

**Pneucia13**  
**13-valent Pneumococcal Polysaccharide Conjugate**  
**Vaccine**

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

Pneucia13

13-valent Pneumococcal Polysaccharide Conjugate Vaccine

Suspension for injection, for intramuscular use.

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The vaccine is supplied as a multi-dose of vial 2.0 mL (4 x 0.5 mL) with suspension for intramuscular injection. Each dose (0.5 mL) of the vaccine contains:

Pneumococcal polysaccharide serotype 1 <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 3 <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 4 <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 5 <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 6A <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 6B <sup>1</sup>	4.4 µg
Pneumococcal polysaccharide serotype 7F <sup>2</sup>	2.2 µg
Pneumococcal polysaccharide serotype 9V <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 14 <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 18C <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 19A <sup>1</sup>	2.2 µg
Pneumococcal polysaccharide serotype 19F <sup>2</sup>	2.2 µg
Pneumococcal polysaccharide serotype 23F <sup>1</sup>	2.2 µg

<sup>1</sup>Conjugated to CRM<sub>197</sub> carrier protein and <sup>2</sup>conjugated to Tetanus Toxoid, all adsorbed on 0.125 mg aluminum phosphate.

For the full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

The vaccine is supplied as a multi-dose of vial 2.0 mL (4 x 0.5 mL) with suspension for intramuscular injection.

One dose of 0.5 mL, a homogeneous white suspension supplied in vial.

The vaccine should be shaken well to obtain a homogeneous milky white suspension. During storage, a white deposit and clear supernatant might be observed due to adjuvant precipitation.

### 4. CLINICAL PARTICULARS

#### 4.1 Indications

Active immunization for prevention of invasive diseases (including bacteremic pneumonia, meningitis, sepsis, bacteremia, etc.) caused by *Streptococcus pneumoniae* serotypes of 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F in infants and children from 2 months (minimum 6 weeks) to 5 years of age.

#### 4.2 Posology and method of administration

The immunization schedules for Pneucia13 should be based on official recommendations.

### Posology

It is recommended that infants who receive a first dose of Pneucia13 complete the vaccination course with Pneucia13.

#### Infants aged 2 months (minimum 6 weeks):

Immunization for 4 doses in total, each of 0.5 mL: Primary series consists of 3 doses, with the first dose recommended at 2 months of age (can be given as early as six weeks of age) and with an interval of 2 months between doses. The fourth (booster) dose is recommended at 12-15 months of age.

#### Infants aged 3 months:

Immunization for 4 doses in total, each of 0.5 mL: Primary series consists of 3 doses, with the first dose recommended at 3 months of age with an interval of 1 month between doses. The fourth (booster) dose is recommended at 12-15 months of age.

#### Infants aged 7-11 months:

Immunization for 3 doses in total, each of 0.5 mL: Primary series consists of 2 doses, with an interval of at least 2 months. The third (booster) dose is recommended at 12-15 months of age, with an interval of at least 2 months after the second dose.

#### Children aged 12-23 months:

Two doses, each of 0.5 mL, with an interval of 2 months.

#### Children aged 2-5 years (<72 months):

One single dose of 0.5 mL.

### Method of administration

Since this product is a suspension containing an adjuvant, shake vigorously immediately prior to use to obtain a homogenous, white suspension in the vaccine container. This product is for intramuscular injection only. The preferred sites for injection are the anterolateral thigh (vastus lateralis muscle) in infants and the deltoid muscle of the upper arm in children. The injection volume is 0.5 mL for each single human dose. Use a new sterile syringe and sterile needle for each injection. The vaccine should not be injected in and/or near the areas where nerve trunks and/or blood vessels may locate.

### **4.3 Contraindications**

Allergic to any active ingredients, excipients, diphtheria toxoid, tetanus toxoid, etc. in this vaccine.

### **4.4 Special warnings and precautions for use**

Only for intramuscular injection, must not be administered by intravascular injection. This vaccine must not be administered in the gluteal region. Care should be taken to avoid injection into or near nerves and blood vessels.

As with other vaccines, administration of Pneucia13 should be postponed for children suffering from acute or severe febrile diseases.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a serious hypersensitivity after immunization.

As with other intramuscular injections, cautionary use for people with thrombocytopenia, any coagulation

disorder, or those receiving anticoagulant therapy.

Pneucia13 will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine, and it will not protect from infectious diseases caused by other *Streptococcus pneumoniae* serotypes or invasive diseases, pneumonia or otitis media caused by other microorganisms.

As with any vaccine, Pneucia13 may not protect all individuals receiving the vaccine from pneumococcal disease.

Safety and immunogenicity for Pneucia13 are not available for people with compromised immune function (such as malignancy and nephrotic syndrome) and vaccination should be based on an individual basis.

In children  $\geq$  24 months old with sickle cell disease, asplenia, HIV infection, chronic diseases or other immunocompromised children, use of this vaccine cannot replace the 23-valent pneumococcal polysaccharide vaccine (PPSV23).

As with injectable vaccines for children, the potential risk of apnoea should be taken into consideration when primary vaccinating premature infants. When vaccinating extremely premature infants ( $\leq$  30 weeks gestation at birth) who are still hospitalized according to recommended procedures, monitoring for at least 48 hours after vaccination with Pneucia13 should be considered. As the benefit of vaccination is high in premature infants, it is not recommended to withhold or postpone vaccination of this vaccine.

In any case, tetanus toxoid in Pneucia13 cannot replace routine Tetanus vaccine immunization.

#### **4.5 Interaction with other medicinal products and forms of interaction**

There are no clinical trials of concomitant use of Pneucia13 with other vaccines. In the Phase III clinical trial of Pneucia13 vaccine, no impact on its immunogenicity was observed when administered with an interval of at least 7 days from other vaccines.

#### **4.6 Fertility, pregnancy and lactation**

Not applicable.

#### **4.7 Effects on ability to drive and use machines**

Not applicable.

#### **4.8 Undesirable effects**

##### **4.8.1 Adverse reactions from clinical studies**

Phase I and phase III clinical trials have been conducted in China, with subjects of 237 and 3420, respectively. Among them, 2206 received one dose of Pneucia13. The systemic safety observation lasted from the initial immunization of the first dose to 30 days after each dose immunization, and the long-term safety observation lasted until 6 months after the full immunization procedures.

Adverse reactions were classified as the recommendation from the Council for International Organizations of Medical Sciences (CIOMS): very common ( $\geq$ 10%), common (1% to 10%, including 1%), and uncommon (0.1% to 1%, including 0.1%), rare (0.01% to 0.1%, including 0.01%), very rare ( $<$ 0.01%).

2 months (minimum 6 weeks) – 6 months old:

## (1) Local adverse reactions

Very common: erythema

Common: swelling

Uncommon: pain, induration

## (2) Systemic adverse reactions

Very common: pyrexia

Common: vomiting, diarrhea, cough, irritability

Uncommon: nausea, mucocutaneous disorder, decreased appetite, somnolence, rhinorrhoea, abdominal distention, viral rash, sputum increased

7-11 months:

## (1) Local adverse reactions

Very common: erythema

Common: swelling

Uncommon: induration, pain

## (2) Systemic adverse reactions

Very common: pyrexia

Common: diarrhea, cough, vomiting

Uncommon: irritability, hypersensitivity, mucocutaneous disorder

12 months – 5 years old:

## (3) Local adverse reactions

Very common: erythema

Common: swelling, pain

Uncommon: pruritus, induration

## (4) Systemic adverse reactions

Very common: pyrexia

Common: cough, diarrhea, vomiting

Uncommon: irritability, hypersensitivity, decreased appetite, rhinorrhoea

## Serious adverse reactions:

There is no vaccine related serious adverse event in the clinical trials for children aged 6 weeks to 5 years (<72 months)

#### 4.8.2 Clinical trials for similar vaccines

Besides adverse reactions in clinical trials of Pneucia13, clinical study reports of similar 13-valent pneumococcal polysaccharide conjugate vaccines include adverse reactions such as urticaria, convulsions (including febrile convulsions), hypotonic-hyporeactivity nasopharyngitis, upper respiratory tract infection, dermatitis allergic, sleep decreased, mouth ulceration, abdominal pain, hyperhidrosis, lacrimation increased, eye discharge, and redness of eyelid.

