



## Clinical trial results:

**A phase IV, open-label, single-center study to evaluate long term immunogenicity up to 10 years after the first booster immunization with Tick Borne Encephalitis vaccine in adults who received 1 of 3 different primary vaccination schedules**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2011-003255-19    |
| Trial protocol           | CZ                |
| Global end of trial date | 30 September 2016 |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v4 (current)  |
| This version publication date  | 30 June 2018  |
| First version publication date | 22 February 2015  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> To align with US Results Summary (minor correction due to re-QC). |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 205335 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01562444 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium,   |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, (44)2089 904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, (44)2089 904466, GSKClinicalSupportHD@gsk.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? | No |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 30 September 2016 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 30 September 2016 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 30 September 2016 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

Immunogenicity Objectives:

To evaluate the persistence of antibody response to a booster vaccine starting 6 years after the booster administration and following subjects up to 10 years after first booster administration.

Protection of trial subjects:

The clinical study was designed, implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki. Eligible subjects were included in the study after providing written (witnessed, where required by law or regulation), Independent Ethics Committee (IEC)-approved informed consent, or, if incapable of doing so, after such consent was provided by a legally acceptable representative of the subject.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 08 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 | Czech Republic: 205 |
| Worldwide total number of subjects   | 205                 |
| EEA total number of subjects         | 205                 |

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)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |

|                      |     |
|----------------------|-----|
| Adults (18-64 years) | 189 |
| From 65 to 84 years  | 16  |
| 85 years and over    | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Subjects who completed V48P7E1 study having received primary vaccination according to rapid (R), conventional (C) or accelerated conventional (AC) schedule were included in the study. Since modified conventional (MC) had not been accepted by health authorities as primary vaccination schedule, this group from V48P7 was not enrolled in this study.

### Pre-assignment

Screening details:

206 subjects were enrolled in the study but one subject was not assigned to any group. Therefore, the number of subjects started is 205.

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 205 |
| Number of subjects completed | 205 |

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | TBE_R Group |

Arm description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to rapid (R) schedule i.e., on days 0, 7 (+3) and 21 (+7) in the parent study (V48P7) and who were administered 1 booster dose of Encepur adults either 12-18 months after R schedule completion or in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination (for those subjects boosted before V48P7E1 study start, the blood draw occurred annually starting from >6 years up to >10 years after booster vaccination).

|  |   |
|--|---|
| Arm type                               | Blood draw  |
| Investigational medicinal product name | Blood draw  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Anticoagulant and preservative solution for blood |
| Routes of administration               | Route of administration not applicable            |

Dosage and administration details:

Annual blood draw at years 6 (Visit 18), 7 (Visit 19), 8 (Visit 20), 9 (Visit 21) and 10 (Visit 22)

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | TBE_C Group |
|------------------|-------------|

Arm description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to conventional (C) schedule i.e., on days 0, 28 (+10) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.

|          |            |
|----------|------------|
| Arm type | Blood draw |
|----------|------------|

|   |   |
|---|---|
| Investigational medicinal product name  | Blood draw  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Anticoagulant and preservative solution for blood |
| Routes of administration  | Route of administration not applicable            |
| Dosage and administration details:  |   |
| Annual blood draw at years 6 (Visit 18), 7 (Visit 19), 8 (Visit 20), 9 (Visit 21) and 10 (Visit 22) |   |
| <b>Arm title</b>  | TBE_AC Group                                      |

**Arm description:**

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to accelerated conventional (AC) schedule i.e., on days 0, 14 (+3) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.

|  |   |
|--|---|
| Arm type                               | Blood draw  |
| Investigational medicinal product name | Blood draw  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Anticoagulant and preservative solution for blood |
| Routes of administration               | Route of administration not applicable            |

**Dosage and administration details:**

Annual blood draw at years 6 (Visit 18), 7 (Visit 19), 8 (Visit 20), 9 (Visit 21) and 10 (Visit 22)

| <b>Number of subjects in period 1</b>   | TBE_R Group | TBE_C Group | TBE_AC Group |
|---|-------------|-------------|--------------|
| Started                                 | 48          | 51          | 106          |
| Completed                               | 43          | 49          | 99           |
| Not completed                           | 5           | 2           | 7            |
| Protocol forbidden medication           | 1           | -           | -            |
| Did not meet entry criteria             | 2           | -           | 3            |
| Unavailable serological results         | -           | 2           | 2            |
| Protocol forbidden concomitant vaccine  | 1           | -           | 1            |
| Did not comply with blood draw schedule | 1           | -           | 1            |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | TBE_R Group |
|-----------------------|-------------|

Reporting group description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to rapid (R) schedule i.e., on days 0, 7 (+3) and 21 (+7) in the parent study (V48P7) and who were administered 1 booster dose of Encepur adults either 12-18 months after R schedule completion or in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination (for those subjects boosted before V48P7E1 study start, the blood draw occurred annually starting from >6 years up to >10 years after booster vaccination).

|                       |             |
|-----------------------|-------------|
| Reporting group title | TBE_C Group |
|-----------------------|-------------|

Reporting group description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to conventional (C) schedule i.e., on days 0, 28 (+10) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.

|                       |              |
|-----------------------|--------------|
| Reporting group title | TBE_AC Group |
|-----------------------|--------------|

Reporting group description:

Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to accelerated conventional (AC) schedule i.e., on days 0, 14 (+3) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.

| Reporting group values | TBE_R Group | TBE_C Group | TBE_AC Group |
|------------------------|-------------|-------------|--------------|
| Number of subjects     | 48          | 51          | 106          |
| Age categorical        |             |             |              |
| Units: Subjects        |             |             |              |

|                            |         |         |         |
|----------------------------|---------|---------|---------|
| Age continuous             |         |         |         |
| Units: years               |         |         |         |
| arithmetic mean            | 42.7    | 41.8    | 42.4    |
| standard deviation         | ± 15.25 | ± 14.34 | ± 14.35 |
| Gender categorical         |         |         |         |
| Units: Subjects            |         |         |         |
| Female                     | 24      | 32      | 55      |
| Male                       | 24      | 19      | 51      |
| Race/Ethnicity, Customized |         |         |         |
| Units: Subjects            |         |         |         |
| White                      | 48      | 51      | 106     |

| Reporting group values | Total |  |  |
|------------------------|-------|--|--|
| Number of subjects     | 205   |  |  |
| Age categorical        |       |  |  |
| Units: Subjects        |       |  |  |

|   |     |  |  |
|---|-----|--|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -   |  |  |
| Gender categorical<br>Units: Subjects                                   |     |  |  |
| Female  | 111 |  |  |
| Male  | 94  |  |  |
| Race/Ethnicity, Customized<br>Units: Subjects                           |     |  |  |
| White   | 205 |  |  |

## End points

### End points reporting groups

|   |              |
|---|--------------|
| Reporting group title   | TBE_R Group  |
| Reporting group description:<br>Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to rapid (R) schedule i.e., on days 0, 7 (+3) and 21 (+7) in the parent study (V48P7) and who were administered 1 booster dose of Encepur adults either 12-18 months after R schedule completion or in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination (for those subjects boosted before V48P7E1 study start, the blood draw occurred annually starting from >6 years up to >10 years after booster vaccination). |              |
| Reporting group title   | TBE_C Group  |
| Reporting group description:<br>Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to conventional (C) schedule i.e., on days 0, 28 (+10) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.  |              |
| Reporting group title   | TBE_AC Group |
| Reporting group description:<br>Subjects who had previously received the Tick borne encephalitis (TBE) primary vaccination according to accelerated conventional (AC) schedule i.e., on days 0, 14 (+3) and 300 (+21) in the parent study (V48P7) and were administered 1 booster dose of Encepur adults in the first extension study, V48P7E1 (NCT00387634), were included in this group. Subjects had blood drawn annually starting from year 6 up to year 10 after booster vaccination.  |              |

### Primary: Percentage of subjects with detectable TBE antibody titers greater than or equal to ( $\geq$ ) 2

|  |   |
|--|---|
| End point title  | Percentage of subjects with detectable TBE antibody titers greater than or equal to ( $\geq$ ) 2 <sup>[1]</sup> |
| End point description:<br>Antibody titers were measured by GlaxoSmithKline (GSK) neutralizing antibody (NT) assay. |   |
| End point type   | Primary   |
| End point timeframe:<br>At Year 6  |   |
| 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group        | TBE_AC Group           |  |
|----------------------------------|------------------------|--------------------|------------------------|--|
| Subject group type               | Reporting group        | Reporting group    | Reporting group        |  |
| Number of subjects analysed      | 48                     | 51                 | 106                    |  |
| Units: Percentage of subjects    |                        |                    |                        |  |
| number (confidence interval 95%) |                        |                    |                        |  |
| Percentage of subjects           | 95.83 (85.75 to 99.49) | 100 (93.02 to 100) | 97.17 (91.95 to 99.41) |  |

## Statistical analyses



No statistical analyses for this end point

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**Primary: Percentage of subjects with detectable TBE antibody titers  $\geq 2$** 

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|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ |
|-----------------|---|

End point description:

Antibody titers were measured by GSK NT assay.

