WHO Technical Report Series, No. 800, 1990

SUMMARY PROTOCOL FOR POLIOMYELITIS VACCINE (ORAL)

Based on Requirements for Biological Substances No. 7 revised 1989

Name and address of manufacturer

_____

_____

Proprietary name

_____

Lot No. of vaccine trivalent blend

_____

Filling lot No.

_____

No. of filled containers

_____

Date on which last determination of virus concentration was started

_____

Shelf-life

_____

Expiry date

_____

Nature and concentration of stabilizer

_____

Volume of vaccine container

_____

Volume of human dose (in drops and/or ml)

_____

Prescribed virus concentration per human dose Type 1

_____

Type 2

_____

Type 3

_____

Nature of any antibiotics present in vaccine and amount per human dose

_____

Production cell tissue

_____

Type 1 *Type 2* *Type 3*

Bulk Nos. of monovalent bulk suspensions blended in trivalent vaccine _____

_____ _____

Date of approval of protocol indicating compliance with Requirements for Biological Substances No. 7 _____

_____ _____

The following sections are intended for the recording of the results of the tests performed during the production of the vaccine, so that the complete document will provide evidence of consistency of production; thus if any test has had to be repeated, this must be indicated. Any abnormal result must be recorded on a separate sheet.

If any cell lot or virus harvest intended for production was rejected during the control testing, this should also be recorded either in the following sections or on a separate sheet.

PRODUCTION IN CELL LINES

Control of source materials

Cell seed

Origin and short history of cell seed

_____

Authority that approved cell seed

_____

Total number of ampoules of cells stored

_____

Method of preparation of cell seed in terms of number of freezes and efforts made to ensure that a homogeneous population is

dispersed into the ampoules

_____

Passage level (or No. of population doublings) of cell seed

_____

Storage conditions

_____

Percentage of total cell-seed ampoules tested

_____

Growth characteristics

_____

Morphological characteristics

_____

Immunological markers

_____

Cytogenetic data

_____

Biochemical data

_____

Results of other identity tests

_____

Results of tests for adventitious agents

_____

Results of tests for tumorigenicity

_____

Capacity for interferon production (if determined)

_____

Viral susceptibility

_____

Manufacturer's working cell bank (MWCB)

Date MWCB was established

_____

Quantity of cells stored

_____

Passage level of MWCB

_____

Storage conditions

_____

Percentage of total MWCB ampoules tested

_____

Results of identity tests

_____

Results of tests for adventitious agents

_____

Results of tests for tumorigenicity

_____

Virus strains

Reference No. of seed lot

_____

Seed virus strain

_____

Substrate used for preparing seed lot

_____

Date(s) of satisfactory test(s) for freedom from adventitious agents

_____

Sterility test

_____

Identity test

_____

Virus concentration

_____

Test for consistency of virus characteristics

Neurovirulence test in monkeys

_____

Result of blood serum test in monkeys prior to inoculation

_____

Date of inoculation of seed lot

_____

Number and species of control

_____

monkeys inoculated test

Quantity ($CCID_{50}$) inoculated in each test monkey

Number of monkeys surviving control

---

without specific symptoms test

Result of histopathological control

---

examination (specify any test

---

abnormal findings)
Test *in vitro*

Control of vaccine production
Control of cell cultures
Ratio of control to production cell cultures or control cultures as proportion of production cell cultures

---

Period of observation of cultures

Ratio or proportion of cultures discarded for nonspecific reasons

---

Results of observation

Tests for haemadsorbing viruses:
Methods

Results

Tests for adventitious agents:

Methods

_____

Results

_____

Identity test

_____

Cell cultures for vaccine production
Tests for adventitious agents:
Methods

_____

Results

_____

Test for bacteri, fungi and mycoplasmas:
Methods

_____

Results

_____

Control of single harvests
Volume harvested

_____

Date of sampling

_____

Tests of neutralized single harvests for adventitious agents:
Methods

_____

Results

_____

Sterility tests:
Methods

_____

Results

_____

Control of bulk suspension
Dates of filtration of bulk

_____

Porosity of filters used

_____

Date of sampling

_____

Identity test:
Method

_____

Result

_____

Virus concentration:
Method

_____

Result

_____

Tests for consistency of virus characteristics
Neurovirulence tests in monkeys:
Species of monkey inoculated

_____

Dose of vaccine virus injected

_____

No. of “valid” monkeys inoculated with
test sample

_____

No. of positive monkeys observed

_____

Reference preparation

_____

Dose of reference virus injected

_____

No. of "valid" monkeys inoculated with reference

_____

No. of positive monkeys observed

_____

Mean Lesion score of test sample

_____

Mean Lesion Score of reference

_____

In vitro rct/40 marker test:

