-label, randomised controlled trial. Lancet Infect Dis, 2018;18:657-665.
3. Anand A, Molodecky NA, **Pallansch MA**, Sutter RW. Immunogenicity of two doses of fractional intradermal inactivated poliovirus vaccine: a novel dose sparing immunization schedule. Vaccine 2017;35:2993-2998
4. Anand A, Zaman K, Estivariz CF, Yunos M, Gary HE Jr, Weldon WC, Bari TI, Oberste MS, Wassilak SG, Luby SP, Heffelfinger JD, **Pallansch MA**. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: a randomized controlled trial. Vaccine 2015;33:6816-22
5. Estívariz CF, Jafari H, Sutter RW, John TJ, Jain V, Agarwal A, Verma H, **Pallansch MA**, Singh AP, Guirguis S, Awale J, Burton A, Bahl S, Chatterjee A, Aylward RB. Immunogenicity of supplemental doses of poliovirus vaccine for children age 6–9 months in Moradabad, India: a community-based, randomised controlled trial. Lancet Infectious Diseases 2015;15:898-904.

Name: M. Steve Oberste
Present position: Chief, Polio and Picornavirus Laboratory Branch, Division of Viral Diseases, CDC
Education background:

	Institution	Year
BS (Genetics)	College of Letters and Sciences, University of California at Davis; Davis, California	1982
PhD (Immunology and Medical Microbiology)	College of Medicine, University of Florida; Gainesville, Florida	1988

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	8333	

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	87
Letters, editorials in peer-reviewed journals	7

Recent publications including publications relevant to the present research protocol:

1. Anand A, Zaman K, Estivariz C, Yunus M, Gary H, Weldon WC, Bari TI, **Oberste MS**, Wassilak S, Luby S, Heffelfinger JD, Pallansch MA. 2015. Early priming with inactivated poliovirus vaccine (IPV) and intradermal fractional dose IPV administered by a microneedle device: A randomized controlled trial. Vaccine 33:6816-6822. (PMID: 26476367)
2. Sáez-Llorens X, Clemens R, LeRoux Roels G, Jimeno, J, Costa Clemens SA, Weldon WC, **Oberste MS**, Molina N, Bandyopadhyay AS. 2016. Immunogenicity and safety of a novel monovalent high-dose inactivated poliovirus type 2 vaccine in infants: a comparative, observer-blind, randomised controlled study. Lancet Infect Dis 16:321-330. (PMID: 26719058)
3. Asturias EJ, Bandyopadhyay AS, Self S, Rivera L, Saez-Llorens X, Lopez E, Melgar M, Gaensbauer JT, Weldon WC, **Oberste MS**, Borate BR, Gast C, Clemens R, Orenstein W, O'Ryan G M, Jimeno J, Costa Clemens SA, Ward J, Rüttimann R. 2016. Humoral and intestinal immunity induced by new schedules of bivalent OPV and one or two doses of IPV in an open, randomised, controlled trial in Latin American infants. Lancet 388:158-169. (PMID: 27212429)
4. Habib MA, Soofi S, Mach O, Samejo T, Alam D, Bhatti Z, Weldon WC, **Oberste MS**, Sutter R, Bhutta ZA. Effect of booster doses of poliovirus vaccine in previously vaccinated children, clinical trial results 2013. Vaccine 34:3803-3809. (PMID: 27269054)
5. Brickley EB, Strauch C, Wieland-Alter W, Connor RI, Lin S, Weiner JA, Ackerman ME, Arita M, Weldon WC, **Oberste MS**, Sáez-Llorens X, Bandyopadhyay AS, Wright PF. 2018. Intestinal immune responses to type 2 oral polio vaccine challenge in infants previously immunized with bOPV and either high-dose or standard IPV. J Infect Dis In Press. (PMID: 29304199)

Name: Jacquelyn Lickness
Present position: Public Health Analyst, Polio Eradication Branch, Global Immunization Division, U.S. CDC
Education background:

Degree	Institution	Year
MPH	Emory University	2014

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	18892	

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	2
Letters, editorials in peer-reviewed journals	

Recent publications including publications relevant to the present research protocol:

1. Lickness JS, Gardner T, Diop OM, et al. Surveillance to Track Progress Toward Polio Eradication – Worldwide, 2018-2019. MMWR Morb Martal Wkly Rep 2020;69:623-629.
2. Bartz FE, **Lickness JS**, Heredia N, Fabiszewski de Aceituno A, Newman KL, Hodge DW, Jaykus L-A, García S, Leon JS. 2017. Contamination of fresh produce by microbial indicators on farms and in packing facilities: elucidation of environmental routes. Appl Environ Microbiol 83:e02984-16. https://doi.org/10.1128/AEM.02984-16.

Name: Jaymin Patel

Present position: Global Immunization Division, CDC, USA

Education background:

Degree	Institution	Year
PhD – Epidemiology	University of North Carolina at Chapel Hill	2016
MPH – Global Epidemiology	Emory University	2011
BS–Biology; BA–Env. Studies	University of North Carolina at Chapel Hill	2008

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	9300	

Publications:

Types of publications	Numbers
Original scientific papers in peer-review journals	20
Papers in conference proceedings	13

Five recent publications including publications relevant to the present research protocol:

1. **Patel JC**, Soeters HM, Diallo AO, et al. MenAfriNet: A Network Supporting Case-Based Meningitis Surveillance and Vaccine Evaluation in the Meningitis Belt of Africa. The Journal of infectious diseases 2019; 220(Supplement_4): S148-s54.
2. **Patel JC**, Diop OM, Gardner T, et al. Surveillance to Track Progress Toward Polio Eradication - Worldwide, 2017-2018. MMWR Morb Mortal Wkly Rep 2019; 68(13): 312-8.
3. **Patel JC**, George J, Vuong J, Potts CC, Bozio C, Clark TA, et al. Rapid Laboratory Identification of Neisseria meningitidis Serogroup C as the Cause of an Outbreak - Liberia, 2017. MMWR Morb Mortal Wkly Rep. 2017 Oct 27;66(42):1144-7.
4. **Patel JC**, Hathaway NJ, Parobek CM, Thwai KL, Madanitsa M, Khairallah C, et al. Increased risk of low birth weight in women with placental malaria associated with P. falciparum VAR2CSA clade. Sci Rep. 2017 Aug 11;7(1):7768.
5. **Patel JC**, Mwapasa V, Kalilani L, et al. Absence of Association Between Sickle Trait Hemoglobin and Placental Malaria Outcomes. The American journal of tropical medicine and hygiene **2016**; 94(5): 1002-7.

Name: Jennifer Anstadt

Present position: Lead Microbiologist, Vaccine Development Laboratory, Polio and Picornavirus Laboratory Branch, Division of Viral Diseases, Centers for Disease Control and Prevention

Education background:

	Institution	Year
BS (Biology)	Fairfield University	2000
PhD (Microbiology & Immunology)	University of North Carolina, Chapel Hill	2007
Postdoctoral Fellow (Pediatric Infectious Diseases)	Vanderbilt University School of Medicine	2012

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	29741394	12 Dec 2021

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	16
Letters, editorials in peer-reviewed journals	2

Recent publications including publications relevant to the present research protocol:

1. Sáez-Llorens X, Bandyopadhyay AS, Gast C, De Leon T, DeAntonio R, Jimeno J, Caballero MI, Aguirre G, Oberste MS, Weldon WC, **Konopka-Anstadt JL**, Modlin J, Bachtiar NS, Fix A, Konz J, Clemens R, Costa-Clemens SA, Rüttimann R. Safety and immunogenicity of two novel live attenuated oral poliovirus type 2 vaccines candidates in healthy children and infants: two randomised trials. (Under review, Lancet)
2. De Coster I, Leroux-Roels I, Bandyopadhyay AS, Gast C, Withanage K, Steenackers K, De Smedt P, Aerssens A, Leroux-Roels G, Oberste MS, **Konopka-Anstadt JL**, Weldon WC, Fix A, Konz J, Wahid R, Modlin J, Clemens R, Costa-Clemens SA, Bachtiar NS, Van Damme P. An evaluation of the safety and immunogenicity of two novel live attenuated serotype 2 oral poliovirus vaccine candidates in healthy adults; a phase 2, partial blind, randomised, placebo-controlled study. (Under review, Lancet)
3. **Konopka-Anstadt JL**, Campagnoli R, Vincent A, Shaw J, Wei L, Wynn NT, Smithee SE, Bujaki E, Te Yeh M, Laassri M, Zagorodnyaya T, Weiner AJ, Chumakov K, Andino R, Macadam A, Kew O, Burns CC. Development of a new oral poliovirus vaccine for the eradication end game using codon deoptimization. NPJ Vaccines. 2020 Mar 20;5:26. eCollection 2020.
4. Schubert RD, Hawes IA, Ramachandran PS, Ramesh A, Crawford ED, Pak JE, Wu W, Cheung CK, O'Donovan BD, Tato CM, Lyden A, Tan M, Sit R, Sowa GA, Sample HA, Zorn KC, Banerji D, Khan LM, Bove R, Hauser SL, Gelfand AA, Johnson-Kerner BL, Nash K, Krishnamoorthy KS, Chitnis T, Ding JZ, McMillan HJ, Chiu CY, Briggs B, Glaser CA, Yen C, Chu V, Wadford DA, Dominguez SR, Ng TFF, Marine RL, Lopez AS, Nix WA, Soldatos A, Gorman MP, Benson L, Messacar K, **Konopka-Anstadt JL**, Oberste MS, DeRisi JL, Wilson MR. Pan-viral serology implicates enteroviruses in acute flaccid myelitis. Nat Med. 2019 Nov;25(11):1748-1752.
5. Lopez A, Lee A, Guo A, **Konopka-Anstadt JL**, Nisler A, Rogers SL, Emery B, Nix WA, Oberste S, Routh J, Patel M. Vital Signs: Surveillance for Acute Flaccid Myelitis - United States, 2018. MMWR Morb Mortal Wkly Rep. 2019 Jul 12;68(27):608-614.
6. Van Damme P, De Coster I, Bandyopadhyay AS, Revets H, Withanage K, De Smedt P, Suykens L, Oberste MS, Weldon WC, Costa-Clemens SA, Clemens R, Modlin J, Weiner AJ, Macadam AJ, Andino R, Kew OM, **Konopka-Anstadt JL**, Burns CC, Konz J, Wahid R, Gast C. The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study. Lancet. 2019 Jul 13;394(10193):148-158.

Name: Cara C. Burns

Present position: Acting Branch Chief, Polio and Picornavirus Laboratory Branch, Division of Viral Diseases, CDC

Education background:

	Institution	Year
B. S. Biochemistry	Texas A& M University, College Station, Texas	1985
PhD Cellular, Viral and Molecular Biology	University of Utah, Salt Lake City, Utah	1991
Postdoctoral training	University of Washington Microbiology Department, Seattle, Washington	1991 - 1998

Ethics Certification:

		If Yes		
		Issuing Authority	Registration No	Valid Until
No ☐	Yes ☒	CDC	30057846	14Jan 2022

Publications:

Type of publication	Number
Original scientific papers in peer-review journals	>50
Letters, editorials in peer-reviewed journals	0

Recent publications including publications relevant to the present research protocol:

1. Fagnant-Sperati CS, Ren Y, Zhou NA, Komen E, Mwangi B, Hassan J, Chepkurui A, Nzunza R, Nyangao J, van Zyl WB, Wolfaardt M, Matsapola PN, Ngwana FB, Jeffries-Miles S, Coulliette-Salmond A, Peñaranda S, Vega E, Shirai JH, Kossik AL, Beck NK, Boyle DS, **Burns CC**, Taylor MB, Borus P, Meschke JS.Fagnant-Sperati CS, et al. Validation of the bag-mediated filtration system for environmental surveillance of poliovirus in Nairobi, Kenya. J Appl Microbiol. 2020 Aug 2. doi: 10.1111/jam.14807. Online ahead of print. J Appl Microbiol. 2020. PMID: 32743931
2. Mary M Alleman, Jaume Jorba, Sharon A Greene, Ousmane M Diop, Jane Iber, Graham Tallis, Ajay Goel, Eric Wiesen, Steven G F Wassilak, Cara C Burns. MMWR Morb Mortal Wkly Rep. 2020 Apr 24;69(16):489-495. doi:10.15585/mmwr.mm6916a1. Update on Vaccine-Derived Poliovirus Outbreaks - Worldwide, July 2019-February 2020 PMID: 32324719 PMCID: PMC7188410 DOI: 10.15585/mmwr.mm6916a1
3. Zhou NA, Fagnant-Sperati CS, Komen E, Mwangi B, Mukubi J, Nyangao J, Hassan J, Chepkurui A, Maina C, van Zyl WB, Matsapola PN, Wolfaardt M, Ngwana FB, Jeffries-Miles S, Coulliette-Salmond A, Peñaranda S, Shirai JH, Kossik AL, Beck NK, Wilmouth R, Boyle DS, Burns CC, Taylor MB, Borus P, Meschke JS.Zhou NA, et al. Feasibility of the Bag-Mediated Filtration System for Environmental Surveillance of Poliovirus in Kenya. Food Environ Virol. 2020 Mar;12(1):35-47. doi: 10.1007/s12560-019-09412-1. Epub 2019 Nov 2. Food Environ Virol. 2020. PMID: 31679104 Free PMC article.
4. Konopka-Anstadt JL, Campagnoli R, Vincent A, Shaw J, Wei L, Wynn NT, Smithee SE, Bujaki E, Te Yeh M, Laassri M, Zagorodnyaya T, Weiner AJ, Chumakov K, Andino R, Macadam A, Kew O, **Burns CC**. Development of a new oral poliovirus vaccine for the eradication end game using codon

deoptimization. NPJ Vaccines. 2020 Mar 20;5:26. doi: 10.1038/s41541-020-0176-7. eCollection 2020.NPJ Vaccines. 2020. PMID: 32218998

5. Estívariz CF, Pérez-Sánchez EE, Bahena A, **Burns CC**, Gary HE Jr, García-Lozano H, Rey-Benito G, Peñaranda S, Castillo-Montufar KV, Nava-Acosta RS, Meschke JS, Oberste MS, Lopez-Martínez I, Díaz-Quiñonez JA.Estívariz CF, et al. Field Performance of Two Methods for Detection of Poliovirus in Wastewater Samples, Mexico 2016-2017. Food Environ Virol. 2019 Dec;11(4):364-373. doi: 10.1007/s12560-019-09399-9. Epub 2019 Sep 30. Food Environ Virol. 2019. PMID: 31571037
6. Van Damme P, De Coster I, Bandyopadhyay A, Prevets H, Withanage K, De Smedt P, Suykens L, Oberste M, Weldon W, Costa-Clemens S, Clemens R, Modlin J, Weiner A, Macadam A, Andino R, Kew O, Konopka-Anstadt J, **Burns CC**, Konz J, Wahid R, and Gast C. A blinded phase 1 study of the safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults. Lancet, Published online June 4, 2019 http://dx.doi.org/10.1016/S0140-6736(19)31279-6
7. Shaw J, Jorba J, Zhao K, Iber J, Chen Q, Adu F, Adeniji A, Bukbuk D, Baba M, Henderson E, Dybdahl-Sissoko N, Macdonald S, Weldon WC, Gumede N, Oberste MS, Kew OM, **Burns CC**. Dynamics of Evolution of Poliovirus Neutralizing Antigenic Sites and Other Capsid Functional Domains during a Large and Prolonged Outbreak. J Virol. 2018 Feb 14. pii: JVI.01949-17. doi: 10.1128/JVI.01949-17. [Epub ahead of print] PubMed PMID: 29444940; PubMed Central PMCID: PMC5899205.
8. Montmayeur AM, Ng TF, Schmidt A, Zhao K, Magaña L, Iber J, Castro CJ, Chen Q, Henderson E, Ramos E, Shaw J, Tatusov RL, Dybdahl-Sissoko N, Endegue-Zanga MC, Adeniji JA, Oberste MS, **Burns CC**. High-Throughput Next-Generation Sequencing of Polioviruses. J Clin Microbiol. 2017 Feb;55(2):606-615. doi: 10.1128/JCM.02121-16. Epub 2016 Dec 7. PMID:27927929
9. **Burns CC**, Kilpatrick DR, Iber JC, Chen Q, Kew OM. Molecular Properties of **Poliovirus** Isolates: Nucleotide Sequence Analysis, Typing by PCR and Real-Time RT-PCR. Methods Mol Biol. 2016;1387:177-212. doi: 10.1007/978-1-4939-3292-4_9.Methods Mol Biol. 2016. PMID: 26983735

Informed Consent (English and Bangla)

Information Sheet for Vaccine recipient and Sibling

Protocol No. PR-20060	Version No. 1.06	Date: 03-12-2020

Protocol Title: Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

Investigator's name: Dr. K. Zaman
Organization: International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)

We would like to invite you to participate in a research project. Please read this information sheet carefully, and if you have any questions about the study do not hesitate to ask from the research staff. Feel free to discuss the project with your family or friends before you make a decision on whether to participate

Background
Polio disease is caused by infection with the poliovirus. Polio can cause paralysis of the legs, arms or the chest muscles and can result in death. There are three types of polioviruses: type 1, type 2, and type 3. To protect children from polio, oral poliovirus vaccines (OPV) and inactivated poliovirus vaccines (IPV) are used. In the EPI vaccination schedule of Bangladesh, children are given fractional IPV (fIPV) at 6 and 14 weeks and bivalent OPV (bOPV) at 6, 10, and 14 weeks.

Infants in Bangladesh are given OPV in the form of bOPV, which protects infants against types 1 and 3. There is also OPV that protects against just one type of poliovirus. These are called monovalent OPV, or mOPV. Monovalent OPV (mOPV) protects infants against type 2 but is only used in very specific situations and not part of routine immunization. After polio disease has been eradicated, the expectation is that OPV will no longer be given to infants but will still be used for outbreak response. A new vaccine that works to protect infants from type 2, called novel OPV, or nOPV2 will likely replace mOPV2 as the vaccine used in places with type 2 outbreaks. But we do not know if it is better to give nOPV2 with bOPV to help protect children against all three types of poliovirus, or if giving nOPV2 and bOPV together affects how well they protect children against polioviruses.

Why is your infant invited to participate in the study as a vaccine recipient?
We are talking to you about this study because you have an infant that will need to receive polio vaccination to be protected against polio disease.

Why is the infant's older sibling invited to participate in the study?
For this study, stool samples will be collected from one sibling of each infant who receives the vaccine. This will help us understand how polio vaccine spreads from a child who receives vaccine to other children in the household.