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

End point timeframe:

At Year 7

Notes:

[2] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group           | TBE_C Group        | TBE_AC Group           |  |
|----------------------------------|-----------------------|--------------------|------------------------|--|
| Subject group type               | Reporting group       | Reporting group    | Reporting group        |  |
| Number of subjects analysed      | 48                    | 51                 | 106                    |  |
| Units: Percentage of subjects    |                       |                    |                        |  |
| number (confidence interval 95%) |                       |                    |                        |  |
| Percentage of subjects           | 93.75 (82.8 to 98.69) | 100 (93.02 to 100) | 95.28 (89.33 to 98.45) |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Percentage of subjects with detectable TBE antibody titers  $\geq 2$** 

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|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ |
|-----------------|---|

End point description:

Antibody titers were measured by GSK NT assay.

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

End point timeframe:

At Year 8

Notes:

[3] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group            | TBE_AC Group         |  |
|----------------------------------|------------------------|------------------------|----------------------|--|
| Subject group type               | Reporting group        | Reporting group        | Reporting group      |  |
| Number of subjects analysed      | 48                     | 51                     | 106                  |  |
| Units: Percentage of subjects    |                        |                        |                      |  |
| number (confidence interval 95%) |                        |                        |                      |  |
| Percentage of subjects           | 89.58 (77.34 to 96.53) | 98.04 (89.55 to 99.95) | 93.4 (86.87 to 97.3) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 2$

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ |
|-----------------|---|

End point description:

Antibody titers were measured by GSK NT assay.

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

End point timeframe:

At Year 9

Notes:

[4] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group            | TBE_AC Group           |  |
|----------------------------------|------------------------|------------------------|------------------------|--|
| Subject group type               | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed      | 48                     | 51                     | 106                    |  |
| Units: Percentage of subjects    |                        |                        |                        |  |
| number (confidence interval 95%) |                        |                        |                        |  |
| Percentage of subjects           | 89.58 (77.34 to 96.53) | 94.12 (83.76 to 98.77) | 92.45 (85.67 to 96.69) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 2$

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ |
|-----------------|---|

End point description:

Antibody titers were measured by GSK NT assay.

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

End point timeframe:

At Year 10

Notes:

[5] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group            | TBE_AC Group         |  |
|----------------------------------|------------------------|------------------------|----------------------|--|
| Subject group type               | Reporting group        | Reporting group        | Reporting group      |  |
| Number of subjects analysed      | 48                     | 51                     | 106                  |  |
| Units: Percentage of subjects    |                        |                        |                      |  |
| number (confidence interval 95%) |                        |                        |                      |  |
| Percentage of subjects           | 89.58 (77.34 to 96.53) | 96.08 (86.54 to 99.52) | 93.4 (86.87 to 97.3) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ |
|-----------------|---|

End point description:

Antibody titers were measured by GSK NT assay.

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

End point timeframe:

At Year 6

Notes:

[6] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group        | TBE_AC Group           |  |
|----------------------------------|------------------------|--------------------|------------------------|--|
| Subject group type               | Reporting group        | Reporting group    | Reporting group        |  |
| Number of subjects analysed      | 48                     | 51                 | 106                    |  |
| Units: Percentage of subjects    |                        |                    |                        |  |
| number (confidence interval 95%) |                        |                    |                        |  |
| Percentage of subjects           | 95.83 (85.75 to 99.49) | 100 (93.02 to 100) | 97.17 (91.95 to 99.41) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ |
|-----------------|---|

End point description:

Antibody titers were measured by GSK NT assay.

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

End point timeframe:

At Year 7

Notes:

[7] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group           | TBE_C Group        | TBE_AC Group           |  |
|----------------------------------|-----------------------|--------------------|------------------------|--|
| Subject group type               | Reporting group       | Reporting group    | Reporting group        |  |
| Number of subjects analysed      | 48                    | 51                 | 106                    |  |
| Units: Percentage of subjects    |                       |                    |                        |  |
| number (confidence interval 95%) |                       |                    |                        |  |
| Percentage of subjects           | 93.75 (82.8 to 98.69) | 100 (93.02 to 100) | 95.28 (89.33 to 98.45) |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$

|  |   |
|--|---|
| End point title  | Percentage of subjects with detectable TBE antibody titers $\geq$ |
| End point description:<br>Antibody titers were measured by GSK NT assay. |   |
| End point type   | Primary   |
| End point timeframe:<br>At Year 8  |   |

Notes:

[8] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group            | TBE_AC Group           |  |
|----------------------------------|------------------------|------------------------|------------------------|--|
| Subject group type               | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed      | 48                     | 51                     | 106                    |  |
| Units: Percentage of subjects    |                        |                        |                        |  |
| number (confidence interval 95%) |                        |                        |                        |  |
| Percentage of subjects           | 89.58 (77.34 to 96.53) | 98.04 (89.55 to 99.95) | 92.45 (85.67 to 96.69) |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$

|  |   |
|--|---|
| End point title  | Percentage of subjects with detectable TBE antibody titers $\geq$ |
| End point description:<br>Antibody titers were measured by GSK NT assay. |   |
| End point type   | Primary   |
| End point timeframe:<br>At Year 9  |   |

Notes:

[9] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group            | TBE_AC Group           |  |
|----------------------------------|------------------------|------------------------|------------------------|--|
| Subject group type               | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed      | 48                     | 51                     | 106                    |  |
| Units: Percentage of subjects    |                        |                        |                        |  |
| number (confidence interval 95%) |                        |                        |                        |  |
| Percentage of subjects           | 89.58 (77.34 to 96.53) | 94.12 (83.76 to 98.77) | 92.45 (85.67 to 96.69) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$

|  |   |
|--|---|
| End point title                                | Percentage of subjects with detectable TBE antibody titers $\geq$ |
| End point description:                         |   |
| Antibody titers were measured by GSK NT assay. |   |
| End point type                                 | Primary   |
| End point timeframe:                           |   |
| At Year 10                                     |   |

Notes:

[10] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                 | TBE_R Group            | TBE_C Group            | TBE_AC Group         |  |
|----------------------------------|------------------------|------------------------|----------------------|--|
| Subject group type               | Reporting group        | Reporting group        | Reporting group      |  |
| Number of subjects analysed      | 48                     | 51                     | 106                  |  |
| Units: Percentage of subjects    |                        |                        |                      |  |
| number (confidence interval 95%) |                        |                        |                      |  |
| Percentage of subjects           | 89.58 (77.34 to 96.53) | 94.12 (83.76 to 98.77) | 93.4 (86.87 to 97.3) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of Geometric Mean Antibody Titers (GMTs)

|  |   |
|--|---|
| End point title  | Evaluation of Geometric Mean Antibody Titers (GMTs) <sup>[11]</sup> |
| End point description:   |   |
| GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate Geometric Mean Ratios (GMRs). Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of |   |

V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[11] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group      |  |
|--|------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 48               | 51                 | 106               |  |
| Units: Titers                            |                  |                    |                   |  |
| geometric mean (confidence interval 95%) |                  |                    |                   |  |
| Baseline GMT pre booster (N=9;51;104)    | 76 (28 to 208)   | 228 (149 to 348)   | 228 (170 to 307)  |  |
| Baseline GMT post booster (N=48;51;105)  | 467 (325 to 670) | 1135 (799 to 1611) | 985 (771 to 1257) |  |
| GMT Year 6                               | 292 (184 to 463) | 293 (187 to 458)   | 221 (162 to 302)  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Evaluation of GMTs

