rivm

# Poliomyelitisvaccin

RVG 17642

Periodic Safety Update Report

01/01/1997 – 31/12/2000

rivm
research for
man and environment

RIJKSINSTITUUT VOOR VOLKSGEZONDHEID EN MILIEU
NATIONAL INSTITUTE OF PUBLIC HEALTH AND THE ENVIRONMENT

# RIVM-Poliomyelitis vaccine

**inactivated – trivalent**

Periodic Safety Update

01/01/1997-31/12/2000

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FOLIO 1228

## Contents



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# 1. Introduction

This is the first safety update on inactivated plain poliomyelitis vaccine, produced by RIVM. It covers the observation period of January 1997 to December 2000.

Inactivated trivalent poliomyelitis vaccine (IPV) produced by RIVM is a suspension of purified and formalin inactivated poliomyelitis virus containing three types of poliomyelitis virus virus: type1: strain Mahoney; type 2: strain MEF 1 and type 3: strain Saukett. The company standard product information is given in Appendix 1.

The vaccine contains per dose of 1 ml for subcutaneous injection:

| | | |
|---|---|---|
| inactivated poliovirus type 1 | : | 40 DU |
| type 2 | : | 8 DU |
| type 3 | : | 32 DU |
| 2-phenoxyethanol | : | 5 mg |
| formaldehyde | : | 0,025 mg |

# 2. World-wide Market Authorization Status

RIVM-IPV has been approved as vaccine for active immunisation against poliomyelitis in 8 countries (Appendix 2). RIVM-IPV was the last time registered in the Netherlands in 1991.

# 3. Update on Regulatory or Manufacturer Actions Taken for Safety Reasons

In the period of January 1997 to December 2000, there have been no license application rejections , product suspensions or restrictions for safety reasons.

# 4. Changes to Referenced Safety Information

The company core safety information of RIVM-IPV (based on the standard product information authorised by the Dutch regulatory authorities in 1991) did not have to be amended for safety reasons during the 4 year period of this review.

# 5. Patient Exposure

## 5.1 Clinical Trials

RIVM-IPV vaccine was used in 1997 in Norway in an open, randomised, controlled, prospective study comparing IPV-VERO and IPV-MK given as primary vaccination at age of 6, 8 and at age of 12 months (immunogenicity, reactogenicity and safety). 74 infants were

included in the study (24 randomised to IPV-MK group). The adverse events reported during this study were:

*Table 1. Adverse events reported the first three days after 1., 2. and 3. dose IPV-Vero or IPV-MK given at age 6, 8 and 16 months. Some infants had more than one adverse event. (*S Sandbu, M Nokleby, O. Helland, L.B. Flugstrud, H.C.Rumke. IPV-VERO vaccine gives high antibody response and is well tolereted in infants. ESPID, 19.annual meeting, Istanbul 2001.*)*

| Adverse events | 1. dose | | 2. dose | | 3. dose | | Total |
|---|---|---|---|---|---|---|---|
| N= | Vero 40 | *MK* 21 | Vero 38 | *MK* 21 | Vero 38 | *MK* 19 | 177 |
| Redness | 2 | 3 | | 1 | 3 | 2 | 11 |
| Tenderness | 3 | 1 | 1 | | 3 | | 8 |
| *Infants (%) with local reactions* | *5 (13)* | *4 (19)* | *1 (3)* | *1 (5)* | *4 (11)* | *2 (11)* | *17 (6)* |
| Fussiness, uneasiness etc. | 13 | 4 | 7 | 2 | 5 | | 31 |
| Less active | | | | | | | |
| Eating less | 1 | | | | | | 1 |
| Crying | 3 | 2 | | 1 | | | 6 |
| Vomiting | 1 | | | | 1 | | 2 |
| Diarrhoea | 1 | | | 1 | | | 2 |
| Fever ≥ 38 °C | 2 | | 1 | 1 | 2 | 2 | 8 |
| Rash | 1 | | | | 3 | | 4 |
| *Infants (%) with systemic adverse event* | 14 (35) | 6 (29) | 8 (21) | 3 (14) | 7 (18) | 2 (11) | 40 (23) |

The adverse events were mostly mild. No participant was withdrawn because of adverse events. More adverse events were reported after the first than after the second or third vaccine dose.