Methods and procedures of the study
If you decide to participate, you will need to bring your infant, the one who will receive the vaccine, to the study clinic a total of four times over a period of 12 weeks, including today's visit. Today's visit requires both the vaccine recipient and the sibling to be present, but for the additional visits you will only need to bring the vaccine recipient. The additional three clinic visits will be when the vaccine

recipient is 10, 14, and 18 weeks of age. Each visit will take about 60 minutes. During today's visit, a doctor will ask questions about your children's health, their vaccinations, and will examine them. For the vaccine recipient, the doctor will also administer study vaccines, collect samples, administer routine childhood vaccines, observe for any reactions to the vaccines, and schedule the next visit; the same activities will take place at the other three study visits. Prior to leaving, the study staff will tell you what to do if the vaccine recipient becomes ill, even if the illness is not related to the study vaccines. In addition, you will be visited or contacted by phone within 2 days of your infant receiving the first study vaccination. The purpose will be for added safety, to check if your infant is experiencing any problems or symptoms.

There are three different groups in this study. A computer will choose your infant's study group. The doctor will not know your infant's study group until the computer does the selection. The doctor will tell you the group assignment. The study vaccines are novel OPV2 (nOPV2) and bOPV. Vaccine recipients will receive either nOPV2 only, nOPV2 plus bOPV, or bOPV only at 6, 10, and 14 weeks of age. The sibling of the vaccine recipient will not receive any study vaccines.

The doctor or nurse will collect a sample of blood (1 ml or less than a quarter teaspoon) each time the vaccine recipient comes for a study clinic visit. You will also be asked to collect small stool samples (8 gm or about the size of an adult thumb) from the vaccine recipient and the enrolled sibling. This will tell us how the vaccine works in the intestines and how it can spread between children in the same household.

For the stool collections, study staff will make visits to your home at 2-3 timepoints, when the vaccine recipient is 7, 8, or 10 weeks of age. The timing of the stool collections will depend on the vaccine recipient's study group. There will be no stool collection from your children after 10 weeks of age. For each stool collection, there will be two or more visits to your household. At the first visit, study staff will give you kits to collect stool from your two children. During the next home visit(s), study staff will pick up the stool kits.

Once study activities are finished, the doctor or nurse will advise you to vaccinate the vaccine recipient with two doses of fIPV. The vaccine recipient may also be advised to receive three doses of bOPV, depending on which group he/she is assigned. These additional doses will make sure that your infant has protection in the blood and intestines against all three types of poliovirus, like other children in Bangladesh. The additional doses will not harm your infant. The doctor or nurse will provide the vaccines and will help you schedule the appointments to come to the clinic.

Risk and benefits

There are benefits from participating in the study. At each visit, a doctor will examine the vaccine recipient and administer polio vaccines at no charge. Other vaccines against childhood diseases will also be provided to the vaccine recipient during the visits at no cost. These include the pentavalent vaccine that protects against diphtheria, tetanus, whooping cough, hepatitis B and *Haemophilus influenzae* B, and the pneumococcal conjugate vaccine that protects against *Streptococcus pneumoniae*. This study will also help the global community because the results will be used to guide how outbreak response activities are conducted around the world.

For the vaccine recipient, there are risks to participating in the study. bOPV contains very small amounts of antibiotics and an allergic reaction to the antibiotics is possible, but very unlikely. nOPV2 does not contain antibiotics. During the study, the vaccine recipient may receive a polio vaccine that is different from other children in Bangladesh. bOPV protects against types 1 and 3 and is given to all infants in

Bangladesh. nOPV2 only protects against type 2 and is not a part of routine immunization. Since nOPV2 is a new vaccine, we have limited data on its safety, although all the data we have from studies suggests that it is safe. We also do not know the duration or extent to which nOPV2 protects against type 2. To ensure that all vaccine recipients in the study are protected against all types of poliovirus, after the study is over your infant will be given two doses of fIPV, which protects against all three types and is given to all infants in Bangladesh through EPI. Your infant will also be given three doses of bOPV based on their study group. This means the risk of your infant becoming sick with any of the poliovirus types is very low.

Although polio-like disease is a risk with OPV, only one in 1-2 million children develop this kind of illness. There is a risk of polio-like disease for the vaccine recipient. We do not know the exact risk of polio-like disease in children who receive nOPV2 or bOPV, although we believe it is similar and very low. There may also be risk of polio-like disease for others in close contact with the vaccine recipient, including the older sibling, but we believe this risk to be very low.

Drawing blood may cause discomfort or pain, and localized bruising, although pressure on the site may prevent or reduce bruising. Although rare, it is possible to get an infection at the site of blood draw or injection. Trained doctors and nurses will use sterile needles and clean materials to collect blood and administer vaccines in order to lower the chance of infection and bruising.

In addition to the expected reactions, there is a chance that the vaccine recipient may experience an unexpected reaction. If the vaccine recipient suffers any illness or injury from participating in the study, free medical care and treatment will be provided in the appropriate hospital. icddr,b will pay the cost of the medical care. In addition, while enrolled in the study, both of your children (the vaccine recipient and older sibling) will receive free medical care for any illnesses or injuries that occur, including those that are unrelated to participating in the study. If either of your children need medical assistance during the study, you may come to icddr,b's health facilities. A study doctor will examine your child and provide medical care according to his/her judgment and local standards.

Privacy, anonymity and confidentiality

Only a few, select study staff will have access to you and your children's personal information, such as name and address. They will need this information to contact you and to follow up with your children. All other study staff will use coded numbers assigned to each child. This includes staff testing the blood and stool samples. If the results of the study are published, you and your children will not be identified by name.

If the vaccine recipient experiences a severe reaction to the vaccine, his/her records may need to be reviewed by other individuals to make sure the study is safe. These people may include the lead study investigator, the safety monitor, or a member of the regulatory agency in Bangladesh. These individuals will not share names or other personal information with anyone not involved in the review.

Future use of information

Information collected in this study may be of use to other researchers, vaccine manufacturers and/or regulatory authorities (national and international). Upon request to icddr,b, information may be shared with these groups in the future. However, you and your children's names and other personal information will not be shared, coded numbers will be shared. This will maintain the same level of privacy, anonymity and confidentiality of information that you and your child will have during the study.

Once testing on blood and stool samples are completed and the results are analysed, it may be necessary to carry out further testing on the samples. Stored samples will be used for further testing, no additional

sample collection will be done. If you consent to allow your children to participate in the study, you are also consenting to this future testing, if necessary.

Some of your children's blood and stool samples will be stored for five years in the icddr,b laboratory. They will be stored because they contain valuable information about protection in children that may be useful for another polio study or other vaccine-preventable disease study. Investigators of future studies will need to obtain permission from icddr,b's research and ethical review committees before they can use any stored samples. Genetic testing will not be performed.

Right not to participate and withdraw

Your consent for your children to participate in this study is voluntary. Your children do not have to take part in this study. Your children may stop taking part at any time during the study. If your children do not participate in the study, they will still have access to vaccines, medical services and other benefits provided by the Government of Bangladesh.

Study staff may take a vaccine recipient or sibling out of the study early if:

- The doctor thinks that the vaccine recipient is too sick to receive one of the study vaccine doses
- He/she receives a polio vaccine from another source before or during the study
- You withdraw your consent for the vaccine recipient to be in the study

Principle of compensation

No monetary compensation will be provided for participating in this study. Money will be provided to pay for the cost of transportation to and from the study clinic. Vaccine recipients and siblings will be provided free medical care for illnesses and injuries while enrolled in the study.

Answering your questions/ Contact persons

If you have any questions or concerns about the study or information form, you may speak to:

Name of local principal investigator: Dr. K. Zaman, Phone: 01713047100

If you have questions about your child's rights as a vaccine recipient in this research study or think that your child may have been harmed, you may contact the IRB Secretariat of the Ethics Review Committee for Research in Human Subjects, icddr,b:

Name: M A Salam Khan Phone: 9886498

Vaccine recipient and Sibling Informed Consent Form

Protocol No. PR-20060	Version No. 1.06	Date: 03-12-2020

Protocol Title: Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

Investigator's name: Dr. K. Zaman
Organization: International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)

I have read the informed consent information sheet, have had the opportunity to ask questions, discuss the study, and have received satisfactory answers.	Yes ☐ No ☐
I understand that I am free to withdraw my children from the study without giving any reason.	Yes ☐ No ☐
I agree to the collection of up to 1 ml of blood (vaccine recipient) and 8 gm of stool (vaccine recipient and older sibling) during each scheduled sample collection.	Yes ☐ No ☐
I agree that unidentified blood/stool samples can be sent to CDC for analysis.	Yes ☐ No ☐
I agree for icddr,b to store blood /stool samples up to five years for future use.	Yes ☐ No ☐
I understand that the information I give is confidential.	Yes ☐ No ☐
I agree to my non-identifiable data being used for future, ethically approved studies.	Yes ☐ No ☐
I agree to being contacted in the future if there are any studies related to this research. I understand that relevant sections of my children's medical notes and data collected during the study may be looked at by individuals from the sponsor organization and by regulatory authorities, where it is relevant to my children taking part in this research. I give my permission for those individuals to have access to my children's records.	Yes ☐ No ☐
I give my consent for my infant (Name: _____) to take part in the study and receive polio vaccines.	Yes ☐ No ☐
I give my consent for his/her sibling (Name: _____) to also take part in this study.	Yes ☐ No ☐

If you agree to our proposal of enrolling your infant (Name:_____) in our study to receive polio vaccines, please indicate that by putting your signature or your left thumb impression at the specified space below.

Thank you for your cooperation.

_____ _____
Signature or left thumb impression of Parent Date

If you also agree to have his/her sibling (Name:_____) to participate in this study, please indicate that by putting your signature or your left thumb impression at the specified space below.

_____ _____
Signature or left thumb impression of Parent Date

_____ _____
Signature of the witness Date

_____ _____
Signature of the PI or his/her representative Date

Answering your questions/ Contact persons
If you have any questions or concerns about the study, information form, or consent form, you may speak to:

Name of local principal investigator: Dr. K. Zaman, Phone: 01713047100

If you have questions about your child's rights as a vaccine recipient in this research study or think that your child may have been harmed, you may contact the IRB Secretariat of the Ethics Review Committee for Research in Human Subjects, icddr,b:

Name: M A Salam Khan Phone: 9886498

অবহিতকরণ সম্মতিপত্র

icddr,b

টিকা গ্রহণকারী এবং তার ভাইবোনের জন্য অবহিতকরণ পত্র

Protocol No. PR-20060	Version No. 1.06	Date: 03-12-2020

Protocol Title: Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

গবেষকের নাম: ডা: কে জামান

সংস্থা: আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র (আইসিডিডিআর,বি)

আপনাকে একটি গবেষণা প্রকল্পে অংশগ্রহণের জন্য আমন্ত্রন জানাতে চাই। অনুগ্রহ করে এই অবহিতকরণ পত্রটি যত্নসহকারে পড়ুন এবং এ গবেষণা সম্পর্কে আপনার কোন প্রশ্ন থাকলে বিনা দ্বিধায় গবেষণা সহকারীকে প্রশ্ন করতে পারেন। গবেষণায় অংশগ্রহণের সিদ্ধান্ত নেয়ার পূর্বে প্রকল্পটি সম্পর্কে আপনার পরিবার ও বন্ধু-বান্ধবের সাথে স্বাধীনভাবে আলোচনা করে নিতে পারেন।

পটভূমি

পোলিও ভাইরাসের সংক্রমণের কারণে পোলিও রোগ হয়ে থাকে। পোলিওর কারণে পা, হাত বা বুকের মাংসপেশী পক্ষাঘাতগ্রস্ত হতে পারে যার কারণে মৃত্যু হতে পারে। তিন ধরণের পোলিও ভাইরাস আছে, টাইপ ১, টাইপ ২ এবং টাইপ ৩। শিশুদের পোলিও রোগ থেকে রক্ষা করার জন্যে আমরা মুখে খাওয়ার পোলিও ভাইরাস টিকা (OPV) এবং ইনএ্যাকটিভেটেড পোলিও ভাইরাস টিকা (IPV) ব্যবহার করে থাকি। বাংলাদেশের ইপিআই টিকাদান কর্মসূচী অনুযায়ী শিশুদের ৬ এবং ১৪ সপ্তাহ বয়সে আইপিভি (IPV) টিকা এবং ৬, ১০ এবং ১৪ সপ্তাহ বয়সে বাইভ্যালেন্ট ওপিভি টিকা দেয়া হয়।

বাংলাদেশের শিশুদের বিওপিভি (bOPV) আবরে ওপিভি (OPV) দেয়া হয়, যেটা টাইপ ১ এবং ৩ থেকে শিশুদেরর রক্ষা করে। আরো এক ধরণের ওপিভি (OPV) আছে যেটি শুধুমাত্র এক ধরণের পোলিও ভাইরাস থেকে রক্ষা করে। এগুলোকে মনোভ্যালেন্ট ওপিভি (OPV) অথবা এমওপিভি (mOPV) বলা হয়। মনোভ্যালেন্ট ওপিভি (mOPV) শিশুদের টাইপ ২ থেকে রক্ষা করে তবে এটা শুধুমাত্র খুবই নির্দিষ্ট পরিস্থিতিতে ব্যবহার করা হয় এবং নিয়মিত টিকাদান কর্মসূচীর অংশ এটা না। পোলিও রোগ নির্মূল হয়ে যাবার পর, এটা আশা করা যায় যে মহামারীর প্রতিক্রিয়া ছাড়া শিশুদের আর ওপিভি (OPV) দেয়া হবে না। এমওপিভি২ (mOPV2) এর পরিবর্তে নভেল ওপিভি (OPV) অথবা এনওপিভি২ (nOPV2) নামে একটি নতুন টিকা শিশুদের টাইপ ২ পোলিও থেকে রক্ষা করার কাজ করবে, এই টিকা টাইপ ২ মহামারীর ক্ষেত্রে ব্যবহার করা হবে। তবে এটা আমাদের জানা নেই যে এনওপিভি২ (nOPV2) এর সাথে বিওপিভি (bOPV) দিলে তা তিন ধরণের পোলিও ভাইরাস থেকে রক্ষা করতে পারবে কিনা, অথবা যদি এনওপিভি২ (nOPV2) এবং বিওপিভি (bOPV) একত্রে শিশুদের দেয়া হয় সেটি পোলিও ভাইরাস থেকে শিশুদেরর রক্ষা করতে সমর্থ কিনা।

কেন আপনার শিশুকে একজন টিকা গ্রহণকারী হিসেবে এ গবেষণায় অংশগ্রহণের জন্য আমন্ত্রণ জানানো হচ্ছে?

আমরা এ গবেষণা সম্পর্কে আপনার সাথে কথা বলছি কারণ আপনার একটি শিশু আছে যাকে পোলিও রোগ থেকে সুরক্ষা দেয়ার জন্য পোলিও টিকা গ্রহণ করতে হবে।

কেন শিশুটির ভাইবোনকে গবেষণায় অংশগ্রহণ করার জন্য আমন্ত্রণ জানানো হচ্ছে?

এই গবেষণায়, প্রত্যেক টিকা গ্রহণকারীর একজন ভাইবোনের কাছ থেকে পায়খানার নমুনা সংগ্রহ করা হবে। এটি আমাদের বুঝতে সাহায্য করবে, টিকা পাওয়া একটি শিশুর কাছ থেকে পোলিও টিকা/ভাইরাস কিভাবে একই পরিবারের অন্যান্য শিশুদের মধ্যে ছড়িয়ে পরে।

পদ্ধতি এবং প্রক্রিয়া

আপনি যদি গবেষণায় অংশগ্রহণের সিদ্ধান্ত নেন তবে আপনার যে শিশুটি টিকা গ্রহণ করবে তাকে, আজকের ভিজিট সহ ১২ সপ্তাহের মধ্যে মোট ৪ বার ক্লিনিকে নিয়ে আসতে হবে। আজকের পরিদর্শনের সময় টিকা গ্রহণকারী এবং তার ভাইবোন উভয়কেই উপস্থিত থাকতে হবে, কিন্তু পরবর্তী অতিরিক্ত পরিদর্শনের সময়গুলোতে শুধুমাত্র টিকা গ্রহণকারীকে আনতে হবে। অতিরিক্ত তিনটি ক্লিনিক পরিদর্শন হবে যখন টিকা গ্রহণকারীর বয়স ১০, ১৪ এবং ১৮সপ্তাহ হবে। প্রতিটি ভিজিটে প্রায় ৬০ মিনিটের মতো সময় লাগবে। আজকের দিনের পরিদর্শনের সময়ে একজন ডাক্তার আপনার শিশুদের স্বাস্থ্য সম্পর্কে, তাদের টিকার বিষয়ে জিজ্ঞেস করবেন এবং তাদের পরীক্ষা করবেন। টিকা গ্রহণকারীর ক্ষেত্রে, ডাক্তার তাকে গবেষণা টিকাও প্রদান করবেন, নমুনা সংগ্রহ করবেন, শিশুর জন্য নির্ধারিত সরকারী সকল টিকা প্রদান করবেন, টিকা দেয়ার পর কোন প্রতিক্রিয়া হয় কিনা তা দেখবেন এবং পরবর্তী পরিদর্শনের তারিখ ঠিক করবেন; গবেষণার অন্যান্য তিনটি পরিদর্শনের সময় একই রকম কায়ক্রম পরিচালনা করা হবে। ক্লিনিক থেকে চলে যাবার পূর্বে টিকা গ্রহণকারীর গবেষণা টিকার সাথে সম্পর্কিত নয় এমন কোন অসুস্থতা যদি হয় তাহলে কি করতে হবে গবেষণাকর্মী তা আপনাকে জানিয়ে দিবেন। এছাড়া, আপনার শিশু প্রথম গবেষণা টিকা পাওয়ার ২ দিনের মধ্যে আপনার বাড়ি পরিদর্শন (ভিজিট) করা হবে বা ফোনে যোগাযোগ করা হবে। সুরক্ষার জন্য এটা করা হবে, আপনার শিশুর কোন সমস্যা বা লক্ষণ দেখা গিয়েছে কিনা এসময়ে তা দেখা হবে।

এই গবেষণায় তিনটি আলাদা গ্রুপ আছে। একটি কম্পিউটারের মাধ্যমে আপনার শিশুর গ্রুপ নির্ধারণ করা হবে। কম্পিউটার না জানানো পর্যন্ত ডাক্তার ও আপনার শিশুর গ্রুপ জানতে পারবে না। ডাক্তার আপনার শিশুর প্রাপ্ত গ্রুপটি জানিয়ে দিবেন। এই গবেষণার টিকাগুলো হলো নভেল ওপিভি২ (nOPV2) এবং বিওপিভি (bOPV)। সকল টিকা গ্রহণকারী ৬, ১০ এবং ১৪ সপ্তাহ বয়সের সময়ে হয়তো শুধুমাত্র nOPV2, nOPV2 এর সাথে bOPV, অথবা শুধুমাত্র bOPV পাবে। টিকা গ্রহণকারীর ভাইবোন কোন গবেষণা টিকা পাবে না।