#### 4.8.3 Post-Marketing Surveillance

In addition to the adverse reactions reported in clinical studies of Pneucia13, post-marketing data for similar 13-valent pneumococcal polysaccharide conjugate vaccines include the following adverse reactions: dermatitis/urticaria at the injection site, localized lymphadenopathy restricted to the vaccination site, severe hypersensitivity reactions (manifested as shock), angioedema, erythema multiforme, mucocutaneous lymph node syndrome, etc. The post-marketing adverse reactions are derived from spontaneous reports, and therefore, their incidence cannot be reliably determined.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

#### Pharmaceutical Industry Reporting Contacts

PT ETANA BIOTECHNOLOGIES INDONESIA

Kawasan Industri Pulogadung, Jl. Rawa Gelam V, Blok. L, Kav. 11-13, Jakarta

Email: [pv@id.etanabiotech.com](mailto:pv@id.etanabiotech.com)

Website: <https://ebi-pharmacovigilance.azurewebsites.net/>

#### MESO Center / National Pharmacovigilance Center

Direktorat Pengawasan Distribusi Produk Terapeutik dan PKRT Badan POM RI Jl.

Percetakan Negara 23 Jakarta Pusat, 10560

No Telp: 021 – 4244 755 ext.111

Fax: 021 – 4288 3485

Email: [pv-center@pom.go.id](mailto:pv-center@pom.go.id) and [Indonesia-meso-badanpom@hotmail.com](mailto:Indonesia-meso-badanpom@hotmail.com)

## 4.9 Overdose

No overdose data are available for the product in recipients.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, pneumococcal vaccines; ATC code: J07AL02

Pneucia13 contains pneumococcal capsular polysaccharides of 1, 3, 4, 5, 6A, 6B, 9V, 14, 18C, 19A and 23F conjugated to carrier protein CRM<sub>197</sub>, as well as pneumococcal capsular polysaccharides of 7F and 19F conjugated to Tetanus Toxoid.

#### Immunogenicity

In the pivotal phase III clinical trial of Pneucia13 in China, a randomized, blinded, positive-controlled non-inferiority design was used to evaluate the immunogenicity and safety of Pneucia13 and the control vaccine (Pneuvia 13) in 3420 children aged 2 months (minimum 6 weeks) to 5 years. 1200 infants aged 2 months (minimum 6 weeks) received Pneucia13 or Pneuvia 13 at a ratio 1:1, with a 2, 4, 6 month primary series (3 doses) and one booster dose at 12-15 months; 600 infants aged 3 months received Pneucia13 only, with a 3, 4, and 5 month primary series (3 doses) and one booster dose at 12-15 months; 564 infants aged 7-11 months received Pneucia13 or Pneuvia 13 at a ratio of 1:1, 2 doses of primary series (with an interval of 2 months) and one booster dose at 12-15 months (with an interval of at least 2 months from the second dose); 528 children aged 12-23 months received Pneucia13 or Pneuvia 13 at a ratio of 1:1, with a 2-dose immunization with an interval of 2 months; 528 children aged 2-5 years received Pneucia13 or Pneuvia 13 at a ratio of 1:1.

IgG antibody concentrations were tested by enzyme-linked immunosorbent assay (ELISA) for all subjects. OPA antibodies were tested by opsonophagocytic activity assay for 864 subjects, to evaluate the ability of immune sera to bind complement and mediate the phagocytosis and killing of pneumococci by phagocytic cells. Immunogenicity parameters were percentage (positive rate) and geometric mean concentration (GMC) of subjects with vaccine serotype-specific IgG antibody concentrations  $\geq 0.35 \mu\text{g/mL}$  at 30 days after primary immunization and 30 days after booster immunization, and the proportion (positive rate) and geometric mean

titer (GMT) of subjects with vaccine serotype-specific OPA antibody titers  $\geq 1:8$ .

Non-inferiority criteria: the lower limit of the two-sided 95% CI for the difference in IgG positive rate (Investigational vaccine – Control vaccine) was greater than -10%, and the lower limit of the two-sided 95% CI for the IgG GMC ratio (Investigational vaccine/Control vaccine) was greater than 0.5.

Immunogenicity results for subjects aged 2 months to 5years are listed in Tables 1~6.

**Table 1 Proportion for subjects aged 2 months old and 3 months old with IgG ≥0.35µg/ml (PPS)**

Serotype	After primary immunization				After booster immunization			
	2 months old		3 months old		2 months old		3 months old	
	PCV-13 (T1) N=550 % (CI*)	Pneumar 13 (C1) N=572 % (CI*)	Difference of rate (T1-C1) % (CI*)	PCV-13 (T2) N=567 % (CI*)	PCV-13 (T1) N=550 % (CI*)	Pneumar 13 (C1) N=575 % (CI*)	Difference of rate (T1-C1) % (CI*)	PCV-13 (T2) N=561 % (CI*)
1	100.00(99.33,100.00)	100.00(99.36,100.00)	0.00 (-0.01,0.01)	100.00 (99.35,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
3	98.55 (97.15,99.37)	90.56 (87.86,92.83)	0.08 (0.05,0.11)	99.29 (98.20,99.81)	99.27 (98.15,99.80)	0.03 (0.02,0.05)	99.47 (98.45,99.89)	
4	99.82 (98.99,100.00)	100.00 (99.36,100.00)	-0.00 (-0.01,0.00)	99.82 (99.02,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	99.82 (99.01,100.00)	
5	94.91 (92.73,96.59)	98.95 (97.73,99.61)	-0.04 (-0.06,-0.02)	94.00 (91.72,95.81)	99.27 (98.15,99.80)	0.00 (-0.01,0.01)	99.64 (98.72,99.96)	
6A	99.82 (98.99,100.00)	99.83 (99.03,100.00)	-0.00 (-0.01,0.00)	99.47 (98.46,99.89)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
6B	100.00 (99.33,100.00)	99.83 (99.03,100.00)	0.00 (-0.00,0.01)	99.82 (99.02,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
7F	100.00 (99.33,100.00)	100.00 (99.36,100.00)	0.00 (-0.01,0.01)	100.00 (99.35,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
9V	99.82 (98.99,100.00)	99.83 (99.03,100.00)	-0.00 (-0.01,0.00)	99.82 (99.02,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
14	100.00 (99.33,100.00)	100.00 (99.36,100.00)	0.00 (-0.01,0.01)	100.00 (99.35,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	99.82 (99.01,100.00)	
18C	99.64 (98.69,99.96)	98.95 (97.73,99.61)	0.01 (-0.00,0.02)	99.47 (98.46,99.89)	100.00 (99.33,100.00)	0.00 (-0.00,0.01)	99.82 (99.01,100.00)	
19A	100.00 (99.33,100.00)	100.00 (99.36,100.00)	0.00 (-0.01,0.01)	100.00 (99.35,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
19F	100.00 (99.33,100.00)	100.00 (99.36,100.00)	0.00 (-0.01,0.01)	100.00 (99.35,100.00)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	
23F	99.82 (98.99,100.00)	99.30 (98.22,99.81)	0.01 (-0.00,0.01)	99.47 (98.46,99.89)	100.00 (99.33,100.00)	0.00 (-0.01,0.01)	100.00 (99.34,100.00)	

Note: N: number of subjects meet data set; CI\*: two sided 95% CI of IgG antibody positive rate; 2 months old: minimum 6 weeks.

T1: investigational CanSinoBIO PCV-13 vaccine in 2 months infant group; T2: investigational CanSinoBIO PCV-13 vaccine in 3 months infant group; C1: Comparator Pneumar 13 vaccine in 2 months infant group.

