



## Clinical trial results:

**A phase III open-label randomised study, to evaluate the immunogenicity and safety of the concomitant administration of V419 (PR5I) given at 2, 3 and 4 months of age with two types of meningococcal serogroup C conjugate (MCC) vaccines given at 3 and 4 months of age, and followed by the administration at 12 months of age of a combined Haemophilus influenzae type b-MCC vaccine.**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2011-002413-11    |
| Trial protocol           | GB                |
| Global end of trial date | 27 September 2013 |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1             |
| This version publication date  | 27 April 2016  |
| First version publication date | 02 August 2015 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | PRI01C |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01553279 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                              |
|------------------------------|----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Sanofi Pasteur MSD S.N.C.                                                                    |
| Sponsor organisation address | 162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367                              |
| Public contact               | Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C.,<br>ClinicalTrialsDisclosure@spmsd.com |
| Scientific contact           | Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C.,<br>ClinicalTrialsDisclosure@spmsd.com |

Notes:

### Paediatric regulatory details

|                                                                      |     |
|----------------------------------------------------------------------|-----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No  |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

|                                                      |                   |
|------------------------------------------------------|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 27 September 2013 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 27 September 2013 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 27 September 2013 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the concomitant administration of PR5I with 2 types of MCC vaccines (MCC-TT and MCC-CRM) to healthy infants at 3 and 4 months of age in terms of antibody seroprotection rate (SPR) to MCC.

Protection of trial subjects:

Healthy subjects with known or suspected hypersensitivity to any of the study vaccines' component or history of a life-threatening reaction to a vaccine containing the same substances as the study vaccines were excluded.

Vaccines were administered by qualified study personnel.

After each vaccination, subjects were kept under observation for at least 30 minutes to ensure their safety. Adequate treatment provisions, including epinephrine, were to be available for immediate use if an anaphylactic or anaphylactoid reaction occurred.

Background therapy: -

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 30 March 2012 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 284 |
| Worldwide total number of subjects   | 284                 |
| EEA total number of subjects         | 284                 |

Notes:

### Subjects enrolled per age group

|                                           |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 284 |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 0   |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Study subjects were enrolled in 11 active centres in the United Kingdom (UK).

### Pre-assignment

Screening details:

292 subjects were screened.

284 subjects were randomised.

282 subjects received all 3 doses of PR5I vaccine and all 2 doses of MCC vaccines (period 1).

281 subjects completed period 1 of the study.

5 subjects discontinued between periods 1 & 2.

276 subjects entered period 2 and received Hib-MCC vaccine.

266 subjects completed the study.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Infant doses            |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

Blinding implementation details:

Not applicable as this study was open-label.

Serology tests were performed by laboratory staffs that were blinded for the group to which each subject was randomised.

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | MCC-TT (period 1) |

Arm description:

Subjects received:

# 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by intramuscular (IM) route: dose 1 at 2 months of age (Visit 1, V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).

# 2 doses of MCC-TT vaccine (NeisVac-C® = Meningococcal group C polysaccharide Conjugate vaccine to tetanus toxoid) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).

# As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).

Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-TT vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-TT vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

|                                        |                          |
|----------------------------------------|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | PR5I vaccine             |
| Investigational medicinal product code | DTaP-HB-IPV-Hib          |
| Other name                             | V419                     |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

0.5 mL, IM route (left thigh), 3 doses: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2), and dose 3 at 4 months of age (V3).

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | NeisVac-C®               |
| Investigational medicinal product code | MCC-TT vaccine           |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:  
0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 2 doses: dose 1 at 3 months of age (V2), and dose 2 at 4 months of age (V3).

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Prevenar 13®             |
| Investigational medicinal product code | PCV-13 vaccine           |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:  
0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MCC-TT vaccine injection-site), 2 doses: dose 1 at 2 months of age (V1), and dose 2 at 4 months of age (V3).

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | MCC-CRM (period 1) |
|------------------|--------------------|

Arm description:

Subjects received:

# 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by IM route: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).

# 2 doses of MCC-CRM vaccine (Menjugate® = Meningococcal group C Conjugate vaccine to CRM-197) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).

# As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).

Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-CRM vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-CRM vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

|                                        |                          |
|----------------------------------------|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | PR5I vaccine             |
| Investigational medicinal product code | DTaP-HB-IPV-Hib          |
| Other name                             | V419                     |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:  
0.5 mL, IM route (left thigh), 3 doses: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2), and dose 3 at 4 months of age (V3).

|                                        |                                                 |
|----------------------------------------|-------------------------------------------------|
| Investigational medicinal product name | Menjugate®                                      |
| Investigational medicinal product code | MCC-CRM vaccine                                 |
| Other name                             |                                                 |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:  
0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 2 doses: dose 1 at 3 months of age (V2), and dose 2 at 4 months of age (V3).

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Prevenar 13®             |
| Investigational medicinal product code | PCV-13 vaccine           |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:  
0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MCC-CRM vaccine injection-site), 2 doses: dose 1 at 2 months of age (V1), and dose 2 at 4 months of age (V3).

| Number of subjects in period 1 | MCC-TT (period 1) | MCC-CRM (period 1) |
|--------------------------------|-------------------|--------------------|
| Started                        | 142               | 142                |
| Completed                      | 140               | 141                |
| Not completed                  | 2                 | 1                  |
| Consent withdrawn by subject   | 1                 | 1                  |
| Lost to follow-up              | 1                 | -                  |

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Toddler dose            |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

Blinding implementation details:

Not applicable as this study was open-label.

Serology tests were performed by laboratory staffs that were blinded for the group to which each subject was randomised.

## Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| Arm title                    | MCC-TT (period 2) |

Arm description:

# Subjects of the "MCC-TT (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).

# As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).

Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).

|                                        |                                                 |
|----------------------------------------|-------------------------------------------------|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Menitorix®                                      |
| Investigational medicinal product code | Hib-MCC vaccine                                 |
| Other name                             |                                                 |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

0.5 mL, IM route (left thigh), 1 dose at 12 months of age (V5).