No local reaction lasted for more than two days. Only one child on IPV-MK had local swelling and redness >2,5 cm after first dose. There were no prolonged periods of screaming or other severe reactions. Most of the infants with systemic adverse events were described as fussy, restless, silent, fretful, more sleepy or less sleepy than usual. A few had periods of crying. One infant had diarrhoea for 6 weeks after 1, vaccine dose, regarded as unrelated to the vaccine. Two infants had fever lasting for three days and one had periods of restlessness unrelated to the vaccine. All other events were short lasting, (<1hour-2 days). All subjects recovered completely.

## 5.2 Market Experience and Total Exposure from January 1997 – December 2000

The total patient exposure can be calculated from the total world –wide sales in the period of January 1997 to December 2000 (table 2).

*Table 2. Sales Volume in the period January 1997 to December 2000*

**Sales volume January 1997 - December 2000**

| Year | All doses |
|---|---|
| 1997 | 597.024 |
| 1998 | 1.986.970 |
| 1999 | 2.302.922 |
| 2000 | 1.277.615 |
| Total | 6.164.531 |

It is estimated that up to 6.164.531 injections of RIVM-IPV in the period of January 1997 to December 2000 were administered world-wide to children and adults.
RIVM-IPV is used to a very limited extent in the Netherlands (4000-5000 per year). There were no adverse events reported during the period of PSUR. In the Netherlands IPV is mostly used in combined DTP-IPV and DT-IPV vaccine.

## 6. Presentation of Individual Case Histories

### 6.1 General Considerations

During the 4 year observation period of January 1997 to December 2000, 66 adverse events associated with the use of RIVM-IPV in 66 subjects have been reported spontaneously from world-wide sources. (Of these reported adverse events, 21 were considered serious.)

### 6.2 Analysis of individual case histories

During the period of this of this safety report, LVO-KO has received 21 reports which were concerned serious adverse events by nature , severity, and/or because of hospitalisation (see table 3 and listing below).

*Table 3. Number of reported serious adverse events 1997-2000*

| | | causality | | | | | |
|---|---|---|---|---|---|---|---|
| diagnosis | hospital stay | certain | probable | possible | improbable | unclassifiable | total |
| convulsions | 1 | - | - | - | 3 | - | 3 |
| respiratory infections | 2 | - | - | - | 2 | - | 2 |
| facial paralysis | 2 | - | - | - | 3 | - | 3 |
| renal failure | 1 | - | - | - | 1 | - | 1 |
| TIA | 1 | - | - | - | 1 | - | 1 |
| urticarial rash illness | 2 | - | - | 2 | - | - | 2 |
| ITP | - | - | - | 1 | - | - | 1 |
| arthrosis/arthritis | 1 | - | - | - | 1- | - | 1 |
| AHOI | 1 | - | - | - | 1 | - | 1 |
| fever | 1 | - | - | - | 1 | - | 1 |
| meningeal irritation | 1 | - | - | - | 1 | - | 1 |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| low back pain | 1 | - | - | - | 1 | - | 1 |
| psoriasis | 1 | - | - | - | 1 | - | 1 |
| atrioventricular block | - | - | - | - | 1 | - | 1 |
| "undefined" | 1 | - | - | - | - | 1 | 1 |
| total | 16 | - | - | 3 | 17 | 1 | 21 |

Only three events were considered possibly related to IPV or one of the other given vaccines . Once a (definite) diagnosis could not be made and the event was regarded unclassifiable.

RIVM-97.919 (Norway)

A 7 year old girl received her probably fourth dose of RIVM-IPV (Lot No 752G). Approximately 12 hours later, while sleeping under a blanket in the sitting room, she had tonic clonic seizures, probably of short duration, without post ictal stupor. She did not have fever.

**Causality:** improbable.

RIVM-97.920 (Norway)

A 22 year old woman received RIVM-IPV and DT "SBL Vaccin" simultaneous on 08.09.1997. The same evening she had a fever, headache, neck- and back pain and photophobia. She was hospitalised. She did not have meningitis, and other serious conditions were excluded. The meningeal irritation lasted for more than one month, during which time she was unwell and complained of dizziness.

**Causality:** improbable.

RIVM-97.921 (Norway)

A 42 year old man received RIVM-IPV (Lot No 750C) with Engerix-B, Havrix and DT vaccine simultaneous on 13.01.1997. Six days after vaccination, he discovered petechiae on his lower extremities. There were also petechiae around his wrists and a couple in his upper pharynx. The diagnosis was idiopathic trombocytopenic purpura, and he was being treated with prednison.