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Evaluation of GMTs <sup>[12]</sup> |
|-----------------|------------------------------------|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[12] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group      |  |
|--|------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 48               | 51                 | 106               |  |
| Units: Titers                            |                  |                    |                   |  |
| geometric mean (confidence interval 95%) |                  |                    |                   |  |
| Baseline GMT pre booster (N=9;51;104)    | 76 (28 to 208)   | 228 (149 to 348)   | 228 (170 to 307)  |  |
| Baseline GMT post booster (N=48;51;105)  | 467 (325 to 670) | 1135 (799 to 1611) | 985 (771 to 1257) |  |

|            |                  |                  |                  |  |
|------------|------------------|------------------|------------------|--|
| GMT Year 7 | 295 (180 to 484) | 343 (212 to 555) | 254 (182 to 355) |  |
|------------|------------------|------------------|------------------|--|

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Evaluation of GMTs <sup>[13]</sup> |
|-----------------|------------------------------------|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At year 8

Notes:

[13] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group      |  |
|--|------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 48               | 51                 | 106               |  |
| Units: Titers                            |                  |                    |                   |  |
| geometric mean (confidence interval 95%) |                  |                    |                   |  |
| Baseline GMT pre booster (N=9;51;104)    | 76 (28 to 208)   | 228 (149 to 348)   | 228 (170 to 307)  |  |
| Baseline GMT post booster (N=48;51;105)  | 467 (325 to 670) | 1135 (799 to 1611) | 985 (771 to 1257) |  |
| GMT Year 8                               | 134 (79 to 227)  | 211 (127 to 352)   | 155 (109 to 221)  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Evaluation of GMTs <sup>[14]</sup> |
|-----------------|------------------------------------|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 9

Notes:

[14] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group      |  |
|--|------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 48               | 51                 | 106               |  |
| Units: Titers                            |                  |                    |                   |  |
| geometric mean (confidence interval 95%) |                  |                    |                   |  |
| Baseline GMT pre booster (N=9;51;104)    | 76 (28 to 208)   | 228 (149 to 348)   | 228 (170 to 307)  |  |
| Baseline GMT post booster (N=48;51;105)  | 467 (325 to 670) | 1135 (799 to 1611) | 985 (771 to 1257) |  |
| GMT Year 9                               | 211 (119 to 375) | 214 (122 to 374)   | 194 (131 to 285)  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Evaluation of GMTs

|  |                                    |
|--|------------------------------------|
| End point title  | Evaluation of GMTs <sup>[15]</sup> |
| End point description:   |                                    |
| GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |                                    |
| End point type   | Primary                            |

End point timeframe:

At Year 10

Notes:

[15] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group      |  |
|--|------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 48               | 51                 | 106               |  |
| Units: Titers                            |                  |                    |                   |  |
| geometric mean (confidence interval 95%) |                  |                    |                   |  |
| Baseline GMT pre booster (N=9;51;104)    | 76 (28 to 208)   | 228 (149 to 348)   | 228 (170 to 307)  |  |
| Baseline GMT post booster (N=48;51;105)  | 467 (325 to 670) | 1135 (799 to 1611) | 985 (771 to 1257) |  |
| GMT Year 10                              | 166 (94 to 295)  | 245 (140 to 428)   | 180 (122 to 265)  |  |



## Statistical analyses

No statistical analyses for this end point

### Primary: Geometric Mean Ratios (GMRs) calculated to pre booster baselines

|                 |  |
|-----------------|--|
| End point title | Geometric Mean Ratios (GMRs) calculated to pre booster baselines <sup>[16]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 6

Notes:

[16] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group          | TBE_C Group         | TBE_AC Group       |  |
|--|----------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group      | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 9                    | 51                  | 104                |  |
| Units: Ratios                            |                      |                     |                    |  |
| geometric mean (confidence interval 95%) |                      |                     |                    |  |
| Ratios                                   | 6.73 (3.23 to 14.02) | 1.28 (0.94 to 1.75) | 0.99 (0.8 to 1.23) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines <sup>[17]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 7

Notes:

[17] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group       |  |
|--|-------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 9                 | 51                  | 104                |  |
| Units: Ratios                            |                   |                     |                    |  |
| geometric mean (confidence interval 95%) |                   |                     |                    |  |
| Ratios                                   | 3.85 (1.48 to 10) | 1.51 (1.01 to 2.25) | 1.13 (0.85 to 1.5) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines <sup>[18]</sup> |
| End point description:   |  |
| GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Year 8  |  |

Notes:

[18] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group        |  |
|--|---------------------|--------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group     |  |
| Number of subjects analysed              | 9                   | 51                 | 104                 |  |
| Units: Ratios                            |                     |                    |                     |  |
| geometric mean (confidence interval 95%) |                     |                    |                     |  |
| Ratios                                   | 0.67 (0.23 to 1.91) | 0.93 (0.6 to 1.44) | 0.69 (0.51 to 0.95) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines <sup>[19]</sup> |
| End point description:   |  |
| GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Year 9  |  |

Notes:

[19] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group       |  |
|--|---------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 9                   | 51                  | 104                |  |
| Units: Ratios                            |                     |                     |                    |  |
| geometric mean (confidence interval 95%) |                     |                     |                    |  |
| Ratios                                   | 1.08 (0.33 to 3.53) | 0.94 (0.57 to 1.54) | 0.85 (0.6 to 1.21) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines <sup>[20]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:<br>At Year 10   |  |

Notes:

[20] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group      |  |
|--|---------------------|---------------------|-------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group   |  |
| Number of subjects analysed              | 9                   | 51                  | 104               |  |
| Units: Ratios                            |                     |                     |                   |  |
| geometric mean (confidence interval 95%) |                     |                     |                   |  |
| Ratios                                   | 0.76 (0.26 to 2.24) | 1.08 (0.68 to 1.69) | 0.8 (0.59 to 1.1) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines

|   |   |
|---|---|
| End point title   | GMRs calculated to post booster baselines <sup>[21]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post |   |

booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[21] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 48                  | 51                  | 105                 |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 0.63 (0.46 to 0.86) | 0.26 (0.19 to 0.35) | 0.22 (0.18 to 0.28) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines <sup>[22]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[22] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group       | TBE_AC Group        |  |
|--|---------------------|-------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group   | Reporting group     |  |
| Number of subjects analysed              | 48                  | 51                | 105                 |  |
| Units: Ratios                            |                     |                   |                     |  |
| geometric mean (confidence interval 95%) |                     |                   |                     |  |
| Ratios                                   | 0.63 (0.41 to 0.96) | 0.3 (0.2 to 0.46) | 0.25 (0.19 to 0.34) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines

|   |   |
|---|---|
| End point title   | GMRs calculated to post booster baselines <sup>[23]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |   |
| End point type  | Primary   |
| End point timeframe:<br>At Year 8   |   |
| Notes:<br>[23] - 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.<br>Justification: The scope of this end point was descriptive, no statistical hypothesis test was performed.             |   |

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group        |  |
|--|---------------------|--------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group     |  |
| Number of subjects analysed              | 48                  | 51                 | 105                 |  |
| Units: Ratios                            |                     |                    |                     |  |
| geometric mean (confidence interval 95%) |                     |                    |                     |  |
| Ratios                                   | 0.29 (0.18 to 0.47) | 0.19 (0.12 to 0.3) | 0.16 (0.11 to 0.22) |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines

|   |   |
|---|---|
| End point title   | GMRs calculated to post booster baselines <sup>[24]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |   |
| End point type  | Primary   |
| End point timeframe:<br>At Year 9   |   |
| Notes:<br>[24] - 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.<br>Justification: The scope of this end point was descriptive, no statistical hypothesis test was performed.             |   |

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group       |  |
|--|---------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 48                  | 51                  | 105                |  |
| Units: Ratios                            |                     |                     |                    |  |
| geometric mean (confidence interval 95%) |                     |                     |                    |  |
| Ratios                                   | 0.45 (0.27 to 0.77) | 0.19 (0.11 to 0.32) | 0.2 (0.14 to 0.28) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines <sup>[25]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 10

Notes:

[25] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group        | TBE_C Group         | TBE_AC Group        |  |
|--|--------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group    | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 48                 | 51                  | 105                 |  |
| Units: Ratios                            |                    |                     |                     |  |
| geometric mean (confidence interval 95%) |                    |                     |                     |  |
| Ratios                                   | 0.36 (0.21 to 0.6) | 0.22 (0.13 to 0.36) | 0.18 (0.13 to 0.26) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups <sup>[26]</sup> |
|-----------------|---|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years,  $\geq 50$  years, and  $\geq 60$  years.