**Table 2. IgG GMCs for subjects aged 2 months old and 3 months old (PPS)**

Serotype	After primary immunization				After booster immunization			
	2 months old		3 months old		2 months old		3 months old	
	PCV-13 (T1) N=550	Prevnar 13 (C1) N=572	Ratio (T1/C1)	PCV-13 (T2) N=567	PCV-13 (T1) N=550	Prevnar 13 (C1) N=575	Ratio (T1/C1)	PCV-13 (T2) N=561
1	2.61 (2.46,2.76)	3.19 (3.02,3.37)	0.82 (0.76,0.88)	3.29 (3.14,3.45)	3.85 (3.63,4.10)	4.11 (3.89,4.35)	0.94 (0.86,1.02)	4.62 (4.35,4.90)
3	1.17 (1.11,1.23)	0.76 (0.73,0.80)	1.53 (1.42,1.64)	1.86 (1.77,1.97)	1.33 (1.26,1.41)	0.92 (0.87,0.96)	1.45 (1.35,1.56)	1.74 (1.65,1.84)
4	2.57 (2.44,2.72)	2.15 (2.04,2.27)	1.20 (1.11,1.29)	3.72 (3.52,3.93)	3.35 (3.14,3.57)	2.57 (2.42,2.74)	1.30 (1.19,1.42)	3.62 (3.38,3.87)
5	0.99 (0.93,1.04)	1.53 (1.45,1.61)	0.65 (0.60,0.70)	0.89 (0.84,0.94)	1.49 (1.40,1.58)	1.66 (1.57,1.75)	0.89 (0.83,0.97)	1.38 (1.31,1.44)
6A	2.35 (2.21,2.50)	3.20 (3.00,3.41)	0.74 (0.67,0.80)	2.06 (1.95,2.18)	4.55 (4.25,4.87)	6.07 (5.66,6.50)	0.75 (0.68,0.83)	4.41 (4.10,4.74)
6B	3.13 (2.96,3.31)	3.77 (3.53,4.02)	0.83 (0.76,0.90)	2.58 (2.43,2.74)	7.66 (7.15,8.21)	9.44 (8.78,10.14)	0.81 (0.74,0.90)	7.01 (6.54,7.52)
7F	10.44 (9.83,11.10)	5.64 (5.34,5.95)	1.85 (1.71,2.01)	12.31 (11.61,13.05)	10.28 (9.68,10.92)	4.94 (4.66,5.23)	2.08 (1.92,2.26)	9.50 (8.96,10.08)
9V	3.53 (3.31,3.77)	2.66 (2.50,2.83)	1.33 (1.21,1.45)	3.95 (3.75,4.17)	3.70 (3.46,3.95)	3.31 (3.11,3.52)	1.12 (1.02,1.22)	3.19 (3.00,3.38)
14	14.23 (13.37,15.15)	15.77 (14.81,16.79)	0.90 (0.83,0.99)	14.17 (13.40,14.98)	17.80 (16.74,18.93)	18.83 (17.79,19.94)	0.95 (0.87,1.03)	17.04 (15.98,18.18)
18C	1.62 (1.53,1.72)	2.55 (2.38,2.72)	0.64 (0.58,0.70)	1.92 (1.82,2.03)	2.23 (2.10,2.38)	3.09 (2.88,3.30)	0.72 (0.66,0.79)	1.70 (1.60,1.80)
19A	6.48 (6.06,6.93)	4.49 (4.24,4.75)	1.45 (1.32,1.58)	7.17 (6.79,7.58)	14.20 (13.27,15.20)	10.42 (9.79,11.09)	1.36 (1.24,1.49)	16.29 (15.24,17.40)
19F	12.95 (12.14,13.80)	4.27 (4.05,4.51)	3.03 (2.79,3.29)	15.95 (14.94,17.04)	15.74 (14.75,16.80)	6.94 (6.55,7.35)	2.27 (2.08,2.47)	18.26 (17.15,19.44)
23F	3.52 (3.28,3.77)	3.37 (3.14,3.61)	1.04 (0.95,1.15)	2.68 (2.53,2.84)	7.61 (7.08,8.18)	7.94 (7.35,8.59)	0.96 (0.86,1.07)	6.09 (5.68,6.54)

Note: N: number of subjects meets protocol set; CI\*: two sided 95%CI of IgG antibody GMC; 2 months old; minimum 6 weeks

TI: investigational CanSinoBIO PCV-13 vaccine in 2 months infant group; T2: investigational CanSinoBIO PCV-13 vaccine in 3 months infant group; C1: Comparator Prevnar 13 vaccine in 2 months infant group.

**Table 3. Proportion of IgG antibody  $\geq 0.35\mu\text{g/ml}$  for subjects aged 7 months to 5 years (PPS)**

Serotype	After primary immunization						After booster immunization					
	7-11 months			12-23 months			2-5 years old			7-11 months		
	PCV-13 (T3) N=263	Prevar 13 (C3) N=261	Difference of rate (T3-C3)	PCV-13 (T4) N=255	Prevar 13 (C4) N=253	Difference of rate (T4-C4)	PCV-13 (T5) N=263	Prevar 13 (C5) N=263	Difference of rate (T5-C5)	PCV-13 (T3) N=266	Prevar 13 (C3) N=263	Difference of rate (T3-C3)
1	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
3	99.24 (97.28, 99.91)	97.70 (95.06, 99.15)	0.02 (-0.01, 0.04)	96.47 (93.41, 98.37)	96.05 (92.85, 98.09)	0.00 (-0.03, 0.04)	97.34 (94.59, 98.92)	93.54 (89.85, 96.19)	0.04 (0.00, 0.07)	99.62 (97.92, 99.99)	98.48 (96.15, 99.58)	0.01 (-0.01, 0.03)
4	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
5	96.58 (93.60, 98.42)	100.00 (98.60, 100.00)	-0.03 (-0.06, -0.01)	96.47 (93.41, 98.37)	100.00 (98.55, 100.00)	-0.04 (-0.06, -0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	98.12 (95.67, 99.39)	100.00 (98.61, 100.00)	-0.02 (-0.04, -0.00)
6A	99.62 (97.90, 99.99)	99.23 (97.26, 99.91)	0.00 (-0.01, 0.02)	99.22 (97.20, 99.90)	100.00 (98.55, 100.00)	-0.01 (-0.02, 0.00)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
6B	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	98.82 (96.60, 99.76)	100.00 (98.55, 100.00)	-0.01 (-0.02, 0.00)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
7F	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
9V	99.62 (97.90, 99.99)	100.00 (98.60, 100.00)	-0.00 (-0.01, 0.00)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
14	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
18C	99.62 (97.90, 99.99)	99.62 (97.88, 99.99)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	99.25 (97.31, 99.91)	100.00 (98.61, 100.00)	-0.01 (-0.02, 0.00)
19A	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
19F	100.00 (98.61, 100.00)	100.00 (98.60, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.56, 100.00)	100.00 (98.55, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.61, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	100.00 (98.61, 100.00)	0.00 (-0.01, 0.01)
23F	99.24 (97.28, 99.91)	99.23 (97.26, 99.91)	0.00 (-0.01, 0.01)	99.61 (97.83, 99.99)	99.60 (97.82, 99.99)	0.00 (-0.01, 0.01)	99.62 (97.90, 99.99)	99.62 (97.90, 99.99)	0.00 (-0.01, 0.01)	100.00 (98.62, 100.00)	99.62 (97.90, 99.99)	0.00 (-0.00, 0.01)

Note: N: number of subjects meets protocol set; CI\*: two sided 95% CI of IgG antibody positive rate

T3: investigational CanSinoBIO PCV-13 vaccine in 7-11 months infant group; C3: Comparator Prevar 13 vaccine in 7-11 months infant group; T4: investigational CanSinoBIO PCV-13 vaccine in 12-23 months children group; C4: Comparator Prevar 13 vaccine in 12-23 months children group; T5: investigational CanSinoBIO PCV-13 vaccine in 2-5 years children group; C5: Comparator Prevar 13 vaccine in 2-5 years children group.