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Prevenar 13®             |
| Investigational medicinal product code | PCV-13 vaccine           |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MMR vaccine injection-site), 1 dose at 12 months of age (V5).

|                                        |              |
|----------------------------------------|--------------|
| Investigational medicinal product name | M-M-RvaxPRO® |
| Investigational medicinal product code | MMR vaccine  |
| Other name                             |              |

|                          |                                                 |
|--------------------------|-------------------------------------------------|
| Pharmaceutical forms     | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use                               |

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 1 dose at 12 months of age (V5).

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | MCC-CRM (period 2) |
|------------------|--------------------|

Arm description:

# Subjects of the "MCC-CRM (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).

# As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).

Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).

|                                        |                                                 |
|----------------------------------------|-------------------------------------------------|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Menitorix®                                      |
| Investigational medicinal product code | Hib-MCC vaccine                                 |
| Other name                             |                                                 |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

0.5 mL, IM route (left thigh), 1 dose at 12 months of age (V5).

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Prevenar 13®             |
| Investigational medicinal product code | PCV-13 vaccine           |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MMR vaccine injection-site), 1 dose at 12 months of age (V5).

|                                        |                                                 |
|----------------------------------------|-------------------------------------------------|
| Investigational medicinal product name | M-M-RvaxPRO®                                    |
| Investigational medicinal product code | MMR vaccine                                     |
| Other name                             |                                                 |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 1 dose at 12 months of age (V5).

| <b>Number of subjects in period 2<sup>[1]</sup></b> | MCC-TT (period 2) | MCC-CRM (period 2) |
|-----------------------------------------------------|-------------------|--------------------|
| Started                                             | 137               | 139                |
| Completed                                           | 134               | 132                |
| Not completed                                       | 3                 | 7                  |
| Consent withdrawn by subject                        | -                 | 5                  |
| Lost to follow-up                                   | 3                 | 2                  |

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Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: # In the MCC-TT arm, 3 subjects discontinued the study between the Infant doses and the Toddler dose: 1 "lost of follow-up" and 2 "consent withdrawn by subject".

# In the MCC-CRM arm, 2 subjects discontinued the study between the Infant doses and the Toddler dose: 2 "consent withdrawn by subject".



## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | MCC-TT (period 1) |
|-----------------------|-------------------|

Reporting group description:

Subjects received:

# 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by intramuscular (IM) route: dose 1 at 2 months of age (Visit 1, V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).

# 2 doses of MCC-TT vaccine (NeisVac-C® = Meningococcal group C polysaccharide Conjugate vaccine to tetanus toxoid) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).

# As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).

Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-TT vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-TT vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | MCC-CRM (period 1) |
|-----------------------|--------------------|

Reporting group description:

Subjects received:

# 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by IM route: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).

# 2 doses of MCC-CRM vaccine (Menjugate® = Meningococcal group C Conjugate vaccine to CRM-197) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).

# As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).

Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-CRM vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-CRM vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

| Reporting group values                                                  | MCC-TT (period 1) | MCC-CRM (period 1) | Total |
|-------------------------------------------------------------------------|-------------------|--------------------|-------|
| Number of subjects                                                      | 142               | 142                | 284   |
| Age categorical                                                         |                   |                    |       |
| Age at Visit 1.                                                         |                   |                    |       |
| Units: Subjects                                                         |                   |                    |       |
| Infants and toddlers (mini: 47 days-maxi: 76 days)                      | 142               | 142                | 284   |
| Age continuous                                                          |                   |                    |       |
| Age in days calculated as (date of vaccination dose 1-date of birth)+1. |                   |                    |       |
| Units: days                                                             |                   |                    |       |
| arithmetic mean                                                         | 62.6              | 61.6               |       |
| standard deviation                                                      | ± 6.7             | ± 7.2              | -     |
| Gender categorical                                                      |                   |                    |       |
| Units: Subjects                                                         |                   |                    |       |
| Female                                                                  | 62                | 67                 | 129   |
| Male                                                                    | 80                | 75                 | 155   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                          |                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                    | MCC-TT (period 1)       |
| Reporting group description:                                                                                                                                                                                                                                                                                                                             |                         |
| Subjects received:                                                                                                                                                                                                                                                                                                                                       |                         |
| # 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by intramuscular (IM) route: dose 1 at 2 months of age (Visit 1, V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3). |                         |
| # 2 doses of MCC-TT vaccine (NeisVac-C® = Meningococcal group C polysaccharide Conjugate vaccine to tetanus toxoid) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).                                                                                                                                                        |                         |
| # As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).                                                                                                                       |                         |
| Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-TT vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-TT vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).                                                                                                                                          |                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                    | MCC-CRM (period 1)      |
| Reporting group description:                                                                                                                                                                                                                                                                                                                             |                         |
| Subjects received:                                                                                                                                                                                                                                                                                                                                       |                         |
| # 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by IM route: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).                          |                         |
| # 2 doses of MCC-CRM vaccine (Menjugate® = Meningococcal group C Conjugate vaccine to CRM-197) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).                                                                                                                                                                             |                         |
| # As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).                                                                                                                       |                         |
| Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-CRM vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-CRM vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).                                                                                                                                        |                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                    | MCC-TT (period 2)       |
| Reporting group description:                                                                                                                                                                                                                                                                                                                             |                         |
| # Subjects of the "MCC-TT (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).                                                                                                                                    |                         |
| # As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).                                                                        |                         |
| Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).                                                                                                                                                            |                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                    | MCC-CRM (period 2)      |
| Reporting group description:                                                                                                                                                                                                                                                                                                                             |                         |
| # Subjects of the "MCC-CRM (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).                                                                                                                                   |                         |
| # As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).                                                                        |                         |
| Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).                                                                                                                                                            |                         |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                               | Combined vaccine groups |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                | Sub-group analysis      |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                        |                         |
| Combined vaccine groups = MCC-TT period 1 and MCC-CRM period 1 combined groups, i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.                                                                                                                                          |                         |

**Primary: Acceptability of the seroprotection rate (SPR) to MCC 1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4)**

|                 |                                                                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Acceptability of the seroprotection rate (SPR) to MCC 1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4) <sup>[1]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

The SPR to MCC (proportion of subjects with anti-MCC antibody (Ab) titre  $\geq 8$  (1/dil)) was determined 1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4). Anti-MCC Ab titres were measured by serum bactericidal antibody with rabbit complement (rSBA).

Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

## End point timeframe:

1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4).

## Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There was no comparison between groups in this end point.

The SPR to MCC was considered as acceptable if the lower bounds of the 2-sided 95% CI for the response rates were greater than 90% (i.e., the prespecified acceptability threshold).

Analysis was based on the 2-sided 95% CI with adjustment for multiplicity for single group proportion, calculated using the exact binomial method for binary variables as defined by D. Collet.

Acceptability criteria were met for MCC in both groups.

| End point values                       | MCC-TT (period 1) | MCC-CRM (period 1) |  |  |
|----------------------------------------|-------------------|--------------------|--|--|
| Subject group type                     | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed            | 121               | 109                |  |  |
| Units: Percentage of subjects          |                   |                    |  |  |
| number (confidence interval 95%)       |                   |                    |  |  |
| Anti-MCC $\geq 8$ (1/dil) (N=121, 109) | 100 (97 to 100)   | 99.1 (95 to 100)   |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Acceptability of the SPR to Hib (PRP) 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)**

|                 |                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Acceptability of the SPR to Hib (PRP) 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

The SPR to Hib (proportion of subjects with anti-polyribosylribitol phosphate (PRP) Ab titre  $\geq 0.15$   $\mu\text{g/mL}$ ) was determined 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

Anti-PRP Ab titres were measured by radioimmunoassay (RIA).

Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Acceptability of the SPR to Hib (based on anti-PRP Ab titre  $\geq 0.15$   $\mu\text{g/mL}$ ) analysis was based on the 2-sided 95% CI for single group proportion, calculated using the exact binomial method for binary variables as defined by D. Collet. If the lower bound of the 2-sided 95% CI was greater than 80% (i.e., the prespecified acceptability threshold), the SPR to Hib was considered as acceptable for the combined vaccine groups. Acceptability criterion was met.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

| End point values                              | Combined vaccine groups |  |  |  |
|-----------------------------------------------|-------------------------|--|--|--|
| Subject group type                            | Subject analysis set    |  |  |  |
| Number of subjects analysed                   | 175                     |  |  |  |
| Units: Percentage of subjects                 |                         |  |  |  |
| number (confidence interval 95%)              |                         |  |  |  |
| Anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ (N=175) | 98.9 (95.9 to 99.9)     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Proportion of subjects with anti-MCC Ab titres $\geq 8$ (1/dil) and $\geq 128$ (1/dil) 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4)

|                 |                                                                                                                                                                                                        |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of subjects with anti-MCC Ab titres $\geq 8$ (1/dil) and $\geq 128$ (1/dil) 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Proportion of subjects with anti-MCC Ab titres  $\geq 8$  (1/dil) and  $\geq 128$  (1/dil) was determined 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).

Anti-MCC Ab titres were measured by rSBA.

Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).

| End point values                                    | MCC-TT (period 1) | MCC-CRM (period 1)  |  |  |
|-----------------------------------------------------|-------------------|---------------------|--|--|
| Subject group type                                  | Reporting group   | Reporting group     |  |  |
| Number of subjects analysed                         | 121               | 109                 |  |  |
| Units: Percentage of subjects                       |                   |                     |  |  |
| number (confidence interval 95%)                    |                   |                     |  |  |
| Post-dose 1 anti-MCC $\geq 8$ (1/dil) (N=102, 84)   | 100 (96.4 to 100) | 96.4 (89.9 to 99.3) |  |  |
| Post-dose 1 anti-MCC $\geq 128$ (1/dil) (N=102, 84) | 98 (93.1 to 99.8) | 84.5 (75 to 91.5)   |  |  |

|                                                         |                    |                  |  |  |
|---------------------------------------------------------|--------------------|------------------|--|--|
| Post-dose 2 anti-MCC $\geq 8$ (1/dil)<br>(N=121, 109)   | 100 (97 to 100)    | 99.1 (95 to 100) |  |  |
| Post-dose 2 anti-MCC $\geq 128$ (1/dil)<br>(N=121, 109) | 99.2 (95.5 to 100) | 99.1 (95 to 100) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titres (GMTs) for MCC 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4)

|                 |                                                                                                                                                      |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titres (GMTs) for MCC 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-MCC Ab titres were measured by rSBA 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).

Ab titres are expressed in 1/dil.

Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).

| End point values                         | MCC-TT (period 1)         | MCC-CRM (period 1)       |  |  |
|------------------------------------------|---------------------------|--------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group          |  |  |
| Number of subjects analysed              | 121                       | 109                      |  |  |
| Units: Titres                            |                           |                          |  |  |
| geometric mean (confidence interval 95%) |                           |                          |  |  |
| Post-Dose 1 anti-MCC GMT (N=102, 84)     | 1353 (1058.4 to 1729.6)   | 285 (201.5 to 403.1)     |  |  |
| Post-Dose 2 anti-MCC GMT (N=121, 109)    | 2024.7 (1689.8 to 2425.9) | 1077.4 (847.5 to 1369.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Ab response rates for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

|                 |                                                                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Ab response rates for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------|

**End point description:**

% of subjects with an Ab titre  $\geq 0.15$   $\mu\text{g/mL}$  for Hib (PRP),  $\geq 10$  mIU/mL for Hepatitis B (HBsAg),  $\geq 0.01$  &  $\geq 0.1$  IU/mL for Diphtheria & Tetanus,  $\geq 8$  (1/dil) for Poliovirus types 1, 2 & 3, and % of pertussis seroresponder subjects (Pertussis toxoid (PT), Filamentous haemagglutinin (FHA), Fimbriae types 2 & 3 (FIM) & Pertactin (PRN)) 1 month Post-Dose 3 of PR5I administered concomitantly with MCC vaccines (V4).