Reduction of titre of bulk sample

_____

Reduction of titre of negative reference

_____

Reduction of titre of positive reference

_____

Result

_____

Additional in *vitro* marker tests:

Test method

_____

Details

_____

Date of test

_____

Result

_____

Final bulk

Preparation of trivalent bulk:

Type 1 *Type 2* *Type3*

Lot No. of trivalent blend _____ _____ _____

Monovalent bulks in blend _____ _____ _____

Volume in blend _____

_____ _____

Nature and volume of stabilizer _____

_____ _____

Nature and volume of diluent _____

_____ _____

Total volume of blend _____

_____ _____

Sterility test:

Date

_____

Media used

_____

Result

_____

Filling and containers:

Total volume of final filling

_____

Date of final filling

_____

No. of vials filled

_____

Test on final filling

_____

Control tests on final product

Identity test

Methods

_____

Result

_____

Tests for bacteria and fungi

Number of containers examined

_____

Method

_____

Result

_____

Virus titration
Identity of reference preparations

_____

Titre of individual virus types

_____

Batch Nos. of antiserum used in test

_____

Date of test

_____

	Vaccine	*Reference*
Results:		
Type 1	_____	_____
Type 2	_____	_____
Type 3	_____	_____

Stability
Method

_____

Result

_____

PRODUCTION IN MONKEY KIDNEY-CELL CULTURES

Control of vaccine production
Monkey species used for production

_____

Quarantine batch No.

_____

Percentage of monkeys surviving quarantine period

_____

Nature and concentration of antibiotics used in production cell culture maintenance medium

_____

Tests for antibodies to simian immuno-deficiency virus and SV40:
Methods

_____

Results

_____

Production details:
Production monkey No.

_____

Date of trypsinizing

_____

No. of cultures prepared

_____

Production cell cultures:
Virus seed lot No.

_____

Virus infectivity/cell ratio

_____

No. of cultures inoculated

_____

Date of inoculation

_____

Date of harvest

_____

Temperature of incubation

_____

Period of incubation

_____

No. of cultures harvested

_____

Tests on pooled supernatant fluids:

Date of sampling from production cell cultures

_____

Tests for adventitious agents

_____

Volume tested/cell culture type

_____

Observation period

_____

Date of completion of tests

_____

Result

_____

Date of sampling from cell cultures inoculated with the pooled fluid

_____

Tests for adventitious agents:

Volume tested/cell culture type

_____

Date of completion of tests

_____

Results

_____

Tests in rabbit kidney-cell cultures:

Volume tested

_____

Date of completion of test

_____

Result

_____

Test of control cell cultures:
Ratio of control to production cell cultures or control cell cultures as proportion of production cell cultures

_____

Period of observation of cultures

_____

Ratio or proportion of cultures discarded for nonspecific reasons

_____

Result

_____

Tests for other adventitious viruses:
Methods

_____

Results

_____

Tests for other adventitious agents:
Methods

_____

Results

_____

Control of single harvests

Volume harvested

_____

Date of sampling

_____

Tests for bacteria, fungi, and mycoplasmas:
Result

_____

Tests on neutralized single harvests in
monkey kidney-cell and human cell

_____

cultures:
Batch No. of antiserum used

_____

Volume tested

_____

Date of starting primary cell culture tests

_____

Period of observation

_____

Date of sampling cell culture fluids

_____

Period of observation

_____

Date of completion of test

_____

Result

_____

Control of bulk suspension
Date of filtration of bulk

_____

Porosity of filters used

_____

Date of sampling

_____

Tests in rabbits:
No. and weight of animals

_____

Date of inoculation

_____

Results of injection

_____

Quantity injected

_____

Results (survival Nos., etc.)

_____

Tests in guinea-pigs:
No. and weight of animals

_____

Date of inoculation

_____

Results of injection

_____

Quantity injected

_____

Results (survival Nos., etc.)

_____

Certification by the manufacturer

Name of head of production (typed)

_____

Certification by person from the control laboratory of the manufacturing company taking overall responsibility for the production and control of the vaccine

I certify that lot No…. of poliomyelitis vaccine (oral), whose number appears on the label of the final container, meets all national requirements and satisfies Part A of the Requirements for Biological Substances No. 7, revised 1989, and (if applicable) addenda 19… for poliomyelitis vaccine (oral).

Signature

_____

Name (typed)

_____

Date

_____