# PUBLIC ASSESSMENT SUMMARY REPORT – PICOVAX® (INACTIVATED POLIOVACCINE)

**What is Picovax®?**

Picovax® is a liquid inactivated poliovaccine adsorbed to aluminium hydroxide with the following composition:

| Components | Quantity/dose (0.5 mL) |
|---|---|
| Poliovirus type 1 (Brunhilde strain), inactivated | ≥ 3.2 DU/SHD |
| Poliovirus type 2 (MEF-1 strain), inactivated | ≥ 0.88 DU/SHD |
| Poliovirus type 3 (Saukett strain), inactivated | ≥ 3.1 DU/SHD |
| Aluminium hydroxide corresponding to Al | 0.5 mg |
| Phenoxyethanol | 2.5 mg |

Other ingredients: Sodium hydroxide, sodium phosphate monobasic monohydrate, sodium chloride, water for injections, Medium 199 (contains phenolsulfonphthalein as pH indicator, vitamins, mineral salts and amino acids including phenylalanine).

Picovax® contains trace amounts of formaldehyde, used for virus inactivation.

*Container*

Picovax® (inactivated poliovaccine) is a liquid vaccine supplied in a Type I glass multi-dose vial containing 5 doses (5 x 0.5 ml, overflow capacity of 5.69 ml), with a pharmaceutical grade siliconised rubber stopper made of chlorobutyl, secured by an aluminium Flip-Off® seal covered by a polypropylene plastic cap of dark grey colour.

Real time and accelerated stability reviewed supports the use of a VVM type 7. If a VVM is required, it will be part of the product label.

Bulk manufacture, formulation, dispensing, packaging and labelling occur in the facilities at AJ Vaccines A/S, 5, Artillerivej, DK-2300 Copenhagen S, Denmark.

**What is Picovax® used for?**

Picovax® is indicated for active immunization against poliomyelitis.

Picovax® is approved for use in persons 6 weeks of age and older.

**How is Picovax® used?**

Picovax® is recommended to be used in a primary vaccination series consisting of 3 doses administered from 6 weeks of age in accordance with official recommendations, with an interval of at least 4 weeks between each dose.

After completion of the primary vaccination series, revaccination with Picovax® can be performed in accordance with official recommendations.

Picovax® can be used in a mixed/sequential schedule with oral poliomyelitis vaccine (OPV) in accordance with official recommendations.

Picovax® is safe and immunogenic when administered with other live or inactivated vaccines. There are no immunogenicity data available on the live or inactivated vaccines, that have been given concomitantly with Picovax. When given concomitantly, the vaccines should be administered at different sites of injection.

The vaccine should be administered intramuscularly only, not intravascularly or intradermally.

**What are the vaccine characteristics?**

Picovax® must be stored between 2-8°C. It must not be frozen. Under these recommended storage conditions, the vaccine is stable for 24 months from the date of manufacture. After first use the vaccine may be stored for a maximum of 28 days in a refrigerator (2°C – 8°C).

The vaccine contains phenoxyethanol 0.5% w/v as a preservative.

Cold chain volume per dose is 6.8241 $cm^3$ in the secondary carton of 10 vials.

**Who is the regulatory authority responsible for its oversight vis a vis WHO?**

The Danish Medicines Agency (DKMA) is the National Regulatory Authority (NRA) of record for WHO prequalification of Picovax®.

Picovax® has been granted a marketing authorization by the DKMA on 29 May 2019 for both domestic use and export.

**How has Picovax® been studied from the clinical point of view?**

The vaccine was studied in six sponsored prelicensure clinical trials. Study 04 in Denmark was a proof of concept study in children 10-15 years of age; study 05 was a dose-investigation in the EPI schedule in the Dominican Republic. Studies 06 and 07 compared the vaccine formulation with full dose IPV in the EPI schedule 6-10-14 weeks (study 06, Philippines) or 2-4-6 months schedule (study 07, Panama) with booster dose response at 9 and 15-18 months respectively.

Non-inferiority of the primary endpoint (seroconversions) was based on the lower 95% Confidence Interval of the difference in the percentage of subjects not exceeding -10 percentage points. Non-inferiority of the secondary endpoint (seroprotection) was based on the lower 95% Confidence Interval of the difference in the percentage of subjects not exceeding -5 percentage points.

Non-inferiority of the vaccine (Picovax®) to IPV has been demonstrated for the primary endpoint when given as primary immunisation at 6, 10 and 14 weeks (study 05, study 06) and 2, 4 and 6 months (study 07).

Non-inferiority of Picovax® to IPV has been demonstrated for the secondary endpoint of seroprotection when given at 6, 10 and 14 weeks (study 05, study 06). In study 07 (2, 4 and 6 months) non-inferiority of Picovax® to IPV has been demonstrated for type 2 and 3 but not for type 1. The lower confidence limit for type 1 was -5.81.

Geometric Mean Titres were universally well above the accepted level of poliovirus type-specific serum neutralizing antibodies for protection but the levels pre- and post-vaccination with Picovax® were

consistently lower than with IPV. The implications for long-term persistence and any associated clinical consequences will be investigated.

Boosting with Picovax® was studied in study 04, study 06 booster and study 07 booster and demonstrated adequate response in children and adolescent. No study was conducted in adults.

The vaccine demonstrated acceptable safety in all age groups studied.

**Other information about evaluation of Picovax®:**

Evaluation of the Picovax® application was based on the NRA quality and clinical reviews provided in CTD format. The vaccine meets WHO Recommendations to assure the quality, safety and efficacy of poliomyelitis vaccine (inactivated), WHO TRS 993, Annex 3. In addition, WHO specific requirements such as the programmatic suitability, the testing for preservative efficacy (with respect to use under the multidose vial policy), stability data (with respect to VVM assignment) and UN specific labelling data were assessed by a team of WHO experts and found to be compliant with their respective guidance.

The manufacturing facility was inspected by a joint team of experts from the DKMA and WHO, and found to be compliant with the standards of Good Manufacturing Practices (GMP) published by the World Health Organization (WHO).

Based on the review of the batch release process, which encompasses lot testing and lot release approval issued by Sciensano (Belgium), acting as a WHO approved contract laboratory (NCL), independent testing in WHO contracted laboratories, as part of the prequalification evaluation, was waived.

Since batch release is not a requirement in Denmark, the batch release process is conducted by Sciensano without DKMA involvement.

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