প্রতিবার ক্লিনিক পরিদর্শনের সময় ডাক্তার অথবা নার্স টিকা গ্রহণকারীর কাছ থেকে খুব অল্প পরিমাণ রক্ত (১ মিলি অথবা বোরাটার চা চামচের চেয়ে কম) সংগ্রহ করবেন। টিকা গ্রহণকারী এবং অন্তর্ভুক্ত/তালিকাভুক্ত তার ভাইবোনের কাছ থেকে খুব অল্প পরিমাণ পায়খানার নমুনাও (৮ গ্রাম বা প্রাপ্তবয়স্ক ব্যক্তির এক বৃদ্ধাঙ্গুলির সমপরিমাণ) সংগ্রহ করার জন্য আপনাকে বলা হবে। টিকা অন্ত্রে কিরকম কাজ করছে এবং কিভাবে এটি একই পরিবারের শিশুদের মধ্যে ছড়িয়ে পরতে পারে তা এর মাধ্যমে আমরা বুঝতে পারবো

টিকা গ্রহণকারীর ৭, ৮ অথবা ১০ সপ্তাহ বয়সের সময় পায়খানা সংগ্রহ করার জন্য গবেষণা কর্মী ২ থেকে ৩ বার আপনার বাড়ি পরিদর্শনের (ভিজিট) জন্য যাবেন। পায়খানার নমুনা সংগ্রহের সময়গুলো টিকা গ্রহণকারী গবেষণার কোন গ্রুপের মধ্যে পরেছে তার উপর নির্ভর করবে। আপনার শিশুর ১০ সপ্তাহ বয়সের পরে আর কোন পায়খানার নমুনা সংগ্রহ করা হবে না। প্রত্যেকবার পায়খানা সংগ্রহ করার জন্য আপনার বাড়িতে দুই অথবা তার অধিক বার করে পরিদর্শনে যাওয়া হবে। প্রথম পরিদর্শনের সময় গবেষণা কর্মী আপনার দুই শিশু থেকে পায়খানা ধরে রাখার জন্য কিট /পাত্র দিয়ে আসবে। পরবর্তী বাড়ি পরিদর্শনের (ভিজিট) সময়, গবেষণা কর্মী পায়খানার কিট/পাত্র গুলো সংগ্রহ করবে।

গবেষণা কার্যক্রম শেষ হয়ে যাবার পর ডাক্তার বা নার্স টিকা গ্রহণকারীকে দুই ডোজের এফআইপিভি (fIPV) দেয়ার জন্য আপনাকে পরামর্শ দিবেন। টিকা গ্রহণকারী কোন গ্রুপে পরেছে তার উপর নির্ভর করে তাকে তিন ডোজের বিওপিভি (bOPV) খাওয়ানোর পরামর্শও দেয়া হতে পারে। অতিরিক্ত এই টিকাগুলো নিশ্চিত করবে যে, বাংলাদেশের অন্যান্য শিশুদের মতো আপনার শিশুর রক্ত এবং অন্ত্র তিন ধরণের পোলিও ভাইরাস থেকে সুরক্ষিত রয়েছে। অতিরিক্ত এই টিকাগুলোর জন্য আপনার শিশুর কোন ধরণের ক্ষতি হবে না। ডাক্তার বা নার্স টিকাগুলো দিবেন এবং নির্ধারিত সময়ে ক্লিনিকে এসে টিকাগুলো পাওয়ার বিষয়ে সময়সূচী তৈরীতে আপনাকে সহায়তা করবেন।

ঝুঁকি এবং সুবিধা

গবেষণায় অংশগ্রহণের সুবিধা রয়েছে। প্রতিটি ভিজিটে একজন ডাক্তার টিকা গ্রহণকারীকে পরীক্ষা করবে এবং বিনামূল্যে পোলিও টিকা দিবে। পরিদর্শনের সময়ে শিশুকালের অন্যান্য রোগের বিরুদ্ধে পাওয়া টিকাগুলোও টিকা গ্রহণকারীকে বিনামূল্যে দিয়ে দেয়া হবে। এ টিকাগুলোর মধ্যে আছে পেন্টাভ্যালেন্ট টিকা যা ডিপথেরিয়া, ধনুষ্টংকার, হুপিং কাশি, হেপাটাইটিস বি এবং হ্যামোফিল্যাস ইনফ্লুয়েঞ্জা বি থেকে রক্ষা করে, এবং নিউমোকোকাল কনজুগেট টিকা স্ট্রেপটোকক্কাস নিউমোনিয়া থেকে রক্ষা করে থাকে। এই গবেষণা বিশ্ব সম্প্রদায়কে সহায়তাও করবে কারণ এই গবেষণার ফলাফলগুলো বিশ্বজুড়ে মহামারী প্রতিক্রিয়া কার্যক্রম পরিচালনা করার নির্দেশক হিসেবে ব্যবহার করা হবে।

এই গবেষণায় অংশগ্রহণে ঝুঁকি রয়েছে। বিওপিভি (bOPV) তে সামান্য পরিমাণ এন্টিবায়োটিক রয়েছে এবং এর কারণে সম্ভাব্য এলার্জিক প্রতিক্রিয়া হতে পারে, যদিও এর সম্ভবনা খুবই সামান্য। গবেষণা চলাকালীন সময়ে টিকা গ্রহণকারীকে বাংলাদেশের অন্যান্য শিশুদের থেকে আলাদা একটি পোলিও টিকা দেয়া হতে পারে। বাংলাদেশের সকল শিশুকেই বিওপিভি (bOPV) দেয়া হয় যা টাইপ ১ এবং ৩ থেকে রক্ষা করে। এনওপিভি২ (nOPV2) শুধুমাত্র টাইপ ২ থেকে রক্ষা করে এবং এটি নিয়মিত টিকাদান কর্মসূচীর অংশ নয়। যেহেতু এনওপিভি২ (nOPV2) একটি নতুন টিকা, তাই এটি নিরাপদ কিনা এ বিষয়ে খুব সীমিত তথ্য আমাদের আছে, যদিও অন্যান্য গবেষণা থেকে প্রাপ্ত সকল তথ্য আমাদের জানায় যে এটি নিরাপদ। টাইপ ২ এর বিরুদ্ধে সুরক্ষা দেয়া এনওপিভি২ (nOPV2) এর সময়কাল বা পরিসরটিও আমাদের জানা নেই। গবেষণায় অংশগ্রহণ করা সকল টিকা গ্রহণকারীর সকল ধরণের পোলিও ভাইরাস থেকে সুরক্ষা নিশ্চিত করার জন্য গবেষণা শেষ হয়ে যাবার পর আপনার শিশুকে দুই ডোজের এফআইপিভি (fIPV) টিকা দিয়ে দেয়া হবে, যা তিন ধরণের পোলিও থেকে রক্ষা করে এবং বাংলাদেশের ইপিআই কার্যক্রমের মাধ্যমে সকল শিশুকে এটা দেয়া হয়। আপনার শিশুকে তার গবেষণা গ্রুপের উপর ভিত্তি করে তিন ডোজের বিওপিভি (bOPV) টিকাও দিয়ে দেয়া হবে। এর মানে হল আপনার শিশুর কোন ধরণের পোলিও ভাইরাসের দ্বারা অসুস্থ হবার সম্ভবনা খুবই কম।

যদিও ওপিভি (OPV) পাওয়ার পরও পোলিওর মতো রোগ হওয়ার ঝুঁকি থাকে, তবে সেটা ১-২ মিলিয়ন শিশুর মধ্য থেকে মাত্র একজনের মধ্যে দেখা যায়। টিকা গ্রহণকারীর পোলিও এর মতো রোগে আক্রান্ত হওয়ার ঝুঁকি রয়েছে। এনওপিভি২ (nOPV2) অথবা বিওপিভি (bOPV) গ্রহণ করা শিশুদের মধ্যে পোলিওর মতো রোগে আক্রান্ত হওয়ার ঝুঁকি কতটা তা আমাদের সঠিক জানা নেই, যদিও আমরা বিশ্বাস করি তা প্রায় একই রকম এবং খুবই সামান্য। টিকা গ্রহণকারীর কাছ থেকে তার বড় ভাইবোন সহ তার কাছাকাছি থাকা অন্যান্যদেরও পোলিও এর মতো রোগ হওয়ার ঝুঁকি থাকতে পারে, কিন্তু আমরা বিশ্বাস করি এই ঝুঁকির পরিমাণ খুবই কম।

রক্ত নেয়ার সময় অস্বস্তি বা ব্যথা, রক্ত নেয়ার স্থানে নীলচে দাগ হতে পারে যদিও জায়গাটি চেপে ধরে এটা প্রতিরোধ বা কমানো যেতে পারে। যদিও দেখা যায় না, রক্ত নেয়ার বা ইঞ্জেকশনের স্থানে সংক্রমনের সম্ভাবনা আছে। প্রশিক্ষিত ডাক্তার এবং নার্স সংক্রমণের বা নীলচে দাগের সম্ভাবনা কমানোর জন্য রক্ত নেয়ার বা ইঞ্জেকশান দেয়ার সময় জীবাণুমুক্ত সুঁই এবং পরিষ্কার সামগ্রী ব্যবহার করবেন।

প্রত্যাশিত প্রতিক্রিয়া ছাড়াও, টিকা গ্রহণকারীর অপ্রত্যাশিত প্রতিক্রিয়া হওয়ার সম্ভাবনা রয়েছে। গবেষণায় অংশগ্রহণের কারনে যদি টিকা গ্রহণকারী কোন অসুস্থতা বা আঘাত পায় তবে যথাযথ হাসপাতালে বিনামূল্যে তার স্বাস্থ্য সেবা ও চিকিৎসার ব্যবস্থা করা হবে। আইসিডিডিআর,বি চিকিৎসা খরচ প্রদান করবে। এছাড়া, গবেষণায় অন্তর্ভুক্ত হবার পর আপনার উভয় শিশু (টিকা গ্রহণকারী এবং তার বড় ভাইবোন) গবেষণায় অংশগ্রহণের সাথে সম্পর্কিত নয় এমন কোন অসুস্থতা হলে বা আঘাত পেলে বিনামূল্যে তার স্বাস্থ্য সেবা পাবে।

গবেষণায় থাকাকালীন আপনার শিশুদের যে কোন একজনেরও যদি চিকিৎসা সংক্রান্ত কোন সহযোগিতার দরকার হয় আপনি আইসিডিডিআর,বি এর স্বাস্থ্য কেন্দ্রে আসতে পারেন। একজন গবেষণা চিকিৎসক আপনার শিশুকে পরীক্ষা করবেন এবং স্থানীয় মানসম্মত চিকিৎসা প্রদান করবেন।

গোপনীয়তা, নামহীনতা ও বিশ্বস্ততা

শুধুমাত্র অল্প কিছু নির্দিষ্ট গবেষণা কর্মী আপনার ও আপনার শিশুদের ব্যক্তিগত তথ্য যেমন নাম, ঠিকানা জানতে পারবে। আপনার সাথে যোগাযোগ এবং আপনার শিশুর ফলোআপ করার জন্য এইসব তথ্য তাদের প্রয়োজন হবে। অন্য সব গবেষণা কর্মীরা আপনার শিশুদের জন্য বরাদ্দ কোড নম্বর ব্যবহার করবে। এদের মধ্যে যারা রক্ত এবং পায়খানার নমুনা পরীক্ষা করবে তারাও রয়েছে। গবেষণার ফলাফল প্রকাশ করা হলে তাতে আপনার ও আপনার শিশুর নাম উল্লেখ করা হবে না।

যদি টিকা গ্রহণকারীর টিকা নেয়ার পর কোন মারাত্মক প্রতিক্রিয়া হয় তখন গবেষণা নিরাপত্তা নিশ্চিত করার জন্য এই গবেষণায় তার থেকে সংগৃহীত তথ্যগুলো দেখার প্রয়োজন হতে পারে। এদের মধ্যে প্রধান গবেষক, নিরাপত্তা পর্যবেক্ষক ও বাংলাদেশের আইনগত সংস্থার সদস্যরা থাকতে পারেন। এইসব ব্যক্তিরা নাম বা অন্যান্য ব্যক্তিগত তথ্য পর্যালোচনায় জড়িত নয় এমন কাউকে জানাবে না।

তথ্যের ভবিষ্যৎ ব্যবহার

এই গবেষণায় সংগৃহীত তথ্য অন্য গবেষক, টিকা উৎপাদনকারী এবং/অথবা আইনগত কতৃপক্ষ (জাতীয়/আন্তর্জাতিক) কর্তৃক ব্যবহৃত হতে পারে। আইসিডিডিআর,বি কে অনুরোধ সাপেক্ষে তথ্য ভবিষ্যতে এই সকল গোষ্ঠীকে প্রদান করা হতে পারে। তবে আপনার ও আপনার শিশুর নাম ও ব্যক্তিগত তথ্য প্রদান করা হবে না, কোড নম্বর প্রদান করা হবে। গবেষণার সময় যেভাবে আপনার ও আপনার শিশুর গোপনীয়তা, নামহীনতা ও বিশ্বস্ততা রক্ষা করা হয়েছে এ ক্ষেত্রেও ঠিক সেভাবে রক্ষা করা হবে।

রক্ত এবং পায়খানা নমুনাগুলোর পরীক্ষা একেবারে শেষ হয়ে যাবার পর এবং ফলাফল বিশ্লেষণ হয়ে যাবার পর, পুনরায় পায়খানার নমুনাগুলোর পরীক্ষা করার প্রয়োজন হতে পারে। পরবর্তী পরীক্ষা করার জন্য সংরক্ষিত পায়খানার নমুনাই ব্যবহার করা হবে, অতিরিক্ত কোন নমুনা সংগ্রহ করা হবে না। আপনি যদি এই গবেষণায় আপনার শিশুদের অংশগ্রহণের বিষয়ে সম্মতি দিয়ে থাকেন, তাহলে ভবিষ্যতে প্রয়োজনানুযায়ী এই অতিরিক্ত পরীক্ষার করার সম্মতিও আপনি দিয়ে থাকবেন।

আপনার শিশুদের রক্ত এবং পায়খানার কিছু নমুনা আইসিডিডিআর,বি এর ল্যাবরেটরীতে পাঁচ বছরের জন্য সংরক্ষণ করা হবে। এ নমুনাগুলো সংরক্ষণ করা হবে যারন এ নমুনা থেকে ছোট শিশুদের সুরক্ষা সম্পর্কে মূল্যবান তথ্য পাওয়া যেতে পারে যা অন্য পোলিও গবেষণা বা অন্যান্য টিকা প্রতিরোধযোগ্য রোগ সম্পর্কে গবেষণার জন্য দরকার হতে পারে। সংরক্ষিত নমুনা ভবিষ্যতে ব্যবহার করার জন্য গবেষকদের আইসিডিডিআর,বি এর গবেষণা ও নৈতিক পর্যালোচনা কমিটি থেকে অনুমতি নিতে হবে। এ নমুনা দিয়ে কোন জীনগত পরীক্ষা করা হবে না।

গবেষণায় অংশগ্রহণ না করার এবং প্রত্যাহারের অধিকার

এই গবেষণায় আপনার শিশুর অংশগ্রহণের জন্য আপনার সম্মতি দেয়ার বিষয়টি স্বেচ্ছামূলক। আপনি না চাইলে এই গবেষণায় আপনার শিশুকে নেয়া হবে না। আপনি যে কোন সময়ে গবেষণায় আপনার শিশুর অংশগ্রহণ বন্ধ করে দিতে পারেন। আপনার শিশু গবেষণায় অংশগ্রহণ না করলেও বাংলাদেশ সরকার প্রদত্ত টিকা, চিকিৎসা সেবা এবং অন্যান্য সুবিধাদি যা সে পেয়ে আসছিল সেগুলো অব্যাহত থাকবে।

গবেষণা কর্মীরা একজন টিকা গ্রহণকারী বা তার ভাইবোনকে গবেষণা থেকে আগেই বাদ দিতে পারেন যদি:

- ডাক্তার মনে করেন যে টিকা গ্রহনকারী এতোটা অসুস্থ যে তাকে গবেষণা টিকার কোন একটি ডোজ দেয়া যাবে না
- গবেষণা চলাকালীন সময়ে বা এর পূর্বে সে অন্য কোন জায়গা থেকে পোলিও টিকা পেয়ে থাকে
- গবেষণা থেকে টিকা গ্রহনকারীর অংশগ্রহণের সম্মতি আপনি প্রত্যাহার করে নিলে

ক্ষতিপূরণের নীতি

এই গবেষণায় অংশগ্রহণের জন্য কোন ধরণের ক্ষতিপূরণ প্রদান করা হবে না। গবেষণা ক্লিনিকে আসা যাওয়ার জন্য যাতায়াত খরচ প্রদান করা হবে। গবেষণায় অন্তর্ভূক্ত হলে অসুস্থতার জন্য বা আঘাত প্রাপ্তির জন্য টিকা গ্রহণকারীরা এবং তার ভাইবোনরা বিনামূল্যে চিকিৎসা সেবা পাবে।

আপনার প্রশ্নের উত্তর দেয়া/ যোগাযোগের ব্যক্তি

এই গবেষণা বা অবহিতকরণ পত্র সম্পর্কে আপনার যদি কোন প্রশ্ন বা জিজ্ঞাসা থাকে তাহলে আপনি কথা বলতে পারেন:

স্থানীয় প্রধান গবেষকের নাম: ডা: কে জামান, ফোন: ০১৭১৩০৪৭১০০

এই গবেষণায় অংশগ্রহণের জন্য টিকা গ্রহণকারীর অধিকার বা সুবিধা সংক্রান্ত প্রশ্ন থাকলে অথবা আপনি যদি মনে করেন আপনার শিশুর ক্ষতি হতে পারে তবে আপনি আইসিডিডিআর,বি এর মানব বিষয়ক গবেষণার নৈতিকতা পর্যালোচনা কমিটির আইআরবি এর সেক্রেটারিয়েট এর সাথে যোগাযোগ করতে পারেন:

নাম: এম এ সালাম খান ফোন: ৯৮৮৬৪৯৮

টিকা গ্রহণকারী এবং তার ভাইবোনের জন্য অবহিতকরণ সম্মতিপত্র

Protocol No. PR-20060	Version No. 1.06	Date: 03-12-2020

Protocol Title: Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

গবেষকের নাম: ডা: কে জামান

সংস্থা: আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র (আইসিডিডিআর,বি)