**Causality:** possible; (causal relation can not be excluded with either of the vaccines )

RIVM-98.836 (Germany)

A 59 year old female patient received a single dose of RIVM-IPV (Lot No 022061) together with Td-pur (Lot No002061) on 28. 03. 1998 Eight days later she developed Quincke's oedema. 12 days after the vaccination, she developed a sensation of coldness and tenseness of her left leg and pain in the lumbar spine. The patient was hospitalised.

**Causality:** improbable.

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RIVM-98.1124 (Germany)

A girl (age unknown) was vaccinated with RIVM-IPV (Lot No 024081) in the upper arm on 09.11.1998. 5 minutes later, the girl complained of chills. 4 hours post vaccination, the patient suffered from fever (39,5° C) and had cyanosis of lips. Emotional lability and uncertain gait were reported. She was hospitalised the same day. Infection of upper respiratory system was diagnosed.

**Causality:** improbable.

RIVM-98.1212 (Germany)

A 29 old woman was vaccinated with RIVM-IPV (Lot No 022041) s.c. and Td-pur (Lot No 002081) simultaneously on 06.02.1998. The next day she experienced small itching skin eruptions which confluent the second day after vaccination. 18 days after vaccination , dermatological examination showed psoriasis of an acute exanthemic type on both backs of the hands, the ventral thighs, the abdomen and extremities.

**Causality:** improbable, according to current scientific knowledge.

RIVM-98.837 (Germany)

A two year old girl received a single dose of RIVM-IPV (Lot No 022033) s.c. on 13. 03. 96. During the following night, the girl was excited, moved convulsively and vomited two times. The girl was hospitalised. On admission the child was restless and experienced right-sided facial convulsion and clonic convulsion of the left hand and the left leg. Reflexes were absent, temperature was normal on admission (except of increase of 38,4° C for 12 hours). Blood gases showed a metabolic and respiratory acidosis. Neonatal convulsions and the state of postnatal cerebral haemorrhage are anamnestically known. EEG was pathological and MRI showed small cerebral scars at the right lateral ventricle. The symptoms were treated with Diazepam and Rivotril.

**Causality:** improbable.

RIVM-98.1160 (Germany)

A 13 year old girl received her first RIVM-IPV (Lot No 022051) s.c. and third dose MMRVax (Lot No 109011C) s.c. into the upper arm 09. 07. 1998. Two days later, right-sided incomplete peripheral facial paralysis was reported. The girl was hospitalised. Family history was positive for idiopathic peripheral facial paralysis. The girl recovered.

**Causality:** improbable.

RIVM-98.1137 (Germany)

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A 66 year old female suffered about 14 days after vaccination with RIVM-IPV and Td-pur (Lot No and vaccination date not known) asthenia and malaise. 4 weeks after vaccination she had acute renal failure. By the time of the report ( December 1998) the condition of the patient had stabilised.

**Causality:** improbable.

RIVM-98.1159 (Germany)

A 67 female was vaccinated with RIVM-IPV for the second time i.m on 25. 09. 1998 Postvaccinal (interval?) she complained about dyspnea on exertion. Atrioventricular block III/II (Type Mobitz) was diagnosed; medically history of arterial hypertension.

**Causality:** improbable.

RIVM-98.1211 (Germany)

A17 year old male received RIVM-IPV (Lot No 022041) s.c. and Td-pur (Lot No 001051) i.m. simultaneously on 31.01.1998. 3 days later he had fever, serous rhinitis and tenderness of a paranasal sinus. He was hospitalised with 40° C fever and lethargy. He was treated with Penicillin, infusions and Novalgin. 6 days later he was discharged without complaints. The symptoms were interpreted as fever caused by an unspecified virus infection. In medical history: 3 weeks before vaccination the patient had a febrile infection with cough and purulent bronchitis.