Seroresponse was defined: (1) If pre-vaccination Ab concentration (cc) was <LLOQ (lower limit of quantification), post-vaccination Ab cc was to be  $\geq$ LLOQ; (2) If pre-vaccination Ab cc was  $\geq$ LLOQ, post-vaccination Ab cc was to be  $\geq$ pre-immunisation levels.

Ab titres were measured by RIA for PRP, enhanced Chemiluminescence assay (ECi) for HBsAg, micrometabolic inhibition test (MIT) for Diphtheria & Poliovirus, and Enzyme-Linked Immunosorbent Assay (ELISA) for Tetanus, PT, FHA, FIM & PRN.

Analysis was done on the Period 1 PPS.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

**End point timeframe:**

1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

| End point values                                 | MCC-TT (period 1)   | MCC-CRM (period 1)  |  |  |
|--------------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                      | 125                 | 105                 |  |  |
| Units: Percentage of subjects                    |                     |                     |  |  |
| number (confidence interval 95%)                 |                     |                     |  |  |
| Anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ (N=93, 82) | 97.8 (92.4 to 99.7) | 100 (95.6 to 100)   |  |  |
| Anti-HBsAg $\geq 10$ mIU/mL (N=93, 82)           | 96.8 (90.9 to 99.3) | 96.3 (89.7 to 99.2) |  |  |
| Anti-Diphtheria $\geq 0.01$ IU/mL (N=125, 104)   | 100 (97.1 to 100)   | 100 (96.5 to 100)   |  |  |
| Anti-Diphtheria $\geq 0.1$ IU/mL (N=125, 104)    | 68 (59.1 to 76.1)   | 74 (64.5 to 82.1)   |  |  |
| Anti-Tetanus $\geq 0.01$ IU/mL (N=122, 105)      | 100 (97 to 100)     | 100 (96.5 to 100)   |  |  |
| Anti-Tetanus $\geq 0.1$ IU/mL (N=122, 105)       | 100 (97 to 100)     | 100 (96.5 to 100)   |  |  |
| Anti-PT seroresponse (N=100, 75)                 | 99 (94.6 to 100)    | 100 (95.2 to 100)   |  |  |
| Anti-FHA seroresponse (N=100, 74)                | 91 (83.6 to 95.8)   | 90.5 (81.5 to 96.1) |  |  |
| Anti-PRN seroresponse (N=100, 73)                | 95 (88.7 to 98.4)   | 90.4 (81.2 to 96.1) |  |  |
| Anti-FIM seroresponse (N=100, 75)                | 96 (90.1 to 98.9)   | 96 (88.8 to 99.2)   |  |  |
| Anti-Polio 1 $\geq 8$ (1/dil) (N=114, 95)        | 100 (96.8 to 100)   | 100 (96.2 to 100)   |  |  |
| Anti-Polio 2 $\geq 8$ (1/dil) (N=106, 89)        | 100 (96.6 to 100)   | 100 (95.9 to 100)   |  |  |
| Anti-Polio 3 $\geq 8$ (1/dil) (N=90, 74)         | 100 (96 to 100)     | 100 (95.1 to 100)   |  |  |

**Statistical analyses**

**Secondary: Geometric Mean Titres (GMTs) for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)**

|                 |                                                                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titres (GMTs) for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

Ab titres were measured by RIA for Hib (PRP), Eci for HBsAg, MIT for Diphtheria & Poliovirus, and ELISA for Tetanus, PT, FHA, FIM & PRN 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

Ab titres are expressed in µg/mL for Hib (PRP), mIU/mL for HBsAg, IU/mL for Diphtheria & Tetanus, ELISA units (EU)/mL for Pertussis (PT, FHA, FIM & PRN), and 1/dil for Poliovirus types 1, 2 & 3. Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

| End point values                         | MCC-TT (period 1)      | MCC-CRM (period 1)     |  |  |
|------------------------------------------|------------------------|------------------------|--|--|
| Subject group type                       | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed              | 125                    | 105                    |  |  |
| Units: Titres                            |                        |                        |  |  |
| geometric mean (confidence interval 95%) |                        |                        |  |  |
| Anti-PRP GMT (N=93, 82)                  | 6.44 (4.7 to 8.83)     | 8.21 (6.08 to 11.09)   |  |  |
| Anti-HBsAg GMT (N=93, 82)                | 195.1 (150.7 to 252.7) | 247.7 (186.3 to 329.3) |  |  |
| Anti-Diphtheria GMT (N=125, 104)         | 0.198 (0.165 to 0.237) | 0.22 (0.181 to 0.268)  |  |  |
| Anti-Tetanus GMT (N=122, 105)            | 1.03 (0.9 to 1.17)     | 0.95 (0.82 to 1.1)     |  |  |
| Anti-PT GMT (N=112, 89)                  | 131.5 (117.2 to 147.6) | 133.3 (118.3 to 150.2) |  |  |
| Anti-FHA GMT (N=112, 88)                 | 50.4 (44.8 to 56.6)    | 50.1 (43.7 to 57.4)    |  |  |
| Anti-PRN GMT (N=112, 87)                 | 90.4 (73.2 to 111.7)   | 106.8 (83.7 to 136.3)  |  |  |
| Anti-FIM GMT (N=112, 89)                 | 401.7 (339.4 to 475.5) | 441.7 (363.2 to 537.2) |  |  |
| Anti-Polio 1 GMT (N=114, 95)             | 214 (164.9 to 277.7)   | 257.9 (193.8 to 343.1) |  |  |
| Anti-Polio 2 GMT (N=106, 89)             | 385.2 (288.2 to 514.9) | 400.6 (290.6 to 552.3) |  |  |
| Anti-Polio 3 GMT (N=90, 74)              | 502.2 (370.2 to 681.4) | 405.1 (284.9 to 576)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of subjects with anti-MCC Ab titres $\geq 8$ (1/dil) and $\geq 128$ (1/dil) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

|                 |                                                                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of subjects with anti-MCC Ab titres $\geq 8$ (1/dil) and $\geq 128$ (1/dil) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Proportion of subjects with anti-MCC Ab titres  $\geq 8$  (1/dil) and  $\geq 128$  (1/dil) determined before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

Anti-MCC Ab titres were measured by rSBA.

Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

| End point values                                         | MCC-TT (period 2)   | MCC-CRM (period 2)  |  |  |
|----------------------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                              | 109                 | 110                 |  |  |
| Units: Percentage of subjects                            |                     |                     |  |  |
| number (confidence interval 95%)                         |                     |                     |  |  |
| Pre Hib-MCC anti-MCC $\geq 8$ (1/dil)<br>(N=89, 94)      | 83.1 (73.7 to 90.2) | 40.4 (30.4 to 51)   |  |  |
| Pre Hib-MCC anti-MCC $\geq 128$ (1/dil)<br>(N=89, 94)    | 40.4 (30.2 to 51.4) | 16 (9.2 to 25)      |  |  |
| Post Hib-MCC anti-MCC $\geq 8$ (1/dil)<br>(N=109, 110)   | 100 (96.7 to 100)   | 97.3 (92.2 to 99.4) |  |  |
| Post Hib-MCC anti-MCC $\geq 128$ (1/dil)<br>(N=109, 110) | 99.1 (95 to 100)    | 95.5 (89.7 to 98.5) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titres (GMTs) for MCC before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

|                 |                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titres (GMTs) for MCC before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose |
|-----------------|---------------------------------------------------------------------------------------------------------|

End point description:

Anti-MCC Ab titres were measured by rSBA before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

Ab titres are expressed in 1/dil.

Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity



evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                                                                                                                      |           |
|----------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                       | Secondary |
| End point timeframe:                                                                                                 |           |
| Before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6). |           |

| End point values                            | MCC-TT (period 2)         | MCC-CRM (period 2)     |  |  |
|---------------------------------------------|---------------------------|------------------------|--|--|
| Subject group type                          | Reporting group           | Reporting group        |  |  |
| Number of subjects analysed                 | 109                       | 110                    |  |  |
| Units: Titres                               |                           |                        |  |  |
| geometric mean (confidence interval 95%)    |                           |                        |  |  |
| Pre Hib-MCC dose anti-MCC GMT (N=89, 94)    | 50.3 (34.4 to 73.4)       | 8.7 (5.9 to 12.9)      |  |  |
| Post Hib-MCC dose anti-MCC GMT (N=109, 110) | 3257.9 (2597.4 to 4086.3) | 580.8 (432.7 to 779.5) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Proportion of subjects with anti-PRP Ab titres $\geq 0.15$ $\mu\text{g/mL}$ and $\geq 1.0$ $\mu\text{g/mL}$ before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

|                 |                                                                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of subjects with anti-PRP Ab titres $\geq 0.15$ $\mu\text{g/mL}$ and $\geq 1.0$ $\mu\text{g/mL}$ before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Proportion of subjects with anti-PRP Ab titres  $\geq 0.15$   $\mu\text{g/mL}$  and  $\geq 1.0$   $\mu\text{g/mL}$  determined before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

Anti-PRP Ab titres were measured by radioimmunoassay (RIA).

Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                                                                                                                      |           |
|----------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                       | Secondary |
| End point timeframe:                                                                                                 |           |
| Before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6). |           |

| End point values                                                | MCC-TT (period 2)   | MCC-CRM (period 2)  |  |  |
|-----------------------------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                                              | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                                     | 110                 | 106                 |  |  |
| Units: Percentage of subjects                                   |                     |                     |  |  |
| number (confidence interval 95%)                                |                     |                     |  |  |
| Pre Hib-MCC anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ (N=82, 87)    | 93.9 (86.3 to 98)   | 95.4 (88.6 to 98.7) |  |  |
| Pre Hib-MCC anti-PRP $\geq 1.0$ $\mu\text{g/mL}$ (N=82, 87)     | 54.9 (43.5 to 65.9) | 56.3 (45.3 to 66.9) |  |  |
| Post Hib-MCC anti-PRP $\geq 0.15$ $\mu\text{g/mL}$ (N=110, 106) | 100 (96.7 to 100)   | 100 (96.6 to 100)   |  |  |
| Post Hib-MCC anti-PRP $\geq 1.0$ $\mu\text{g/mL}$ (N=110, 106)  | 99.1 (95 to 100)    | 100 (96.6 to 100)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titres (GMTs) for Hib (PRP) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

|                 |                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titres (GMTs) for Hib (PRP) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose |
|-----------------|---------------------------------------------------------------------------------------------------------------|

End point description:

Anti-PRP Ab titres were measured by RIA before (Pre Hib-MCC dose) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose).

Ab titres are expressed in  $\mu\text{g/mL}$ .

Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Note: (N=\*\*\*, \*\*\*) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Before (Pre Hib-MCC dose) and 1 month after Hib-MCC toddler dose administration (Post Hib-MCC dose).

| End point values                            | MCC-TT (period 2)        | MCC-CRM (period 2)    |  |  |
|---------------------------------------------|--------------------------|-----------------------|--|--|
| Subject group type                          | Reporting group          | Reporting group       |  |  |
| Number of subjects analysed                 | 110                      | 106                   |  |  |
| Units: Titres                               |                          |                       |  |  |
| geometric mean (confidence interval 95%)    |                          |                       |  |  |
| Pre Hib-MCC dose anti-PRP GMT (N=82, 87)    | 1.09 (0.81 to 1.45)      | 1.18 (0.9 to 1.55)    |  |  |
| Post Hib-MCC dose anti-PRP GMT (N=110, 106) | 100.19 (81.05 to 123.86) | 121 (101.11 to 144.8) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Global summary of safety from D1 to D15 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

|                 |                                                                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Global summary of safety from D1 to D15 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine) |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Adverse events (AEs) were recorded as follows:

1/ From D1 to D5 after each vaccination: # temperature (at least 1  $\geq 38.0^{\circ}\text{C}$ ), # solicited injection-site adverse reactions (ISRs: erythema, pain, and swelling) by injection-site (PR5I or MCC vaccine), and # solicited systemic AEs (crying, decreased appetite, irritability, pyrexia, somnolence, and vomiting).