আমি অবহিতকরণ সম্মতিপত্রটি পড়েছি, আমার এই গবেষণা সম্পর্কে প্রশ্ন করার এবং আলোচনা করার সুযোগ ছিল এবং আমি আমার প্রশ্নের সন্তোষজনক উত্তর পেয়েছি।	হ্যাঁ ☐ না ☐
আমি বুঝেছি যে, কোন কারন দেখানো ছাড়াই গবেষণা থেকে বিরত থাকার স্বাধীনতা আমার আছে।	হ্যাঁ ☐ না ☐
প্রতিটি নির্ধারিত সময়সূচী অনুযায়ী নমুনা সংগ্রহের সময়ে আমি ১ মি.লি রক্ত (টিকা গ্রহণকারী) এবং ৮ গ্রাম পরিমাণ পায়খানা (টিকা গ্রহণকারী এবং তার বড় ভাইবোন) দিতে সম্মত আছি।	হ্যাঁ ☐ না ☐
আমি অসণাক্ত/অজ্ঞাত রক্ত/পায়খানার নমুনা পরীক্ষার জন্য সিডিসি তে পাঠাতে সম্মত আছি।	হ্যাঁ ☐ না ☐
আমি রক্ত/পায়খানার নমুনা ভবিষ্যতে ব্যবহারের জন্য আইসিডিডিআর,বি তে পাচ বছর পর্যন্ত সংরক্ষণ করতে সম্মত আছি।	হ্যাঁ ☐ না ☐
আমি বুঝেছি যে, আমার দেয়া তথ্যাবলী গোপনীয়।	হ্যাঁ ☐ না ☐
আমার অ-সণাক্তকরণযোগ্য তথ্যসমূহ ভবিষ্যতে নৈতিকভাবে অনুমোদিত গবেষণাসমূহে ব্যবহারে আমি সম্মত আছি।	হ্যাঁ ☐ না ☐
এই গবেষণার সাথে সম্পর্কিত ভবিষ্যত যদি কোন গবেষণা থাকে তবে আমার সাথে যোগাযোগের ব্যাপারে আমি সম্মত আছি। আমি এও বুঝেছি যে, এই গবেষণা চলাকালীন আমার শিশুদের থেকে সংগৃহীত মেডিকেল নোট এবং তথ্যাদির প্রাসঙ্গিক অংশ প্রয়োজনে স্পন্সর সংস্থা এবং নিয়ন্ত্রনকারী কর্তৃপক্ষরা দেখতে পারেন, যা এই গবেষণায় আমার শিশুর অংশগ্রহণের সাথে সম্পর্কিত। ঐ সকল ব্যক্তিদের আমি আমার শিশুদের তথ্যসমূহ দেখার অনুমতি প্রদান করছি।	হ্যাঁ ☐ না ☐
আমি আমার শিশুকে (নাম: _____) এই গবেষণায় অংশগ্রহণের জন্য এবং পোলিও টিকা গ্রহণের বিষয়ে আমি সম্মত আছি।	হ্যাঁ ☐ না ☐
আমি এই গবেষণায় তার ভাইবোনের (নাম: _____) অংশগ্রহণের বিষয়েও সম্মত আছি।	হ্যাঁ ☐ না ☐

আপনি যদি আমাদের গবেষণায় পোলিও টিকা গ্রহণের ক্ষেত্রে আপনার শিশুর (নাম: _____) অন্তর্ভুক্তির বিষয়ে আমাদের প্রস্তাবে রাজী থাকেন তবে অনুগ্রহ করে নিচের নির্ধারিত স্থানে আপনার সাক্ষর অথবা বাম বৃদ্ধাঙ্গুলির ছাপ দিয়ে তা নির্দিষ্ট করুন।

আপনার সহযোগিতার জন্য আপনাকে ধন্যবাদ।

_____ _____

পিতামাতার সাক্ষর অথবা বাম বৃদ্ধাঙ্গুলির ছাপ তারিখ

আপনি যদি এই গবেষণায় তার ভাইবোনের (নাম: _____) অংশগ্রহণের বিষয়েও রাজী হয়ে থাকেন তবে অনুগ্রহ করে নিচের নির্ধারিত স্থানে আপনার সাক্ষর অথবা বাম বৃদ্ধাঙ্গুলির ছাপ দিয়ে তা নির্দিষ্ট করুন।

.

_____ _____

পিতামাতার সাক্ষর অথবা বাম বৃদ্ধাঙ্গুলির ছাপ তারিখ

_____ _____

স্বাক্ষীর সাক্ষর তারিখ

_____ _____

পিআই অথবা তার প্রতিনিধির সাক্ষর তারিখ

আপনার প্রশ্নের উত্তর দেয়া/ যোগাযোগের ব্যক্তি

এই গবেষণা, অবহিতকরণ পত্র বা সম্মতিপত্র সম্পর্কে আপনার কোন প্রশ্ন বা জিজ্ঞাসা থাকলে আপনি কথা বলতে পারেন:

স্থানীয় প্রধান গবেষকের নাম: ডা: কে জামান, ফোন: ০১৭১৩০৪৭১০০

এই গবেষণায় অংশগ্রহণের জন্য টিকা গ্রহণকারী হিসেবে আপনার শিশুর অধিকার বা সুবিধা সংক্রান্ত প্রশ্ন থাকলে অথবা আপনি যদি মনে করেন আপনার শিশুর ক্ষতি হতে পারে তবে আপনি আইসিডিডিআর, বি এর মানব বিষয়ক গবেষণার নৈতিকতা পর্যালোচনা কমিটির আইআরবি এর সেক্রেটারিয়েট এর সাথে যোগাযোগ করতে পারেন:

নাম: এম এ সালাম খান ফোন: ৯৮৮৬৪৯৮

Appendix A: Study Forms

- Screening Form
- Clinic Visit at 6 weeks of Age – Vaccine Recipient
- Clinic Visit at 6 weeks of Age – Sibling
- Phone Call or Home Visit 24–48 hours after 6-week Vaccination
- Household Visit at 7 weeks of Age
- Household Visit at 8 weeks of Age
- Household Visit at 10 weeks of Age
- Clinic Visit at 10 weeks of Age
- Clinic Visit at 14 weeks of Age
- Clinic Visit at 18 weeks of Age
- Adverse Event Form
- Discontinuation Tracking Form – Vaccine Recipient
- Discontinuation Tracking Form – Sibling
- Protocol Deviation Tracking Form

nOPV2 and bOPV Study **PID** ☐☐☐☐☐

Screening Form

Date of interview (dd/MMM/yy): ☐☐/☐☐☐/☐☐

Vaccine recipient's name: _____

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐ Sex: F / M

Demographics

Father's education (circle): No formal school / Primary / Middle / High school / Graduate

Mother's education (circle): No formal school / Primary / Middle / High school / Graduate

Eligibility criteria for vaccine recipient

1. Child's residence within the study area? Yes / No

2. Child NOT planning to travel/move in the next 3 months that would prevent them for coming for study visits? Yes / No

3. Child born in single birth? Yes / No

4. Child born after 37 weeks of pregnancy? Yes / No

5. At least one sibling <10 years living in the household? Yes / No

Is this child eligible for participation in the study as a vaccine recipient? Yes / No

- *Child is ELIGIBLE if all answers to questions 1-5 are YES, proceed to question 6.*
- *Child is NOT ELIGIBLE if any of the answers to questions 1-5 is NO. If the child is **NOT** eligible, **STOP**.*

6. How many siblings does the vaccine recipient have that are <10 years of age? _____

- *For each sibling <10 years of age, complete the eligibility questions below. Then, ask the mother to bring the youngest eligible sibling to the Clinic Visit at 6 Weeks of Age, along with the sibling's vaccination records.*

Eligibility criteria for sibling

Siblings' name: _____

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐ Sex: F / M

1. Child will be <10 years of age at the time of enrollment (when the vaccine recipient is 42-48 days of age)? Yes / No

2. Child resides in the same household as the eligible vaccine recipient? Yes / No

3. Child will be available to participate in study activities for the next month ? Yes / No

4. Child has NOT participated in a previous poliovirus vaccine clinical trial. Yes / No

Screening Form (page for additional siblings)

Eligibility criteria for sibling

Siblings' name: ____

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐ Sex: F / M

1. Child will be <10 years of age at the time of enrollment (when the vaccine recipient is 42-48 days of age)? Yes / No
2. Child resides in the same household as the eligible vaccine recipient? Yes / No
3. Child will be available to participate in study activities for the next month ? Yes / No
4. Child has NOT participated in a previous poliovirus vaccine clinical trial. Yes / No

Eligibility criteria for sibling

Siblings' name: ____

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐ Sex: F / M

1. Child will be <10 years of age at the time of enrollment (when the vaccine recipient is 42-48 days of age)? Yes / No
2. Child resides in the same household as the eligible vaccine recipient? Yes / No
3. Child will be available to participate in study activities for the next month ? Yes / No
4. Child has NOT participated in a previous poliovirus vaccine clinical trial. Yes / No

Eligibility criteria for sibling

Siblings' name: ____

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐ Sex: F / M

1. Child will be <10 years of age at the time of enrollment (when the vaccine recipient is 42-48 days of age)? Yes / No
2. Child resides in the same household as the eligible vaccine recipient? Yes / No
3. Child will be available to participate in study activities for the next month ? Yes / No
4. Child has NOT participated in a previous poliovirus vaccine clinical trial. Yes / No

Screening Form

Is one or more of the children eligible to be a sibling participant? Yes / No

- *Child is ELIGIBLE if all answers to sibling eligibility questions 1-4 are YES. If multiple children are eligible, select the youngest eligible sibling for participation in the trial. Explain what the child's participation in the study will involve and provide the information sheet.*
- *Child is NOT ELIGIBLE if any of the answers to sibling eligibility questions 1-4 is NO. If NONE of the children are eligible to be sibling participants,* ***STOP****.*

Are parents interested in their children participating in the study? Yes / No

- *If parents* ***ARE NOT*** *interested, ask them the following.*

Why are you not interested in having your children participate in the study? *(Circle all that apply)*

Study purpose unclear / Busy-No time / Other (specify):_____

Name of father: _____Name of mother: _____

Address: _____Section_____Upzila:_____District: _____

Cell phone: _____ Scheduled date for first study visit (dd/MMM/yy): ☐☐/☐☐☐/☐☐

Name and signature of study staff: _____

Clinic Visit at 6 weeks of Age – Vaccine Recipient

Date of visit (dd/MMM/yy): ☐☐/☐☐☐/☐☐

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐ Sex: F / M

Demographics

Father's education (circle): No formal school / Primary / Middle / High school / Graduate

Mother's education (circle): No formal school / Primary / Middle / High school / Graduate

Eligibility criteria for vaccine recipient

1. Child's residence within the study area? Yes / No
2. Child 6 weeks of age? Yes / No
3. Child and family NOT planning to travel / move in the next 3 months that would prevent them from coming for study follow-up visits? Yes / No
4. Child born in single birth? Yes / No
5. Child born after 37 weeks of pregnancy? Yes / No
6. No diagnosis or suspicion of immunodeficiency in the child or family member? Yes / No
7. Child has NO known coagulation disorders that contraindicates venipuncture or injection? Yes / No
8. Child has NOT received OPV or IPV before? Yes / No
9. Child does not have a medical condition that contraindicates bOPV or nOPV2 administration? Yes / No

   If no, specify _____

10. Child has at least one sibling < 10 years living in the household? Yes / No

Is this child eligible for participation in the study as a vaccine recipient? Yes / No

- *Child is ELIGIBLE if all answers to questions 1-10 are YES. If the child is eligible, proceed to the next section.*
- *Child is NOT ELIGIBLE if any of the answers to questions 1-10 is NO. If the child is **NOT** eligible, **STOP**.*

Do the parents give consent for their child to participate in the study as a vaccine recipient? Yes / No

- *If parents **DO NOT** consent, ask them the following. When finished, thank them for their time and **STOP.***

Why are you not interested in having your child participate in the study? *(Circle all that apply)* Study purpose unclear / Vaccine concerns / Reluctant to blood draw / More than two vaccine injections at first visit / Busy-No time / Other (specify):_____

- *If parents **DO** consent, continue with the study procedures.*

Clinic Visit at 6 weeks of Age – Vaccine Recipient

1. Is the child currently breastfed? No breastfeeding / Partial breastfeeding / Exclusive breastfeeding

2. Has the child received BCG? Yes / No

   2a. If yes, date of vaccination (dd/MMM/yy): ☐☐/☐☐☐/☐☐

3. Has the child received any other vaccine to date? Yes / No

   3a. If yes, specify: _____

   3b. Date of vaccination (dd/MMM/yy) ☐☐/☐☐☐/☐☐

4. Has any other child in the household received OPV since the infant was born? Yes / No

   4a. If yes, specify: _____

5. Has the child had diarrhea in the last 24 hours (≥ 3 loose stools in 24 hours)? Yes / No

   5a. If yes, specify: duration of diarrhea ☐☐ days

6. Is the child on any immunosuppressive medications? Yes / No 6a. If yes, specify _____

Physical Exam

7. Temperature: ☐☐.☐ °Celsius 8. Length #1: ☐☐☐.☐ cm 10. Weight #1: ☐☐.☐ kg

   9. Length #2: ☐☐☐.☐ cm 11. Weight #2: ☐☐.☐ kg

Blood Collection

12. Blood sample collected? Yes / No 12a. If not, why? _____

13. Sufficient quantity (1 ml)? Yes / No 13a. If insufficient, why? _____

14. Time of collection (hh:mm): ☐☐:☐☐

Study Group Allocation and Vaccine Administration

15. Specify which study group the child was allocated *(select the answer)*:

    A: nOPV2 @ 6, 10, and 14 weeks
    B: nOPV2 + bOPV @ 6, 10, and 14 weeks
    C: bOPV @ 6, 10, and 14 weeks

Clinic Visit at 6 weeks of Age – Vaccine Recipient

Vaccine Administration

If Study Arm A or B

16. nOPV2 administered? Yes / No 16a. If not, reason: _____

If administered: 16b. Time of vaccine administration (hh:mm): ☐☐:☐☐

16c. Expiration (mmm/yy): ☐☐☐/☐☐

If Study Arm B or C

17. bOPV administered? Yes / No 17a. If not, reason: _____

If administered: 17b. Time of vaccine administration (hh:mm): ☐☐:☐☐

17c. Expiration (mmm/yy): ☐☐☐/☐☐

18. BCG administered? Yes / No 18a. If no and infant has yet to receive BCG, provide reason not given during today's visit: _____

If administered: 18b. Site of administration: Right arm / Left arm

19. Pentavalent administered? Yes / No 19a. If not, reason: _____

If administered: 19b. Dose: Penta1 / Penta2 / Penta3

19c. Site of administration: Right thigh / Left thigh

20. PCV administered? Yes / No 20a. If not, reason: _____

If administered: 20b. Dose: PCV1 / PCV2 / PCV3

20c. Site of administration: Right thigh / Left thigh

Observe for 30 minutes after vaccine administration:

21. Any symptoms? Yes / No

21a. If yes, specify *(complete Adverse Event Form, if required)*: _____

_____

Schedule next visit date (dd/MMM/yy):

Name and signature of medical officer: _____

nOPV2 and bOPV Study **PID** ☐☐☐☐☐

Clinic Visit at 6 weeks of Age – Sibling

Date of birth (dd/MMM/yy): ☐☐/☐☐☐/☐☐

Current age in years: ☐☐

Sex: F / M

Eligibility criteria for sibling

1. Child is <10 years of age Yes / No
2. Child resides in the same household as the study vaccine recipient? Yes / No
3. Child will be available to participate in study activities for the next month? Yes / No
4. Child has NOT participated in a previous poliovirus vaccine clinical trial. Yes / No

Is this child eligible to be a sibling in the study? Yes / No

- *Child is ELIGIBLE if all answers to questions 1-4 are YES. If the child is eligible, explain what the child's participation in the study will involve and provide the information sheet.*
- *Child is NOT ELIGIBLE if any of the answers to questions 1-4 is NO. If the child is **NOT** eligible, **STOP**. The sibling and vaccine recipient are not eligible to continue with study enrollment. Enrollment cannot continue for the vaccine recipient unless an eligible sibling is brought to the clinic to be enrolled on the same day.*

Do the parents give consent for their child to participate in the study? Yes / No

- *If parents **DO NOT** consent, ask them the following. When finished, thank them for their time and **STOP.***

Why are you not interested in having your child participate in the study? *(Circle all that apply)* Study purpose unclear Busy-No time / Other (specify):_____

- *If parents **DO** consent, continue with the study procedures.*

Polio vaccination history:

1. Is the vaccination card present? Yes / No
   Note: If present, answer questions below based on the vaccination card.
2. Has the child ever received bOPV? Yes / No
   2a. If yes, how many doses of bOPV? _____
   2b. Date of most recent bOPV vaccination (dd/MMM/yy): ☐☐/☐☐☐/☐☐

Clinic Visit at 6 weeks of Age – Sibling

3. Has the child ever received tOPV? Yes / No

3a. If yes, how many doses of tOPV? _____

3b. Date of most recent tOPV vaccination (dd/MMM/yy): ☐☐/☐☐☐/☐☐

4. Has the child ever received fIPV? Yes / No

4a. If yes, how many doses of fIPV? _____

4b. Date of most recent fIPV vaccination (dd/MMM/yy): ☐☐/☐☐☐/☐☐

5. Has the child ever received IPV? Yes / No

5a. If yes, how many doses of IPV? _____

5b. Date of most recent IPV vaccination (dd/MMM/yy): ☐☐/☐☐☐/☐☐

Name and signature of medical officer: _____

Phone Call or Home Visit 24–48 hours after 6-week vaccination

To be completed for vaccine recipients in all Arms

Date of call/visit (dd/MMM/yy**):** ☐☐/☐☐☐/☐☐

Time of call/visit (hh:mm)**:** ☐☐ ☐☐

Adverse events

Since the vaccine recipient was at the clinic for the "Clinic Visit at 6 weeks", have they had any of the following symptoms?

1. Fever: ☐ No ☐ Yes If yes, please describe _____

   If yes, and thermometer available: ☐ Grade 1: 37.5° C- 38.0 ° C ☐ Grade 2: 38.1° C- 39.0 ° C ☐ Grade 3: >39.0 ° C

2. Vomiting: ☐ No ☐ Yes If yes, ☐ Grade 1: 1 episode/24 hours ☐ Grade 2: 2-5 episodes/24 hours ☐ Grade 3: ≥ 6 episodes/24 hours

3. Abnormal crying: ☐ No ☐ Yes If yes, ☐ Grade 1: < 1hour ☐ Grade 2: 1-3 hours ☐ Grade 3: >3 hours

4. Drowsiness: ☐ No ☐ Yes If yes, ☐ Grade 1: Sleepier than usual or less interested in surroundings ☐ Grade 2: Not interested in surroundings or did not wake up for a feed ☐ Grade 3: Sleeping most of the time or difficult to wake up

5. Poor feeding: ☐ No ☐ Yes If yes, ☐ Grade 1: Eating less than normal ☐ Grade 2: Missed 1 or 2 feeds completely ☐ Grade 3: Refuses ≥3 feeds or refuses most feeds

6. Irritability: ☐ No ☐ Yes If yes, ☐ Grade 1: Easily consolable

☐ Grade 2: Requiring increased attention

☐ Grade 3: Inconsolable

7. Other Adverse Events (24–48 hours after 6-week vaccination) ☐ No ☐ Yes

If yes, specify: _____

If yes: ☐ Grade 1 (Mild): An AE which is easily tolerated by the participants, causing minimal discomfort and not interfering with everyday activities.

☐ Grade 2 (Moderate): An AE which is sufficiently discomforting to interfere with normal everyday activities.

☐ Grade 3 (Severe): An AE which prevents normal, everyday activities.

If parent responds Yes to any of the above, fill out an AE form.

Name of medical officer:_____ Signature: _____

Household Visit at 7 weeks of Age

To be completed for participants in Arm A only

<u>Home Visit #1</u>: To be completed on the day the stool kits are delivered to the parents.