**Causality:** improbable.

RIVM-99.0196 (Germany)

A 31 year old man was vaccinated with Adsorbed Diphtheria Vaccine Behring for adults (Lot No not known) on 21.01 1999. and with RIVM-IPV (Lot No not known) on 28.011999. On 29.01.1999. the patient experienced a flu-like syndrome and paresthesia of the left half of his face. Two days later, he could not close his left eye, had difficulties in whistling and also felt weakness of both arms. The patient was hospitalised. On 01.02.1999, the analysis of liquor. revealed an increase in the cell count (18/3 lymphocytic leukocytes) and an oligoclonal gammaglobulinopathy of intrathecal IgG-synthesis.
On 04.03.1999. the facial nerve paralyse had almost completely recovered

**Causality:** improbable.

RIVM-99.0136 (Germany)

A 60 year old male patient, was vaccinated with RIVM-IPV (Lot No not known) and Diphtheria vaccine (Lot No not known) simultaneous i.m. (M. deltoideus) on 08.01.1999. Two days later, the patient suffered from high fever and was hospitalised.

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Diagnosis; "Allergic reaction on right gluteus" (on a scar after total prosthetic replacement on 11.11.1998).

**Causality:** improbable.

RIVM-99.0549 (Germany)

A 8 months old girl was vaccinated with RIVM-IPV and Diphtheria and Tetanus Vaccine from Merieux simultaneously. 2 and 6 days after vaccination, she had relapsing non-febrile convulsions. Lumbar puncture findings were normal. The girl recovered.

**Causality:** improbable.

RIVM-99.1347 (Germany)

A 52 year old male patient with known diabetes mellitus, received his first IPV-Polio (Lot No and producer unknown).on 28.10.1998. 22 days later, the patient noticed a right sided facial paresis and ataxia. The CSF shows lymphocytic pleocytosis (1432/3). The preliminary diagnosis of neuro-borreliosis was made.

**Causality:** improbable.

RIVM-00.1300 (Germany)

A 49 year old female was vaccinated with RIVM-IPV (Lot No 028012) and Td-Merieux simultaneous on 31. 08 1999. 22 days after vaccination, she complained about vision disturbance and speech disorder (sensoric and motoric aphasia), hemiparesis, paraesthesia and deafness. Almost all symptoms disappeared within 30 minutes. A relapse occurred in the evening of the same day. The symptoms were interpreted as transient ischemic attack. At the time of reporting (17. 01. 2000), the patient is still complaining about slight paresthesia of the right hand and forearm. Cranial MRI, CT, transcranial duplex sonography were without relevant abnormalities.

**Causality:** improbable.

RIVM-00.1301 (Germany)

A 16 year old female patient was vaccinated simultaneously with RIVM-IPV ( Lot No 031011) and Gen H-B-Vax ( Lot No 668011) into the musculus deltoideus. After 12 hours she developed pustules, papules, redness (local?), nettle rash, shivering attacks, fever and malaise. The patient was admitted to the hospital. At the time of report (19.01.2000) the patient had recovered and been discharged from the hospital.

**Causality:** possible.

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RIVM-00.1302 (Germany)

A 68 year old female patient was vaccinated with RIVM-IPV (Lot No unknown) for the first time on 29.09.1999. 4 days later she had swelling of fingers and back of both hands. An underlying arthrosis of dig.I (left hand) and dig.II (right hand ) treated with Prednisolon 7.5 mg/day and Paracetamol is known. For further investigations she was hospitalised on 26.10.1999. Rheumatoid arthritis was suspected.

**Causality:** improbable.

RIVM-00.1303 (Germany)

A patient (no further information given) was simultaneously vaccinated with inactivated polio vaccine (manufacturer unknown) and Td-pur (in January 2000?). 4 hours later the patient experienced pain in limbs, nephralgia, face swelling and exhaustion. The symptoms improved after cortisone was given. The patient was hospitalised. At the time of reporting (10.02.2000) the patient still experienced face swelling and exhaustion.

**Causality:** unclassifiable (insufficient data)

RIVM-00.1304 (Germany)

A 2 year old boy was vaccinated on 14.10.1999. with RIVM-IPV (Lot no. B030021; no further information given). The next day fever and upper airway infection ware reported and three days later obstructive bronchitis was diagnosed. 22 days after vaccination the patient suffered from haemorrhagic oedema on both legs that started with intense feeling of pain and cried uncontrollably for hours. He was hospitalised for 6days (no specific therapy; no hematuria. On 15.11.1999 the patient had nearly recovered.

**Causality:** improbable.

RIVM-00.1304 (Germany)

A 61 year old woman was vaccinated for the first time with RIVM-IPV (Lot No 030021) in her right upper arm on 13.03.2000. Additionally she received a Td vaccine (manufacture unknown). Redness, swelling, maculopapular exanthema and urticaria occurred on the day of vaccination on both arms, later also on both feet, hands and the whole body, especially on the upper thighs.. She was hospitalised from 23. to 31.03. 2000 (insufficient data for erythema exudativum multiforme.