**Table 4 IgG antibody GMC for subjects aged 7 months to 5 years (PPS)**

Serotype	After primary immunization						After booster immunization					
	7-11 months			12-23 months			2-5 years old			7-11 months		
	PCV-13 (T3) N=263	Prevar 13 (C3) N=261	Ratio (T3/C3)	PCV-13 (T4) N=255	Prevar 13 (C4) N=253	Ratio (T4/C4)	PCV-13 (T5) N=263	Prevar 13 (C5) N=263	Ratio (T5/C5)	PCV-13 (T3) N=266	Prevar 13 (C3) N=263	Ratio (T3/C3)
1	2.88 (2.68, 3.10)	3.30 (3.07, 3.54)	0.87 (0.79, 0.97)	3.17 (2.97, 3.38)	3.89 (3.63, 4.18)	0.81 (0.74, 0.90)	3.76 (3.50, 4.04)	4.62 (4.31, 4.96)	0.81 (0.74, 0.90)	3.38 (3.13, 3.66)	3.89 (3.60, 4.20)	0.87 (0.78, 0.97)
3	1.52 (1.42, 1.64)	1.01 (0.94, 1.09)	1.50 (1.36, 1.67)	1.12 (1.04, 1.20)	0.88 (0.81, 0.94)	1.27 (1.15, 1.41)	0.93 (0.86, 1.00)	0.83 (0.76, 0.90)	1.12 (1.00, 1.26)	1.95 (1.79, 2.13)	1.18 (1.10, 1.27)	1.65 (1.47, 1.85)
4	2.81 (2.60, 3.04)	2.21 (2.04, 2.40)	1.27 (1.14, 1.43)	3.47 (3.24, 3.72)	3.31 (3.08, 3.57)	1.05 (0.95, 1.16)	5.77 (5.26, 6.33)	4.91 (4.47, 5.40)	1.18 (1.03, 1.34)	2.73 (2.53, 2.95)	2.26 (2.06, 2.47)	1.21 (1.08, 1.36)
5	1.04 (0.96, 1.13)	1.95 (1.82, 2.09)	0.53 (0.48, 0.59)	0.90 (0.84, 0.96)	1.94 (1.81, 2.08)	0.46 (0.42, 0.51)	1.63 (1.52, 1.76)	2.01 (1.87, 2.16)	0.81 (0.73, 0.90)	1.24 (1.14, 1.35)	2.11 (1.96, 2.27)	0.59 (0.53, 0.66)
6A	1.51 (1.39, 1.65)	1.67 (1.52, 1.84)	0.90 (0.80, 1.03)	1.91 (1.75, 2.09)	2.24 (2.03, 2.47)	0.85 (0.75, 0.97)	2.48 (2.22, 2.76)	2.56 (2.32, 2.82)	0.97 (0.84, 1.12)	2.32 (2.13, 2.53)	3.20 (2.90, 3.53)	0.73 (0.64, 0.83)
6B	2.02 (1.85, 2.20)	1.82 (1.65, 2.00)	1.11 (0.97, 1.26)	2.72 (2.47, 2.99)	2.91 (2.64, 3.21)	0.93 (0.81, 1.07)	4.33 (3.86, 4.85)	4.16 (3.69, 4.69)	1.04 (0.88, 1.23)	3.43 (3.12, 3.77)	3.90 (3.50, 4.35)	0.88 (0.76, 1.01)
7F	9.77 (8.97, 10.63)	5.44 (5.05, 5.87)	1.79 (1.60, 2.01)	8.10 (7.52, 8.72)	6.07 (5.65, 6.51)	1.34 (1.21, 1.48)	5.56 (5.14, 6.01)	5.97 (5.47, 6.51)	0.93 (0.83, 1.05)	13.60 (12.43, 14.88)	5.64 (5.23, 6.09)	2.41 (2.14, 2.71)
9V	2.24 (2.06, 2.42)	2.25 (2.04, 2.49)	0.99 (0.87, 1.13)	2.68 (2.47, 2.92)	2.89 (2.64, 3.16)	0.93 (0.82, 1.05)	3.61 (3.25, 4.01)	3.71 (3.35, 4.10)	0.97 (0.84, 1.13)	2.57 (2.36, 2.80)	2.71 (2.47, 2.97)	0.95 (0.84, 1.07)
14	11.41 (10.60, 12.29)	14.66 (13.55, 15.85)	0.78 (0.70, 0.87)	10.37 (9.68, 11.11)	14.24 (13.30, 15.25)	0.73 (0.66, 0.80)	17.29 (15.16, 19.71)	19.63 (17.20, 22.39)	0.88 (0.73, 1.06)	15.48 (14.38, 16.65)	18.25 (16.85, 19.78)	0.85 (0.76, 0.94)
18C	1.89 (1.73, 2.06)	2.21 (2.04, 2.40)	0.85 (0.76, 0.96)	2.88 (2.67, 3.11)	3.13 (2.87, 3.41)	0.92 (0.82, 1.03)	5.96 (5.38, 6.61)	5.80 (5.20, 6.48)	1.03 (0.88, 1.19)	1.85 (1.71, 2.01)	2.33 (2.14, 2.54)	0.80 (0.71, 0.89)
19A	5.67 (5.27, 6.11)	4.73 (4.40, 5.09)	1.20 (1.08, 1.33)	7.24 (6.73, 7.78)	6.94 (6.43, 7.48)	1.04 (0.94, 1.16)	11.08 (10.09, 12.17)	11.71 (10.67, 12.86)	0.95 (0.83, 1.08)	8.49 (7.84, 9.19)	6.19 (5.72, 6.70)	1.37 (1.23, 1.53)
19F	11.20 (10.18, 12.33)	3.89 (3.61, 4.19)	2.88 (2.55, 3.25)	9.98 (9.25, 10.76)	5.23 (4.85, 5.63)	1.91 (1.72, 2.12)	9.90 (9.07, 10.80)	7.93 (7.27, 8.65)	1.25 (1.10, 1.41)	15.41 (13.93, 17.04)	4.34 (4.00, 4.71)	3.55 (3.12, 4.04)
23F	2.35 (2.14, 2.59)	1.70 (1.55, 1.86)	1.38 (1.21, 1.58)	2.65 (2.46, 2.85)	2.38 (2.18, 2.61)	1.11 (0.99, 1.25)	4.87 (4.32, 5.49)	3.87 (3.43, 4.36)	1.26 (1.06, 1.49)	3.33 (3.06, 3.64)	3.12 (2.81, 3.45)	1.07 (0.94, 1.22)

Note: N: number of subjects meets protocol set; CI\*: two sided 95%CI of IgG antibody GMC; T3: investigational CanSinoBIO PCV-13 vaccine in 7-11 months infant group; C3: Comparator Prevar 13 vaccine in 7-11 months infant group; T4: investigational CanSinoBIO PCV-13 vaccine in 12-23 months children group; C4: Comparator Prevar 13 vaccine in 12-23 months children group; T5: investigational CanSinoBIO PCV-13 vaccine in 2-5 years children group; C5: Comparator Prevar 13 vaccine in 2-5 years children group.

**Table 5. Proportion of subjects with OP A antibody titers ≥ 1:8 for all age groups (PPS)**

Serotype	After primary immunization												After booster immunization	
	2 months			7-11 months			12-23 months			2-5 years old			2 months	
	PCV-13 N=137	Prevar 13 N=140	PCV-13 N=89	Prevar 13 N=88	PCV-13 N=90	Prevar 13 N=91	PCV-13 N=96	Prevar 13 N=96	PCV-13 N=136	Prevar 13 N=136				
1	99.27 (96.00, 99.98)	100.00 (97.40, 100.00)	94.38 (87.37, 98.15)	97.73 (92.03, 99.72)	91.11 (83.23, 96.08)	95.60 (89.13, 98.79)	94.79 (88.26, 98.29)	96.88 (91.14, 99.35)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
3	99.27 (96.00, 99.98)	98.57 (94.93, 99.83)	100.00 (95.94, 100.00)	100.00 (95.89, 100.00)	100.00 (95.98, 100.00)	100.00 (96.03, 100.00)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
4	100.00 (97.34, 100.00)	100.00 (97.40, 100.00)	100.00 (95.94, 100.00)	100.00 (95.89, 100.00)	100.00 (95.98, 100.00)	100.00 (96.03, 100.00)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
5	93.43 (87.90, 96.95)	100.00 (97.40, 100.00)	85.39 (76.32, 91.99)	100.00 (95.89, 100.00)	74.44 (64.16, 83.06)	94.51 (87.64, 98.19)	51.04 (40.63, 61.39)	100.00 (96.23, 100.00)	94.12 (88.74, 97.43)	100.00 (97.32, 100.00)				
6A	99.27 (96.00, 99.98)	100.00 (97.40, 100.00)	98.88 (93.90, 99.97)	100.00 (95.89, 100.00)	98.89 (93.96, 99.97)	96.70 (90.67, 99.31)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
6B	100.00 (97.34, 100.00)	99.29 (96.08, 99.98)	94.38 (87.37, 98.15)	95.45 (88.77, 98.75)	97.78 (92.20, 99.73)	95.60 (89.13, 98.79)	97.92 (92.68, 99.75)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
7F	100.00 (97.34, 100.00)	100.00 (97.40, 100.00)	100.00 (95.94, 100.00)	100.00 (95.89, 100.00)	100.00 (95.98, 100.00)	100.00 (96.03, 100.00)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
9V	100.00 (97.34, 100.00)	100.00 (97.40, 100.00)	100.00 (95.94, 100.00)	98.86 (93.83, 99.97)	100.00 (95.98, 100.00)	100.00 (96.03, 100.00)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
14	99.27 (96.00, 99.98)	99.29 (96.08, 99.98)	100.00 (95.94, 100.00)	100.00 (95.89, 100.00)	100.00 (95.98, 100.00)	100.00 (96.03, 100.00)	98.96 (94.33, 99.97)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
18C	100.00 (97.34, 100.00)	100.00 (97.40, 100.00)	96.63 (90.46, 99.30)	100.00 (95.89, 100.00)	98.89 (93.96, 99.97)	98.90 (94.03, 99.97)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
19A	100.00 (97.34, 100.00)	100.00 (97.40, 100.00)	100.00 (95.94, 100.00)	100.00 (95.89, 100.00)	100.00 (95.98, 100.00)	100.00 (96.03, 100.00)	98.96 (94.33, 99.97)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
19F	99.27 (96.00, 99.98)	99.29 (96.08, 99.98)	97.75 (92.12, 99.73)	98.86 (93.83, 99.97)	96.67 (90.57, 99.31)	98.90 (94.03, 99.97)	100.00 (96.23, 100.00)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				
23F	99.27 (96.00, 99.98)	99.29 (96.08, 99.98)	98.88 (93.90, 99.97)	97.73 (92.03, 99.72)	98.89 (93.96, 99.97)	97.80 (92.29, 99.73)	98.96 (94.33, 99.97)	100.00 (96.23, 100.00)	100.00 (97.32, 100.00)	100.00 (97.32, 100.00)				

Note: N: number of subjects meets protocol set; CI\*: two sided 95%CI for proportion of subjects with OPA antibody titers ≥ 1:8

Table 6 OPA antibody GMT for all age groups (PPS)

Serotype	After primary immunization												After booster immunization										
	2 months				7-11 months				12-23 months				2-5 years old		2 months								
	PCV-13 N=137	Prevnar 13 N=140	PCV-13 N=89	Prevnar 13 N=88	PCV-13 N=90	Prevnar 13 N=91	PCV-13 N=96	Prevnar 13 N=96	PCV-13 N=136	Prevnar 13 N=136	PCV-13 N=137	Prevnar 13 N=140	PCV-13 N=89	Prevnar 13 N=88	PCV-13 N=90	Prevnar 13 N=91	PCV-13 N=96	Prevnar 13 N=96	PCV-13 N=136	Prevnar 13 N=136			
1	64.52 (54.34, 76.61)	82.51 (67.79, 100.43)	47.86 (36.31, 63.08)	80.59 (62.98, 103.14)	31.82 (25.11, 40.33)	43.10 (33.91, 54.77)	58.24 (42.66, 79.51)	61.38 (47.25, 79.75)	201.76 (167.99, 242.32)	218.77 (179.76, 266.25)	267.14 (228.63, 312.14)	176.85 (151.17, 206.90)	280.43 (243.07, 323.53)	273.00 (235.21, 316.87)	185.42 (161.24, 213.24)	172.48 (148.57, 200.24)	235.05 (196.90, 280.60)	201.09 (165.60, 244.20)	388.85 (334.67, 451.80)	388.85 (229.73, 309.20)	266.52 (229.73, 309.20)		
3	1696.09 (1474.93, 1950.40)	1694.93 (1465.91, 1959.73)	1495.03 (1272.05, 1757.08)	1380.59 (1171.74, 1626.66)	2631.87 (2165.10, 3199.27)	2688.68 (2198.68, 3287.87)	5217.19 (4385.46, 6206.67)	4882.70 (4157.99, 5733.73)	3745.48 (3223.64, 4351.78)	3745.48 (3223.64, 4351.78)	1696.09 (1474.93, 1950.40)	1694.93 (1465.91, 1959.73)	1495.03 (1272.05, 1757.08)	1380.59 (1171.74, 1626.66)	2631.87 (2165.10, 3199.27)	2688.68 (2198.68, 3287.87)	5217.19 (4385.46, 6206.67)	4882.70 (4157.99, 5733.73)	3745.48 (3223.64, 4351.78)	3745.48 (3223.64, 4351.78)	3245.96 (2752.51, 3827.86)	3245.96 (2752.51, 3827.86)	
4	99.29 (72.03, 136.88)	482.13 (412.70, 563.23)	29.41 (21.94, 39.42)	151.57 (124.61, 184.38)	13.43 (9.88, 18.26)	92.95 (66.90, 129.15)	10.49 (7.10, 15.51)	204.72 (162.66, 257.66)	241.31 (173.42, 335.78)	572.43 (496.14, 660.43)	99.29 (72.03, 136.88)	482.13 (412.70, 563.23)	29.41 (21.94, 39.42)	151.57 (124.61, 184.38)	13.43 (9.88, 18.26)	92.95 (66.90, 129.15)	10.49 (7.10, 15.51)	204.72 (162.66, 257.66)	241.31 (173.42, 335.78)	572.43 (496.14, 660.43)	572.43 (496.14, 660.43)	10256.74 (8673.02, 12129.66)	10256.74 (8673.02, 12129.66)
5	3414.20 (2705.04, 4309.26)	5690.83 (4750.80, 6816.86)	1760.46 (1317.25, 2352.79)	2736.14 (2203.17, 3398.04)	5980.41 (4536.39, 7884.11)	4913.92 (3385.37, 7132.63)	5557.29 (4443.70, 6949.93)	6319.75 (5142.08, 7767.13)	8310.48 (6841.70, 10094.57)	8310.48 (6841.70, 10094.57)	3414.20 (2705.04, 4309.26)	5690.83 (4750.80, 6816.86)	1760.46 (1317.25, 2352.79)	2736.14 (2203.17, 3398.04)	5980.41 (4536.39, 7884.11)	4913.92 (3385.37, 7132.63)	5557.29 (4443.70, 6949.93)	6319.75 (5142.08, 7767.13)	8310.48 (6841.70, 10094.57)	8310.48 (6841.70, 10094.57)	10256.74 (8673.02, 12129.66)	10256.74 (8673.02, 12129.66)	
6A	2433.14 (2046.97, 2892.16)	2692.76 (2147.39, 3376.65)	863.06 (549.84, 1354.68)	1129.24 (748.13, 1704.49)	4135.98 (3014.32, 5675.01)	3046.04 (2032.74, 4564.45)	4573.43 (3293.37, 6351.02)	5207.37 (4231.84, 6407.79)	8249.30 (6686.77, 10994.93)	8833.50 (7095.36, 10994.93)	2433.14 (2046.97, 2892.16)	2692.76 (2147.39, 3376.65)	863.06 (549.84, 1354.68)	1129.24 (748.13, 1704.49)	4135.98 (3014.32, 5675.01)	3046.04 (2032.74, 4564.45)	4573.43 (3293.37, 6351.02)	5207.37 (4231.84, 6407.79)	8249.30 (6686.77, 10994.93)	8833.50 (7095.36, 10994.93)	8833.50 (7095.36, 10994.93)	8833.50 (7095.36, 10994.93)	
6B	21024.32 (18152.20, 24350.88)	15161.14 (13175.95, 17445.44)	25368.69 (20589.68, 31256.94)	8311.71 (7211.35, 9579.96)	39583.25 (33086.75, 47355.31)	17248.59 (14213.01, 20932.50)	25088.01 (21679.81, 29031.99)	21140.82 (17997.50, 24833.14)	21546.00 (18777.59, 24722.56)	11435.93 (10049.84, 13013.19)	21024.32 (18152.20, 24350.88)	15161.14 (13175.95, 17445.44)	25368.69 (20589.68, 31256.94)	8311.71 (7211.35, 9579.96)	39583.25 (33086.75, 47355.31)	17248.59 (14213.01, 20932.50)	25088.01 (21679.81, 29031.99)	21140.82 (17997.50, 24833.14)	21546.00 (18777.59, 24722.56)	11435.93 (10049.84, 13013.19)	11435.93 (10049.84, 13013.19)	11435.93 (10049.84, 13013.19)	
7F	1645.53 (1408.42, 1922.55)	1550.95 (1314.42, 1830.05)	1329.58 (1049.72, 1684.04)	1709.45 (1280.27, 2282.52)	3425.08 (2729.11, 4298.52)	3723.45 (3010.18, 4605.73)	5894.19 (4786.51, 7258.22)	6539.99 (5495.94, 7782.37)	1929.21 (1663.58, 2237.25)	2221.24 (1876.91, 2628.73)	1645.53 (1408.42, 1922.55)	1550.95 (1314.42, 1830.05)	1329.58 (1049.72, 1684.04)	1709.45 (1280.27, 2282.52)	3425.08 (2729.11, 4298.52)	3723.45 (3010.18, 4605.73)	5894.19 (4786.51, 7258.22)	6539.99 (5495.94, 7782.37)	1929.21 (1663.58, 2237.25)	2221.24 (1876.91, 2628.73)	2221.24 (1876.91, 2628.73)	2221.24 (1876.91, 2628.73)	
9V	3847.74 (3086.64, 4796.51)	3526.90 (2818.15, 4413.91)	2344.10 (1961.08, 2801.93)	2767.64 (2314.44, 3309.59)	3447.71 (2807.82, 4233.41)	4138.67 (3433.06, 4989.30)	6332.07 (4824.98, 8309.90)	7482.51 (6023.99, 9294.17)	3639.87 (3080.09, 4301.38)	3836.43 (3159.09, 4659.00)	3847.74 (3086.64, 4796.51)	3526.90 (2818.15, 4413.91)	2344.10 (1961.08, 2801.93)	2767.64 (2314.44, 3309.59)	3447.71 (2807.82, 4233.41)	4138.67 (3433.06, 4989.30)	6332.07 (4824.98, 8309.90)	7482.51 (6023.99, 9294.17)	3639.87 (3080.09, 4301.38)	3836.43 (3159.09, 4659.00)	3836.43 (3159.09, 4659.00)	3836.43 (3159.09, 4659.00)	
14	1126.10 (938.00, 1351.91)	2424.58 (2020.54, 2909.41)	423.78 (309.84, 579.64)	798.31 (646.39, 985.93)	1691.44 (1295.27, 2208.78)	1849.70 (1417.27, 2414.07)	2382.24 (1884.39, 3011.62)	2832.33 (2300.58, 3487.00)	2690.79 (2219.45, 3262.24)	2845.63 (2428.41, 3334.55)	1126.10 (938.00, 1351.91)	2424.58 (2020.54, 2909.41)	423.78 (309.84, 579.64)	798.31 (646.39, 985.93)	1691.44 (1295.27, 2208.78)	1849.70 (1417.27, 2414.07)	2382.24 (1884.39, 3011.62)	2832.33 (2300.58, 3487.00)	2690.79 (2219.45, 3262.24)	2845.63 (2428.41, 3334.55)	2845.63 (2428.41, 3334.55)	2845.63 (2428.41, 3334.55)	
18C	2752.83 (2325.80, 3258.26)	2031.98 (1711.06, 2413.09)	1698.13 (1341.71, 2149.24)	1605.41 (1275.97, 2019.90)	3686.14 (3065.41, 4432.56)	2995.44 (2438.89, 3678.98)	3301.96 (2551.16, 4273.71)	4118.02 (3269.75, 5186.59)	5563.22 (4839.25, 6395.50)	4829.45 (4170.44, 5592.59)	2752.83 (2325.80, 3258.26)	2031.98 (1711.06, 2413.09)	1698.13 (1341.71, 2149.24)	1605.41 (1275.97, 2019.90)	3686.14 (3065.41, 4432.56)	2995.44 (2438.89, 3678.98)	3301.96 (2551.16, 4273.71)	4118.02 (3269.75, 5186.59)	5563.22 (4839.25, 6395.50)	4829.45 (4170.44, 5592.59)	4829.45 (4170.44, 5592.59)	4829.45 (4170.44, 5592.59)	
19A	1440.21 (1210.15, 1714.01)	545.52 (466.39, 638.07)	1141.87 (858.25, 1519.21)	519.43 (416.03, 648.53)	1516.83 (1103.50, 2084.97)	982.95 (787.96, 1226.20)	2283.29 (1904.10, 2737.99)	1288.58 (1058.67, 1568.43)	2394.17 (2077.35, 2759.30)	1171.53 (1025.41, 1338.46)	1440.21 (1210.15, 1714.01)	545.52 (466.39, 638.07)	1141.87 (858.25, 1519.21)	519.43 (416.03, 648.53)	1516.83 (1103.50, 2084.97)	982.95 (787.96, 1226.20)	2283.29 (1904.10, 2737.99)	1288.58 (1058.67, 1568.43)	2394.17 (2077.35, 2759.30)	1171.53 (1025.41, 1338.46)	1171.53 (1025.41, 1338.46)	1171.53 (1025.41, 1338.46)	
19F	7673.09 (6104.85, 9644.17)	7288.41 (5706.15, 9309.40)	3011.41 (2141.00, 4235.69)	3180.59 (2193.92, 4610.98)	8125.45 (6055.05, 10903.79)	6390.47 (4551.71, 8972.02)	6692.46 (5094.31, 8791.99)	4987.88 (3998.22, 6222.51)	18517.82 (15682.04, 21866.40)	15690.48 (12818.02, 19206.64)	7673.09 (6104.85, 9644.17)	7288.41 (5706.15, 9309.40)	3011.41 (2141.00, 4235.69)	3180.59 (2193.92, 4610.98)	8125.45 (6055.05, 10903.79)	6390.47 (4551.71, 8972.02)	6692.46 (5094.31, 8791.99)	4987.88 (3998.22, 6222.51)	18517.82 (15682.04, 21866.40)	15690.48 (12818.02, 19206.64)	15690.48 (12818.02, 19206.64)	15690.48 (12818.02, 19206.64)	
23F																							

Note: N: number of subjects meets protocol set; C\*: two-sided 95%CI for OP A antibody GMT.

## 5.2 Pharmacokinetic properties

Not applicable.

## 5.3 Preclinical safety data

Non-clinical data obtained from single dose and repeated dose toxicology and local tolerance studies showed that Pneucia13 is safe and well tolerated in animals.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Aluminum phosphate (adjuvant)  
Polysorbate 80  
Sodium chloride  
Succinic acid  
Water for Injection

## 6.2 Incompatibilities

This vaccine must not be mixed with other medicinal products.

## 6.3 Shelf life

Please use before the expiration date printed on the label or box

## 6.4 Special precautions for storage

### Storage condition:

The vaccine should be stored and transported under 2°C - 8 °C. Protect from light.

The product is used for a **MAXIMUM of 7 DAYS** after opened.

**DO NOT FREEZE.** Discard if the vaccine is frozen.

Keep the product in places out of children's reach

### Instructions for use:

- Homogenize the vials by shaking for 10 times until homogenous.
- Use a new sterile syringe for each injection
- Disinfect the rubber stopper with 70% alcohol before puncturing and drawing the dose, and consistently maintain aseptic conditions during vaccine withdrawal
- Duration of vaccine withdrawing should not exceed 60 seconds.
- The dose is 0.5 mL given intramuscularly, with care to avoid injection into or near nerves and blood vessel.
- The vaccine should be shake for 10 times before withdrawing the next dose.
- The product is used for a **MAXIMUM OF 7 DAYS** after opened.
- Once opened, multi-dose vials should be kept in a clean, tightly sealed container at a temperature between +2°C and +8°C, protect from light.
- The second, third, and fourth vaccine doses can be stored in the vaccine vial
- Adhering the use of storage duration and other conditions are the responsibility of the user

### 6.5 Nature and contents of container

2.0 mL suspension for injection in vial clear type I with a rubber stopper (halogenated butyl) and aluminum plastics combined caps.

### 6.6 Special precautions for disposal and other handling

During storage, a white deposit and clear supernatant may be observed.

The vaccine should be shaken well to obtain a homogeneous white suspension. Do not use it if there are clots that cannot be shaken apart, or found any foreign matters, discoloration or unclear labels.

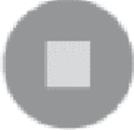
No special requirements for disposal.

Any unused vaccine or waste material should be disposed of properly in accordance with local requirements.

## 7 How to read Vaccine Vial Monitor

Vaccine Vial Monitors (VVMs) is on the vial label of Pneucia13. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level. **Please kindly check the indicator before using it.**

The interpretation of the VVM is simple. Focus on the central square. Its color will change progressively. As long as the color of this square is lighter than the color of the outer circle, then the vaccine can be used. As soon as the color of the central square is the same color as the outer circle or of a darker color than the outer circle, then the vial should be discarded. Please find the following example for reference.

<p>A</p> 		<p>Square lighter than circle</p> <p><b>Use vaccine if the expiry date has not been passed</b></p>
<p>B</p> 		<p>Square darkened but lighter than circle</p> <p><b>Use vaccine if the expiry date has not been passed</b></p>
<p>C</p> 		<p>Discard point:</p> <p>Square is the same colour as the circle</p> <p><b>DO NOT USE VACCINE</b></p>
<p>D</p> 		<p>Beyond the discard point:</p> <p>Square is darker than the circle</p> <p><b>DO NOT USE VACCINE</b></p>

**8 REGISTERED BY**

PT Etana Biotechnologies Indonesia

Jakarta – Indonesia

**9 PACKAGING AND MARKETING AUTHORISATION NUMBER**

Box, 50 vials @ 2.0 mL (4 x 0.5 mL doses)

No. Reg.: XXXXXXXXXXXXXXXXX

**10 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorization: {DD MM YYYY}

**11 DATE OF REVISION OF THE TEXT**

First version dated MM/DD/YYYY

**HARUS DENGAN RESEP DOKTER**



## Leaflet Kemasan: Informasi bagi Pengguna

### Pneucia13

13-valent Pneumococcal Polysaccharide Conjugate Vaccine  
Suspensi untuk injeksi

**Bacalah seluruh isi leaflet ini dengan cermat sebelum anak Anda menerima vaksin ini karena leaflet ini memuat informasi penting untuk Anda.**

- ✧ Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- ✧ Jika Anda memiliki pertanyaan lebih lanjut, hubungi dokter, apoteker, atau perawat Anda.
- ✧ Vaksin ini diresepkan hanya untuk anak Anda. Jangan diberikan kepada orang lain.
- ✧ Jika anak Anda merasakan efek samping apa pun, hubungi dokter, apoteker, atau perawat Anda. Ini termasuk segala bentuk efek samping yang tidak tercantum di dalam leaflet ini. Lihat bagian 4.

#### Isi leaflet ini:

1. Penjelasan tentang Pneucia13 dan kegunaannya
2. Yang perlu Anda ketahui sebelum anak Anda menerima Pneucia13
3. Cara pemberian Pneucia13
4. Kemungkinan efek samping
5. Cara menyimpan Pneucia13
6. Isi kemasan dan informasi lainnya

#### 1. Penjelasan tentang Pneucia13 dan kegunaannya

Pneucia13 adalah vaksin pneumokokus yang diberikan kepada anak-anak berusia 2 bulan (minimal 6 minggu) hingga 5 tahun untuk membantu melindungi terhadap penyakit seperti: meningitis (peradangan selaput otak), sepsis atau bakteremia (bakteri dalam aliran darah), pneumonia (infeksi paru-paru) yang disebabkan oleh 13 jenis bakteri *Streptococcus pneumoniae*.

Pneucia13 memberikan perlindungan terhadap 13 jenis bakteri *Streptococcus pneumoniae*.

Vaksin ini bekerja dengan membantu tubuh membuat antibodi sendiri, yang melindungi anak Anda terhadap penyakit ini.

#### 2. Yang perlu Anda ketahui sebelum anak Anda menerima Pneucia13

##### Jangan gunakan Pneucia13 jika anak Anda:

- ✧ alergi (hipersensitif) terhadap zat aktif atau bahan lain dalam vaksin ini (tercantum dalam bagian 6).

- ✧ mengalami infeksi berat disertai demam (lebih dari 38°C). Jika hal ini terjadi pada anak Anda, maka vaksinasi akan ditunda hingga anak Anda merasa lebih baik. Beri tahu dokter, apoteker, atau perawat Anda terlebih dahulu jika anak Anda mengalami infeksi ringan.

### **Peringatan dan tindakan pencegahan:**

Jika anak Anda memiliki kondisi berikut, silahkan hubungi dokter, apoteker, atau perawat Anda:

- ✧ Memiliki masalah medis saat ini atau sebelumnya setelah menerima dosis vaksin konjugat pneumokokus seperti reaksi alergi atau masalah pernapasan.
- ✧ Memiliki masalah pendarahan atau mudah memar.
- ✧ Memiliki sistem kekebalan tubuh yang lemah (seperti akibat infeksi HIV), ia mungkin tidak mendapatkan manfaat penuh dari Pneucia13.
- ✧ Jika anak Anda tidak responsif atau mengalami kejang setelah vaksinasi, segera hubungi dokter Anda.
- ✧ Informasikan kepada dokter, apoteker, atau perawat Anda sebelum vaksinasi jika anak Anda lahir sangat prematur (pada atau sebelum 30 minggu kehamilan), karena risiko potensial henti napas dapat terjadi setelah vaksinasi.
- ✧ Seperti halnya vaksin lainnya, Pneucia13 tidak akan melindungi semua orang yang divaksinasi.
- ✧ Pneucia13 hanya dapat melindungi terhadap infeksi pada anak-anak yang disebabkan oleh 13 jenis *Streptococcus pneumoniae* yang tercakup dalam vaksin. Vaksin ini tidak akan melindungi terhadap agen infeksius lain yang dapat menyebabkan penyakit invasif, pneumonia, atau otitis media.

### **Obat/vaksin lain dan Pneucia13**

Informasikan kepada dokter, apoteker, atau perawat Anda jika anak Anda sedang, baru baru ini, atau mungkin akan mengonsumsi obat lain, atau baru saja menerima vaksin lain.

### **3. Cara Pemberian Pneucia13**

Dokter atau perawat akan menyuntikkan dosis vaksin Pneucia13 yang direkomendasikan (0,5 mL) ke bagian otot lengan atau otot tengah paha anak Anda.

#### Bayi berusia 2 bulan (minimal 6 minggu):

Biasanya, anak Anda harus menerima tiga suntikan vaksin primer dan satu dosis *booster*.

Suntikan pertama dapat diberikan sejak usia 2 bulan (minimal enam minggu).

Setiap suntikan akan diberikan dengan jarak dua bulan.

Suntikan keempat (*booster*) akan diberikan pada usia 12-15 bulan.

#### Bayi berusia 2 bulan (minimal 6 minggu):

Biasanya, anak Anda harus menerima tiga suntikan vaksin primer dan satu dosis *booster*.

Suntikan pertama dapat diberikan sejak usia 3 bulan.

Setiap suntikan akan diberikan dengan jarak satu bulan.

Suntikan keempat (*booster*) akan diberikan pada usia 12-15 bulan.

Menurut rekomendasi resmi di negara Anda, jadwal alternatif dapat digunakan oleh penyedia layanan kesehatan Anda. Silakan hubungi dokter, apoteker, atau perawat Anda untuk informasi lebih lanjut.

Bayi dan anak-anak berusia 7 bulan – 5 tahun yang belum divaksinasi:

Bayi berusia **7 hingga 11 bulan** harus menerima tiga suntikan. Suntikan kedua akan diberikan dengan jarak dua bulan setelah suntikan pertama. Suntikan ketiga akan diberikan pada usia 12-15 bulan, dengan jarak setidaknya dua bulan dari suntikan kedua.

Anak-anak berusia **12 hingga 23 bulan** harus menerima dua suntikan. Setiap suntikan akan diberikan dengan jarak setidaknya dua bulan.

Anak-anak berusia **2 hingga 5 tahun** harus menerima satu suntikan dosis.

#### **4. Kemungkinan Efek Samping**

Seperti semua vaksin yang ada, vaksin Pneucia13 dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Berikut ini adalah efek samping untuk bayi berusia 2 bulan (minimal 6 minggu) hingga 6 bulan:

Efek samping yang paling umum (mengacu pada kejadian  $\geq 10\%$ ):

- Kemerahan di lokasi injeksi
- Demam

Efek samping yang umum [(mengacu pada kejadian 1-10% (termasuk 1%))]:

- Pembengkakan di lokasi injeksi
- Muntah, diare, batuk, iritabilitas

Efek samping yang tidak umum [mengacu pada kejadian 0,1-1% (termasuk 0,1%)]:

- Nyeri, indurasi di tempat suntikan
- Mual, gangguan mukokutan, nafsu makan menurun, mengantuk, pilek, perut kembung, ruam virus, peningkatan sputum

Efek samping pada bayi berusia 7 bulan hingga 11 bulan:

Efek samping yang paling umum (mengacu pada insidensi  $\geq 10\%$ ):

- Kemerahan di tempat suntikan
- Demam

Efek samping yang umum [(mengacu pada insidensi 1-10% (termasuk 1%))]:

- Bengkak di tempat suntikan
- Diare, batuk, muntah

Efek samping yang jarang terjadi [mengacu pada kejadian 0,1-1% (termasuk 0,1%)]:

- Indurasi di tempat suntikan, nyeri di tempat suntikan
- Iritabilitas, reaksi alergi, gangguan mukosa kulit

Efek samping pada bayi berusia 12 bulan hingga 5 tahun:

Efek samping yang paling umum (mengacu pada insidensi  $\geq 10\%$ ):

- Kemerahan di tempat suntikan

- Demam

Efek samping yang umum [(mengacu pada insidensi 1-10% (termasuk 1%))]:

- Bengkak di tempat suntikan, nyeri di tempat suntikan
- Diare, batuk, muntah

Efek samping yang jarang terjadi [mengacu pada kejadian 0,1-1% (termasuk 0,1%)]:

- Pruritus di tempat suntikan, indurasi di tempat suntikan
- Iritabilitas, reaksi alergi, nafsu makan menurun, pilek

Hubungi dokter, apoteker, atau perawat anak Anda jika mengalami efek samping apa pun, termasuk yang tidak tercantum dalam brosur ini.