Date stool kits delivered (dd/mm/yy): ☐☐/☐☐/☐☐

1. Were there any problems in giving the two stool kits to the parents? Yes / No

   1a. If yes, explain _____

Name and signature of study staff: _____

<u>Home Visit #2</u>: To be completed on the day the stool samples are picked up.

For vaccine recipient:

1. Stool sample collected? Yes / No 1a. If no stool obtained, why not? _____
2. Date of stool collection (dd/mm/yyyy): ☐☐/☐☐ /☐☐
3. Time of collection (hh:mm): ☐☐ : ☐☐
4. Sufficient quantity (8 grams)? Yes / No 4a. If insufficient, specify reasons: _____

For sibling:

5. Stool sample collected? Yes / No 5a. If no stool obtained, why not? _____
6. Date of stool collection (dd/mm/yyyy): ☐☐/☐☐ /☐☐
7. Time of collection (hh:mm): ☐☐ : ☐☐
8. Sufficient quantity (8 grams)? Yes / No 8a. If insufficient, specify reasons: _____

Name and signature of study staff: _____

<u>Data Entry</u>: To be completed when data entered into RedCap

Date of data entry in RedCap (dd/mm/yyyy): ☐☐/☐☐ /☐☐

Name and signature of person entering data: _____

Household Visit at 8 weeks of Age

To be completed for vaccine recipients in all Arms

<u>Home Visit #1</u>: To be completed on the day the stool kits are delivered to the parents.

Date stool kits delivered (dd/mm/yy): ☐☐/☐☐/☐☐

1. Were there any problems in giving the two stool kits to the parents? Yes / No

   1a. If yes, explain _____

Name and signature of study staff: _____

<u>Home Visit #2</u>: To be completed on the day the stool samples are picked up.

For study vaccine recipient:

1. Stool sample collected? Yes / No 1a. If no stool obtained, why not? _____
2. Date of stool collection (dd/mm/yyyy): ☐☐/☐☐ /☐☐
3. Time of collection (hh:mm): ☐☐ : ☐☐
4. Sufficient quantity (8 grams)? Yes / No 4a. If insufficient, specify reasons: _____

For sibling of study vaccine recipient:

5. Stool sample collected? Yes / No 5a. If no stool obtained, why not? _____
6. Date of stool collection (dd/mm/yyyy): ☐☐/☐☐ /☐☐
7. Time of collection (hh:mm): ☐☐ : ☐☐
8. Sufficient quantity (8 grams)? Yes / No 8a. If insufficient, specify reasons: _____

Name and signature of study staff: _____

<u>Data Entry</u>: To be completed when data entered into RedCap

Date of data entry in RedCap (dd/mm/yyyy): ☐☐/☐☐ /☐☐

Name and signature of person entering data: _____

Household Visit at 10 weeks of Age

To be completed for vaccine recipients in all Arms

<u>Home Visit #1</u>: To be completed on the day the stool kits are delivered to the parents.

Date stool kits delivered (dd/mm/yy): ☐☐/☐☐/☐☐

1. Were there any problems in giving the two stool kits to the parents? Yes / No

   1a. If yes, explain _____

Name and signature of study staff: _____

<u>Home Visit #2</u>: To be completed on the day the stool samples are picked up.

For study vaccine recipient:

1. Stool sample collected? Yes / No 1a. If no stool obtained, why not? _____
2. Date of stool collection (dd/mm/yyyy): ☐☐/☐☐ /☐☐
3. Time of collection (hh:mm): ☐☐ : ☐☐
4. Sufficient quantity (8 grams)? Yes / No 4a. If insufficient, specify reasons: _____

For sibling of study vaccine recipient:

5. Stool sample collected? Yes / No 5a. If no stool obtained, why not? _____
6. Date of stool collection (dd/mm/yyyy): ☐☐/☐☐ /☐☐
7. Time of collection (hh:mm): ☐☐ : ☐☐
8. Sufficient quantity (8 grams)? Yes / No 8a. If insufficient, specify reasons: _____

Name and signature of study staff: _____

<u>Data Entry</u>: To be completed when data entered into RedCap

Date of data entry in RedCap (dd/mm/yyyy): ☐☐/☐☐ /☐☐

Name and signature of person entering data: _____

Clinic Visit at 10 weeks of Age

Date of visit (dd/mm/yy**):** ☐☐/☐☐/☐☐

Clinical History

1. Is the child currently breastfed? No breastfeeding / Partial breastfeeding / Exclusive breastfeeding
2. Has the child received any vaccine since last visit? Yes / No 2a. If yes, specify: _____
   2b. Date of vaccination (dd/mm/yy): ☐☐/☐☐/☐☐
3. Has any other child in the household received OPV since the last clinic visit ? Yes / No 3a. If yes, specify: _____
4. Has the child had diarrhea in the last 24 hours (≥ 3 loose stools in 24 hours)? Yes / No
   4a. If yes, specify: duration of diarrhea in days: ☐☐
   (If the child currently has fever >38.3°C, blood in stools, vomiting or signs of dehydration, do not continue with study procedures. Provide advice and referral as required.)
5. Has the child been sick since the last study visit? Yes / No 5a. If yes, specify: _____
6. Is the child on any immunosuppressive medications? Yes / No 6a. If yes, specify _____

Physical Exam

7. Temperature: ☐☐.☐ °Celsius 8. Length #1: ☐☐☐.☐ cm 10. Weight #1 ☐☐.☐ kg
   9. Length #2: ☐☐☐.☐ cm 11. Weight #2 ☐☐.☐ kg

Blood Collection

12. Blood sample collected? Yes / No 12a. If not, why? _____
13. Sufficient quantity (1 ml)? Yes / No 13a. If insufficient, why? _____
14. Time of collection (hh:mm): ☐☐:☐☐

Vaccine Administration

If Study Arm A or B

15. nOPV2 administered? Yes / No 15a. If not, reason: _____
    If administered: 15b. Time of vaccine administration (hh:mm): ☐☐:☐☐
    15c. Expiration (mmm/yy): ☐☐☐/☐☐

If Study Arm B or C

16. bOPV administered? Yes / No 16a. If not, reason: _____
    If administered: 16b. Time of vaccine administration (hh:mm): ☐☐:☐☐
    16c. Expiration (mmm/yy): ☐☐☐/☐☐

Clinic Visit at 10 weeks of Age (ctd.)

17. Pentavalent administered? Yes / No 17a. If not, reason: _____

If administered: 17b. Dose: Penta1 / Penta2 / Penta3

17c. Site of administration: Right thigh / Left thigh

18. PCV administered? Yes / No 18a. If not, reason: _____

If administered: 18b. Dose: PCV1 / PCV2 / PCV3

18c. Site of administration: Right thigh / Left thigh

Observe for 30 minutes after vaccine administration:

19. Any symptoms? Yes / No

19a. If yes, specify *(complete Adverse Event Form, if required)*: _____

_____

The following questions correspond to sibling of the study vaccine recipient. Note: the sibling does not need to be present for this visit.

20. Has the child received any poliovirus vaccines (bOPV, fIPV) since last visit? Yes / No

20a. If yes, specify: _____ ☐☐/☐☐/☐☐

20b. Date of vaccination (dd/mm/yy):

21. Has the child had diarrhea in the last 24 hours (≥ 3 loose stools in 24 hours)? Yes / No

21a. If yes, specify: duration of diarrhea in days ☐☐

22. Has the child been sick since the last study visit? Yes / No 22a. If yes, specify: _____

23. Is the child on any immunosuppressive medications? Yes / No 23a. If yes, specify _____

Schedule next visit date (dd/mm/yy): ☐☐/☐☐/☐☐

Name and signature of medical officer: _____

Clinic Visit at 14 weeks of Age

Date of visit (dd/mm/yy**):** ☐☐/☐☐/☐☐

Clinical History

1. Is the child currently breastfed? No breastfeeding / Partial breastfeeding / Exclusive breastfeeding
2. Has the child received any vaccine since last visit? Yes / No 2a. If yes, specify: _____
   2b. Date of vaccination (dd/mm/yy): ☐☐/☐☐/☐☐
3. Has any other child in the household received OPV since the last clinic visit? Yes / No 3a. If yes, specify: _____
4. Has the child had diarrhea in the last 24 hours (≥ 3 loose stools in 24 hours)? Yes / No
   4a. If yes, specify: duration of diarrhea in days: ☐☐
   (If the child currently has fever >38.3°C, blood in stools, vomiting or signs of dehydration, do not continue with study procedures. Provide advice and referral as required.)
5. Has the child been sick since the last study visit? Yes / No 5a. If yes, specify: _____
6. Is the child on any immunosuppressive medications? Yes / No 6a. If yes, specify _____

Physical Exam

7. Temperature: ☐☐.☐ °Celsius 8. Length #1: ☐☐☐.☐ cm 10. Weight #1: ☐☐.☐ kg
   9. Length #2: ☐☐☐.☐ cm 11. Weight #2 ☐☐.☐ kg

Blood Collection

12. Blood sample collected? Yes / No 12a. If not, why? _____
13. Sufficient quantity (1 ml)? Yes / No 13a. If insufficient, why? _____
14. Time of collection (hh:mm): ☐☐:☐☐

Vaccine Administration

If Study Arm A or B

15. nOPV2 administered? Yes / No 15a. If not, reason: _____
    If administered: 15b. Time of vaccine administration (hh:mm): ☐☐:☐☐
    15c. Expiration (mmm/yy): ☐☐☐/☐☐

Clinic Visit at 14 weeks of Age (ctd.)

If Study Arm B or C

16. bOPV administered? Yes / No 16a. If not, reason: _____

If administered: 16b. Time of vaccine administration (hh:mm): ☐☐:☐☐

16c. Expiration (mmm/yy): ☐☐☐/☐☐

17. Pentavalent administered? Yes / No 17a. If not, reason: _____

If administered: 17b. Dose: Penta1 / Penta2 / Penta3

17c. Site of administration: Right thigh / Left thigh

18. PCV administered? Yes / No 18a. If not, reason: _____

If administered: 18b. Dose: PCV1 / PCV2 / PCV3

18c. Site of administration: Right thigh / Left thigh

Observe for 30 minutes after vaccine administration:

19. Any symptoms? Yes / No

19a. If yes, specify *(complete Adverse Event Form, if required)*: _____

_____

Schedule next visit date (dd/mm/yy): ☐☐/☐☐/☐☐

Name and signature of medical officer: _____

nOPV2 and bOPV Study **PID** ☐☐☐☐☐

Clinic Visit at 18 weeks of Age

Date of visit (dd/mm/yy**):** ☐☐/☐☐/☐☐

Clinical History

1. Is the child currently breastfed? No breastfeeding / Partial breastfeeding / Exclusive breastfeeding
2. Has the child received any vaccine since last visit? Yes / No 2a. If yes, specify: _____
   2b. Date of vaccination (dd/mm/yy): ☐☐/☐☐/☐☐
3. Has any other child in the household received OPV since the last clinic visit? Yes / No 3a. If yes, specify: _____
4. Has the child had diarrhea in the last 24 hours (≥ 3 loose stools in 24 hours)? Yes / No
   4a. If yes, specify: duration of diarrhea in days: ☐☐
   (If the child currently has fever >38.3°C, blood in stools, vomiting or signs of dehydration, do not continue with study procedures. Provide advice and referral as required.)
5. Has the child been sick since the last study visit? Yes / No 5a. If yes, specify: _____
6. Is the child on any immunosuppressive medications? Yes / No 6a. If yes, specify _____

Physical Exam

7. Temperature: ☐☐.☐ °Celsius
8. Length #1: ☐☐☐.☐ cm
9. Length #2: ☐☐☐.☐ cm
10. Weight #1 ☐☐.☐ kg
11. Weight #2 ☐☐.☐ kg

Blood Collection

12. Blood sample collected? Yes / No 12a. If not, why? _____
13. Sufficient quantity (1 ml)? Yes / No 13a. If insufficient, why? _____
14. Time of collection (hh:mm): ☐☐:☐☐

Schedule next visit date to begin routine polio vaccination schedule (dd/mm/yy): ☐☐/☐☐/☐☐

Name and signature of medical officer: _____

nOPV2 and bOPV Study **PID** ☐☐☐☐☐

Adverse Event Form

Date of report (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Report Status: ☐ Initial Report ☐ Follow-up Report ☐ Final report

Initials of parent providing information: ☐☐☐

Vaccine recipient date of birth (dd/mm/yy): ☐☐/☐☐/☐☐

Description of the event

Is this a solicited (from the 24–48 hours after 6-week vaccination) or unsolicited AE? Solicited / Unsolicited

Date of onset (dd/mm/yy): ☐☐/☐☐/☐☐ Time of onset (hh:mm): ☐☐:☐☐

Describe briefly relevant clinical symptoms and signs: _____

Results of diagnostic tests performed: _____

Medications prescribed: _____

Diagnosis (*circle:* Current / Final): _____

Severity *(circle what applies)***:** Mild / Moderate / Severe

Did any of the following occur or are present? *(if present, report immediately as a Serious Adverse Event)*

Paralysis, severe disability or incapacity, or substantial disruption of the ability to conduct normal functions	Yes / No
Anaphylaxis	Yes / No
Hospitalization or prolongation of existing hospitalization	Yes / No
Death	Yes / No
Life-threatening event	Yes / No

Outcome *(circle what applies)***:** Ongoing / Resolved without sequela / Resolved with sequela / Death

Date when event resolved or death (dd/mm/yy): ☐☐/☐☐/☐☐

Did this AE lead to discontinuation from the study or from future vaccinations? Yes / No

Adverse Event Form (cont.)

Study group allocation: Specify which study group the child was allocated *(circle the answer)*:

A: nOPV2 @ 6, 10, and 14 weeks
B: nOPV2 + bOPV @ 6, 10, and 14 weeks
C: bOPV @ 6, 10, and 14 weeks

Study vaccines administered:

Clinic visit	Study vaccines administered	Date (DD/MMM/YY)	Lot & batch number
6 weeks of age		___ / _____ / ___	
10 weeks of age		___ / _____ / ___	
14 weeks of age		___ / _____ / ___	

Routine immunization vaccines administered:

Clinic visit	Vaccines administered
At birth	
6 weeks of age	
10 weeks of age	
14 weeks of age	
18 weeks of age	
At any other age, specify age_____	

Signature of study investigator/s: _____

To be completed by the principal investigator

Is the event related to the study vaccine?

☐ Unrelated ☐ Possibly related ☐ Probably related ☐ Definitely related

If unrelated to the vaccine, provide a reasonable explanation for the event *(e.g., other vaccine, blood collection, medical collection, etc.)* _____

_____

_____

Name and signature of PI: _____ Date ☐☐/☐☐☐/☐☐

Discontinuation Tracking Form – Vaccine Recipient

Date of the report (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Date of study discontinuation (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Note: This is the date the vaccine recipient is withdrawn from the study and may not be the same date as the report

Last clinic visit *(circle one)*: 6 weeks / 10 weeks / 14 weeks

Date of last study clinic visit (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Reasons *(circle one of the choices listed below)*:

Discontinuation criteria as mentioned in study protocol:

1. Parent withdrew consent for participation (i.e., did not want child to participate any further).
2. The vaccine recipient received **polio vaccine** outside of the study. ***(Complete protocol deviation form)***
3. Parent refused to allow collection of blood at 6 weeks of age. ***(Complete protocol deviation form)***
4. Study staff were unable to collect blood at 6 weeks of age ***(Complete protocol deviation form)***
5. Since enrolment, the vaccine recipient was diagnosed with a medical condition in which continued participation in the study posed a health risk (for example, immunodeficiency or bleeding disorder).
6. The vaccine recipient began taking immunosuppressive medications.
7. The PI withdrew or parent refused participation because the vaccine recipient experienced a serious adverse event, not death, in which continued participation in the study posed a health risk. **(*Complete Adverse Event form)***
8. The PI withdrew or parent refused participation because the vaccine recipient experienced an adverse event, not serious AE, in which continued participation in the study posed a health risk. **(*Complete Adverse Event form)***
9. Withdrawal by investigator (specify reason): _____

Other reasons why vaccine recipient may not continue in the study:

10. The vaccine recipient died. **(*Complete Adverse Event form)***
11. The PI withdrew because the parent and vaccine recipient could not be located (i.e., lost to follow-up).
12. Other (specify reason): _____

_____

Name of medical officer:_____ Signature: _____

Discontinuation Tracking Form – Sibling

Date of the report (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Date of study discontinuation (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Note: This is the date the sibling is withdrawn from the study and may not be the same date as the report

Last study visit *(circle one)*: 6 weeks / 7 weeks / 8 weeks / 10 weeks

Date of last study visit (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Reasons *(circle one of the choices listed below)*:

Discontinuation criteria as mentioned in study protocol:

1. Vaccine recipient was discontinued from the study.
2. Parent withdrew consent for sibling's participation (i.e., did not want child to participate any further).
3. The sibling received **polio vaccine** during their participation in the study. ***(Complete protocol deviation form)***
4. Withdrawal by investigator (specify reason): _____

Other reasons why vaccine recipient may not continue in the study:

5. The sibling died.
6. The PI withdrew because the parent and sibling could not be located (i.e., lost to follow-up).
7. Other (specify reason): _____

_____

Name of medical officer:_____ Signature: _____

Protocol Deviation Tracking Form

Complete this form for protocol deviations and protocol violations.

Date of the report (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Date of protocol deviation (dd/mm/yy)**:** ☐☐/☐☐/☐☐

Note: This is the date the protocol deviation occurred, may not be the same date as the report.

1. Describe the protocol deviation: _____

_____

_____

2. Reason for protocol deviation *(circle one answer)*
   - Vaccine recipient illness
   - Vaccine recipient (or parent) unable to comply
   - Parental refusal
   - Sibling unable to comply
   - Other, Specify _____
   - Laboratory error
   - Clinic error
   - Investigator/study decision
3. Deviation category *(circle one answer)**:***
   - Eligibility / enrolment
   - Protocol procedure / assessment
   - Clinic visit schedule
   - Study vaccine type or dosing
   - Biological specimen collection or processing
4. Describe steps taken to resolve or avoid recurrence of the deviation:

_____

_____

5. Did the deviation result in an **adverse event**? Yes / No **(*If Yes, complete an Adverse Event Form)***
6. Did the deviation result in vaccine recipient discontinuation? Yes / No

(*If Yes, complete Vaccine recipient Discontinuation Tracking Form)*

Name of medical officer:_____Signature: _____

Appendix B: Microneutralization Test for Polio Antibodies

Prepared by	Date Adopted	Supersedes Procedure
William Weldon	4/2/2014	12_10_10

Introduction

The polio microneutralization assay measures neutralizing antibody titers to poliovirus types 1, 2, and 3 using 96-well microtiter plates (it is termed "microneutralization" because the original neutralization assay was performed using larger volumes on culture tubes). The principle of the test is that the anti-poliovirus antibodies in a serum sample will bind to the virus and block infection of susceptible cells. Because poliovirus is cytopathic, virus that is not bound by antibody infects and lyses cells. The amount of neutralizing antibody is quantitated as a 50% endpoint titer; that is, the dilution of serum that protects 50% of susceptible cells from poliovirus infection and cytopathic effect.