**Causality:** possible; ( causal relation cannot be excluded with either vaccine )

## 6.3 Summary tabulatios

45 non-serious adverse events were reported (see table 4.)

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*Table 4. Number of reported non-serious adverse events 1997 – 2000 (of which assessed as adverse reaction)*

| Body System<br>*Adverse Event* | Non-serious adverse events (with possible causal relation) |
|---|---|
| **Administration site conditions** | |
| Injection site reaction | 1 (-) |
| Injection site inflammation | 13 (13) |
| *subtotal* | **14 (13)** |
| **General disorders** | |
| Fever | 5 (3) |
| Myasthenia | 1 (-) |
| Headache | 1 (1) |
| Crying | 1 (1) |
| Malaise | 1 (1) |
| Myalgia | 1 (-) |
| Coxitis fugax | 1 (-) |
| False positive laboratory test | 1 (-) |
| *subtotal* | **12 (6)** |
| **Skin & subcutaneous disorders** | |
| Rash | 10 (5) |
| *subtotal* | **10 (5)** |
| **Gastro-intestinal disorders** | |
| Gastro-enteritis | 1 (-) |
| Nausea | 1 (-) |
| *subtotal* | **2 (-)** |
| **Vascular disorders** | |
| Faint | 3 (3) |
| Hypotension | 1 (1) |
| Hypertension | 1 (-) |
| Paroxysmal event | 1 (-) |
| *subtotal* | **6 (4)** |
| **Respiratory, thoracic & mediastinal disorders** | |
| Respiratory infection | 1 (-) |
| *subtotal* | **1 (-)** |
| Total | **45 (28)** |

## 7. Studies

### 7.1 Newly Analyzed Company sponsored studies

In the period of PSUR, RIVM-IPV vaccine was used in 1997 in Norway in an open, randomized, controlled, prospective study. The reported adverse events were mild and short lasting and did not cause any child to be withdrawn from the study. More adverse events were reported after the first than after the second or third vaccine dose. Some of the systemic events (fever and rash, diarrhea etc) obviously had other causes than the vaccine. In a few cases the parents reported other reason for fever ( a cold, teething, other family members had some symptoms).

## 8. Overall Safety Evaluation

From data in this safety report and from the cumulative experience it is concluded that no amendments to the company core safety information need to be done.

### 8.1 Increased Frequency of Reports

There is no evidence of an increase in the frequency of adverse event reported during the period of PSUR (66 AE's/6.164.531 administered injections) compared with RIVM-IPV company clinical safety update for the period 1991-1996 (230 AE's/4.150.244 distributed doses). Variations in relatively small numbers of reports could represent chance variation over the years as well as changes in physician awareness of reporting a possible reaction.

### 8.2 Drug interactions

No clinically relevant drug interactions are known. There have been no spontaneous reports of drug interaction.

### 8.3 Overdose

There have been no reports of overdose during the period of this PSUR.

### 8.4 Drug abuse

RIVM-IPV is recommended for active immunisation in children from 2 months of age and older. There is no abuse potential for this vaccine.

### 8.5 Experience during pregnancy or lactation

Long clinical experience indicates no adverse effects of inactivated trivalent polyomyelitis vaccine on pregnancy or on the health of the foetus/newborn child.
RIVM-IPV can be used during pregnancy and breast-feeding.

## 8.6 Conclusions

It may be concluded that RIVM-IPV is safe. It may cause minor side-effects. The adverse events indicated in the company safety information and approved for the standard product information are in general confirmed.

# PREPARATOMTALE

## 1. LEGEMIDLETS NAVN

Poliovaksine Inaktivert "RIVM"
Injeksjonsvæske, suspensjon.
Vaksine mot poliomyelitt (inaktivert), D-antigen fra poliovirus type 1 (40 E), 2 (8 E) og 3 (32 E)

## 2. KVALITATIV OG KVANTITATIV SAMMENSETNING

1 dose (1 ml) inneholder:

| | | |
|---|---|---|
| Inaktivert poliovirus type 1 | (Mahoney) | 40 enheter D-antigen |
| Inaktivert poliovirus type 2 | (MEF) | 8 enheter D-antigen |
| Inaktivert poliovirus type 3 | (Saukett) | 32 enheter D-antigen |

Poliovaksine Inaktivert "RIVM" er trivalent poliovaksine framstilt av poliovirus type 1, 2 og 3, dyrket på nyreceller fra ape og inaktivert med formaldehyd.