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

End point timeframe:

At Year 6

Notes:

[26] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values  | TBE_R Group           | TBE_C Group        | TBE_AC Group          |  |
|---|-----------------------|--------------------|-----------------------|--|
| Subject group type  | Reporting group       | Reporting group    | Reporting group       |  |
| Number of subjects analysed                               | 35                    | 39                 | 81                    |  |
| Units: Percentage of subjects                             |                       |                    |                       |  |
| number (confidence interval 95%)                          |                       |                    |                       |  |
| 15-49 years: Antibody Titers $\geq 2$                     | 94.29 (80.84 to 99.3) | 100 (90.97 to 100) | 96.3 (89.56 to 99.23) |  |
| $\geq 50$ years: Antibody Titers $\geq 2$<br>(N=13;12;25) | 100 (75.29 to 100)    | 100 (73.54 to 100) | 100 (86.28 to 100)    |  |
| $\geq 60$ years: Antibody Titers $\geq 2$<br>(N=4;3;7)    | 100 (39.76 to 100)    | 100 (29.24 to 100) | 100 (59.04 to 100)    |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups <sup>[27]</sup> |
|-----------------|---|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years,  $\geq 50$  years, and  $\geq 60$  years.

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

End point timeframe:

At Year 7

Notes:

[27] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values  | TBE_R Group           | TBE_C Group        | TBE_AC Group           |  |
|---|-----------------------|--------------------|------------------------|--|
| Subject group type  | Reporting group       | Reporting group    | Reporting group        |  |
| Number of subjects analysed                               | 35                    | 39                 | 81                     |  |
| Units: Percentage of subjects                             |                       |                    |                        |  |
| number (confidence interval 95%)                          |                       |                    |                        |  |
| 15-49 years: Antibody Titers $\geq 2$                     | 91.43 (76.94 to 98.2) | 100 (90.97 to 100) | 93.83 (86.18 to 97.97) |  |
| $\geq 50$ years: Antibody Titers $\geq 2$<br>(N=13;12;25) | 100 (75.29 to 100)    | 100 (73.54 to 100) | 100 (86.28 to 100)     |  |
| $\geq 60$ years: Antibody Titers $\geq 2$<br>(N=4;3;7)    | 100 (39.76 to 100)    | 100 (29.24 to 100) | 100 (59.04 to 100)     |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups

|  |   |
|--|---|
| End point title  | Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups <sup>[28]</sup> |
| End point description:<br>Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, $\geq 50$ years, and $\geq 60$ years. |   |
| End point type   | Primary   |
| End point timeframe:<br>At Year 8  |   |

Notes:

[28] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                                       | TBE_R Group            | TBE_C Group            | TBE_AC Group           |  |
|--|------------------------|------------------------|------------------------|--|
| Subject group type                                     | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                            | 35                     | 39                     | 81                     |  |
| Units: Percentage of subjects                          |                        |                        |                        |  |
| number (confidence interval 95%)                       |                        |                        |                        |  |
| 15-49 years: Antibody Titers $\geq 2$                  | 88.57 (73.26 to 96.8)  | 97.44 (86.52 to 99.94) | 92.59 (84.57 to 97.23) |  |
| $\geq 50$ years: Antibody Titers $\geq 2$ (N=13;12;25) | 92.31 (63.97 to 99.81) | 100 (73.54 to 100)     | 96 (79.65 to 99.9)     |  |
| $\geq 60$ years: Antibody Titers $\geq 2$ (N=4;3;7)    | 100 (39.76 to 100)     | 100 (29.24 to 100)     | 100 (59.04 to 100)     |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups

|  |   |
|--|---|
| End point title  | Percentage of subjects with detectable TBE antibody titers $\geq 2$ by age groups <sup>[29]</sup> |
| End point description:<br>Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, $\geq 50$ years, and $\geq 60$ years. |   |
| End point type   | Primary   |
| End point timeframe:<br>At Year 9  |   |

Notes:

[29] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                      | TBE_R Group           | TBE_C Group            | TBE_AC Group        |  |
|---------------------------------------|-----------------------|------------------------|---------------------|--|
| Subject group type                    | Reporting group       | Reporting group        | Reporting group     |  |
| Number of subjects analysed           | 35                    | 39                     | 81                  |  |
| Units: Percentage of subjects         |                       |                        |                     |  |
| number (confidence interval 95%)      |                       |                        |                     |  |
| 15-49 years: Antibody Titers $\geq 2$ | 88.57 (73.26 to 96.8) | 92.31 (79.13 to 98.38) | 91.36 (83 to 96.45) |  |



|   |                        |                    |                    |  |
|---|------------------------|--------------------|--------------------|--|
| ≥ 50 years: Antibody Titers ≥ 2<br>(N=13;12;25) | 92.31 (63.97 to 99.81) | 100 (73.54 to 100) | 96 (79.65 to 99.9) |  |
| ≥ 60 years: Antibody Titers ≥ 2<br>(N=4;3;7)    | 100 (39.76 to 100)     | 100 (29.24 to 100) | 100 (59.04 to 100) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with detectable TBE antibody titers ≥ 2 by age groups <sup>[30]</sup> |
|-----------------|--|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

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

End point timeframe:

At Year 10

Notes:

[30] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                                | TBE_R Group            | TBE_C Group            | TBE_AC Group           |  |
|---|------------------------|------------------------|------------------------|--|
| Subject group type                              | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                     | 35                     | 39                     | 81                     |  |
| Units: Percentage of subjects                   |                        |                        |                        |  |
| number (confidence interval 95%)                |                        |                        |                        |  |
| 15-49 years: Antibody Titers ≥ 2                | 88.57 (73.26 to 96.8)  | 94.87 (82.68 to 99.37) | 92.59 (84.57 to 97.23) |  |
| ≥ 50 years: Antibody Titers ≥ 2<br>(N=13;12;25) | 92.31 (63.97 to 99.81) | 100 (73.54 to 100)     | 96 (79.65 to 99.9)     |  |
| ≥ 60 years: Antibody Titers ≥ 2<br>(N=4;3;7)    | 100 (39.76 to 100)     | 100 (29.24 to 100)     | 100 (59.04 to 100)     |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with detectable TBE antibody titers ≥ 10 by age groups <sup>[31]</sup> |
|-----------------|---|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years, ≥ 50 years, and ≥ 60 years.

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

End point timeframe:

At Year 6

Notes:

[31] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values   | TBE_R Group           | TBE_C Group        | TBE_AC Group          |  |
|--|-----------------------|--------------------|-----------------------|--|
| Subject group type   | Reporting group       | Reporting group    | Reporting group       |  |
| Number of subjects analysed                                | 35                    | 39                 | 81                    |  |
| Units: Percentage of subjects                              |                       |                    |                       |  |
| number (confidence interval 95%)                           |                       |                    |                       |  |
| 15-49 years: Antibody Titers $\geq 10$                     | 94.29 (80.84 to 99.3) | 100 (90.97 to 100) | 96.3 (89.56 to 99.23) |  |
| $\geq 50$ years: Antibody Titers $\geq 10$<br>(N=13;12;25) | 100 (75.29 to 100)    | 100 (73.54 to 100) | 100 (86.28 to 100)    |  |
| $\geq 60$ years: Antibody Titers $\geq 10$<br>(N=4;3;7)    | 100 (39.76 to 100)    | 100 (29.24 to 100) | 100 (59.04 to 100)    |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$ by age groups

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq 10$ by age groups <sup>[32]</sup> |
|-----------------|--|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years,  $\geq 50$  years, and  $\geq 60$  years.

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

End point timeframe:

At Year 7

Notes:

[32] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values   | TBE_R Group           | TBE_C Group        | TBE_AC Group           |  |
|--|-----------------------|--------------------|------------------------|--|
| Subject group type   | Reporting group       | Reporting group    | Reporting group        |  |
| Number of subjects analysed                                | 35                    | 39                 | 81                     |  |
| Units: Number of subjects                                  |                       |                    |                        |  |
| number (confidence interval 95%)                           |                       |                    |                        |  |
| 15-49 years: Antibody Titers $\geq 10$                     | 91.43 (76.94 to 98.2) | 100 (90.97 to 100) | 93.83 (86.18 to 97.97) |  |
| $\geq 50$ years: Antibody Titers $\geq 10$<br>(N=13;12;25) | 100 (75.29 to 100)    | 100 (73.54 to 100) | 100 (86.28 to 100)     |  |
| $\geq 60$ years: Antibody Titers $\geq 10$<br>(N=4;3;7)    | 100 (39.76 to 100)    | 100 (29.24 to 100) | 100 (59.04 to 100)     |  |

## Statistical analyses

No statistical analyses for this end point

---

**Primary: Percentage of subjects with detectable TBE antibody titers  $\geq$  10 by age groups**

---

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ 10 by age groups <sup>[33]</sup> |
|-----------------|--|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years,  $\geq$  50 years, and  $\geq$  60 years.