The test takes approximately seven days to complete, from the dilution of sera to staining and reading plates, and data analysis. Each test serum is run in triplicate and diluted from 1:8 to 1:1024; a single 96-well plate contains four test sera (Figure 1). This test may be performed manually, automated, or in a combination of the two approaches (Figure 2). For large studies, automation is recommended.

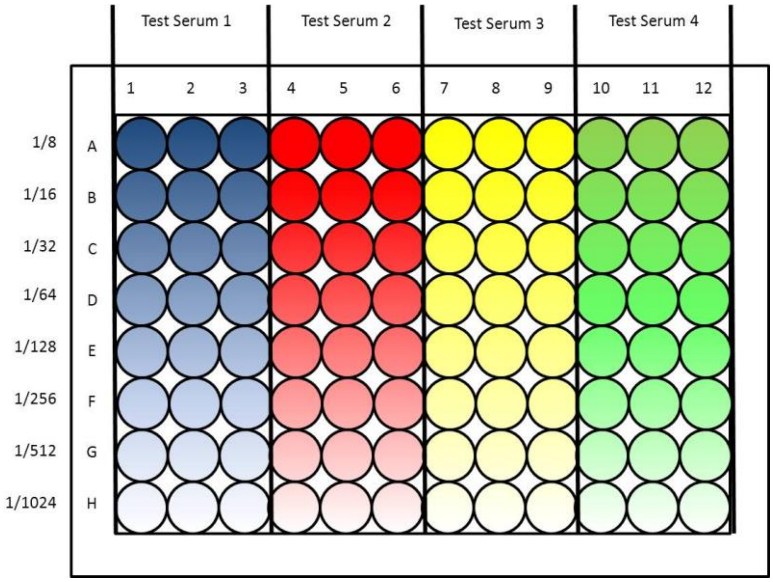


Figure 1. 96-well plate setup for Polio Serology

For a single run, up to 96 sera, which fit on 72 plates (24 plates per serotype), can be tested. For most purposes, the Sabin vaccine strains are used, but other poliovirus strains can be used. Control plates are generated for each run and consist of three back titration plates with no antibody added (one for each Sabin virus) and a cell control plate (no virus or antibody added, to assess cell viability). At the end of each run, control plates are checked for accurate dilution of each Sabin poliovirus (back titration plates) or cell monolayer confluency (cell control plate).

If more than seven sera are being tested, the samples must be randomized using a balanced block randomization scheme with integrated controls. Included in each run is a control serum designated In-House Reference Serum (IHRS), which is pooled from serum samples with high neutralizing antibody titers to each Sabin poliovirus.

The IHRS is tested in multiple replicates, on multiple plates in each run, to provide a measure of assay variability within a run.

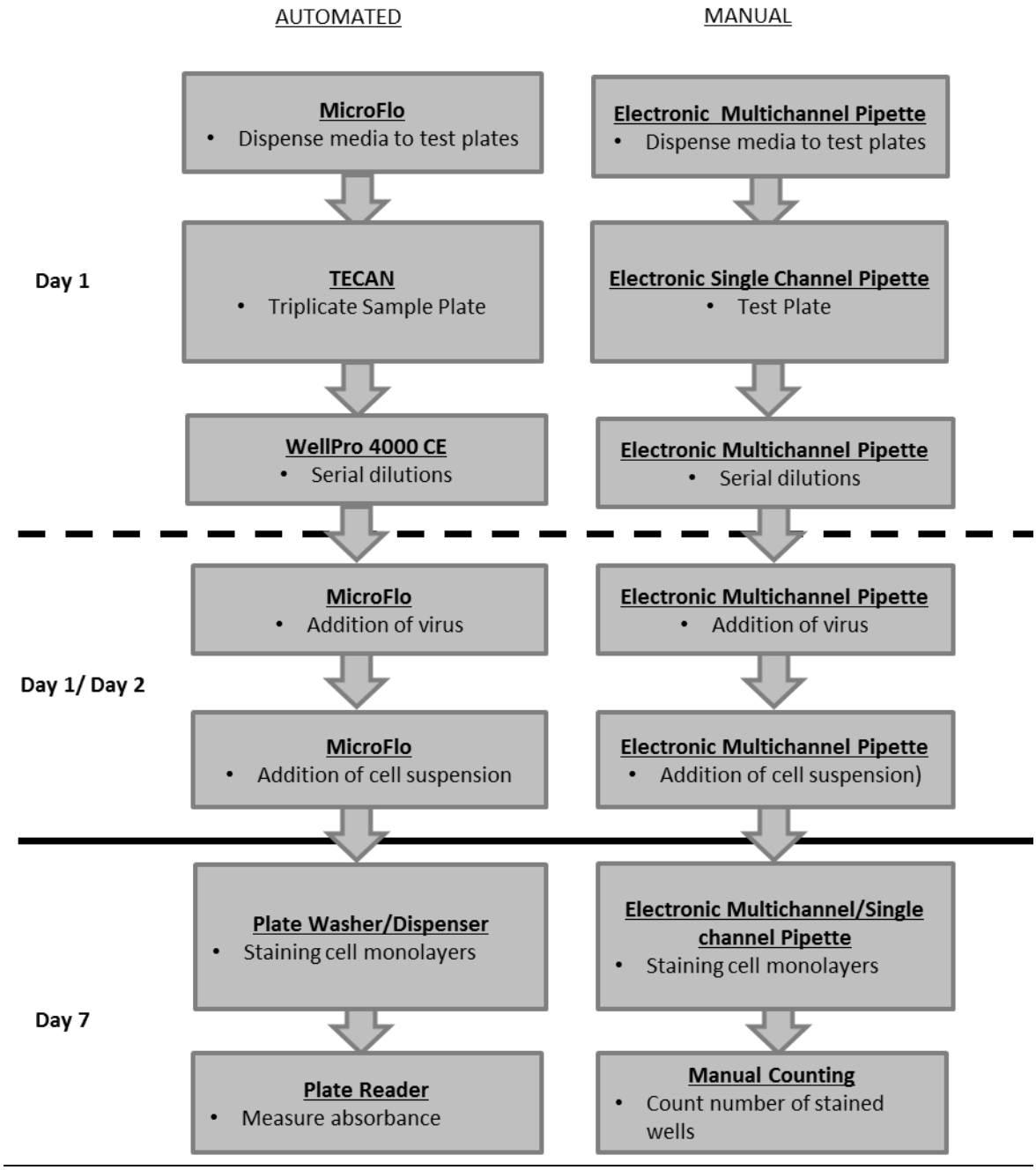


Figure 2. Workflow for automated poliovirus microneutralization assay

Materials and Equipment

Most of these items may be substituted with equivalent items from other manufacturers/suppliers but alternative materials must be validated against an appropriate standard.

Consumables

- T-150 tissue culture flasks (Corning, #430823)
- 96-well tissue culture, clear, sterile plates (Corning, #3997)

- Low evaporation lids (Corning, #3931)
- 96-well tissue culture, clear, sterile, (Corning #3997)
- Plastic wrap (e.g., Saran Wrap)
- Deep-well 96-well microplate, 2.2 ml capacity. (VWR, #40002-014)
- Mat lids for 2.0 mL microplates (VWR, #400002-018)
- Sterile pipettes; 10 ml, 25 ml (Falcon, #357551, #357325)
- Single-channel pipettes:
    - Manual: LTS 20, 200, 1000 (Rainin)
    - Electronic: 10-300, 50-1000 (Biohit)
- 12-channel pipettes
    - Electronic: 10-300, 50-1200 (Biohit)
- Pipette tips
    - Rainin: RT-L200F, RT-L1000F, RT-L10F
    - Biohit: 350 µL, 1000 µL, 1200 µL
- WellPro 250 µL sterile pipette tips (ProGroup)

Cells and Media
- HEp-2C cells (ATCC # CCL23)
- Cell culture media
    - Eagle's Minimum Essential Media (EMEM)(Gibco, #11095-072)
    - Penicillin/streptomycin (Gibco, #15140)
    - Fetal Bovine Serum - Optima (Atlanta Biologicals, #S12450)
    - 0.05% Trypsin-EDTA (Gibco, #25300)
- Nalgene 500 mL, 0.20 µm filter (Nalgene, #450-0020)

Antigens and Control Sera
- In House Reference Sera (developed in-house)(See Note 1.4.4)
- Sabin virus stocks grown in HEp2-C cells

Staining
- Crystal violet stain (0.05% crystal violet, 0.5% Tween-20, 50% ethanol, in H_2O)

To prepare crystal violet stock solution:

2 g	crystal violet (Sigma, C-3386)
1000 ml	95% ethanol

Mix together overnight, with stirring, until dissolved; may be stored up to one year at room temperature

To prepare working dilution crystal violet solution:

250 ml	crystal violet stock solution
5 ml	Tween-20 (Fisher Scientific, #BP337-100)
750 ml	deionized H_20

Equipment and Automation
- CO_2 water-jacketed incubator (ThermoFisher Model 3110 or equivalent)
- WellPro 4000 CE (ProGroup)
- EL406 plate washer and dispenser (BioTek)

- MicroFlo dispenser (BioTek)
- Evo 100 (Tecan)
- TC20 Automatic Cell Counter (BioRad)
- PerkinElmer Victor X4 Multimode plate reader or equivalent

Protocol

In the week preceding the test runs:

1. Assign sera randomly to each run using a balanced block randomization scheme (see Note 3).
2. Use the list generated by the randomization scheme to label plates and organize sera to be tested. Each test serum is run in triplicate, so four sera may be run on each plate (Figure 1). Each plate is duplicated two more times, yielding three plates, one for each poliovirus serotype. There will also be a back-titration plate for each serotype, and one cell control plate per run.
3. In this example of a randomized sample list (Table 1), serum sample number 0000000001 will be in run number 420, position 4 on plates 5 (PV1), 29 (PV2), and 53 (PV3). The in-house reference serum (IHRS) is in position 2 on plates 7 (PV1), 30 (PV2), and 55 (PV3).

RUN [a]	PV1 Plate[b]	PV2 Plate[b]	PV3 Plate[b]	Position[c]	Sample ID[d]
420	5	28	53	1	0000000001
420	5	28	53	2	0000000002
420	5	28	53	3	0000000006
420	5	28	53	4	0000000009
420	6	29	54	1	0000000011
420	6	29	54	2	0000000030
420	6	29	54	3	0000000025
420	6	29	54	4	0000000041
420	7	30	55	1	0000000013
420	7	30	55	2	IHRS
420	7	30	55	3	0000000038
420	7	30	55	4	0000000051

Table 1. Example of randomized sample list for poliovirus microneutralization assay.
[a] each run of 1-96 sera
[b] PV1, polio type 1; PV2, polio type 2; PV3, polio type 3
[c] see Figure 1
[d] unique specimen ID

4. For each run, the IHRS is tested an average of 4-6 times, depending on the number of samples being randomized (see Note 4).
5. The labelling of the assay plates should reflect the setup of the serology run reflected in the randomized list. A suggested plate labelling scheme is shown in Figure 3.

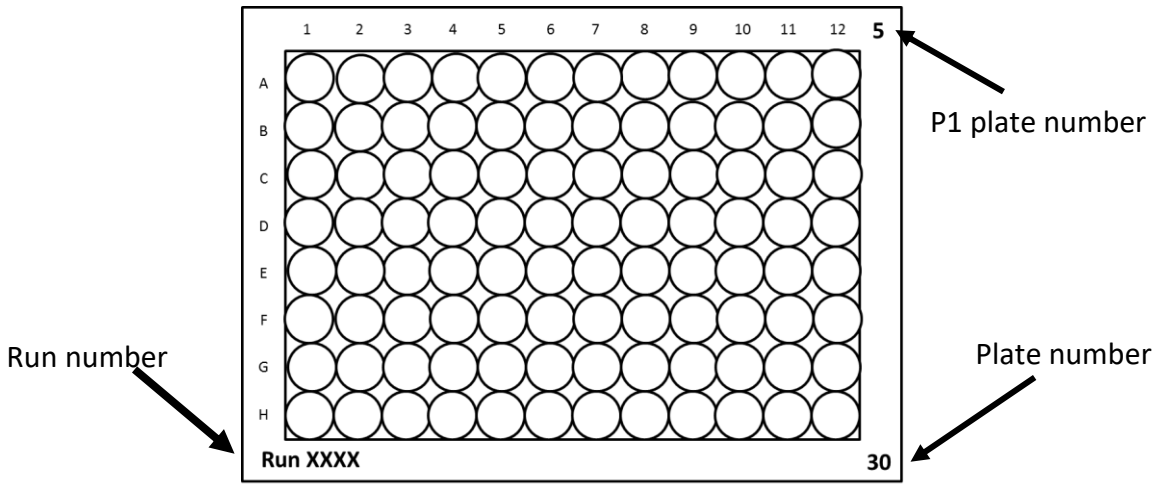


Figure 3. Suggested labeling scheme for assay plates.

6. Prepare MEM+ 2% FBS and MEM+10% FBS:
    a. FBS must be inactivated at 56°C for 30 minutes and filtered with a Nalgene 0.2 µm filter
    b. Add 1 mL of streptomycin/penicillin to 1000 mL of EMEM (0.1%)
    c. Add 20 ml (2%) or 100 mL (10%) of fetal bovine serum to 1000 ml bottle of EMEM
    d. MEM+10% FBS is used for maintaining HEp2-C cells and generating the cell suspension.
    e. MEM+2% FBS is used for filling the assay plates, diluting sera, and diluting the virus.

Prior to each test run:

5. 24-48 hours before each run, seed T-150 flasks with 30 ml of HEp2-C cells at 5 x 10^5 cells/ml.
    a. Approximately 3-4 flasks are needed for one run of 96 sera
6. Incubate flasks at 37°C, 5% CO_2, in a humidified atmosphere for 24 to 48 hours to ensure that cell monolayers are confluent the day assay runs are started.

OPTIONAL - One day before test run:

The following steps can be done the day of the run or the day before the addition of the virus.

1. Manually aliquot 100 µl of each serum sample into deep-well polypropylene microplate, sealed with a mat lid, and heat inactivated at 56°C in a water bath for 30 minutes.
2. Store at 4°C until ready to generate the triplicate sample plates (no more than 24 hours).
3. Prepare IHRS for testing (See Note 4)
4. Use a multichannel pipette to add 300 µl MEM+2% FBS to 100 µl heat-inactivated test serum aliquots (for a final dilution of 1:4)
5. For a full run (i.e. 96 sera), label two stacks of 12 microplates for each serotype (Figure 3).
    a. Use a lidded microplate for the top of each stack, with the low evaporation lid
    b. The 11 remaining microplates can be lidded or lidless; removal of lids is required for many automation systems
    c. Cell control and back titration plates can be set up in lidded plates

AUTOMATED

A6. Use the MicroFlo reagent dispenser program “MEDIA 25UL” to add 25 µl MEM 2% FBS to the test plates.

a. This program adds 25 µl MEM+2% FBS to all wells for each test plate and the back titration plates (PV1, PV2, and PV3).

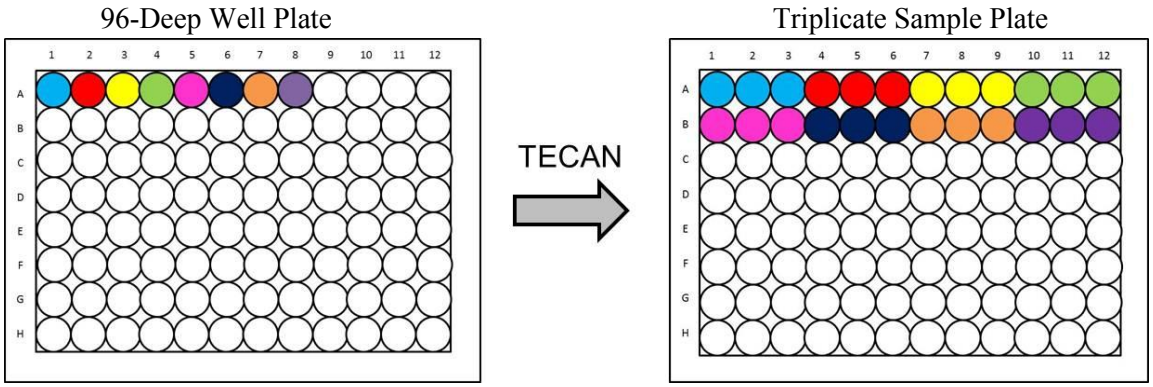
b. For the cell control plate, a total of 50 µl MEM+2% FBS should be added to each well. This plate can be filled twice using the “MEDIA 25UL” program.

A7. Use the TECAN programs “1 or 2 plate triplicate transfer” to make triplicate sample plates (Figures 4A).

a. This program will transfer 100 µL of test serum in a deep-well plate (from Step 3) in triplicate to a triplicate sample plate.

A8. Using electronic single-channel pipette, transfer 25 µL of test serum from triplicate sample plate (Step 6) to three different test plates (one for each serotype) (Figure 4B).

A



B

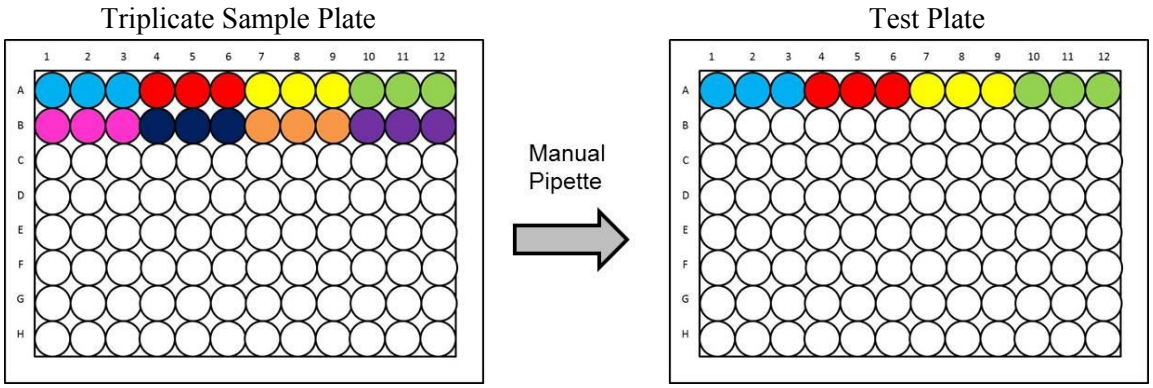
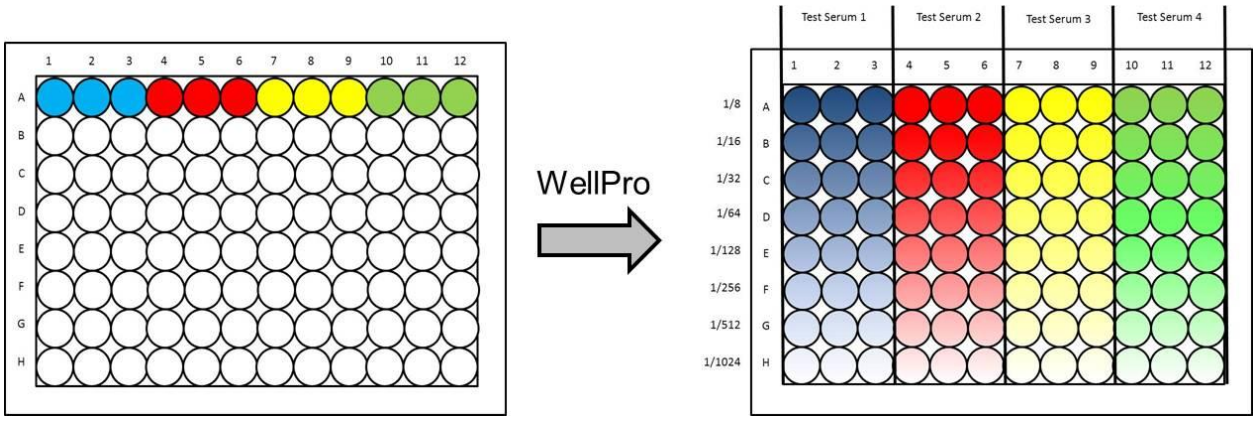


Figure 4. . For each run, 100 µl of sample is transferred from sample plate to dilution plates in triplicate (enough for starting three 25 µl sample dilutions) (A). For simplicity, only the first 8 samples are shown in the deep 96--well plate. The TECAN configuration will allow for triplicates in consecutive order. This step can transfer 96 samples from one 96-deep well plate to a 96-well triplicate sample plate in 22 min. (B) Using a 12-channel manual pipette, each row of from the triplicate sample plate is transferred to a test plate in triplicate for each serotype.