2/ From D1 to D15 after each vaccination: unsolicited ISRs (including erythema, pain, and swelling from D6 to D15) by injection-site (PR5I or MCC vaccine), and # unsolicited systemic AEs.

AEs at injection sites were always considered as related to vaccine (ISRs). The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not.

Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

Percentages of subjects reporting AEs that occurred after any infant dose vaccination are presented hereafter.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 (D1) to D15 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

| End point values                                 | MCC-TT (period 1)   | MCC-CRM (period 1)  |  |  |
|--------------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                      | 142                 | 142                 |  |  |
| Units: Percentage of subjects                    |                     |                     |  |  |
| number (confidence interval 95%)                 |                     |                     |  |  |
| At least 1 AE (D1-D15)                           | 98.6 (95 to 99.8)   | 97.2 (92.9 to 99.2) |  |  |
| At least 1 vaccine-related AE (D1-D15)           | 98.6 (95 to 99.8)   | 96.5 (92 to 98.8)   |  |  |
| At least 1 ISR at PR5I site (D1-D15)             | 88.7 (82.3 to 93.4) | 87.3 (80.7 to 92.3) |  |  |
| At least 1 solicited ISR at PR5I site (D1-D5)    | 88.7 (82.3 to 93.4) | 87.3 (80.7 to 92.3) |  |  |
| At least 1 unsolicited ISR at PR5I site (D1-D15) | 6.3 (2.9 to 11.7)   | 11.3 (6.6 to 17.7)  |  |  |
| At least 1 ISR at MCC site (D1-D15)              | 72.5 (64.4 to 79.7) | 66.2 (57.8 to 73.9) |  |  |
| At least 1 solicited ISR at MCC site (D1-D5)     | 72.5 (64.4 to 79.7) | 65.5 (57.1 to 73.3) |  |  |
| At least 1 unsolicited ISR at MCC site (D1-D15)  | 2.8 (0.8 to 7.1)    | 2.8 (0.8 to 7.1)    |  |  |
| At least 1 systemic AE (D1-D15)                  | 98.6 (95 to 99.8)   | 94.4 (89.2 to 97.5) |  |  |
| At least 1 vaccine-related systemic AE (D1-D15)  | 97.9 (94 to 99.6)   | 93.7 (88.3 to 97.1) |  |  |
| At least 1 solicited systemic AE (D1-D5)         | 97.2 (92.9 to 99.2) | 93 (87.4 to 99.6)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects reporting ISRs at PR5I injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (3 doses of PR5I vaccine)

|                 |                                                                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects reporting ISRs at PR5I injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (3 doses of PR5I vaccine) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

#### End point description:

ISRs occurring after any infant dose of PR5I vaccine (3 doses) were recorded as follows:

# From D1 to D5 after each vaccination: solicited ISRs, i.e., erythema, pain, and swelling at PR5I injection-site.

# From D1 to D15 after each vaccination: unsolicited ISRs (including erythema, pain, and swelling from D6 to D15) at PR5I injection-site.

AEs at injection-site were always considered as related to vaccine (ISRs).

The percentage of subjects presenting at least once the following ISRs that occurred after any infant dose vaccination is reported hereafter.

Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

# Solicited ISRs: from Day 1 (D1) to D5 after any infant dose of PR5I vaccine (3 doses).

# Unsolicited ISRs: from Day 1 (D1) to D15 after any infant dose of PR5I vaccine (3 doses).

| End point values                               | MCC-TT (period 1) | MCC-CRM (period 1) |  |  |
|------------------------------------------------|-------------------|--------------------|--|--|
| Subject group type                             | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed                    | 142               | 142                |  |  |
| Units: Percentage of subjects                  |                   |                    |  |  |
| number (not applicable)                        |                   |                    |  |  |
| Solicited injection-site erythema (D1-D5)      | 71.1              | 64.8               |  |  |
| Solicited injection-site pain (D1-D5)          | 63.4              | 66.2               |  |  |
| Solicited injection-site swelling (D1-D5)      | 51.4              | 47.2               |  |  |
| Unsolicited injection-site bruising (D1-D15)   | 1.4               | 4.2                |  |  |
| Unsolicited injection-site dermatitis (D1-D15) | 0                 | 0.7                |  |  |
| Unsolicited injection-site erythema (D6-D15)   | 0                 | 0.7                |  |  |
| Unsolicited injection-site induration (D1-D15) | 1.4               | 0.7                |  |  |
| Unsolicited injection-site mass (D1-D15)       | 3.5               | 2.1                |  |  |
| Unsolicited injection-site pain (D6-D15)       | 0                 | 0.7                |  |  |
| Unsolicited injection-site rash (D1-D15)       | 1.4               | 0.7                |  |  |

|                                            |   |     |  |  |
|--------------------------------------------|---|-----|--|--|
| Unsolicited injection-site warmth (D1-D15) | 0 | 2.1 |  |  |
|--------------------------------------------|---|-----|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects reporting ISRs at MCC-TT or MCC-CRM injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (2 doses of MCC-TT or MCC-CRM vaccine)

|                 |                                                                                                                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects reporting ISRs at MCC-TT or MCC-CRM injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (2 doses of MCC-TT or MCC-CRM vaccine) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

#### End point description:

ISRs occurring after any infant dose of MCC-TT or MCC-CRM vaccine (2 doses) were recorded as follows:

# From D1 to D5: solicited ISRs, i.e., erythema, pain, and swelling at MCC injection-site.

# From D1 to D15: unsolicited ISRs (including erythema, pain, and swelling from D6 to D15) at MCC injection-site.

AEs at injection-site were always considered as related to vaccine (ISRs).

The percentage of subjects presenting at least once the following ISRs that occurred after any infant dose vaccination is reported hereafter.

Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

# Solicited ISRs: from Day 1 (D1) to D5 after any infant dose of MCC-TT or MCC-CRM vaccine (2 doses).

# Unsolicited ISRs: from Day 1 (D1) to D15 after any infant dose of MCC-TT or MCC-CRM vaccine (2 doses).

| End point values                               | MCC-TT (period 1) | MCC-CRM (period 1) |  |  |
|------------------------------------------------|-------------------|--------------------|--|--|
| Subject group type                             | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed                    | 142               | 142                |  |  |
| Units: Percentage of subjects                  |                   |                    |  |  |
| number (not applicable)                        |                   |                    |  |  |
| Solicited injection-site erythema (D1-D5)      | 56.3              | 45.8               |  |  |
| Solicited injection-site pain (D1-D5)          | 41.5              | 45.8               |  |  |
| Solicited injection-site swelling (D1-D5)      | 35.9              | 28.2               |  |  |
| Unsolicited injection-site bruising (D1-D15)   | 1.4               | 2.1                |  |  |
| Unsolicited injection-site induration (D1-D15) | 0.7               | 0                  |  |  |
| Unsolicited injection-site rash (D1-D15)       | 0.7               | 0                  |  |  |
| Unsolicited injection-site warmth (D1-D15)     | 0                 | 0.7                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects reporting solicited systemic adverse events (AEs) from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

|                 |                                                                                                                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects reporting solicited systemic adverse events (AEs) from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

#### End point description:

Solicited systemic AEs (crying, decreased appetite, irritability, pyrexia, somnolence, and vomiting) were recorded from D1 to D5 after each vaccination.

The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not.

The percentage of subjects presenting at least once the following solicited systemic AEs (vaccine-related or not) that occurred after any infant dose vaccination is presented hereafter.

Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

From Day 1 (D1) to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

| End point values              | MCC-TT (period 1) | MCC-CRM (period 1) |  |  |
|-------------------------------|-------------------|--------------------|--|--|
| Subject group type            | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed   | 142               | 142                |  |  |
| Units: Percentage of subjects |                   |                    |  |  |
| number (not applicable)       |                   |                    |  |  |
| Crying (D1-D5)                | 85.9              | 81                 |  |  |
| Decreased appetite (D1-D5)    | 63.4              | 64.8               |  |  |
| Irritability (D1-D5)          | 88                | 81                 |  |  |
| Pyrexia (D1-D5)               | 11.3              | 10.6               |  |  |
| Somnolence (D1-D5)            | 81.7              | 78.9               |  |  |
| Vomiting (D1-D5)              | 40.1              | 49.3               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects reporting temperature $\geq 38.0^{\circ}\text{C}$ , $>38.5^{\circ}\text{C}$ & $>39.5^{\circ}\text{C}$ from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

|                 |                                                                                                                                                                                                                                                 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects reporting temperature $\geq 38.0^{\circ}\text{C}$ , $>38.5^{\circ}\text{C}$ & $>39.5^{\circ}\text{C}$ from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

#### End point description:

Maximum temperatures recorded with no adjustments to the measurement route were reported from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

The percentage of subjects presenting at least once temperature  $\geq 38.0^{\circ}\text{C}$ ,  $> 38.5^{\circ}\text{C}$ , and  $> 39.5^{\circ}\text{C}$  is presented hereafter.

Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

|                                                                                                                             |           |
|-----------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                              | Secondary |
| End point timeframe:                                                                                                        |           |
| From Day 1 (D1) to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine). |           |

| End point values                        | MCC-TT (period 1) | MCC-CRM (period 1) |  |  |
|-----------------------------------------|-------------------|--------------------|--|--|
| Subject group type                      | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed             | 142               | 142                |  |  |
| Units: Percentage of subjects           |                   |                    |  |  |
| number (not applicable)                 |                   |                    |  |  |
| Temperature $\geq 38.0^{\circ}\text{C}$ | 11.3              | 10.6               |  |  |
| Temperature $> 38.5^{\circ}\text{C}$    | 1.4               | 2.1                |  |  |
| Temperature $> 39.5^{\circ}\text{C}$    | 0                 | 0                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

- # From D1 to D15 after each vaccination during Period 1: unsolicited non-serious systemic AEs.
- # From D1 to D15 after each vaccination: serious AEs (SAEs) and deaths, vaccine-related or not.
- # Throughout the study: deaths and vaccine-related SAEs.

Adverse event reporting additional description:

Analysis of AEs was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

Unsolicited non-serious systemic AEs (vaccine-related or not) with incidence  $\geq 2\%$  are presented hereafter.

1 subject from the MCC-CRM group reported 2 vaccine-related SAEs.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 16.1   |

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | MCC-TT (period 1) |
|-----------------------|-------------------|

Reporting group description:

# Subjects received 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib) by IM route at 2, 3, & 4 months of age + 2 doses of MCC-TT vaccine (NeisVac-C) by IM route at 3 & 4 months of age + routine vaccination, i.e., PCV-13 vaccine (Prevenar 13) by IM route at 2 & 4 months of age.

# Respectively, 71 (50.0%) subjects reported at least 1 unsolicited systemic AE, and 38 (26.8%) subjects reported at least 1 vaccine-related unsolicited systemic AE within 15 days after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT vaccine).

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | MCC-CRM (period 1) |
|-----------------------|--------------------|

Reporting group description:

# Subjects received 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib) by IM route at 2, 3 & 4 months of age + 2 doses of MCC-CRM vaccine (Menjugate) by IM route at 3 & 4 months of age + routine vaccination, i.e., PCV-13 vaccine (Prevenar 13) by IM route at 2 & 4 months of age.