For hjelpestoffer, se pkt. 6.1.

## 3. LEGEMIDDELFORM

Injeksjonsvæske, suspensjon.
Klar, oransje-gul til oransje-rød suspensjon.

## 4. KLINISKE EGENSKAPER

### 4.1 Indikasjoner

Profylakse mot poliomyelitt

### 4.2 Dosering og administrasjonsmåte

Basisvaksinasjon omfatter 3 doser (1 ml/dose). Intervallet mellom 1. og 2. dose må være minst 1 måned, helst 2 måneder. Dersom det går mer enn 6 måneder mellom 1. og 2. dose, må basisvaksinasjon startes på nytt. 3. dose gis 6-12 måneder etter 2. dose. Doser og intervall er de samme for alle aldre (spedbarn, barn og voksne). I det norske barnevaksinasjonsprogrammet gis poliovaksine vanligvis ved 3, 5 og 11-12 måneders alder. I tillegg gis 2 boosterdoser; én ved skolestart og én i ungdomsskolen.

Ved reiser til områder med høy insidens anbefales revaksinasjon med 1 dose hvert 10. år.

Vaksinen skal injiseres subcutant.

### 4.3 Kontraindikasjoner

Overfølsomhet overfor virkestoffene, ett eller flere av hjelpestoffene eller rester fra framstillingsprosessen (neomycin, streptomycin og polymyxinB).
Alvorlig reaksjon etter tidligere vaksinasjon med samme vaksine.
Akutt sykdom med feber over 38 °C.

### 4.4 Advarsler og forsiktighetsregler

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Som ved all vaksinasjon, må den vaksinerte overvåkes i minst 20 minutter. Utstyr til behandling av en eventuell anafylaktisk reaksjon, inkludert adrenalin injeksjonsvæske, skal være tilgjengelig for øyeblikkelig bruk.
Vaksinen må ikke injiseres intravenøst.

### 4.5 Interaksjon med andre legemidler og andre former for interaksjon
Ingen kjente reaksjoner med andre legemidler.. Vaksinen kan gis samtidig med andre vaksiner, men på separate injeksjonssteder.

### 4.6 Graviditet og amming
Vaksinen bør ikke gis under graviditet, bortsett fra til gravide ved opphold i områder med høy smitterisiko.
Vaksinen bør ikke gis under amming.

### 4.7 Påvirkning av evnen til å kjøre bil eller bruke maskiner
Vaksinen antas ikke å påvirke evnen til å kjøre bil eller betjene maskiner.

### 4.8 Bivirkninger
Vanlige (>1/100, < 1/10):
*Lokale:* Lett ømhet og rubor på injeksjonsstedet.
*Systemiske:* Lett feber og uvelfølelse.
Sjeldne (>1/10 000, <1/1000):
Allergiske reaksjoner i form av generalisert urticaria.

### 4.9 Overdosering
Det er ingen rapporterte tilfeller av overdosering

## 5. FARMAKOLOGISKE EGENSKAPER

### 5.1 Farmakodynamiske egenskaper
Farmakoterapeutisk gruppe: Virusvaksiner, ATC-kode J07B F03.
Immunitet oppnås kort tid etter 2. vaksinedose og forsterkes etter 3. dose. Etter basisvaksinasjon (3 vaksinedoser) varer immuniteten i minst 5 år.

### 5.2 Farmakokinetiske egenskaper
Ikke relevant

### 5.3 Prekliniske sikkerhetsdata
Ikke dokumentert

## 6. FARMASØYTISKE OPPLYSNINGER

### 6.1 Fortegnelse over hjelpestoffer
2- fenoksyetanol , formaldehyd, medium 199 (inneholder 61 forskjellige ingredienser, hovedsakelig aminosyrer og vitaminer) og fenolrødt.