A9. Use the WellPro program “SD25” to perform 2-fold serial dilutions (Figure 5).

a. This program will transfer 25 µL of the diluted serum in row A to row B, then from row B to row C, etc.

b. For row H, 25 µL will be aspirated and discarded with the tips, to maintain the correct total volume.
c. For each transfer, the program will mix the diluted serum a total of 4 times.
d. Using this program will produce serum dilutions ranging from 1:8 to 1:1024.
e. This step generates the test plates, ready for addition of virus and cells.



Test Plate Diluted Test Plate

Figure 5. Each test serum is serially diluted (2-fold) from 1:8 to 1:1024 in triplicate. This is repeated for each test plate designated for poliovirus serotypes 1, 2, or 3.

A10. Arrange the plates in stacks of 12-13; use a lid to cover the top plate of each stack of plates and wrap in plastic Saran wrap.
A11. Plates can be stored overnight at 4°C.

MANUAL

M5. Use electronic multichannel pipette to dispense 25 µL MEM+2% FBS to the test plates.
   a. Add 25 µl MEM+2% FBS to each well of the back titration plates (PV1, PV2, and PV3).
   b. Add 50 µl MEM+2% FBS to each well of the cell control plate.
M6. Use an electronic multichannel pipette to transfer 25 µL of each test serum (from Step 3) to each test plate in triplicate (Figure 4B).
M7. Using a multichannel pipette, make serial 2-fold dilutions from row A to row H. (serum dilution will range from 1:8 to 1:1024) (see Figure 5 for plate layout).
   a. Discard 25 µL from row H to make final volume for all wells 25 µL.
M8. Cover the top plate of each stack of plates and wrap in plastic wrap.
M9. Plates can be stored overnight at 4°C.

Day of run:

1. Dilute each virus in MEM+2% FBS to contain 100 $CCID_{50}$ according to Table 2.
   a. Prepare sufficient virus challenge suspension for the number of sera to be tested; each plate requires approximately 2.5 ml of diluted challenge virus.
2. Prepare the back titrations of each poliovirus serotype in MEM+2% FBS. Titrate each virus from 100 $CCID_{50}$ a further three 10-fold steps (Figure 6).

Sabin 1 (NIBSC 01/528) 100 $TCID_{50}$ = $10^{-5.28}$							100 $TCID_{50}$	10 $TCID_{50}$	1 $TCID_{50}$	0.1 $TCID_{50}$
Virus	100 µL	100 µL	100 µL	100 µL	800 µL		7 mL	100 µL	100 µL	100 µL
Medium	38 µL	900 µL	900 µL	900 µL	7.2 mL		63 mL	900 µL	900 µL	900 µL
Sabin 2 (NIBSC 01/530) 100 $TCID_{50}$ = $10^{-5.2}$										
Virus	100 µL	100 µL	100 µL	100 µL	800 µL		7 mL	100 µL	100 µL	100 µL
Medium	82 µL	900 µL	900 µL	900 µL	7.2 mL		63 mL	900 µL	900 µL	900 µL
Sabin 3 (NIBSC 01/532) 100 $TCID_{50}$ = $10^{-4.68}$										
Virus	100 µL	100 µL	100 µL		800 µL		7 mL	100 µL	100 µL	100 µL
Medium	82 µL	900 µL	900 µL		7.2 mL		63 mL	900 µL	900 µL	900 µL

Working Stock

Back Titration Plate

Table 2. Example Virus Dilution for 100 $TCID_{50}$ and Back Titration Plate for Sabin type 1, 2, and 3

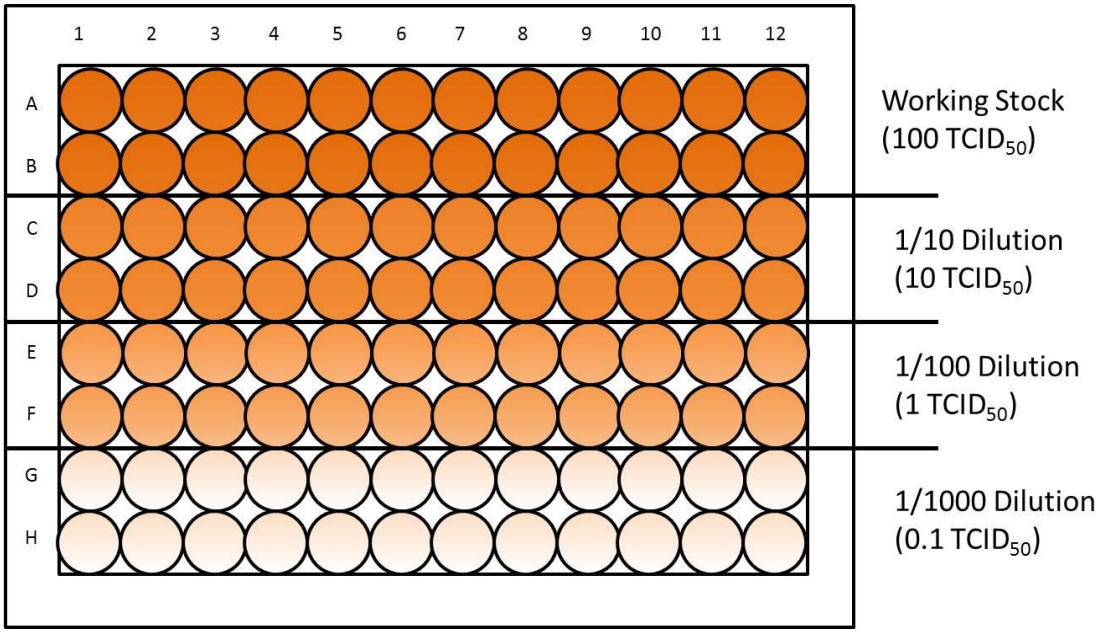


Figure 6. Layout for back titration plate. A back titration plate is made for each virus tested in the microneutralization assay.

AUTOMATED

A3. Use the MicroFlo program VIRUS 25UL to add 25 µl of 100 $CCID_{50}$ of relevant poliovirus antigen to all wells in the diluted serum test plates. Use a different sterile dispensing cartridge for each virus.

MANUAL

M3. Use an electronic, multichannel pipette to add 25 µL of 100 $CCID_{50}$ of relevant poliovirus antigen to all wells in the diluted test plates.

M4. Prepare back titration plate (Figure 6) for each Sabin strain using dilutions prepared in step 2 (Table 2).

a. Add 25 µl of 100 $TCID_{50}$ of virus to rows A and B (i.e., 24 wells/dilution)

b. Add 25 µl of the next three 10-fold dilutions to rows C and D, E and F, and G and H, respectively (See Table 2 for dilutions).

c. Change pipette tips between each dilution

M5. Wrap all plates in plastic wrap and incubate for 3 hours at 35°C and 5% CO_2

M6. During serum-virus incubation, wash HEp2-C monolayer cell cultures (from 150 cm^2 flasks), trypsinize, and count cells using automatic cell counter (BioRad) or a hemocytometer.

M7. Prepare a cell suspension in MEM+10% FBS to contain 3 x 10^5 cells/ml. Prepare a sufficient volume of cells: each plate requires approximately 2.5 ml of cell suspension, and every run requires 3-4 confluent 150 cm^2 flasks. Store cells in glass bottle at 4°C until ready to use.

AUTOMATED

A4. Use MicroFlo program "CELL 25UL" to add 25 µl of prepared cell suspension to each well of every plate.

MANUAL

M8. Use a repeating, multichannel pipette to add 25 µL of prepared cell suspension to each well of every plate.
M9. Wrap all plates in plastic wrap, in stacks of 12-13 plates. *To prevent spills and cross-contamination, avoid abrupt handling of plates.*
M10. Carefully transfer plates to incubator for 5 days incubation at 35°C and 5% CO_2.

Plate washing and staining.

AUTOMATED
A1. After 5 days incubation, use the Biotek EL406 to wash and stain plates with crystal violet solution.
A2. This will aspirate wells and dispense 50 µL of crystal violet stain (0.05%) to all wells.
A3. Incubate for a minimum of 40 minutes at room temperature.
A4. Run wash program
a. This program will aspirate the crystal violet stain then fill all wells with 250 µL of tap water and aspirate.
b. This process will be repeated 3 more times to completely remove any excess crystal violet stain in the test plates prior to reading.

MANUAL
M1. After 5 days incubation, aspirate/discard media with multichannel pipette into freshly made 0.5% sodium hypochlorite solution.
M2. Using a repeating, multichannel pipette, add 50 µL crystal violet stain (0.05%) to all plates.
M3. Incubate for a minimum of 40 minutes at room temperature.
M4. Aspirate/discard stain with multichannel pipette, fill each well with tap water (approximately 250-300 µL), and discard.
a. Repeat washing step 3 more times.
M5. Allow plates to dry at room temperature for approximately 30 minutes.
M6. Plates should be kept at room temperature until results are calculated and results are reported.

Notes

1. Data Collection

AUTOMATED
A1. Read plates with ELISA reader at 595 nm wavelength.
a. Data from plate reader can be processed using macros written in Visual Basic for Microsoft Excel.
b. Use an absorbance cutoff value of ≥ 0.8 as positive for neutralization (i.e., intact monolayer).
c. Automatically calculate the titer for each specimen using Formula 1 below (Step 2).

MANUAL
M1. For each triplicate test serum, count the total number of wells positive for neutralization (i.e., purple wells).
M2. To calculate titer:

Formula 1
Titer = (# positive wells / # replicates) + 2.5

a. To calculate reciprocal titer:

Formula 2

Reciprocal titer = 2^{titer}

M3. For the neutralization titers, the upper limit of detection is 10.5 and the lower limit is 2.5, which is considered negative.

2. Cross-checking stained plates

1. To ensure accuracy, each plate is cross checked to verify correct order of plates and compare plate staining pattern to electronic data file to verify titer.
2. Due to the variance of the assay, there is a statistical likelihood that some wells will have virus not neutralizied by antibody despite neutralization at lower serum dilutions.
3. To account for this, stained plates should be checked for these situations and the data corrected according to the following guidelines (Figure 7).

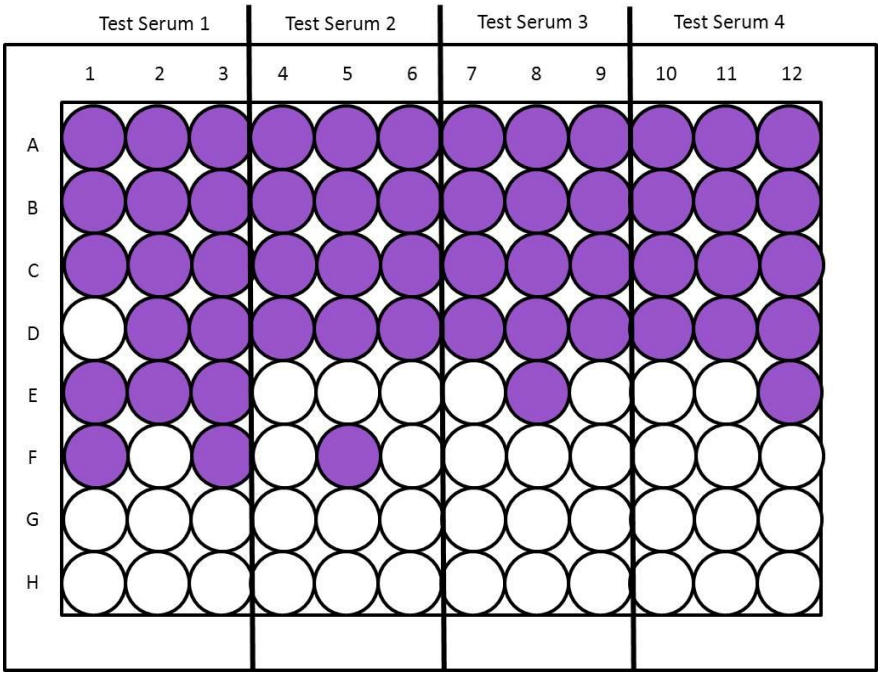


Figure 7. Example of cross-checking a crystal violet stained 96-well plate for poliovirus serology assay.

Example 1

a. For Test Serum 1, the reader software will automatically read this as a titer of 7.83 (1:227)
b. By cross-checking the plate, we will count D1 as positive for neutralization because the 1:128 and 1:256 dilutions (E1 and F1) are positive for neutralization (i.e., purple).
c. Using Formula 1, the titer is adjusted to 8.17 (1:288)

Example 2

a. For Test Serum 2, the reader software will automatically read this as a titer of 6.83 (1:114)
b. By cross-checking the plate, we will count F5 as negative for neutralization because the 1:64 dilutions (D4, D5, and D6) are negative for viral growth

3. Summary of Randomization Process

1. For each study, the specimen number, study site, study arm, patient number, and the unique ID for each specimen.
2. Each run needs to have 4-6 in-house reference sera.
    a. Based on the total number of runs and the number of divisions per plate, the program will also determine how many plates will be required.
    b. The function determines how many unique subjects exist in the file and how many unique study groups exist (where a study group is a unique combination of study site and study arm for multi-site or multi-arm studies). Each study group will be evenly represented in each run, so the program assigns the subjects within each study group randomly and evenly amongst the runs.
    c. After each subject identifier is assigned a run number, all sera associated with those subject identifiers are assigned to the same run.
    d. Finally, plate numbers and plate positions are randomly assigned to the sera within each run, and a spreadsheet of the randomized sera is created, in MS Excel format.
3. At the prompt, enter in the first run number for this group of serology runs.
4. At the next prompt, enter in the code that represents the first specimen per subject (for example SE1) in the input file.
5. At the next prompt, select the path and name of the output file.
6. A dialog box will appear when the process is complete.
7. Review the output to confirm that all samples were included in the randomized output.

4. In-House Reference Serum (IHRS)

1. The in-house reference serum should be established by measuring polio neutralizing antibody titers in a population of immunized subjects.
2. Multiple sera with high neutralization titers (≥ 7.5) should be pooled to generate a high-volume control.
3. Make 100 µL aliquots of the pooled sera to be stored at -20°C for future use. Once thawed, IHRS aliquots must be stored at 4°C for no more than 3-4 days.
4. To prepare the IHRS for use in the serology assay, adjust the initial dilution such that the endpoint titer is reached on the 3-5 dilution on an assay plate.

   Make the initial dilution of the IHRS and transfer to the wells that are designated for the IHRS in the randomized list (See Table 1).

Appendix C: Summary of Laboratory Methods for Stool Testing

Stool samples will be stored at -20°C until analysis. Poliovirus genomes will be detected using a Sabin multiplex real-time RT-PCR (rRT-PCR) assay of total nucleic acid extracted from stool suspensions (50%, w/v) [14]. Virus titrations will be performed as described previously [14]. For stool samples with $>10^5$ $CCID_{50}$ per ml, stool suspensions (10% w/v in EMEM) will be prepared for high resolution sequencing. For stools with low Ct values in Sabin 2 realtime PCR assays, a subset of the stool samples will be subjected to virus isolation/expansion prior to RNA extraction and high resolution sequencing. Virus will be amplified in HEp-2C (ATCC, CCL-23) cells maintained in EMEM supplemented with 2% fetal bovine serum (Atlanta Biologicals). Confluent monolayers of HEp-2C cells in 24-well cell culture cluster plates (Costar) will be inoculated with 50 µL of each 10% stool suspension (4 wells, at least 50 $CCID_{50}$ per well) and incubated for 3 days at 33°C, 5% CO_2. Following two freeze-thaw cycles, cell lysate will be pooled from the 4 wells, and virus isolates will be harvested following removal of cell debris by centrifugation at 3000 x *g* for 10 minutes.

Sequence and data analysis will be performed on viral RNA isolated from both culture-amplified virus and from 10% stool suspensions, using a previously described methods [14]. In brief, viral RNA will be isolated from 140 µl amplified virus stock or stool suspension using a QIAamp Viral RNA mini kit (Qiagen). cDNA preparation and first round amplification of nearly-full-length genome will be performed using poliovirus-specific primers near the ends of the genome, followed by semi-nested PCR using a poliovirus-specific primer at the 5' end of the genome and a Sabin 2-specific primer in the carboxy terminus of VP1. The other half of the genome will be amplified by Sabin 2-specific primer at the amino terminus of VP1 and poliovirus-specific primer at the 3' end of the genome. Library preparation by Nextera XT (Illumina) and paired-end sequencing using MiSeq reagents on a MiSeq instrument to generate FASTQ files.

Data analysis will be performed using the appropriate reference sequence and sequence analysis pipeline. Sequencing reads will be mapped against all three Sabin vaccine reference sequences to

generate coverage plots. As needed, amplicons will be analyzed using long-read sequencing methods (MinIon or PacBio), to confirm the genome structure.

Appendix D: External Reviews

Reviewer 1

Name of Reviewer: Ondrej Mach
Position: POL Research team Lead
Institution: WHO

EVALUATION FORM

Title:

Summary of Referee's Opinions: Rank Score

	High	Medium	Low
Quality of project	X		
Adequacy of project design	X		
Suitability of methodology	X		
Feasibility within time period	X		
Appropriateness of budget		X	
Potential value of field of knowledge	X		

CONCLUSIONS

I support the project proposal

a) without qualification	X
b) with qualification	
c) on technical grounds	
d) on level of financial support	

I do not support the project proposal

Name of Reviewer: _____Ondrej Mach_____

Signature:_____ .Date:___20/03/2020_____
Position: ___POL Research team Lead_____
Institution: ___WHO_____

Detailed Comments: (Please use additional page if necessary.)