### **Efek samping lain dari vaksin yang dipasarkan**

Laporan studi klinis dan pengawasan pasca-pemasaran dari vaksin konjugat polisakarida pneumokokus 13-valen yang serupa yang juga telah dipasarkan mencakup reaksi efek samping seperti urtikaria, kejang (termasuk kejang demam), kejadian hipotonik-hiporesponsif, nasofaringitis, infeksi saluran pernapasan atas, dermatitis alergi, ulserasi mulut, nyeri perut, hiperhidrosis, peningkatan lakrimasi, mata berair, dan kemerahan pada kelopak mata.

### **Pelaporan dugaan efek samping**

Pelaporan dugaan efek samping setelah otorisasi produk obat penting dilakukan. Hal ini memungkinkan pemantauan berkelanjutan terhadap keseimbangan manfaat/risiko produk obat. Tenaga Kesehatan profesional diminta untuk melaporkan setiap dugaan reaksi efek samping.

Kontak Pelaporan Industri Farmasi

PT Etana Biotechnologies Indonesia  
Kawasan Industri Pulogadung, Jl. Rawa Gelam V, Blok. L, Kav. 11-13, Jakarta  
Email: [pv@id.etanabiotech.com](mailto:pv@id.etanabiotech.com)  
Website: <https://ebi-pharmacovigilance.azurewebsites.net/>

MESO Center/National Pharmacovigilance Center

Direktorat Pengawasan Distribusi Produk Terapetik dan PKRT Badan POM RI  
Jl. Percetakan Negara 23 Jakarta Pusat, 10560  
No Telp: 021 – 4244 755 ext.111  
Fax: 021 – 4288 3485  
Email: [pv-center@pom.go.id](mailto:pv-center@pom.go.id) dan [Indonesia-meso-badanpom@hotmail.com](mailto:Indonesia-meso-badanpom@hotmail.com)

## **5. Cara Menyimpan Pneucia13**

Jauhkan vaksin ini dari pandangan dan jangkauan anak-anak.

Jangan menggunakan vaksin ini setelah tanggal kedaluwarsa yang tertera pada karton dan label setelah tanda EXP.

Simpan dan transportasikan di dalam lemari pendingin (2°C - 8°C). Lindungi dari cahaya.

Produk digunakan **MAKSIMAL 7 HARI** setelah dibuka.

Setelah dibuka vial multi-dose harus disimpan pada suhu antara +2°C hingga +8°C

Jangan dibekukan. Buang jika vaksin sudah membeku.

Selama penyimpanan, akan teramati adanya endapan putih dan supernatan yang bening. Kondisi ini tidaklah menunjukkan tanda kerusakan.

Jangan membuang obat melalui saluran pembuangan air atau bersama sampah rumah tangga. Tanyakan apoteker Anda cara membuang vaksin yang sudah tidak digunakan lagi. Langkah-langkah ini akan membantu melindungi lingkungan.

## 6. Isi kemasan dan informasi lainnya Apa saja kandungan Pneucia13:

Zat aktifnya adalah polisakarida yang terkonjugasi dengan CRM197 atau Tetanus Toxoid yang terdiri dari:

2,2 µg polisakarida untuk serotipe 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F

4,4 µg polisakarida untuk serotipe 6B

1 dosis (0,5 mL) mengandung protein pembawa CRM197 dan Tetanus Toxoid, yang diserap pada aluminium fosfat (0,125 mg aluminium).

Bahan lainnya adalah polisorbitat 80, natrium klorida, asam suksinat, dan air untuk injeksi.

## Seperti apa bentuk Pneucia13 dan isi kemasannya

Vaksin ini berupa suspensi putih homogen untuk injeksi, tersedia dalam vial multidosis 2,0 mL (4 x 0,5 mL).

Box, 50 vial @2,0 mL (4 x 0,5 mL dosis)

**HARUS DENGAN RESEP DOKTER**

## Nomor Izin Edar

No. Reg: XXXXXXXXXXXXXXXXX

## Produsen

PT Etana Biotechnologies Indonesia.

Jakarta – Indonesia

Leaflet ini terakhir kali direvisi pada MM/DD/YYYY

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## Informasi berikut ditujukan hanya untuk tenaga kesehatan:

Selama penyimpanan, endapan putih dan supernatan jernih dapat teramati

Periksa secara visual keberadaan partikel benda asing dan/atau wujud fisik yang tidak normal; jangan digunakan jika ditemukan salah satunya.

1. Kocok vial sebanyak 10 kali untuk membentuk suspensi putih yang homogen.

2. Gunakan jarum suntik steril baru untuk setiap injeksi
3. Disinfeksi pada *rubber stopper* dengan alcohol 70% sebelum penusukan dan pengambilan dosis vaksin harus dilakukan secara konsisten untuk menjaga kondisi aseptik
4. Durasi penarikan vaksin tidak boleh lebih dari 60 detik.
5. Berikan dosis vaksin 0,5 mL secara intramuskular
6. Kocok vial sebanyak 10 kali sebelum penarikan dosis berikutnya.
7. Produk digunakan **MAKSIMAL 7 HARI** setelah dibuka.
8. Setelah dibuka, simpan vial yang sudah dibuka dalam wadah tertutup bersih dan rapat, serta simpan pada suhu antara +2°C hingga +8°C dan terlindung dari cahaya
9. Dosis vaksin kedua, ketiga, dan keempat dapat disimpan pada vial vaksin
10. Penggunaan waktu penyimpanan dan kondisi lainnya adalah tanggung jawab pengguna

Pneucia13 hanya untuk penggunaan intramuskular. Jangan diberikan secara intravena atau dengan injeksi intramuskular gluteal, dan pastikan jarum suntik tidak menusuk pembuluh darah selama injeksi.

Dilarang mencampur Pneucia13 dengan vaksin lain dalam alat suntik yang sama. Pneucia13 harus segera disuntikkan setelah diambil ke dalam alat suntik.

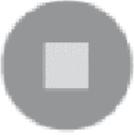
Pneucia13 dapat diberikan pada waktu yang sama dengan vaksin anak lainnya; dalam hal ini harus digunakan pada lokasi vaksinasi yang berbeda.

Setiap produk yang tidak digunakan atau materi limbah harus dibuang sesuai dengan persyaratan setempat.

### Bagaimana cara membaca Vaccine Vial Monitor

Vaccine Vial Monitors (VVMs) terdapat pada label kemasan Pneucia13. Ini merupakan titik indikator yang sensitif terhadap waktu dan suhu, yang memberikan informasi mengenai akumulasi paparan panas yang telah diterima vial. VVM memberi peringatan kepada pengguna apabila paparan panas kemungkinan besar telah menurunkan kualitas vaksin melebihi batas yang dapat diterima. **Harap periksa indikator terlebih dahulu sebelum digunakan.**

Interpretasi VVM sangat mudah. Fokus pada kotak dibagian tengah. Warnanya akan berubah secara bertahap. Selama warna segi empat lebih terang dibandingkan dengan warna lingkaran luar, maka vaksin masih dapat digunakan. Jika warna segi empat sama dengan atau lebih gelap dari lingkaran luar, maka

 A		Segi empat lebih terang dari lingkaran  <b>Gunakan vaksin bila belum kedaluwarsa</b>
 B		Segi empat berubah gelap tapi lebih terang dari lingkaran  <b>Gunakan vaksin lebih dahulu bila belum kedaluwarsa</b>
 C		Batas untuk tidak digunakan lagi: Segi empat berwarna sama dengan lingkaran  <b>JANGAN GUNAKAN VAKSIN</b>
 D		Melewati Batas Buang: Segi empat lebih gelap dari lingkaran  <b>JANGAN GUNAKAN VAKSIN</b>

vaksin harus dibuang. Silahkan lihat contoh berikut sebagai referensi.