### 6.2 Uforlikeligheter
Vaksinen må ikke blandes med andre legemidler.

### 6.3 Holdbarhet
2 år. Etter anbrudd av beholder må vaksinen brukes innen 8 timer.

### 6.4 Oppbevaringsbetingelser
Oppbevares ved 2 °C - 8 °C (i kjøleskap).
Må ikke fryses.

### 6.5 Emballasje (type og innhold)
Vaksinen leveres i:
- Ampuller: 10 x 1 ml.
- Hetteglass 10 ml.

### 6.6 Instruksjoner vedrørende bruk og håndtering samt destruksjon
Før bruk må ampuller/hetteglass undersøkes visuelt for å kunne avsløre fremmedpartikler eller misfarging. Dersom slike forandringer oppdages, må vaksinen kastes.
Før bruk må vaksinen ristes.
Ikke anvendt vaksine samt avfall bør destrueres i overensstemmelse med lokale krav.

## 7. INNEHAVER AV MARKEDSFØRINGSTILLATELSEN

*Representant i Norge:*
Statens institutt for folkehelse
Postboks 4404 Nydalen
0403 Oslo

## 8. MT-NUMMER
8051

## 9. MT-DATO FØRSTE GANG / SISTE FORNYELSE
14.11.1994 / 31.11.2000

## 10. OPPDATERINGSDATO
22.06.2001

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RIVM – Poliomyelitis vaccine, inactivated, trivalent is authorized and placed on the following markets under several brand names:

- The Netherlands
- Norway
- Finland
- Denmark and Iceland
- Germany
- Switzerland
- Italy
- Israel

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# Periodic Safety Update Report for Inactivated Poliomyelitis Vaccine (IPV)

| | |
|---|---|
| Marketing authorisation number: | RVG 17642 |
| Marketing authorisation holder: | Nederlands Vaccin Instituut<br>Antonie v Leeuwenhoeklaan 11<br>3720 AL BILTHOVEN<br>The Netherlands |
| Period covered by this report: | 1 January 2001-1 January 2006 |
| International birth date: | 1982 |
| Date of report: | 28 February 2006 |
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| Approved by: | Carla W.G. Hoitink, PhD, Manager Regulatory & Medical Unit |

Bilthoven, 28 February 2006

..... (RJF Burgmeijer)

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## EXECUTIVE SUMMARY

IPV has been used in the Netherlands since 1982. The marketing authorisation was granted under RVG 17642 by the Dutch Medicines Evaluation Board as per 25 August 1994. In the period 1982-1994 the product was licensed according to the regulations of the so-called 'Committee ex article 14' of the Health Council of the Netherlands. The National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu, RIVM) was marketing authorisation holder (MAH) of the product from 25 August 1994 till 1 January 2003, on which date the Netherlands Vaccine Institute, a former part of the RIVM, was founded.
As a consequence of this reorganisation, NVI became MAH on January, 1st 2003.

The use of the product in the Netherlands itself is very limited (12,269 doses during the entire Analysis Period (AP) of this PSUR). NVI did not receive any spontaneous report of an adverse event after use in the Netherlands. However, the product produced by NVI was during the analysis period exported to six countries in considerable quantities (> 5 million doses). NVI is not the MAH in those countries. Since the exported product is identical to the product used in the Netherlands, we consider it appropriate to report in this PSUR the reports we received from abroad in order to evaluate the safety profile of the vaccine.

To our knowledge no clinical trials were performed and no individual case histories describing serious adverse events (SAEs) or non-serious unlisted adverse events (AEs) associated with IPV were published during the AP.

The safety data collected for IPV during the AP did not give rise to concern about the safety of the vaccine and did not lead to a proposal for adapting the summary of product characteristics (SPC).

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## LIST OF APPENDICES

**ABBREVIATIONS**

| | |
|---|---|
| AE | Adverse Event |
| AP | Analysis Period |
| DLP | Data Lock Point |
| HHE | Hypotonic hyporesponsive episode |
| ICH | International Conference on Harmonisation |
| IPV | Inactivated (or injectable) poliomyelitis vaccine |
| Lareb | National Registration and Evaluation of Adverse events |
| LTR | Laboratory for the Evaluation of the NIP (part of RIVM) |
| MAH | Marketing Authorisation Holder |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MKC | Monkey Kidney Cells |
| NIP | National Immunisation Program |
| NVI | Netherlands Vaccine Institute |
| PSUR | Periodic Safety Update Report |
| RIVM | National Institute for Public Health and the Environment |
| RMU | Regulatory & Medical Unit |
| RVG | Register van Geneesmiddelen (Register of Medicinal Products) |
| SAE | Serious Adverse Event |
| SPC | Summary of Product Characteristics |