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

End point timeframe:

At Year 8

Notes:

[33] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values  | TBE_R Group            | TBE_C Group            | TBE_AC Group        |  |
|---|------------------------|------------------------|---------------------|--|
| Subject group type                                      | Reporting group        | Reporting group        | Reporting group     |  |
| Number of subjects analysed                             | 35                     | 39                     | 81                  |  |
| Units: Percentage of subjects                           |                        |                        |                     |  |
| number (confidence interval 95%)                        |                        |                        |                     |  |
| 15-49 years: Antibody Titers $\geq$ 10                  | 88.57 (73.26 to 96.8)  | 97.44 (86.52 to 99.94) | 91.36 (83 to 96.45) |  |
| $\geq$ 50 years: Antibody Titers $\geq$ 10 (N=13;12;25) | 92.31 (63.97 to 99.81) | 100 (73.54 to 100)     | 96 (79.65 to 99.9)  |  |
| $\geq$ 60 years: Antibody Titers $\geq$ 10 (N=4;3;7)    | 100 (39.76 to 100)     | 100 (29.24 to 100)     | 100 (59.04 to 100)  |  |

---

**Statistical analyses**

---

No statistical analyses for this end point

---

**Primary: Percentage of subjects with detectable TBE antibody titers  $\geq$  10 by age groups**

---

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq$ 10 by age groups <sup>[34]</sup> |
|-----------------|--|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years,  $\geq$  50 years, and  $\geq$  60 years.

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

End point timeframe:

At Year 9

Notes:

[34] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values   | TBE_R Group            | TBE_C Group            | TBE_AC Group        |  |
|--|------------------------|------------------------|---------------------|--|
| Subject group type   | Reporting group        | Reporting group        | Reporting group     |  |
| Number of subjects analysed                                | 35                     | 39                     | 81                  |  |
| Units: Percentage of subjects                              |                        |                        |                     |  |
| number (confidence interval 95%)                           |                        |                        |                     |  |
| 15-49 years: Antibody Titers $\geq 10$                     | 88.57 (73.26 to 96.8)  | 92.31 (79.13 to 98.38) | 91.36 (83 to 96.45) |  |
| $\geq 50$ years: Antibody Titers $\geq 10$<br>(N=13;12;25) | 92.31 (63.97 to 99.81) | 100 (73.54 to 100)     | 96 (79.65 to 99.9)  |  |
| $\geq 60$ years: Antibody Titers $\geq 10$<br>(N=4;3;7)    | 100 (39.76 to 100)     | 100 (29.24 to 100)     | 100 (59.04 to 100)  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with detectable TBE antibody titers $\geq 10$ by age groups

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with detectable TBE antibody titers $\geq 10$ by age groups <sup>[35]</sup> |
|-----------------|--|

End point description:

Age groups defined based on age at entry to V48P7E1 study: 15 to 49 years,  $\geq 50$  years, and  $\geq 60$  years.

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

End point timeframe:

At Year 10

Notes:

[35] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values   | TBE_R Group            | TBE_C Group            | TBE_AC Group           |  |
|--|------------------------|------------------------|------------------------|--|
| Subject group type   | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                                | 35                     | 39                     | 81                     |  |
| Units: Percentage of subjects                              |                        |                        |                        |  |
| number (confidence interval 95%)                           |                        |                        |                        |  |
| 15-49 years: Antibody Titers $\geq 10$                     | 88.57 (73.26 to 96.8)  | 94.87 (82.68 to 99.37) | 92.59 (84.57 to 97.23) |  |
| $\geq 50$ years: Antibody Titers $\geq 10$<br>(N=13;12;25) | 92.31 (63.97 to 99.81) | 91.67 (61.52 to 99.79) | 96 (79.65 to 99.9)     |  |
| $\geq 60$ years: Antibody Titers $\geq 10$<br>(N=4;3;7)    | 100 (39.76 to 100)     | 66.67 (9.43 to 99.16)  | 100 (59.04 to 100)     |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of 15-49 years

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of 15-49 years <sup>[36]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[36] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group       |  |
|--|------------------|--------------------|--------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group    |  |
| Number of subjects analysed              | 35               | 39                 | 81                 |  |
| Units: Titers                            |                  |                    |                    |  |
| geometric mean (confidence interval 95%) |                  |                    |                    |  |
| Baseline GMT pre booster (N=9;39;79)     | 76 (27 to 215)   | 253 (153 to 417)   | 263 (185 to 375)   |  |
| Baseline GMT post booster (N=35;39;80)   | 638 (413 to 984) | 1299 (861 to 1959) | 1008 (757 to 1343) |  |
| GMT Year 6                               | 332 (186 to 593) | 341 (197 to 590)   | 235 (160 to 344)   |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Evaluation of GMTs in the age group of 15-49 years

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of 15-49 years <sup>[37]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[37] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group       |  |
|--|------------------|--------------------|--------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group    |  |
| Number of subjects analysed              | 35               | 39                 | 81                 |  |
| Units: Titers                            |                  |                    |                    |  |
| geometric mean (confidence interval 95%) |                  |                    |                    |  |
| Baseline GMT pre booster (N=9;39;79)     | 76 (27 to 215)   | 253 (153 to 417)   | 263 (185 to 375)   |  |
| Baseline GMT post booster (N=35;39;80)   | 638 (413 to 984) | 1299 (861 to 1959) | 1008 (757 to 1343) |  |
| GMT Year 7                               | 304 (164 to 564) | 384 (214 to 691)   | 250 (166 to 375)   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of 15-49 years

|  |  |
|--|--|
| End point title  | Evaluation of GMTs in the age group of 15-49 years <sup>[38]</sup> |
| End point description:   |  |
| GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Year 8  |  |
| Notes:   |  |
| [38] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.  |  |

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group       |  |
|--|------------------|--------------------|--------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group    |  |
| Number of subjects analysed              | 35               | 39                 | 81                 |  |
| Units: Titers                            |                  |                    |                    |  |
| geometric mean (confidence interval 95%) |                  |                    |                    |  |
| Baseline GMT pre booster (N=9;39;79)     | 76 (27 to 215)   | 253 (153 to 417)   | 263 (185 to 375)   |  |
| Baseline GMT post booster (N=35;39;80)   | 638 (413 to 984) | 1299 (861 to 1959) | 1008 (757 to 1343) |  |
| GMT Year 8                               | 151 (80 to 287)  | 219 (119 to 402)   | 160 (105 to 243)   |  |

## Statistical analyses

No statistical analyses for this end point

**Primary: Evaluation of GMTs in the age group of 15-49 years**

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of 15-49 years <sup>[39]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 9

Notes:

[39] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group       |  |
|--|------------------|--------------------|--------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group    |  |
| Number of subjects analysed              | 35               | 39                 | 81                 |  |
| Units: Titers                            |                  |                    |                    |  |
| geometric mean (confidence interval 95%) |                  |                    |                    |  |
| Baseline GMT pre booster (N=9;39;79)     | 76 (27 to 215)   | 253 (153 to 417)   | 263 (185 to 375)   |  |
| Baseline GMT post booster (N=35;39;80)   | 638 (413 to 984) | 1299 (861 to 1959) | 1008 (757 to 1343) |  |
| GMT Year 9                               | 218 (107 to 443) | 211 (108 to 413)   | 191 (120 to 305)   |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Evaluation of GMTs in the age group of 15-49 years**

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of 15-49 years <sup>[40]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 10

Notes:

[40] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group        | TBE_AC Group       |  |
|--|------------------|--------------------|--------------------|--|
| Subject group type                       | Reporting group  | Reporting group    | Reporting group    |  |
| Number of subjects analysed              | 35               | 39                 | 81                 |  |
| Units: Titers                            |                  |                    |                    |  |
| geometric mean (confidence interval 95%) |                  |                    |                    |  |
| Baseline GMT pre booster (N=9;39;79)     | 76 (27 to 215)   | 253 (153 to 417)   | 263 (185 to 375)   |  |
| Baseline GMT post booster (N=35;39;80)   | 638 (413 to 984) | 1299 (861 to 1959) | 1008 (757 to 1343) |  |
| GMT Year 10                              | 188 (92 to 382)  | 266 (136 to 520)   | 200 (126 to 319)   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of ≥ 50 years

|                 |   |
|-----------------|---|
| End point title | Evaluation of GMTs in the age group of ≥ 50 years <sup>[41]</sup> |
|-----------------|---|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[41] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group       | TBE_AC Group      |  |
|--|------------------|-------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group   | Reporting group   |  |
| Number of subjects analysed              | 13               | 12                | 25                |  |
| Units: Titers                            |                  |                   |                   |  |
| geometric mean (confidence interval 95%) |                  |                   |                   |  |
| Baseline GMT pre booster (N=0;12;25)     | 0 (0 to 0)       | 163 (77 to 348)   | 145 (86 to 244)   |  |
| Baseline GMT post booster                | 201 (111 to 364) | 733 (395 to 1361) | 914 (595 to 1403) |  |
| GMT Year 6                               | 207 (107 to 401) | 178 (89 to 355)   | 183 (114 to 295)  |  |

## Statistical analyses

No statistical analyses for this end point



**Primary: Evaluation of GMTs in the age group of  $\geq 50$  years**

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 50$ years <sup>[42]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[42] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group       | TBE_AC Group      |  |
|--|------------------|-------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group   | Reporting group   |  |
| Number of subjects analysed              | 13               | 12                | 25                |  |
| Units: Titers                            |                  |                   |                   |  |
| geometric mean (confidence interval 95%) |                  |                   |                   |  |
| Baseline GMT pre booster (N=0;12;25)     | 0 (0 to 0)       | 163 (77 to 348)   | 145 (86 to 244)   |  |
| Baseline GMT post booster                | 201 (111 to 364) | 733 (395 to 1361) | 914 (595 to 1403) |  |
| GMT Year 7                               | 272 (126 to 588) | 237 (107 to 528)  | 270 (155 to 470)  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Evaluation of GMTs in the age group of  $\geq 50$  years**

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 50$ years <sup>[43]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 8

Notes:

[43] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group       | TBE_AC Group      |  |
|--|------------------|-------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group   | Reporting group   |  |
| Number of subjects analysed              | 13               | 12                | 25                |  |
| Units: Titers                            |                  |                   |                   |  |
| geometric mean (confidence interval 95%) |                  |                   |                   |  |
| Baseline GMT pre booster (N=0;12;25)     | 0 (0 to 0)       | 163 (77 to 348)   | 145 (86 to 244)   |  |
| Baseline GMT post booster                | 201 (111 to 364) | 733 (395 to 1361) | 914 (595 to 1403) |  |
| GMT Year 8                               | 98 (39 to 245)   | 189 (73 to 492)   | 142 (73 to 275)   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of $\geq 50$ years

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 50$ years <sup>[44]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 9

Notes:

[44] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group       | TBE_AC Group      |  |
|--|------------------|-------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group   | Reporting group   |  |
| Number of subjects analysed              | 13               | 12                | 25                |  |
| Units: Titers                            |                  |                   |                   |  |
| geometric mean (confidence interval 95%) |                  |                   |                   |  |
| Baseline GMT pre booster (N=0;12;25)     | 0 (0 to 0)       | 163 (77 to 348)   | 145 (86 to 244)   |  |
| Baseline GMT post booster                | 201 (111 to 364) | 733 (395 to 1361) | 914 (595 to 1403) |  |
| GMT Year 9                               | 193 (74 to 505)  | 224 (82 to 609)   | 202 (101 to 403)  |  |

## Statistical analyses

No statistical analyses for this end point

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**Primary: Evaluation of GMTs in the age group of  $\geq 50$  years**

---

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 50$ years <sup>[45]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 10

Notes:

[45] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group      | TBE_C Group       | TBE_AC Group      |  |
|--|------------------|-------------------|-------------------|--|
| Subject group type                       | Reporting group  | Reporting group   | Reporting group   |  |
| Number of subjects analysed              | 13               | 12                | 25                |  |
| Units: Titers                            |                  |                   |                   |  |
| geometric mean (confidence interval 95%) |                  |                   |                   |  |
| Baseline GMT pre booster (N=0;12;25)     | 0 (0 to 0)       | 163 (77 to 348)   | 145 (86 to 244)   |  |
| Baseline GMT post booster                | 201 (111 to 364) | 733 (395 to 1361) | 914 (595 to 1403) |  |
| GMT Year 10                              | 119 (47 to 302)  | 189 (72 to 496)   | 129 (66 to 251)   |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Evaluation of GMTs in the age group of  $\geq 60$  years**

---

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 60$ years <sup>[46]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[46] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group     | TBE_C Group       | TBE_AC Group     |  |
|--|-----------------|-------------------|------------------|--|
| Subject group type                       | Reporting group | Reporting group   | Reporting group  |  |
| Number of subjects analysed              | 4               | 3                 | 7                |  |
| Units: Titers                            |                 |                   |                  |  |
| geometric mean (confidence interval 95%) |                 |                   |                  |  |
| Baseline GMT pre booster (N=0;3;7)       | 0 (0 to 0)      | 64 (13 to 316)    | 69 (24 to 197)   |  |
| Baseline GMT post booster                | 173 (71 to 425) | 573 (203 to 1616) | 498 (253 to 982) |  |
| GMT Year 6                               | 189 (52 to 688) | 96 (22 to 427)    | 76 (29 to 202)   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of $\geq 60$ years

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 60$ years <sup>[47]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[47] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group     | TBE_C Group       | TBE_AC Group     |  |
|--|-----------------|-------------------|------------------|--|
| Subject group type                       | Reporting group | Reporting group   | Reporting group  |  |
| Number of subjects analysed              | 4               | 3                 | 7                |  |
| Units: Titers                            |                 |                   |                  |  |
| geometric mean (confidence interval 95%) |                 |                   |                  |  |
| Baseline GMT pre booster (N=0;3;7)       | 0 (0 to 0)      | 64 (31 to 316)    | 69 (24 to 197)   |  |
| Baseline GMT post booster                | 173 (71 to 425) | 573 (203 to 1616) | 498 (253 to 982) |  |
| GMT Year 7                               | 133 (26 to 677) | 120 (18 to 789)   | 105 (31 to 360)  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of $\geq 60$ years

|  |  |
|--|--|
| End point title  | Evaluation of GMTs in the age group of $\geq 60$ years <sup>[48]</sup> |
| End point description:   |  |
| GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Year 8  |  |

Notes:

[48] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group     | TBE_C Group       | TBE_AC Group     |  |
|--|-----------------|-------------------|------------------|--|
| Subject group type                       | Reporting group | Reporting group   | Reporting group  |  |
| Number of subjects analysed              | 4               | 3                 | 7                |  |
| Units: Titers                            |                 |                   |                  |  |
| geometric mean (confidence interval 95%) |                 |                   |                  |  |
| Baseline GMT pre booster (N=0;3;7)       | 0 (0 to 0)      | 64 (13 to 316)    | 69 (24 to 197)   |  |
| Baseline GMT post booster                | 173 (71 to 425) | 573 (203 to 1616) | 498 (253 to 982) |  |
| GMT Year 8                               | 128 (26 to 620) | 81 (13 to 504)    | 71 (21 to 234)   |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Evaluation of GMTs in the age group of $\geq 60$ years

|  |  |
|--|--|
| End point title  | Evaluation of GMTs in the age group of $\geq 60$ years <sup>[49]</sup> |
| End point description:   |  |
| GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Year 9  |  |

Notes:

[49] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group     | TBE_C Group       | TBE_AC Group     |  |
|--|-----------------|-------------------|------------------|--|
| Subject group type                       | Reporting group | Reporting group   | Reporting group  |  |
| Number of subjects analysed              | 4               | 3                 | 7                |  |
| Units: Titers                            |                 |                   |                  |  |
| geometric mean (confidence interval 95%) |                 |                   |                  |  |
| Baseline GMT pre booster (N=0;3;7)       | 0 (0 to 0)      | 64 (13 to 316)    | 69 (24 to 197)   |  |
| Baseline GMT post booster                | 173 (71 to 425) | 573 (203 to 1616) | 498 (253 to 982) |  |
| GMT Year 9                               | 224 (52 to 965) | 67 (12 to 362)    | 128 (42 to 385)  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Evaluation of GMTs in the age group of $\geq 60$ years

|                 |  |
|-----------------|--|
| End point title | Evaluation of GMTs in the age group of $\geq 60$ years <sup>[50]</sup> |
|-----------------|--|

End point description:

GMTs by visit were tabulated for each vaccine schedule. Baselines pre booster and post booster vaccination titers were used as denominators to calculate GMRs. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 10

Notes:

[50] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group     | TBE_C Group       | TBE_AC Group     |  |
|--|-----------------|-------------------|------------------|--|
| Subject group type                       | Reporting group | Reporting group   | Reporting group  |  |
| Number of subjects analysed              | 4               | 3                 | 7                |  |
| Units: Titers                            |                 |                   |                  |  |
| geometric mean (confidence interval 95%) |                 |                   |                  |  |
| Baseline GMT pre booster (N=0;3;7)       | 0 (0 to 0)      | 64 (13 to 316)    | 69 (24 to 197)   |  |
| Baseline GMT post booster                | 173 (71 to 425) | 573 (203 to 1616) | 498 (253 to 982) |  |
| GMT Year 10                              | 181 (35 to 928) | 57 (9 to 377)     | 72 (21 to 248)   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines in the age group of 15-49 years <sup>[51]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:<br>At Year 6  |  |

Notes:

[51] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group          | TBE_C Group         | TBE_AC Group      |  |
|--|----------------------|---------------------|-------------------|--|
| Subject group type                       | Reporting group      | Reporting group     | Reporting group   |  |
| Number of subjects analysed              | 9                    | 39                  | 79                |  |
| Units: Ratios                            |                      |                     |                   |  |
| geometric mean (confidence interval 95%) |                      |                     |                   |  |
| Ratios                                   | 6.73 (3.02 to 15.01) | 1.35 (0.92 to 1.98) | 0.92 (0.7 to 1.2) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines in the age group of 15-49 years <sup>[52]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:<br>At Year 7  |  |

Notes:

[52] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group          | TBE_C Group         | TBE_AC Group        |  |
|--|----------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group      | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 9                    | 39                  | 79                  |  |
| Units: Ratios                            |                      |                     |                     |  |
| geometric mean (confidence interval 95%) |                      |                     |                     |  |
| Ratios                                   | 3.85 (1.34 to 11.04) | 1.52 (0.92 to 2.52) | 0.96 (0.68 to 1.38) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of 15-49 years <sup>[53]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 8

Notes:

[53] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group        |  |
|--|---------------------|--------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group     |  |
| Number of subjects analysed              | 9                   | 39                 | 79                  |  |
| Units: Ratios                            |                     |                    |                     |  |
| geometric mean (confidence interval 95%) |                     |                    |                     |  |
| Ratios                                   | 0.67 (0.22 to 2.08) | 0.87 (0.5 to 1.49) | 0.62 (0.42 to 0.91) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of 15-49 years <sup>[54]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 9



Notes:

[54] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group        | TBE_C Group         | TBE_AC Group        |  |
|--|--------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group    | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 9                  | 39                  | 79                  |  |
| Units: Ratios                            |                    |                     |                     |  |
| geometric mean (confidence interval 95%) |                    |                     |                     |  |
| Ratios                                   | 1.08 (0.3 to 3.88) | 0.84 (0.45 to 1.54) | 0.73 (0.47 to 1.12) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of 15-49 years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of 15-49 years <sup>[55]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 10

Notes:

[55] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group        |  |
|--|---------------------|--------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group     |  |
| Number of subjects analysed              | 9                   | 39                 | 79                  |  |
| Units: Ratios                            |                     |                    |                     |  |
| geometric mean (confidence interval 95%) |                     |                    |                     |  |
| Ratios                                   | 0.76 (0.24 to 2.48) | 1.05 (0.6 to 1.85) | 0.78 (0.52 to 1.16) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to pre booster baselines in the age group of ≥ 50 years <sup>[56]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 6

Notes:

[56] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[57]</sup> | 12                  | 25                  |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.09 (0.75 to 1.59) | 1.27 (0.98 to 1.64) |  |

Notes:

[57] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

## Primary: GMRs calculated to pre booster baselines in the age group of $\geq 50$ years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of $\geq 50$ years <sup>[58]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 7

Notes:

[58] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group        | TBE_AC Group        |  |
|--|-------------------|--------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group    | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[59]</sup> | 12                 | 25                  |  |
| Units: Ratios                            |                   |                    |                     |  |
| geometric mean (confidence interval 95%) |                   |                    |                     |  |
| Ratios                                   | ( to )            | 1.45 (1.01 to 2.1) | 1.87 (1.45 to 2.41) |  |

Notes:

[59] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of $\geq 50$ years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of $\geq 50$ years <sup>[60]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 8

Notes:

[60] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[61]</sup> | 12                  | 25                  |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.16 (0.62 to 2.17) | 0.98 (0.63 to 1.52) |  |

Notes:

[61] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of $\geq 50$ years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of $\geq 50$ years <sup>[62]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 9

Notes:

[62] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[63]</sup> | 12                  | 25                  |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.37 (0.71 to 2.65) | 1.39 (0.88 to 2.21) |  |

Notes:

[63] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of ≥ 50 years

|                        |  |
|------------------------|--|
| End point title        | GMRs calculated to pre booster baselines in the age group of ≥ 50 years <sup>[64]</sup>  |
| End point description: | GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |
| End point type         | Primary  |
| End point timeframe:   | At Year 10   |

Notes:

[64] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[65]</sup> | 12                  | 25                  |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.16 (0.63 to 2.12) | 0.89 (0.58 to 1.35) |  |

Notes:

[65] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of ≥ 60 years

|                        |  |
|------------------------|--|
| End point title        | GMRs calculated to pre booster baselines in the age group of ≥ 60 years <sup>[66]</sup>  |
| End point description: | GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |
| End point type         | Primary  |

End point timeframe:

At Year 6

Notes:

[66] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group        | TBE_AC Group      |  |
|--|-------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group   | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 0 <sup>[67]</sup> | 3                  | 7                 |  |
| Units: Ratios                            |                   |                    |                   |  |
| geometric mean (confidence interval 95%) |                   |                    |                   |  |
| Ratios                                   | ( to )            | 1.5 (0.76 to 2.97) | 1.1 (0.7 to 1.72) |  |

Notes:

[67] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

## Primary: GMRs calculated to pre booster baselines in the age group of $\geq 60$ years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of $\geq 60$ years <sup>[68]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 7

Notes:

[68] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[69]</sup> | 3                   | 7                   |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.88 (0.97 to 3.64) | 1.52 (0.99 to 2.35) |  |

Notes:

[69] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

## Primary: GMRs calculated to pre booster baselines in the age group of $\geq 60$ years

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines in the age group of $\geq 60$ years <sup>[70]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:<br>At Year 8  |  |

Notes:

[70] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[71]</sup> | 3                   | 7                   |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.27 (0.44 to 3.66) | 1.03 (0.51 to 2.05) |  |

Notes:

[71] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

## Primary: GMRs calculated to pre booster baselines in the age group of $\geq 60$ years

|  |  |
|--|--|
| End point title  | GMRs calculated to pre booster baselines in the age group of $\geq 60$ years <sup>[72]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start). |  |
| End point type   | Primary  |
| End point timeframe:<br>At Year 9  |  |

Notes:

[72] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group        |  |
|--|-------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 0 <sup>[73]</sup> | 3                   | 7                   |  |
| Units: Ratios                            |                   |                     |                     |  |
| geometric mean (confidence interval 95%) |                   |                     |                     |  |
| Ratios                                   | ( to )            | 1.05 (0.37 to 2.94) | 1.85 (0.94 to 3.64) |  |

Notes:

[73] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to pre booster baselines in the age group of $\geq 60$ years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to pre booster baselines in the age group of $\geq 60$ years <sup>[74]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using pre booster vaccination titers as baseline. Pre booster vaccination titer: GMT at Day 0 of V48P7E1 prior to booster vaccine administration (excluding subjects who received the booster before V48P7E1 study start).

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

End point timeframe:

At Year 10

Notes:

[74] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group       | TBE_C Group         | TBE_AC Group       |  |
|--|-------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group   | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 0 <sup>[75]</sup> | 3                   | 7                  |  |
| Units: Ratios                            |                   |                     |                    |  |
| geometric mean (confidence interval 95%) |                   |                     |                    |  |
| Ratios                                   | ( to )            | 0.89 (0.39 to 2.06) | 1.04 (0.6 to 1.81) |  |

Notes:

[75] - There were no subjects in the TBE\_R group with baselines calculated using pre booster values

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of 15-49 years <sup>[76]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[76] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group       |  |
|--|---------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 35                  | 39                  | 80                 |  |
| Units: Ratios                            |                     |                     |                    |  |
| geometric mean (confidence interval 95%) |                     |                     |                    |  |
| Ratios                                   | 0.52 (0.35 to 0.78) | 0.26 (0.18 to 0.38) | 0.23 (0.18 to 0.3) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of 15-49 years <sup>[77]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[77] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group        |  |
|--|---------------------|--------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group     |  |
| Number of subjects analysed              | 35                  | 39                 | 80                  |  |
| Units: Ratios                            |                     |                    |                     |  |
| geometric mean (confidence interval 95%) |                     |                    |                     |  |
| Ratios                                   | 0.48 (0.28 to 0.81) | 0.3 (0.18 to 0.49) | 0.24 (0.17 to 0.35) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of 15-49 years <sup>[78]</sup> |
|-----------------|---|



End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type Primary

End point timeframe:

At Year 8

Notes:

[78] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group       | TBE_AC Group        |  |
|--|---------------------|-------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group   | Reporting group     |  |
| Number of subjects analysed              | 35                  | 39                | 80                  |  |
| Units: Ratios                            |                     |                   |                     |  |
| geometric mean (confidence interval 95%) |                     |                   |                     |  |
| Ratios                                   | 0.24 (0.13 to 0.43) | 0.17 (0.1 to 0.3) | 0.16 (0.11 to 0.23) |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

End point title GMRs calculated to post booster baselines in the age group of 15-49 years<sup>[79]</sup>

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

End point type Primary

End point timeframe:

At Year 9

Notes:

[79] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group       |  |
|--|---------------------|--------------------|--------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group    |  |
| Number of subjects analysed              | 35                  | 39                 | 80                 |  |
| Units: Ratios                            |                     |                    |                    |  |
| geometric mean (confidence interval 95%) |                     |                    |                    |  |
| Ratios                                   | 0.34 (0.18 to 0.66) | 0.16 (0.09 to 0.3) | 0.19 (0.12 to 0.3) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of 15-49 years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of 15-49 years <sup>[80]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 10

Notes:

[80] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group        | TBE_AC Group      |  |
|--|---------------------|--------------------|-------------------|--|
| Subject group type                       | Reporting group     | Reporting group    | Reporting group   |  |
| Number of subjects analysed              | 35                  | 39                 | 80                |  |
| Units: Ratios                            |                     |                    |                   |  |
| geometric mean (confidence interval 95%) |                     |                    |                   |  |
| Ratios                                   | 0.29 (0.15 to 0.56) | 0.2 (0.11 to 0.38) | 0.2 (0.13 to 0.3) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of ≥ 50 years

|                 |  |
|-----------------|--|
| End point title | GMRs calculated to post booster baselines in the age group of ≥ 50 years <sup>[81]</sup> |
|-----------------|--|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 6

Notes:

[81] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group        | TBE_C Group         | TBE_AC Group       |  |
|--|--------------------|---------------------|--------------------|--|
| Subject group type                       | Reporting group    | Reporting group     | Reporting group    |  |
| Number of subjects analysed              | 13                 | 12                  | 25                 |  |
| Units: Ratios                            |                    |                     |                    |  |
| geometric mean (confidence interval 95%) |                    |                     |                    |  |
| Ratios                                   | 1.03 (0.7 to 1.52) | 0.24 (0.16 to 0.37) | 0.2 (0.15 to 0.27) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 50$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 50$ years <sup>[82]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[82] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group      |  |
|--|---------------------|---------------------|-------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group   |  |
| Number of subjects analysed              | 13                  | 12                  | 25                |  |
| Units: Ratios                            |                     |                     |                   |  |
| geometric mean (confidence interval 95%) |                     |                     |                   |  |
| Ratios                                   | 1.36 (0.79 to 2.33) | 0.32 (0.18 to 0.57) | 0.3 (0.2 to 0.44) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 50$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 50$ years <sup>[83]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 8

Notes:

[83] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 13                  | 12                  | 25                  |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 0.49 (0.23 to 1.04) | 0.26 (0.12 to 0.57) | 0.16 (0.09 to 0.27) |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 50$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 50$ years <sup>[84]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 9

Notes:

[84] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 13                  | 12                  | 25                  |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 0.96 (0.44 to 2.08) | 0.31 (0.14 to 0.68) | 0.22 (0.13 to 0.39) |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 50$ years

|   |   |
|---|---|
| End point title   | GMRs calculated to post booster baselines in the age group of $\geq 50$ years <sup>[85]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |   |
| End point type  | Primary   |
| End point timeframe:<br>At Year 10  |   |

Notes:

[85] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 13                  | 12                  | 25                  |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 0.59 (0.28 to 1.24) | 0.26 (0.12 to 0.55) | 0.14 (0.08 to 0.24) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 60$ years

|   |   |
|---|---|
| End point title   | GMRs calculated to post booster baselines in the age group of $\geq 60$ years <sup>[86]</sup> |
| End point description:<br>GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start. |   |
| End point type  | Primary   |
| End point timeframe:<br>At Year 6   |   |

Notes:

[86] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 4                   | 3                   | 7                   |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 1.09 (0.47 to 2.55) | 0.17 (0.06 to 0.45) | 0.15 (0.08 to 0.29) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 60$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 60$ years <sup>[87]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 7

Notes:

[87] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 4                   | 3                   | 7                   |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 0.77 (0.21 to 2.86) | 0.21 (0.05 to 0.96) | 0.21 (0.08 to 0.57) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 60$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 60$ years <sup>[88]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 8

Notes:

[88] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group        | TBE_C Group         | TBE_AC Group        |  |
|--|--------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group    | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 4                  | 3                   | 7                   |  |
| Units: Ratios                            |                    |                     |                     |  |
| geometric mean (confidence interval 95%) |                    |                     |                     |  |
| Ratios                                   | 0.74 (0.2 to 2.72) | 0.14 (0.03 to 0.64) | 0.14 (0.05 to 0.38) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 60$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 60$ years <sup>[89]</sup> |
|-----------------|---|

End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

End point timeframe:

At Year 9

Notes:

[89] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group         | TBE_AC Group        |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed              | 4                   | 3                   | 7                   |  |
| Units: Ratios                            |                     |                     |                     |  |
| geometric mean (confidence interval 95%) |                     |                     |                     |  |
| Ratios                                   | 1.29 (0.43 to 3.84) | 0.12 (0.03 to 0.41) | 0.26 (0.11 to 0.58) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: GMRs calculated to post booster baselines in the age group of $\geq 60$ years

|                 |   |
|-----------------|---|
| End point title | GMRs calculated to post booster baselines in the age group of $\geq 60$ years <sup>[90]</sup> |
|-----------------|---|

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End point description:

GMR values were tabulated by vaccine schedule using post booster vaccination titers as baseline. Post booster vaccination titer: GMT at Day 21 of V48P7E1 (for subjects who received booster in V48P7E1); Day 0 for subjects who received booster before V48P7E1 study start.

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

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End point timeframe:

At Year 10

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Notes:

[90] - 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: The scope of this end point was descriptive, no statistical hypothesis test was performed.

| End point values                         | TBE_R Group         | TBE_C Group       | TBE_AC Group        |  |
|--|---------------------|-------------------|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group   | Reporting group     |  |
| Number of subjects analysed              | 4                   | 3                 | 7                   |  |
| Units: Ratios                            |                     |                   |                     |  |
| geometric mean (confidence interval 95%) |                     |                   |                     |  |
| Ratios                                   | 1.05 (0.31 to 3.49) | 0.1 (0.02 to 0.4) | 0.14 (0.06 to 0.36) |  |

## Statistical analyses

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No statistical analyses for this end point



## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

Not applicable (NA)

Adverse event reporting additional description:

The study was intended to evaluate the persistence of antibody response up to 10 years after booster vaccine administration. Safety profile of the vaccine was not evaluated as per study protocol. Hence, there are no safety results as per planned analysis.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |    |
|-----------------|----|
| Dictionary name | NA |
|-----------------|----|

|                    |    |
|--------------------|----|
| Dictionary version | NA |
|--------------------|----|

Frequency threshold for reporting non-serious adverse events: 5 %

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### Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The study was intended to evaluate the persistence of antibody response up to 10 years after booster vaccine administration. Safety profile of the vaccine was not evaluated as per study protocol. Hence, there are no safety results as per planned analysis.

## **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