This is an important study that will provided much needed additional clinical trial data for nOPV and first data on co-administration of nOPV and bOPV. I fully support this study.

Response: Thanks

Reviewer 2

Name: Professor Dr. Md. Shafiqul Islam
Position: Former Professor and Head, Department of Epidemiology,
Institution: National Institute of Preventive and Social Medicine (NIPSOM).

Title: Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

Summary of Referee's Opinions: Please see the following table to evaluate the various aspects of the proposal by checking the appropriate boxes. Your detailed comments are sought on a separate, attached page.

	Rank Score		
	High	**Medium**	**Low**
Quality of project	√		
Adequacy of project design	√		
Suitability of methodology	√		
Feasibility within time period	√		
Appropriateness of budget	√		
Potential value of field of knowledge	√		

CONCLUSIONS

I support the application:

a) without qualification √

b) with qualification

- on technical grounds ☐
- on level of financial support ☐

I do not support the application ☐

Name of Referee: Professor Dr. Md. Shafiqul Islam

Signature : 

Date : 13/04/2020

Position: Former Professor and Head, Department of Epidemiology,

Institution: National Institute of Preventive and Social Medicine (NIPSOM).

Detailed Comments

Please briefly provide your opinions of this proposal, giving special attention to the originality and feasibility of the project, its potential for providing new knowledge and the justification of financial support sought; include suggestions for modifications (scientific or financial) where you feel they are justified. (Use additional pages if necessary)

Title: Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV

PI : Dr. K Zaman

Name of Reviewer : Prof. Dr. Md. Shafiqul Islam

Comments:

Wild poliovirus type 2 (WPV2) was declared eradicated in 2015 and type 2 oral poliovirus vaccine (OPV2) was withdrawn globally in May 2016. Monovalent OPV2 (mOPV2) is stockpiled for responding to circulating type 2 vaccine-derived poliovirus (cVDPV2) outbreaks. However, Sabin polioviruses in OPV can revert to neurovirulence and there is evidence that mOPV2 vaccines used to control cVDPV2 outbreaks have generated new VDPV2 emergences that have led to cVDPV2 outbreaks. Novel OPV2 (nOPV2) candidates have been developed with improved genetic stability to reduce the risk of seeding new VDPVs. Findings from a phase 1 clinical trial in adults demonstrated the safety and immunogenicity of two nOPV2 candidates. Preliminary results from phase 2 clinical trials in adults and children also suggest that the nOPV2 vaccines are safe and immunogenic. It is expected that nOPV2 would replace mOPV2 for responding to type 2 outbreaks. Outbreak response for cVDPV2 also offers the opportunity to close immunity gaps to polioviruses types 1 and 3. It is important to get data on the immunogenicity of co-administered nOPV2 and bOPV, compared to either vaccine given alone. No study has yet assessed the immunogenicity of co-administered nOPV2 and bOPV. So, this is an important study to fill up this knowledge gap.

This is an open-label, non-inferiority, inequality balanced five arm randomized clinical trial assessing immunogenicity of poliovirus vaccines. Vaccine recipient will be enrolled and randomized at 6 weeks to one of five arms:
A: nOPV2 candidate 1 @ 6, 10, and 14 weeks
B: nOPV2 candidate 1 + bOPV @ 6, 10, and 14 weeks
C: nOPV2 candidate 2 @ 6, 10, and 14 weeks
D: nOPV2 candidate 2 + bOPV @ 6, 10, and 14 weeks
E: bOPV @ 6, 10, and 14 weeks

This is a well written research protocol. The investigators as well as this prestigious organization have long experience of conducting vaccine trial research project. This research project has the potential to play an important role to guide Global Polio Eradication Initiative (GPEI), including WHO, in making policy for responding to polio outbreaks with the goal of eradication of polio worldwide.

Prof. Dr. Md. Shafiqul Islam
Former Professor and Head, Department of Epidemiology,
NIPSOM,
Mohakhali, Dhaka 1212.

Response: Thanks

Check-List

Check-list for Submission of Research Protocol
For Consideration of the Research Review Committee (RRC)
[Please check all appropriate boxes]

1. Has the proposal been reviewed, discussed and cleared by all listed investigators?

   ☒ Yes ☐ No

   If the response is No, please clarify the reasons:

2. Has the proposal been peer-reviewed externally?

   ☒ Yes ☐ No ☐ External Review Exempted

   If the response is 'No' or "External Review Exempted", please explain the reasons:

   If the response is "Yes", please indicate if all of their comments have been addressed?

   ☒ Yes (please attach)

   ☐ No (please indicate reason(s)):

3. Has the budget been reviewed and approved by icddr,b's Finance?

   ☒ Yes ☐ No (reason): _____

4. Has the Ethics Certificate(s) been attached with the Protocol?

   ☒ Yes ☐ No

   If the answer is 'No', please explain the reasons:

_____ _____

Signature of the Principal Investigator Date

E-mail approvals of Investigators

From: Dr. Mohammad Yunus
Sent: Wednesday, June 24, 2020 8:37 AM
To: Dr. K. Zaman <kzaman@icddrb.org>; Asma Binte Aziz <asma.aziz@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>
Subject: RE: Approval for submission of nOPV+BOPV protocol

Dear Dr. Zaman,
I approve the protocol entitled "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV" for submission to RRC.
Thank you very much and best wishes.
Md. Yunus

From: Dr. K. Zaman
Sent: Tuesday, June 23, 2020 8:31 PM
To: Dr. Mohammad Yunus; Asma Binte Aziz; Masuma Hoque
Subject: Approval for submission of nOPV+BOPV protocol

Dear All,
We need your approval for submission to the RRC of the following protocol :
"Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV".

Please find attached the protocol.
Appreciate if you please give it urgently (planning to submit tomorrow).

Best regards
Zaman

From: Asma Binte Aziz
Sent: Tuesday, June 23, 2020 8:34 PM
To: Dr. K. Zaman <kzaman@icddrb.org>
Cc: Dr. Mohammad Yunus <myunus@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>
Subject: Re: Approval for submission of nOPV+BOPV protocol

Dear Sir,
Thanks.
Please proceed for RRC submission.

Best Regards,
Asma

On 23 Jun, 2020, at 8:31 PM, Dr. K. Zaman <kzaman@icddrb.org> wrote:

Dear All,
We need your approval for submission to the RRC of the following protocol :

“Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV".

Please find attached the protocol.
Appreciate if you please give it urgently (planning to submit tomorrow).

Best regards
Zaman

From: Masuma Hoque
Sent: Tuesday, June 23, 2020 8:44 PM
To: Dr. K. Zaman
Cc: M.A Salam Khan
Subject: Approval

Zaman Bhai,

I approve submission of the following protocol to the RRC :

“Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV".

Sincerely
Masuma

From: Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) [mailto:lxq6@cdc.gov]
Sent: Wednesday, June 10, 2020 6:58 PM
To: Dr. K. Zaman <kzaman@icddrb.org>
Cc: Masuma Hoque <masuma.hoque@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Asma Binte Aziz <asma.aziz@icddrb.org>
Subject: nOPV2 + bOPV trial protocol

Dear Dr. Zaman,

Attached is an updated nOPV2 + bOPV trial protocol.

The following items need to be added, but otherwise I think this is ready for RRC submission.

1. Translated consent form
2. Second external reviewer form

Please let me know if there’s anything else you need from our side.
Best wishes,
Amanda

From: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) [mailto:dvi5@cdc.gov]
Sent: Monday, June 22, 2020 8:12 AM
To: Dr. K. Zaman <kzaman@icddrb.org>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An,

Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

Dear Zaman,
I approve the submission to RRC.

Best regards,
Abhijeet

From: Dr. K. Zaman <kzaman@icddrb.org>
Sent: Saturday, June 20, 2020 2:04 PM
To: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: nOPV2 + bOPV trial protocol

Dear All,

My sincere thanks to you all for reviewing the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV". We need your approval for submission to our Research Review Committee.

Requesting to write "Approve for submission".

Kindest regards

Zaman

Dr. K. Zaman
Senior Scientist, Enteric and Respiratory Infections
Infectious Diseases Division

From: Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) [mailto:bex4@cdc.gov]
Sent: Monday, June 22, 2020 6:11 PM
To: Dr. K. Zaman <kzaman@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

Dear Zaman,
I approve for submission.
Best regards,

Cindi

From: Dr. K. Zaman <kzaman@icddrb.org>
Sent: Saturday, June 20, 2020 2:04 PM
To: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: nOPV2 + bOPV trial protocol

Dear All,

My sincere thanks to you all for reviewing the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV". We need your approval for submission to our Research Review Committee.

Requesting to write "Approve for submission".

Kindest regards

Zaman

Dr. K. Zaman
Senior Scientist, Enteric and Respiratory Infections
Infectious Diseases Division

From: Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) [mailto:cge3@cdc.gov]
Sent: Monday, June 22, 2020 7:01 PM
To: Dr. K. Zaman <kzaman@icddrb.org>
Subject: RE: nOPV2 + bOPV trial protocol

Dear Zaman
I approve for submission.

Best Regards
Conchi

From: Dr. K. Zaman <kzaman@icddrb.org>
Sent: Saturday, June 20, 2020 2:04 PM
To: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: nOPV2 + bOPV trial protocol

Dear All,

My sincere thanks to you all for reviewing the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV". We need your approval for submission to our Research Review Committee.

Requesting to write "Approve for submission".

Kindest regards

Zaman

Dr. K. Zaman
Senior Scientist, Enteric and Respiratory Infections
Infectious Diseases Division

From: An, Qian (CDC/DDPHSIS/CGH/GID) [mailto:fei8@cdc.gov]
Sent: Wednesday, June 24, 2020 12:39 AM
To: Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Dr. K. Zaman <kzaman@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

Dear Dr. Zaman,

I approve for the submission.
Thanks,
Qian

From: Pallansch, Mark A. (CDC/DDID/NCIRD/OD) [mailto:map1@cdc.gov]
Sent: Sunday, June 21, 2020 10:54 PM
To: Dr. K. Zaman <kzaman@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

I approve for submission.

MAP

From: Dr. K. Zaman <kzaman@icddrb.org>
Sent: Saturday, June 20, 2020 2:04 PM
To: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD)

<mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: nOPV2 + bOPV trial protocol

Dear All,

My sincere thanks to you all for reviewing the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV". We need your approval for submission to our Research Review Committee.

Requesting to write "Approve for submission".

Kindest regards

Zaman

Dr. K. Zaman
Senior Scientist, Enteric and Respiratory Infections
Infectious Diseases Division

From: Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>
Sent: Tuesday, June 23, 2020 2:07 PM
To: Dr. K. Zaman <kzaman@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

Dear Dr Zaman
I approve for submission

Best
SW

Steven Wassilak MD
Global Immunization Division, CDC, H24-2
Tel: +1 404 639 1867
Mob: +1 770 331 7695
email: swassilak@cdc.gov or sgw1@cdc.gov

From: Oberste, Steve (CDC/DDID/NCIRD/DVD) [mailto:mbo2@cdc.gov]
Sent: Sunday, June 21, 2020 7:18 AM
To: Dr. K. Zaman <kzaman@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

Zaman:

I approve for submission.

Steve

From: Dr. K. Zaman <kzaman@icddrb.org>
Sent: Saturday, June 20, 2020 2:04 PM
To: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>; Snider, Cynthia J. (CDC/DDPHSIS/CGH/GID) <bex4@cdc.gov>; Estivariz, Concepcion (Conchi) (CDC/DDPHSIS/CGH/GID) <cge3@cdc.gov>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Pallansch, Mark A. (CDC/DDID/NCIRD/OD) <map1@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Oberste, Steve (CDC/DDID/NCIRD/DVD) <mbo2@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>
Subject: nOPV2 + bOPV trial protocol

Dear All,

My sincere thanks to you all for reviewing the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV". We need your approval for submission to our Research Review Committee.

Requesting to write "Approve for submission".

Kindest regards

Zaman

Dr. K. Zaman
Senior Scientist, Enteric and Respiratory Infections
Infectious Diseases Division

From: Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) [mailto:wxx3@cdc.gov]
Sent: Tuesday, June 23, 2020 10:36 PM
To: Dr. K. Zaman <kzaman@icddrb.org>; An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>
Cc: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol

Dear Dr. Zaman,
I approve for submission.
Thank you,

J. Sunshine Lickness, MPH | Surveillance, Innovation and Research Team – Global Immunization Division – Center for Global Health – US Centers for Disease Control and Prevention | Tel (office): 404-639-8039 | Mobile: 678-519-8389 | E-mail: wxx3@cdc.gov

From: Dr. K. Zaman <kzaman@icddrb.org>
Sent: Tuesday, June 23, 2020 12:32 PM
To: An, Qian (CDC/DDPHSIS/CGH/GID) <fei8@cdc.gov>; Wassilak, Steve (CDC/DDPHSIS/CGH/GID) <sgw1@cdc.gov>; Lickness, Jacquelyn S. (CDC/DDPHSIS/CGH/GID) <wxx3@cdc.gov>

Cc: Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: RE: nOPV2 + bOPV trial protocol
Importance: High

Dear All,

I am not sure if I missed your mail.

My sincere thanks to you all for reviewing the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV".

We need your approval for submission to our Research Review Committee.

Requesting to write "Approve for submission".

Kindest regards

Zaman

Dr. K. Zaman
Senior Scientist, Enteric and Respiratory Infections
Infectious Diseases Division

From: Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>
Sent: Monday, November 23, 2020 9:14 AM
To: Patel, Jaymin (CDC/DDPHSIS/CGH/GID) <isr0@cdc.gov>; Anstadt, Jennifer (CDC/DDID/NCIRD/DVD) <yrq1@cdc.gov>; Burns, Cara C. (CDC/DDID/NCIRD/DVD) <zqd1@cdc.gov>; Ananda Bandyopadhyay <Ananda.Bandyopadhyay@gatesfoundation.org>; Jillian Gauld <jgauld@idmod.org>; Mike Famulare <mfamulare@idmod.org>
Cc: Dr. K. Zaman <kzaman@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: Approval of nOPV2-bOPV protocol from

Dear all,

Thanks very much for your contributions to the protocol "Immunogenicity of novel monovalent oral poliovirus vaccine type 2 (nOPV2) with and without bivalent OPV". Revised versions of the protocol are attached.

Icddr,b needs your approval for submission to their Research Review Committee. If you approve, please respond to this email with "**Approve for submission**".

Best wishes,
Amanda

From: Patel, Jaymin (CDC/DDPHSIS/CGH/GID) <isr0@cdc.gov>
Sent: Monday, November 23, 2020 9:17 AM
To: Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>
Subject: RE: Approval of nOPV2-bOPV protocol from

Approve for submission

Jaymin Patel, PhD, MPH
LCDR, U.S. Public Health Service
Epidemiologist, Global Immunization Division
Centers for Disease Control and Prevention
Office: (404) 718-5539 | Cell: (252) 347-1908
Email: isr0@cdc.gov

Sent: Monday, November 23, 2020 10:48 AM
To: Ananda Bandyopadhyay <Ananda.Bandyopadhyay@gatesfoundation.org>; Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>; Patel, Jaymin (CDC/DDPHSIS/CGH/GID) <isr0@cdc.gov>; Burns, Cara C. (CDC/DDID/NCIRD/DVD) <zqd1@cdc.gov>; Jillian Gauld <jgauld@idmod.org>; Mike Famulare <mfamulare@idmod.org>
Cc: Dr. K. Zaman <kzaman@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: RE: Approval of nOPV2-bOPV protocol from

Thanks Amanda,

Approve for submission.

Best,
Jenn

From: Ananda Bandyopadhyay <Ananda.Bandyopadhyay@gatesfoundation.org>
Sent: Monday, November 23, 2020 10:35 AM
To: Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>; Patel, Jaymin (CDC/DDPHSIS/CGH/GID) <isr0@cdc.gov>; Anstadt, Jennifer (CDC/DDID/NCIRD/DVD) <yrq1@cdc.gov>; Burns, Cara C. (CDC/DDID/NCIRD/DVD) <zqd1@cdc.gov>; Jillian Gauld <jgauld@idmod.org>; Mike Famulare <mfamulare@idmod.org>
Cc: Dr. K. Zaman <kzaman@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: RE: Approval of nOPV2-bOPV protocol from

Approve for submission.

Best wishes,
Ananda

From: Jillian Gauld <jgauld@idmod.org>
Sent: Thursday, November 26, 2020 11:30 AM
To: Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>; Anstadt, Jennifer (CDC/DDID/NCIRD/DVD) <yrq1@cdc.gov>; Ananda Bandyopadhyay <Ananda.Bandyopadhyay@gatesfoundation.org>; Patel, Jaymin (CDC/DDPHSIS/CGH/GID) <isr0@cdc.gov>; Burns, Cara C. (CDC/DDID/NCIRD/DVD) <zqd1@cdc.gov>; Mike Famulare <mfamulare@idmod.org>
Cc: Dr. K. Zaman <kzaman@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: RE: Approval of nOPV2-bOPV protocol from

Hi Amanda,

Apologies for catching this in the 11th hour, but can we add the following clarification (bolded) to the power calculation simulation statement on page 32?

"Using our nOPV2 simulation model, we estimate prevalence and 95% CI of shedding to be 53% among vaccine recipients (46.4 – 59.5%) and 23% (17.8 – 28.8%) among siblings **under the age of 5**.

Otherwise, approve for submission and happy holidays!

Jillian

From: Mike Famulare <mfamulare@idmod.org>
Sent: Monday, November 30, 2020 9:57 AM
To: Jillian Gauld <jgauld@idmod.org>; Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>; Anstadt, Jennifer (CDC/DDID/NCIRD/DVD) <yrq1@cdc.gov>; Ananda Bandyopadhyay <Ananda.Bandyopadhyay@gatesfoundation.org>; Patel, Jaymin (CDC/DDPHSIS/CGH/GID) <isr0@cdc.gov>; Burns, Cara C. (CDC/DDID/NCIRD/DVD) <zqd1@cdc.gov>
Cc: Dr. K. Zaman <kzaman@icddrb.org>; Masuma Hoque <masuma.hoque@icddrb.org>; Anand, Abhijeet (CDC/DDPHSIS/CGH/GID) <dvi5@cdc.gov>
Subject: Re: Approval of nOPV2-bOPV protocol from

Hi Ananda,

I approve with Jillian's correction.

Mike

From: Burns, Cara C. (CDC/DDID/NCIRD/DVD) <zqd1@cdc.gov>
Sent: Thursday, December 3, 2020 12:59 PM
To: Wilkinson, Amanda (CDC/DDPHSIS/CGH/GID) <lxq6@cdc.gov>
Subject: RE: Approval of nOPV2-bOPV protocol from

Amanda,
I approve of the revised protocol for submission.

Thanks,

Cara

Cara C. Burns, PhD
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