# Respectively, 57 (40.1%) subjects reported at least 1 unsolicited systemic AE, and 37 (26.1%) subjects reported at least 1 vaccine-related unsolicited systemic AE within 15 days after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-CRM vaccine).

| Serious adverse events                               | MCC-TT (period 1)                                                                                                       | MCC-CRM (period 1) |  |
|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|--------------------|--|
| Total subjects affected by serious adverse events    |                                                                                                                         |                    |  |
| subjects affected / exposed                          | 6 / 142 (4.23%)                                                                                                         | 4 / 142 (2.82%)    |  |
| number of deaths (all causes)                        | 0                                                                                                                       | 0                  |  |
| number of deaths resulting from adverse events       | 0                                                                                                                       | 0                  |  |
| General disorders and administration site conditions |                                                                                                                         |                    |  |
| Crying                                               | Additional description: Transient (2 days), severe intensity, occurring concomitantly with abdominal pain in 1 subject. |                    |  |
| subjects affected / exposed                          | 0 / 142 (0.00%)                                                                                                         | 1 / 142 (0.70%)    |  |
| occurrences causally related to treatment / all      | 0 / 0                                                                                                                   | 1 / 1              |  |
| deaths causally related to treatment / all           | 0 / 0                                                                                                                   | 0 / 0              |  |
| Hypothermia                                          |                                                                                                                         |                    |  |



|                                                 |                                                                                                                 |                 |  |
|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-----------------|--|
| subjects affected / exposed                     | 1 / 142 (0.70%)                                                                                                 | 0 / 142 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                                                                                           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Gastrointestinal disorders                      |                                                                                                                 |                 |  |
| Abdominal pain                                  | Additional description: Transient (2 days), severe intensity, occurring concomitantly with crying in 1 subject. |                 |  |
| subjects affected / exposed                     | 0 / 142 (0.00%)                                                                                                 | 1 / 142 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0                                                                                                           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                                                                                                                 |                 |  |
| Choking                                         |                                                                                                                 |                 |  |
| subjects affected / exposed                     | 0 / 142 (0.00%)                                                                                                 | 1 / 142 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0                                                                                                           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Infections and infestations                     |                                                                                                                 |                 |  |
| Croup infectious                                |                                                                                                                 |                 |  |
| subjects affected / exposed                     | 1 / 142 (0.70%)                                                                                                 | 0 / 142 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                                                                                           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Gastroenteritis salmonella                      |                                                                                                                 |                 |  |
| subjects affected / exposed                     | 0 / 142 (0.00%)                                                                                                 | 1 / 142 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0                                                                                                           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Gastroenteritis viral                           |                                                                                                                 |                 |  |
| subjects affected / exposed                     | 0 / 142 (0.00%)                                                                                                 | 1 / 142 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0                                                                                                           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Respiratory syncytial virus bronchiolitis       |                                                                                                                 |                 |  |
| subjects affected / exposed                     | 1 / 142 (0.70%)                                                                                                 | 0 / 142 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                                                                                           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0                                                                                                           | 0 / 0           |  |
| Sepsis neonatal                                 |                                                                                                                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 142 (0.70%) | 0 / 142 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 142 (0.70%) | 0 / 142 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Weight gain poor                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 142 (0.70%) | 0 / 142 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                     | MCC-TT (period 1) | MCC-CRM (period 1) |  |
|-------------------------------------------------------|-------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                   |                    |  |
| subjects affected / exposed                           | 71 / 142 (50.00%) | 57 / 142 (40.14%)  |  |
| Injury, poisoning and procedural complications        |                   |                    |  |
| Contusion                                             |                   |                    |  |
| subjects affected / exposed                           | 0 / 142 (0.00%)   | 3 / 142 (2.11%)    |  |
| occurrences (all)                                     | 0                 | 3                  |  |
| Gastrointestinal disorders                            |                   |                    |  |
| Constipation                                          |                   |                    |  |
| subjects affected / exposed                           | 4 / 142 (2.82%)   | 3 / 142 (2.11%)    |  |
| occurrences (all)                                     | 4                 | 3                  |  |
| Diarrhoea                                             |                   |                    |  |
| subjects affected / exposed                           | 11 / 142 (7.75%)  | 8 / 142 (5.63%)    |  |
| occurrences (all)                                     | 11                | 8                  |  |
| Teething                                              |                   |                    |  |
| subjects affected / exposed                           | 7 / 142 (4.93%)   | 1 / 142 (0.70%)    |  |
| occurrences (all)                                     | 7                 | 1                  |  |
| Vomiting                                              |                   |                    |  |
| subjects affected / exposed                           | 3 / 142 (2.11%)   | 3 / 142 (2.11%)    |  |
| occurrences (all)                                     | 3                 | 3                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| Respiratory, thoracic and mediastinal disorders |                  |                  |  |
| Cough                                           |                  |                  |  |
| subjects affected / exposed                     | 12 / 142 (8.45%) | 6 / 142 (4.23%)  |  |
| occurrences (all)                               | 12               | 6                |  |
| Nasal congestion                                |                  |                  |  |
| subjects affected / exposed                     | 4 / 142 (2.82%)  | 2 / 142 (1.41%)  |  |
| occurrences (all)                               | 4                | 2                |  |
| Rhinorrhoea                                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 142 (2.11%)  | 4 / 142 (2.82%)  |  |
| occurrences (all)                               | 3                | 4                |  |
| Skin and subcutaneous tissue disorders          |                  |                  |  |
| Rash                                            |                  |                  |  |
| subjects affected / exposed                     | 8 / 142 (5.63%)  | 6 / 142 (4.23%)  |  |
| occurrences (all)                               | 8                | 6                |  |
| Psychiatric disorders                           |                  |                  |  |
| Insomnia                                        |                  |                  |  |
| subjects affected / exposed                     | 4 / 142 (2.82%)  | 1 / 142 (0.70%)  |  |
| occurrences (all)                               | 4                | 1                |  |
| Infections and infestations                     |                  |                  |  |
| Nasopharyngitis                                 |                  |                  |  |
| subjects affected / exposed                     | 11 / 142 (7.75%) | 12 / 142 (8.45%) |  |
| occurrences (all)                               | 11               | 12               |  |
| Rhinitis                                        |                  |                  |  |
| subjects affected / exposed                     | 8 / 142 (5.63%)  | 6 / 142 (4.23%)  |  |
| occurrences (all)                               | 8                | 6                |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported