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**Immunogenicity and safety of monovalent
RIVM meningococcal B OMP vesicle F91
vaccine administered to children that received
hexavalent meningococcal B vaccine
2.5 years ago**

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This investigation has been performed by order and for the account of the Chief Inspectorate of Health Care (IGZ), within the framework of project V/000012/03/AE, clinical studies with meningococcal B vaccine.

Abstract Nederlands

Dit rapport beschrijft een follow-up studie naar veiligheid en immunogeniciteit van monovalent P1.7^h,4 OMV vaccin (MonoMen) gebruikt als boostervaccinatie in kinderen eerder gevaccineerd met hexavalent MenB vaccin. De deelnemers aan deze studie zijn in het kader van een eerdere studie gevaccineerd met hexavalent MenB vesicle vaccin of met HepB vaccin (controle groep). Tijdens de studie traden geen ernstige bijwerkingen op. Systemische bijwerkingen werden vooral gerapporteerd tijdens de 2e en 3e dag na vaccinatie. Lokale bijwerkingen, die over het algemeen 3 dagen duurden, kwamen vaker voor. De stijging van de GMT van bactericide antistoffen tegen P1.7^h,4 in kinderen geprimeerd met hexavalent MenB was aanzienlijk hoger dan die in kinderen die HepB ontvingen. Ongeveer 80% van de kinderen die een immuunrespons tegen P1.7^h,4 vertoonden na de primaire serie met hexavalent MenB vaccin, reageerde ook met een immuunrespons op de boostervaccinatie met MonoMen, hetgeen wijst op de aanwezigheid van een immunologisch geheugen. Opmerkelijke titerstijgingen tegen stammen niet aanwezig in het monovalente vaccin werden waargenomen, deze worden waarschijnlijk veroorzaakt door kruisreagerende antistoffen. Ondanks een wat lagere respons tegen het subtype P1.7^h,4 na primaire vaccinatie serie met het hexavalente vaccin, wordt een adequate respons tegen deze stam gezien na de booster met MonoMen. Op grond van deze resultaten in combinatie met de resultaten van de fase II trial met MonoMen in peuters lijkt MonoMen een veilig en zeer immunogeen vaccin.

Abstract English

This report describes the results with respect to immunogenicity as well as reactogenicity of a monovalent P1.7^h,4 OMV vaccine (MonoMen) used as booster vaccination in children previously vaccinated with a hexavalent MenB vaccine. The participants in this study were immunised in 1995-1996 with hexavalent MenB vesicle vaccine or with hepatitis B vaccine (control group). The booster vaccination with MonoMen was well tolerated. No serious adverse events occurred during the study. Most systemic adverse reactions were observed during day 2 and 3. Local reactions, which generally lasted for three days, were more common than systemic reactions. The rise of the GMT of bactericidal antibodies against P1.7^h,4 in children primed with MenB was much higher as compared to children who received the HepB vaccine. About 80% of the children with an immune response after the primary series with the hexavalent vaccine, also showed an immune response after the booster vaccination with MonoMen which indicates the presence of an immunological memory for these children. Remarkably, immune responses against strains not present in MonoMen were also observed. Cross-reacting antibodies possibly cause these responses. In spite of the somewhat weak response against P1.7^h,4 after the primary vaccination series with the hexavalent vaccine, an adequate response against this strain was found after boosting with MonoMen. Based on these results in combination with the results of the phase II trial with MonoMen in toddlers MonoMen seems a safe and highly immunogenic vaccine.

Preface

Participating organisations and investigators

1. ROTTERDAM

- Sophia Kinderziekenhuis / Academisch Ziekenhuis Rotterdam

2. BILTHOVEN

- LVO, Laboratory for Clinical Vaccine Research

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- All colleagues who participated in the discussion of this study.

Abbreviations

| | |
|-------------------------|---|
| AlPO ₄ | aluminium phosphate |
| °C | Degrees centigrade |
| 95%CI | 95% Confidence Interval |
| CRF | Case Report Form |
| ELISA | Enzyme Linked Immunosorbent Assay |
| GMT | Geometric Mean Titre |
| HB-VAX [®] DNA | Hepatitis B vaccine |
| Hib | Haemophilus influenzae type b |
| HepB | Hepatitis B |
| ITT | Intention-To-Treat (analyses) |
| LPS | lipopolysaccharide |
| LVO | Laboratory for Clinical Vaccine Research (<i>Laboratorium voor Veldonderzoek vaccins</i>) |
| LVO-BI | LVO Bio- and Immunochemistry section (<i>LVO afdeling bio- en immunochemie</i>) |
| LVO-KO | LVO Clinical Research section (<i>LVO afdeling klinisch onderzoek</i>) |
| MenB | Meningococcal B |
| MonoMen | monovalent meningococcal vaccine expressing P1.7 ^h ,4 PorA |
| OMP | Outer Membrane Protein (of <i>N. meningitidis</i>) |
| OMV | Outer Membrane Vesicle (of <i>N. meningitidis</i>) |
| PEA | Immunisation Administration (<i>Provinciale Entadministratie</i>) |
| PorA | class 1 OMP porin protein |
| PP | Per Protocol (analyses) |
| RC | Resort Centre of the School Health Service (<i>Resort Centrum Schoolartsdienst</i>) |
| RIVM | National Institute of Public Health and the Environment (<i>Rijksinstituut voor Volksgezondheid en Milieu</i>) |
| RVP | National Childhood Immunisation Programme (<i>Rijksvaccinatieprogramma</i>) |
| SBA | serum bactericidal activity |
| SIS | Serum Information System |
| SKZ | Sophia Kinderziekenhuis/Academisch Ziekenhuis Rotterdam |
| VR | variable region of class 1 OMP |
| UTN | Unique Trial Number |

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Samenvatting

Achtergrond

Sinds vaccinatie tegen *Haemophilus influenzae* type b in 1993 is opgenomen in het Rijksvaccinatieprogramma wordt bacteriële meningitis in Nederland voornamelijk veroorzaakt door *Neisseria meningitidis* (meningococ). Meningococcen ziekten, zoals meningitis en/of sepsis, komen vooral voor bij kinderen, zowel in de eerste levensjaren als op school- en adolescenten leeftijd. In West Europa is de meningococcen B serogroep verantwoordelijk voor 70-75% van alle gevallen. In het RIVM is een vesicle vaccin ontwikkeld dat klasse 1 buitenmembraan eiwitten bevat van zes verschillende meningococcen subtypen. Klinische studies hebben aangetoond dat het vaccin immunogeen is in zuigelingen, kleuters en schoolkinderen en dat de aard en ernst van de bijwerkingen na vaccinatie acceptabel zijn.

Methode

Een groep kinderen die in 1995-1996 deelgenomen heeft aan de studie met het hexavalente RIVM meningococcen vaccin werd benaderd voor deelname aan de huidige studie waarin zij eenmalig werden gevaccineerd met monovalent P1.7^h,4 OMV vaccin (MonoMen). Lokale en algemene bijwerkingen werden gedurende één week na vaccinatie geregistreerd. Bloedmonsters werden vlak voor en 4-6 weken na vaccinatie afgenomen. De serum bactericide antistof (SBA) respons werd gemeten tegen zes isogene varianten van stam H44/76 waarin elk PorA eiwit van het hexavalente vaccin (subtypen P1.7,16 - P1.19,15 - P1.5^c,10 - P1.12,13 & P1.7^h,4) individueel tot expressie is gebracht.

Resultaten

Tijdens de studie traden geen ernstige bijwerkingen op. Systemische bijwerkingen werden vooral gerapporteerd tijdens de 2e en 3e dag na vaccinatie. De meest frequent gerapporteerde klachten waren hangerigheid, hoofdpijn en verminderde eetlust (resp. 8%, 7% en 6%). Koorts, één van de meest voorkomende systemische bijwerkingen na vaccinatie, werd in deze studie voor slechts 1-3% van de kinderen gerapporteerd. Lokale bijwerkingen kwamen aanzienlijk vaker voor, met name milde pijn rond de injectieplaats (35-78%). Na de boostervaccinatie was de stijging van de GMT van bactericide antistoffen tegen P1.7^h,4 aanzienlijk hoger in kinderen geprimeerd met het hexavalente MenB vaccin vergeleken met de kinderen gevaccineerd met het HepB vaccin. Circa 80% van de kinderen die een immuunrespons tegen P1.7^h,4 vertoonden na de primaire serie met het hexavalente MenB vaccin in de vorige studie, reageerde ook in deze studie met een immuunrespons. Ofschoon met een monovalent vaccin geboosterd werd, werden onverwachte titerstijgingen gemeten tegen de andere stammen. Deze responsen waren het meest duidelijk voor de stammen P1.5^c,10 en P1.5,2 en wordt waarschijnlijk veroorzaakt door kruisreagerende antistoffen.

Discussie

De aard en ernst van de bijwerkingen na vaccinatie zijn acceptabel. Er zijn geen ernstige bijwerkingen opgetreden. De studie toont aan dat priming met het hexavalente MenB vaccin geleid heeft tot de ontwikkeling van een immunologisch geheugen. Ondanks de wat slechtere respons tegen subtype P1.7^h,4 na de primaire serie leidt boostering met het monovalente vaccin nu wel tot een adequate respons tegen P1.7^h,4.

Summary

Background

Bacterial meningitis in the Netherlands is predominantly caused by *Neisseria meningitidis* (meningococcus) since introduction of vaccination against *Haemophilus influenzae* type b in the National Childhood Immunization Program in 1993. Meningococcal diseases (meningitis and septicemia) predominantly occur in childhood, both in young infants and at school- and adolescent age. Meningococcus serogroup B causes 70-75% of meningococcal disease in Western Europe. The RIVM has developed a vesicle vaccine that contains class 1 outer membrane proteins of six different meningococci subtypes. Clinical studies have proven that the vaccine is well tolerated and immunogenic in infants, toddlers and school children.

Methods

Children who participated in the study with the RIVM hexavalent OMV vaccine in 1995-'96 were asked to participate in the current study in which a booster vaccination with monovalent P1.7^h,4 OMV vaccine (MonoMen) was administered. Local and systemic adverse reactions were assessed during the week after vaccination. Blood for antibody assays was taken before and 4-6 weeks after vaccination. The serum bactericidal antibody (SBA) response was assessed against six isogenic variants of strain H44/76 in which each PorA of the hexavalent vaccine (subtypes P1.7,16 - P1.19,15 - P1.5,2 - P1.5^c,10 - P1.12,13 & P1.7^h,4) was expressed individually.

Results

The booster vaccination was well tolerated, no serious adverse reactions were reported during the study. Most systemic adverse reactions occurred during day 2 and 3, with highest percentages for drowsiness, headache and less appetite (respectively 8%, 7% en 6%). Fever, one of the most common systemic reactions after vaccination in children, was only reported for 1-3% of the children. Local reactions were more common than systemic reactions. Mild pain at the injection site was reported for 35-78% of the children.

The rise of the GMT of bactericidal antibodies against subtype P1.7^h,4 in children primed with the hexavalent vaccine was much higher as compared to children vaccinated with HepB. About 80% of the children with an immune response against P1.7^h,4 after the primary series with the hexavalent MenB vaccine in the earlier study also showed an immune response after the booster vaccination with MonoMen. Unexpected immune responses against strains not present in MonoMen were observed. These responses were most pronounced for the strains P1.5^c,10 en P1.5,2. Cross-reacting antibodies possibly cause these responses.

Discussion

The frequency and nature of adverse reactions after vaccination are acceptable. No serious adverse events occurred. This study shows that priming with the RIVM hexavalent meningococcal OMV vaccine leads to the development of an immunological memory. In spite of a weaker response against P1.7^h,4 after vaccination with the hexavalent vaccine, an adequate response against this strain was found after boosting with MonoMen.

1. Introduction

In the Netherlands bacterial meningitis is predominantly caused by the *Neisseria meningitidis* (meningococcus) since vaccination against *Haemophilus influenzae* type b (Hib) was included in the National Childhood Immunisation Program (RVP) in 1993¹. Besides meningitis, the microorganism causes the serious syndrome of meningococcal septic shock. Mortality of meningococcal infections in children is 5-15% (30-90 cases/year). Survivors suffer serious and often permanent neurological sequelae like hearing loss, convulsive disorders, paralysis or mental retardation. Other complications are arthritis, vasculitis, peripheral necrosis, pericarditis, hydrocephalus and cranial nerve damage². Meningococcal disease occurs predominantly in two age clusters: 0-4 year olds (24 cases per 100,000 inhabitants) and 15-19 year olds (8 cases per 100,000 inhabitants)³.

Meningococci are heterogeneous with respect to the expression of surface antigens. They can be divided into twelve serogroups on the basis of variation in polysaccharides on the bacterial capsula. Second classification (serotyping) is based on differences in the class 2/3 outer membrane (OM) proteins (porin B), while serosubtyping is based on variations of class 1 OM proteins (porin A or PorA). Since class 1 OM proteins have two separate variable regions (VR1 and VR2), two separate serosubtyping epitopes can be recognised on one PorA protein, resulting in designations as P1.5,2 and P1.7,16^{4,5,6}. In the Netherlands, over 90% of the cases of meningococcal disease are caused by serogroups A, B and C, of which serogroup B is the most common (75-80%)¹.

Effective polysaccharide vaccines against the serogroups A and C are available, but a serogroup B polysaccharide vaccine is poorly immunogenic in humans. Moreover, the use of this vaccine has been discouraged because of the presence of closely related, and probably cross-reacting antigens in the human brain tissue^{7,8,9}. Therefore, a genetically engineered vaccine containing class 1 outer membrane proteins of six meningococcal B subtypes has been developed in the RIVM^{10,11,12}. These six subtypes (P1.7,16, P1.19,15, P1.5,2, P1.5^c,10, P1.12,13 and P1.7^h,4) currently represent 75-80% of case isolates of serogroup B in the Netherlands. Other OM proteins such as class 2/3 and 4 protein, as well as the B-capsular polysaccharide are not expressed in the vaccine due to gene deletions. The expression of class 5 protein is low. Side effects found after vaccination were infrequent and mild. In infants, the hexavalent vaccine was shown to be immunogenic, although a fourth booster dose of vaccine was required after the primary series to induce a significant serum bactericidal antibody (SBA) response. There were differences in the magnitudes of SBA responses on the different PorA's¹⁴. Similar results were found for toddlers and school children^{14,15}. In Norway, a monovalent OM vesicle vaccine was developed. The estimated efficacy of this vaccine in teenagers is 57%¹⁶. Another monovalent vaccine, developed in Cuba, showed that the efficacy varied by age: 74% in children aged 48 months or older, 47% in children aged 24 to 47 months, and 37% in children aged less than 24 months¹⁷. The Norwegian and the Cuban vaccines contain the subtypes B:15:P1.7,16 and B:4:P1.19,15 respectively, which only represent a small minority of the case isolates in the Netherlands (~10% of serogroup B isolates)⁴. None of the vaccines shows efficacy in infants.

In the Netherlands as well as in other Western European countries and New Zealand, P1.4 strains are the most prevalent ones among the meningococcal subtypes. However, compared to the other PorA's the anti-P1.4 response induced by the RIVM hexavalent vaccine was weak. For this reason, a monovalent model vaccine, using a vaccine production strain expressing P1.7^h,4 PorA (designated F91), was developed using production methods that

were further improved compared to the production of the hexavalent vaccine¹². The reactogenicity and immunogenicity of this monovalent vaccine was investigated in a phase II clinical trial in toddlers¹⁸. Preliminary results showed that side effects were infrequent and mild. Immunogenicity was compared for two monovalent vaccines that differed in adjuvant (either aluminium-phosphate or aluminium-hydroxide). The best immunogenicity was found for the vaccine absorbed to aluminium-phosphate. This vaccine was used to revaccinate children who were vaccinated with hexavalent meningococcal vaccine (or hepatitis B vaccine as a control) in a previous trial¹⁵.

The aim of this follow-up study was to investigate whether the hexavalent vaccine used in the primary series in the earlier study in 1995-96 has stimulated the induction of P1.4 specific memory. Therefore, the immunogenicity of the RIVM monovalent meningococcal B vesicle vaccine was assessed in healthy children previously vaccinated with hexavalent MenB vaccine. In addition, the reactogenicity of the monovalent MenB vaccine was investigated. The results of this study are described in this report.

2. Materials and methods

The study protocol “Onderzoek naar de aanwezige immuniteit bij een groep Rotterdamse kinderen, 2,5 jaar na inenting met een hexavalent meningokokken B vesicle vaccin”¹⁹ was approved by the Institutional Ethics Review Board of the Sophia Children’s Hospital and the University Hospital in Rotterdam.

2.1 Vaccine

The vaccine (MonoMen) used in this study is a white opaque suspension, filled in 3 ml glass vials, closed with rubber stopper and sealed with an aluminium capsule. The filling volume is 0.7 ml. The vaccine contains per dose of 0.5 ml:

- 17 µg meningococcal OM vesicle protein, corresponding with 15 µg of specific P1.7^h,4 class 1 protein (PorA) from seed strain F91
 - 11 µmol Al-salt (1.34 mg AlPO₄)
 - 50 µg (0.01% (w/v)) thiomersal
 - 50 mg (10 % (w/v)) sucrose
- in 10 mM Tris/HCl buffer, pH 7.4.

The manufacturer distributed the vials of the trial vaccines to the Immunisation Administration (PEA) without breaking the cold chain and all vaccines were stored at 2-8 °C throughout the study. The study personnel transported the vaccines from the PEA to the study site on the day of administration. At the Resort Centre of the School Health Service (RC) the vaccines were transferred to the refrigerator used for RVP vaccines, and during house calls the vaccines remained in insulated containers. At the end of the study each vial of the vaccine that has not been used for vaccinating a participant was returned to the Clinical Trial Monitor.

2.2 Participants

All children who participated in the trial “Study on the safety and immunogenicity of the RIVM hexavalent meningococcal B vesicle vaccine in children of 2-3 and 7-8 years of age in Rotterdam”¹⁵ were invited to participate in the present study by direct mailing. These children were born in 1993 (5-6 years of age) or 1988 (10-11 years of age) and living in the city of Rotterdam and surroundings. In the earlier study these children were immunised with a high or low dose hexavalent MenB vesicle vaccine or with hepatitis B vaccine (control group), according to a three-dose schedule with respectively 2 and 6 months interval between vaccinations.

2.3 Study design and procedures

After evaluation of inclusion and exclusion criteria and signing of an informed consent form by the parents, the child was enrolled. To link the results of this study with those of the earlier study, the children received the same Unique Trial Number (UTN) as used in 1995-96. So, the numbers 1-300 were used for the 5-6 years old children and the numbers 400-700 for the 10-11 years old children.

2.3.1 Study design by immunisation group

| Time (months): | | <0 | 0 | 1 | 7 | >7 |
|---|-------------------------|----|----------------------------------|--|----------------------------------|----------------|
| Study group (based on former study): | | | | | | |
| MenB | <i>Activity:</i> intake | | MonoMen | | | |
| | | | B ₁ O ₁ | B ₂ E ₁ | | |
| HepB | <i>Activity:</i> intake | | MonoMen | MonoMen | MonoMen | |
| | | | B ₁ O ₁ | B ₂ O ₂ E ₁ | O ₃ E ₂ | E ₃ |

Legend:

| | |
|--------------------|---|
| MenB: | received meningococcal B5 or B10 vesicle vaccine in the study in 1995-96 |
| HepB: | received HB-VAX [®] DNA vaccine in the study in 1995-96 |
| MonoMen: | immunisation with monovalent MenB vesicle vaccine |
| B ₁ : | blood sample before first vaccination |
| B ₂ : | blood sample 4-6 weeks after first vaccination |
| O ₁₋₃ : | observation of adverse reactions by trained observer 18-30 hours after vaccination 1, 2 and 3 |
| E ₁₋₃ : | evaluation of adverse reactions observed by parents in the week after vaccination 1, 2 and 3 |

2.3.2 Injection

All participants were immunised with the AlPO₄-adsorbed monovalent MenB vesicle vaccine at the RC's or at home. The vaccine was administered by intramuscular injection in the upper arm (deltoid or triceps muscle) depending on physician or research nurse preference. The site, date, time of injection and vaccine lot number were recorded on the CRF. Two extra monovalent MenB vaccinations were offered to the children who received the control vaccine (HB-VAX[®] DNA) in the previous study in 1995-'96, to complete a three-dose schedule with respectively 1 and 6 months interval between vaccinations.

2.3.3 Blood sampling and storage

Blood was sampled by venipuncture after application of the local anaesthetic lidocain/prilocain [EMLA[™]] by physicians or trained research nurses at the participant's home or at the RC. Blood samples were taken before and 1 month after the first vaccination, and sent to the RIVM by regular mail. Upon arrival serum was separated and stored at -20°C at LVO-BI. Aliquots for blinded antibody measurements were distributed with a Multiprobe (Canberra Packard, SOP 12N-APP-34). To secure blinded measurements, tubes with serum specimens were marked with a code, which did not reveal the timing of the blood sample or the study group.

2.3.4 Evaluation of adverse reactions

Serious adverse events were to be communicated immediately to the RIVM by the investigator. Specific systemic symptoms (fever [temperature \geq 38.5 °C], headache, drowsiness, unusual crying, less appetite, nausea, joint complaints, cutaneous symptoms, absence from school, use of medication, visit doctor or hospital, and illness in family) and the occurrence of local symptoms (redness, swelling, pain, itching and reduced use of the arm)

were assessed by a trained observer at 18-30 hours after each administration of the vaccine. Parents recorded occurrence of the symptoms during the rest of the week after vaccination in a 7-days diary, which was used to complete the CRF at the next study visit.

2.4 Antibody assays

2.4.1 Serum Bactericidal Activity (SBA) Assay

Bactericidal activity of antibodies against isogenic variants of strain H44/76 was determined as described by Peeters and Rouppe van der Voort^{22,23}.

In short, 2-fold dilutions of heat inactivated sera (30 min at 56°C), $2.5\text{--}5.0 \times 10^2$ c.f.u. bacteria and complement (final concentration 10% (v/v)) were incubated in a microtitre plate for 60 minutes at 37°C in 5% CO₂. Subsequently 7 µl of this suspension was spotted onto GC agar plates. Six isogenic strains (P1.7,16, P1.19,15, P1.5,2, P1.5^c,10, P1.12,13 and P1.7^h,4) with the same set of alleles as present in the two trivalent vaccine strains in the hexavalent vaccine of 1995-'96 were used. As control strain for PorA specificity the PorA negative mutant strain H1.5 was used. After 18-20h incubation at 37°C in 5% CO₂, the colonies from time zero were counted. The average number of c.f.u. at time zero was set at 100%. The serum bactericidal titre was reported as the reciprocal of the serum dilution yielding > 90% killing. For SBA with 50% killing titres the suspension of bacteria and complement was diluted 1:5 before spotting them on GC agar plates, further the same method was used as described above. Antibodies detected in the SBA Assay show class 1 OMP (bactericidal) specificity that is assumed to correlate with protective immunity. In earlier studies SBA titres of 1:4 or more were presumed to be associated with protection against clinical disease^{24,25,26}.

2.4.2 Monovalent ELISA

Since a monovalent vaccine vesicle (lot: 98MEN111 code 6.1) was used as ELISA-coat, antibodies detected in the ELISA show specificity against OMP from the F91 monovalent meningococcal P1.7^h,4 strain, which constitutes the monovalent vaccine¹⁸. In short, after overnight coating of the microtitre plates at room temperature threefold serial dilutions of serum samples were incubated for 2 hours at 37°C. After incubation with peroxidase conjugated goat anti-human IgG-F_c for 2 hours at 37°C, TMB-substrate colouring reaction was read at 450 nm. IgG antibody titres are expressed as the dilution that gives an extinction of 50% from the sum of OD_{max} and OD_{min}, where OD_{max} is the maximum OD₄₅₀ of a known high positive serum and OD_{min} is the correction for the background.

2.5 Data handling and validation

CRF data have been entered in a computer by a company, specialised in data entry (Wegener Direct Marketing Group Data Services, the Netherlands). Antibody titres were obtained later, but are an integral part of the final CRF. These antibody data are entered into the Serological Information System (SIS, SOP 12C-ALG-40 & 12C-ALG-41) by LVO-BI, and handed over to LVO-KO as an Excel worksheet. Clinical and serological data have been imported in a LVO database [MS Access 2.0²⁰] for storage and analysis. For further statistical analysis the data have been exported to SPSS [version 9.0 for Windows²¹]. After each step, checks were made to ensure that the correct data were used for final reporting.

During all clinical stages of the study, monitoring visits were made to each study facility (all RC's, PEA, SKZ). The monitor checked all of the informed consents and CRF's.

2.6 Data editing and protocol adherence

After entering all data in a computer database, a final assessment of protocol adherence was made. On the basis of this protocol adherence, data analyses were divided in Per Protocol (PP-) analyses and Intention-to-treat (ITT-) analyses. Because the outcomes of both analyses are almost identical, results of the PP-analyses are not shown in this report.

All data from a child were excluded from the PP- as well as the ITT-analyses in the following situations:

- doubtful fulfilment of inclusion or exclusion criteria, as specified in the study protocol,
- children that did receive vaccines other than the lots specified in the study protocol or children for which the vaccine lot was not filled out on the CRF.

Children were excluded only from the PP-analyses from the moment the protocol violation had occurred in the situations listed below:

- interval between second blood sample and vaccination differed from the interval specified in the protocol (4-6 weeks after vaccination),
- interval between vaccination and observation of adverse events differed from the interval specified in the protocol (18-30 hours after vaccination),
- doubts about time of blood sampling or vaccination recorded on the CRF.

2.7 Statistical analysis

For the analyses, the participants were divided into groups based on their age (5-6 years or 10-11 years), and the study vaccine they received in the earlier study in 1995-'96 (low dose MenB, high dose MenB or HepB). Numbers and percentages of local and systemic adverse reactions were assessed for each observation. Chi square or Fisher's exact tests were used to compare both vaccine groups and both age groups with respect to local and systemic adverse reactions after vaccination. For the former HepB group, these analyses were also done for adverse events occurring after the second and the third vaccination (data not available yet).

All serological results of the present study and of the blood sample after the primary vaccination series with the hexavalent vaccine are described by individual line listings.

Because SBA titres $\geq 1:4$ were presumed to be associated with protection against clinical disease^{24,25,26}, percentages of participants with these titres were calculated. ELISA and SBA results were transformed to logarithmic values to calculate GMT's and 95% CI's.

Mann-Whitney U test was used to compare pre- and post revaccination titres between the MenB and the HepB group. To assess the dose effect of priming Mann-Whitney U test was used to compare both pre- and post revaccination SBA titres between the low and high dose groups. For the SBA assay, an immune response was defined as ≥ 4 -fold rise in antibody titre compared with the prevaccination titre. Percentages of immune responders were assessed and Chi square test or Fisher's exact test was used to compare these percentages between the low dose MenB group and the HepB group, between the high dose MenB group and the HepB group, and between both MenB groups.

3. Results

3.1 Study population

A total of 177 participants were enrolled in the study and an informed consent was obtained from all parents (Table 1). The study population can be divided in 5-6 years old (N=77) and 10-11 years old children (N=100). These children have been recruited from a total population of 357 children, 189 toddlers and 168 school children, who participated in a study with the hexavalent MenB vaccine in 1995-96. The population of the present study includes 87 female and 90 male participants (ratio: 0.97). The UTN's of the participants excluded for (part of) the analyses and the reasons of exclusions are shown in Table 2. One participant in the low dose MenB group (UTN=284) was lost to follow-up after the first observation following vaccination.

3.2 Adverse reactions

The numbers of evaluable participants for the adverse events analyses after the first vaccination are given in Table 3. None of the children had any adverse reaction within 15 minutes after vaccination. Moreover, no serious adverse events occurred during the week after vaccination. The frequencies of adverse events were compared between the former MenB groups and the former HepB group for 5-6 years old children as well as for 10-11 year olds (data not shown). In general, the frequencies were a little higher in the HepB group, especially for the 10-11 years old. For most adverse events however these differences were not statistically significant. Therefore, all data were pooled. Table 5A shows the numbers of systemic adverse reactions in 5-6 and 10-11 years old children monitored for seven days after vaccination. Results on the local adverse reactions are given in Table 5B. To visualise these data in a diagram, both age groups were pooled and the local adverse reactions were dichotomised (Figure 1 & 2). Most systemic adverse reactions were found during the second and third day after vaccination. Drowsiness, headache and less appetite were the most frequently reactions seen in that period (resp 8%, 7% and 6%). Absence from school during the first three days after vaccination was reported for 3% of the participants, especially the 10-11 years olds. Local reactions were much more common than systemic reactions. In most participants with local reactions, complaints lasted for three days. There were no signs of increasing intensity of symptoms during subsequent days in the week after vaccination. Mild pain was the most frequent adverse event (76% at day 1 and 44% at day 2-3). Redness, swelling and reduced use of the injected arm during day 1-3 occurred less frequent (resp 17-26%, 14-17%, and 3-15%). Itching was a rare local reaction (2-6%). The occurrence of adverse reactions in 5-6 year olds was compared with that in 10-11 year olds by Chi square test or Fisher's exact test. Overall, the two age groups were comparable. However, school absence at day 1, pain at day 2-3, and reduced use of the injected arm at day 4-7 occurred statistically significant more often in the older children (for all $p \leq 0.04$).

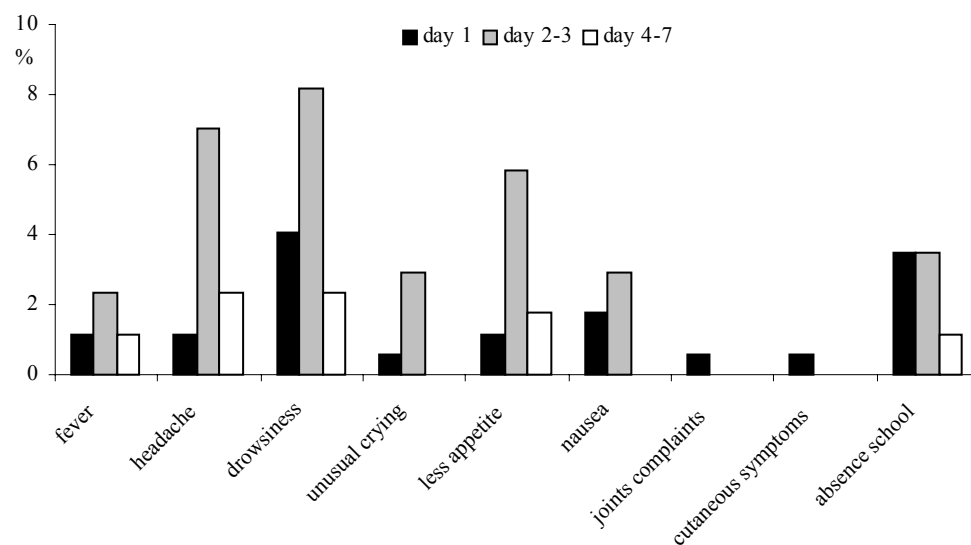


Figure 1. Systemic adverse reactions

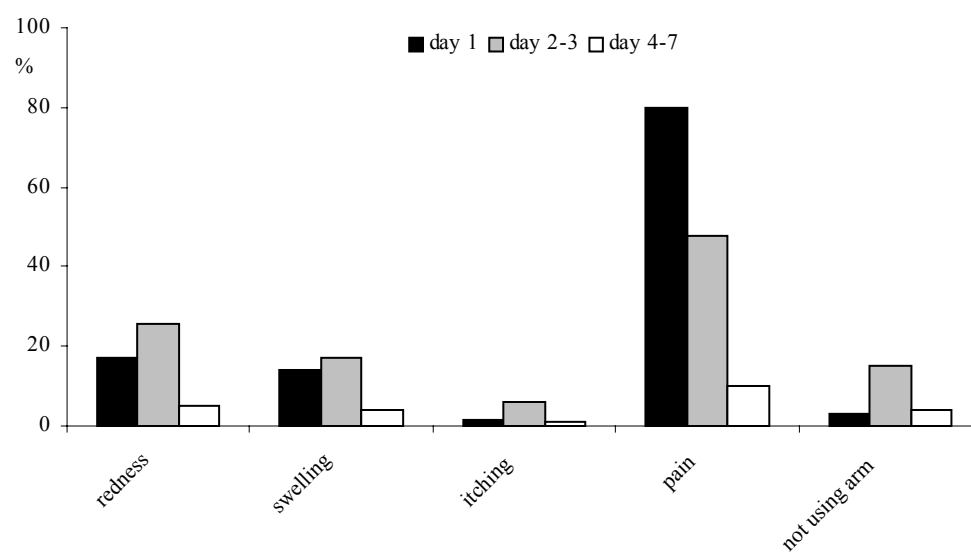


Figure 2. Local adverse reactions

3.3 Antibody response

Table 4 shows the numbers of evaluable participants for the serological analyses. The few discrepancies in the totals of serological tests can be explained by the missing of some blood samples, because of an unsuccessful venipuncture or because the children were lost to follow-up. Furthermore, for some participants the size of blood samples obtained was too small to permit completion of all serological tests.

The participants in this study received three hexavalent meningococcal vaccines or three hepatitis B vaccines in 1995-96. One month after this primary vaccination series, a blood sample was taken for specific antibody measurements. These serological results for SBA as well as ELISA were combined with the results of the current study and described by individual line listings (Appendix 3). In addition with the study in 1995-'96, now SBA against the PorA negative mutant strain (H1.5), 50% SBA titres against strain P1.7^h,4, and monovalent ELISA against P1.7^h,4 were performed.

3.3.1 SBA Assay

The SBA response against the PorA negative strain H1.5 was assessed as control for the PorA specificity. For two participants (UTN=241 and 406) a titre $\geq 1:32$ against H1.5 was measured before the revaccination. Neither of these two children showed an immune response against H1.5 (for UTN=241 the titre after revaccination was 1:32, while the post vaccination titre for UTN=406 was missing).

Percentages participants with reciprocal SBA titres $\geq 1:4$ before and after vaccination are shown in Table 6A and 6B. These data are visualised in Figure 3 and 4.

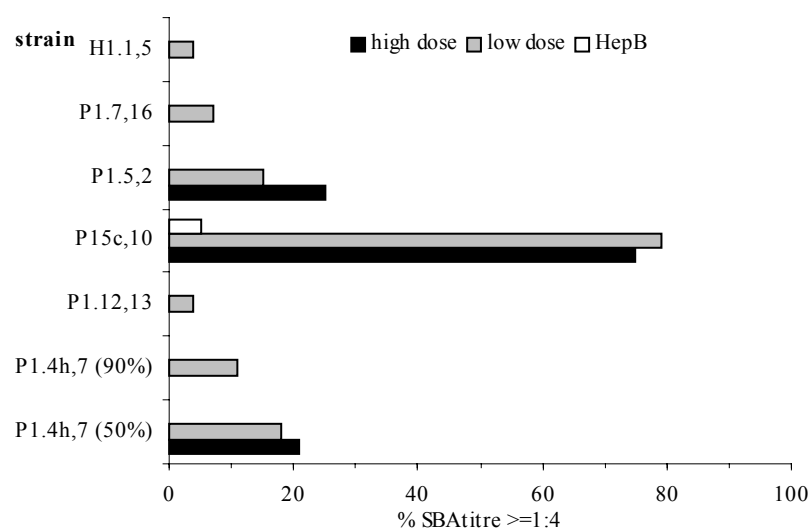
SBA GMT's and 95% CI's against the meningococcal strains were calculated per study group. These data from the blood sample after the primary series with the hexavalent vaccine are summarised in Table 7A and 7B, and those from the blood samples before and after the booster vaccination are shown in Table 8A and 8B. After the primary vaccination series, particularly in the young age group very high SBA titres were measured against the strains P1.5^c,10 and P1.5,2. Before vaccination with the monovalent MenB vaccine, all SBA titres were decreased enormously. Although the anti-P1.5^c,10 and P1.5,2 titres were still the highest measured just before the revaccination, the decrease in titre was most pronounced for these two strains. One month after the revaccination with MonoMen, a rise of the anti-P1.7^h,4 GMT was found in children primed with the hexavalent meningococcal vaccine in 1995-96. The titres after this booster were about two times higher as compared to the titres after the primary series with the hexavalent vaccine. After vaccination with MonoMen the SBA GMT's against the other strains present in the hexavalent vaccine also rose in children primed with this vaccine. The highest titres after vaccination were measured against P1.5^c,10.

However, after the MonoMen booster these titres were about 10 times smaller as compared to those after the primary serie, although this varied by serosubtype.

The post booster vaccination anti-P1.7^h,4 titres were significantly higher in both MenB groups compared to the HepB group, indicating that the primary vaccination series with the hexavalent MenB vaccine had indeed primed the children's immune system. Other statistically significant differences between the MenB groups and the HepB group in both pre- and post revaccination titres are marked with an asterisk in Table 8.

No statistically significant differences in SBA titres between the low and high dose groups were found before vaccination with MonoMen. After vaccination, the anti-P1.7^h,4 titres were higher in the high dose group as compared to the low dose. However, this difference was only statistically significant in the 5-6 years old children.

Pre vaccination



Post vaccination

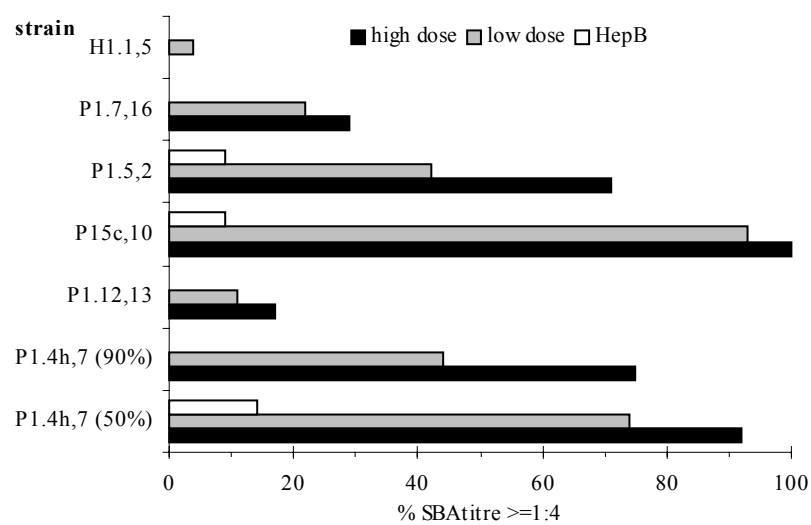
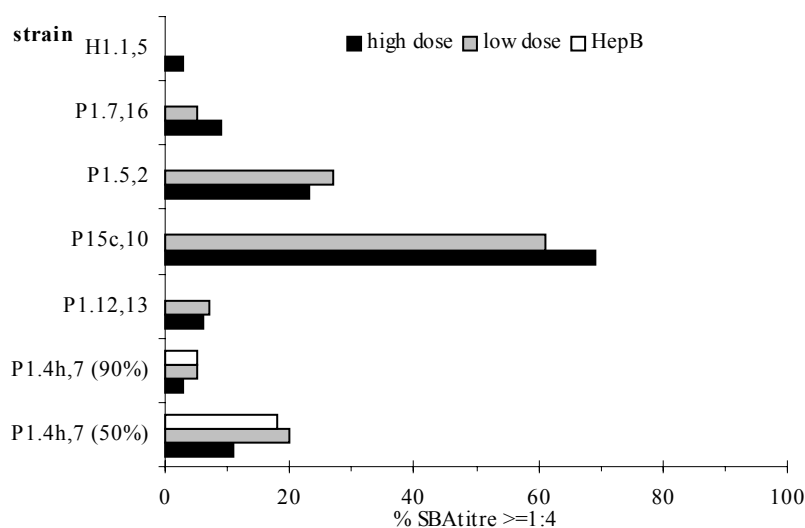


Figure 3. Percentages of 5-6 years old with SBA titre $\geq 1:4$

Pre vaccination



Post vaccination

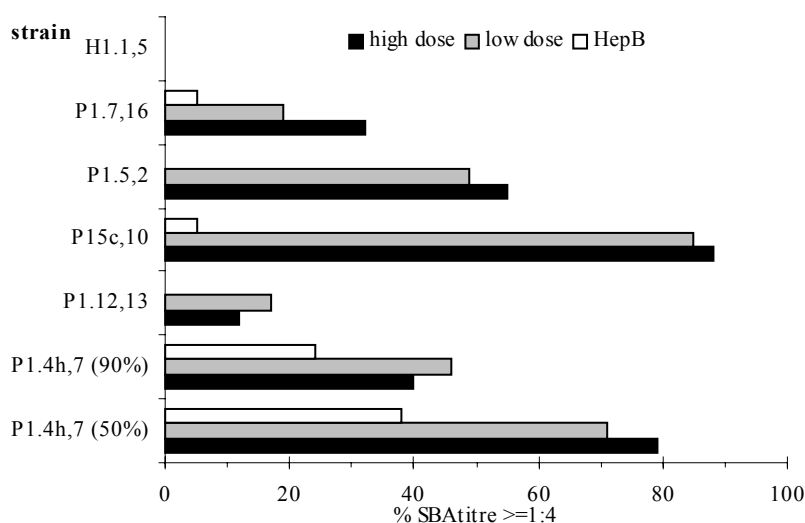
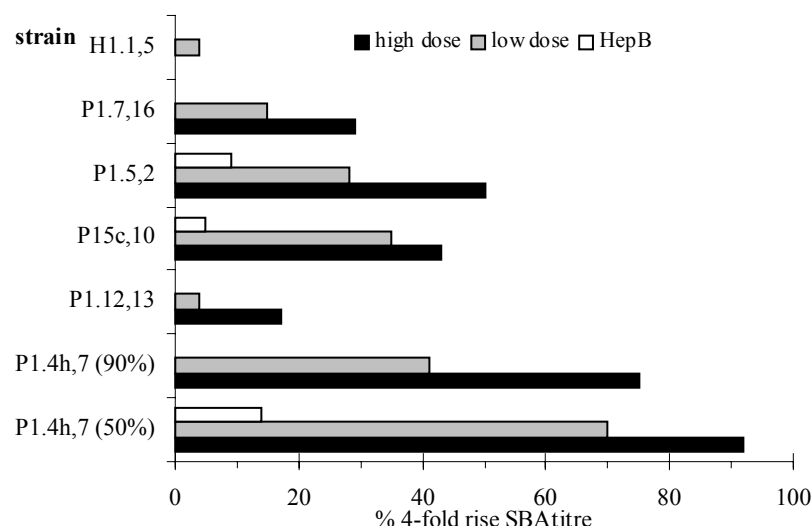


Figure 4. Percentages of 10-11 years old with SBA titre $\geq 1:4$

The percentages immune responders, i.e. children showing a fourfold rise in SBA titre, are shown in Table 9 and Figure 5. High percentages were found for the strains P1.7^h,4; upto 75% for the SBA assay with 90% killing and even over 90% for the SBA assay with 50% killing in the 5-6 year olds. These percentages were somewhat smaller in the 10-11 year olds, respectively 41% and 70%. Moreover, considerable percentages were also measured for the strains P1.5^c,10, P1.5,2 and P1.7,16. After pooling both age groups, statistically significant higher percentages immune responders were found in both MenB groups as compared to the HepB group for the strains P1.7^h,4 (both SBA assays with 90% and 50% killing), P1.5^c,10, P1.5,2 and P1.7,16. For P1.7^h,4 (SBA assay with 90% killing) the percentage immune responders was statistically significant higher in the high dose MenB group as compared to the low dose group. In the subpopulation of children showing a fourfold rise in SBA titre

after the primary series the percentages immune responders after the MonoMen booster were computed per strain (Table 10). About 80% of this subpopulation showed a 4-fold rise in SBA-titre against P1.7^h,4. For the other strains an immune response was seen for less then 40% of these children.

5-6 years old



10-11 years old

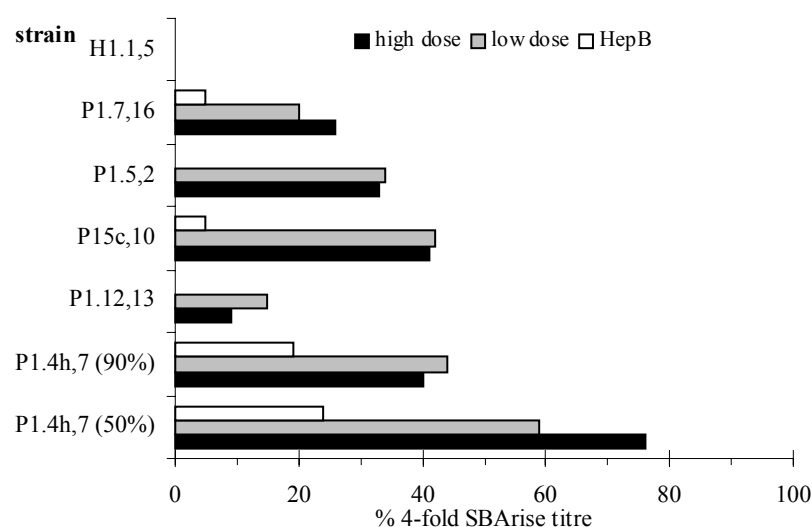


Figure 5. Percentages of participants with rise in SBA titre ≥ 4

3.3.2 ELISA

Table 11A and 11B show ELISA GMT's and 95% CI's before and after vaccination with MonoMen. Both pre and post vaccination anti-P1.7^h,4 ELISA titres were significantly higher in both MenB groups as compared to the HepB group. Higher post vaccination titres were observed in the high dose MenB group as compared to the low dose, but this was not statistically significant. Besides, no statistically significant differences in ELISA titres were found comparing both age groups, although the titres in the 5-6 year old children were in general higher.

4. Discussion

4.1 Adverse reactions

This study showed that a booster vaccination with MonoMen was well tolerated. No serious adverse events occurred during the study. Observed frequencies of adverse reactions for children primarily vaccinated with low or high dose MenB or with HepB were comparable. In general, no relevant differences were found between the two age groups. Most systemic adverse reactions occurred during day 2-3, with the 'highest' percentages for drowsiness, headache, and less appetite (resp 8%, 7% and 6%). Fever, one of the most common systemic reactions after vaccination in children, was only reported for 1-3% of the children. Local reactions, which generally lasted for three days, were much more common than systemic reactions. Pain, the most frequently reported adverse reaction, occurred in 80% of the children at day 1 and in 48% at day 2-3. However, it must be emphasised that this concerned only mild pain. Five children used analgesics because of probably vaccine-related symptoms like a painful arm, headache, nausea, fever, drowsiness and/or loss of appetite. A virus infection or a cold was reported for three other children, two of which used analgesics and the other used eardrops. Adverse reactions reported by these children (fever, headache, drowsiness, loss of appetite and/or school absence) might be caused by an infection instead of the vaccination. In Rotterdam MonoMen was also tested in 2-3 years old children vaccinated according to a 2+1- or 3+1-schedule²⁷. The vaccine was also well tolerated there, even though the frequencies of some systemic adverse reactions were somewhat higher as compared to the current study. Frequently reported reactions in that study²⁷ were drowsiness (upto 15%) and less appetite (upto 8%). On the other hand, local reactions were more common in the current study. In the study with MonoMen in toddlers²⁷, mild pain was the most common local reaction (50% compared to 80% in this study). Previously, the hexavalent RIVM vesicle vaccine was shown to be safe in studies in Rotterdam and Gloucestershire UK^{14,15,36}; the rate and severity of the observed adverse reactions were acceptable and no serious adverse events occurred.

4.2 Antibody response

4.2.1 Response to booster vaccination

Antibodies detected in the SBA assay show class 1 OMP (bactericidal) specificity that is assumed to correlate with specific protective immunity. The SBA response in this study was assessed against the six meningococcal B subtypes of the old hexavalent vaccine used for priming of the participants, and against the PorA negative mutant strain H1.5. None of the children responded with a SBA titre rise ≥ 4 against H1.5, demonstrating the PorA specificity of the antibody response after vaccination.

In the 2.5 years after the primary series all SBA titres had declined. Less than 6% of the children had titres $\geq 1:4$ against P1.7^h,4 (SBA assay with 90% killing), P1.12,13, P1.7,16 and P1.19,15. However, about 70% of the children still had SBA titres $\geq 1:4$ against P1.5^c,10 and 20% against P1.5,2. SBA titres of 1:4 or more are suggested to be associated with protection against clinical disease^{24,25,26}.

After vaccination with MonoMen a rise of the GMT of bactericidal antibodies against P1.7^h,4 was found for both MenB groups, though the percentage of risers was highest for the participants primed with the high dose. For the HepB group only a moderate rise of the anti-P1.7^h,4 GMT was observed. An immune response (i.e. at least 4-fold rise in SBA titre) against P1.7^h,4 with 90% killing was observed for 41-75% of the children, for SBA with 50%

killing these percentages were 59-92%. About 80% of the children showing an immune response against P1.7^h,4 after the primary series with the hexavalent vaccine also showed an immune response after the booster vaccination. This indicates the presence of an immunologic memory for children primed with the hexavalent MenB vaccine, which is most pronounced for the high dose vaccine.

In many studies with meningococcal vaccines^{14,29,32}, 50% killing was used as cut-off point for the SBA assay. In this study the serum bactericidal titre against P1.7^h,4 was assessed for 50% as well as 90% killing. Of course higher titres were measured for the 50% killing assay. For the comparability of studies, it seems important to make an international decision with respect to the most useful cut-off criterion.

Highest GMT's against P1.7^h,4 were measured for the younger age group. In children primed with the high dose hexavalent MenB vaccine the difference between both age groups was even statistically significant ($p < 0.05$). Obviously, the same age dependent effect was observed with respect to the percentages immune responders. This is consistent with the findings of earlier studies with the hexavalent MenB vaccine in Gloucestershire and Rotterdam^{14,15} (lower GMT's were found in the higher age groups). Also in a trial in Chile²⁸ comparing the Norwegian against the Cuban monovalent meningococcal B OMP vaccine (resp. strain B:15:P1.7,16:L3,7 and CU385/83 B:4:P1.15) higher response rates were found for the youngest children. In contrast, one study with the Cuban vaccine in Brazil²⁹ showed lower titres in the youngest age groups.

Immunogenicity was also assessed by measurements of antibodies directed against P1.7^h,4 in an ELISA. Overall, the results with respect to SBA and ELISA were comparable but no correlation between the results of these assays was found.

4.2.2 Cross-reactivity

Remarkable rises of GMT's against the others strains present in the hexavalent MenB vaccine were observed after vaccination with MonoMen. These rises were only moderate for P1.7,16 and P1.12,13. However, 40% of the participants showed a 4-fold titre rise against P1.5^c,10 and 36% against P1.5,2, as compared to 41-92% against P1.7^h,4. In earlier studies in Gloucestershire and Rotterdam^{14,15} P1.5^c,10 and P1.5,2 were found to be the most immunogenic components following vaccination with the hexavalent MenB vesicle vaccine. Taking into account only the percentages of children showing a 4-fold rise against P1.5,2 and P1.5^c,10 might give an overestimation of the booster effect of MonoMen against these strains. The GMT's against P1.5^c,10 and P1.5,2 after the booster were much lower as compared to those measured after the primary series with the hexavalent vaccine. Whereas the GMT's of bactericidal antibodies against P1.7^h,4 after the booster were higher as compared to those after the primary series. This indicates that the immune responses against P1.5^c,10 and P1.5,2 after the booster vaccination with MonoMen are possibly caused by cross-reacting antibodies. These antibodies might be directed against determinants that are situated partly inside and partly outside the PorA variable regions. Another explanation might be that memory cells are triggered to produce antibodies against these other subtypes. Martin et al.³⁰ studied the effect of PorA serosubtype variation of SBA target strains on the immune response in sera of children immunised with the hexavalent vaccine. The SBA response was found to be largely dependent on the homology with the inducing PorA. A lower SBA was found in these sera to isogenic strains with even modest sequence variations³⁰. Rouppe van der Voort et al.¹³ investigated the epitope specificity and cross-reactivity of the induced PorA-specific bactericidal antibodies by use of isogenic strains with loop deletions or point mutations in their PorA. After vaccination with the hexavalent vaccine some of the participants were found to develop PorA-specific bactericidal antibodies that did not depend

on either loops 1 and/or 4 of PorA. It was concluded that this might point to common but still unknown epitopes.

A survey in Norway³¹ including a cross-reactivity study indicates that rather dissimilar meningococcal strains have antigens in common which are functional in SBA assay. The Norwegian meningococcal vaccine made from a B:15:P1.7,16:L3,7 strain unexpectedly induced bactericidal antibodies against an A:4/21:P1.9:L.10 strain. Since the Norwegian vaccine in contrast with the RIVM vaccine, contains many antigens (including LPS) and there is extensive heterogeneity in the human response, it seems likely that bactericidal antibodies may be induced by several antigens^{32,33}. Perkins et al.²⁶ studied the SBA response against heterologous *N. meningitidis* strains after vaccination with the Norwegian or Cuban vaccine. Some cross-reactivity against the heterologous strains was found, though the proportion of SBA responders against the homologous strains was higher. A study in Chile²⁸ also demonstrated SBA cross-reactivity between the respective heterologous vaccine strains in recipients of the Norwegian and Cuban vaccine. However, it is important to stress differences in the production methods of the RIVM, Norwegian, and Cuban MenB vaccines. Both Norwegian and Cuban vaccines are based on one single *N. meningitidis* strain representative of the epidemics^{34,17}. The RIVM vaccine was also derived from a patient isolate, but it has been further genetically engineered³⁵. This leads to differences in the composition of these three vaccines, with respect to the types and doses of the meningococcal antigens: the Norwegian and Cuban vaccine contain many antigens whereas the RIVM vaccine contains only specific antigens (PorA).

5. Conclusions and recommendations

The frequency and nature of the adverse reactions after vaccination with MonoMen are acceptable. No serious adverse events occurred during the study.

The booster vaccination with MonoMen led to an adequate SBA response against the subtype P1.7^h,4 in children primed with the hexavalent MenB vaccine. An immune response (i.e. rise in SBA titre ≥ 4) was seen for 70-90% of the participants for the SBA assay with 50% killing and for 40-75% for the SBA assay with 90% killing.

Study results with respect to SBA assay with 90% killing showed that the RIVM hexavalent meningococcal OMV vaccine had induced the development of an immunological memory in at least 80% of the children.

Although a monovalent vaccine was administered as a booster dose, immune responses were measured against the five other strains present in the hexavalent vaccine used in the primary series. Cross-reacting antibodies to PorA probably cause these responses.

For the comparability of different studies, it seems preferable to make an international decision with respect to the cut-off point for the SBA assay (50% or 90% killing).

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Declaration of quality control

Undersigned states herewith that the research presented in this report has been carried out according to the OECD principles of Good Clinical Practice (GCP) and that this report reflects a complete, correct and reliable overview of the results obtained.

GCP inspections of the experiments and reports submitted to the management research team leader took place on:

| | |
|-----------------|------------------------|
| Inspection Date | Type of Inspection |
| 16-03-99 | Study Initiation Visit |

This report was inspected on 17 October 2000
Inspection of report no. V/000012.002

Quality control officer:

name : M.C. Jongerius
laboratory : Laboratory for Clinical Vaccine Research

Appendix 1 Mailing list

| | |
|--------|---|
| 1 | Hoofdinspecteur Preventieve en Curatieve Gezondheidszorg |
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| 4 | Gezondheidsraad, Den Haag voorzitter |
| 5 | Gezondheidsraad, Den Haag secretaris werkgroep RVP |
| 6 | Medisch Ethische Commissie AZR/EUR, Rotterdam |
| 7-9 | Prof. Dr R. de Groot |
| 10-17 | GGD Rotterdam en omstreken |
| 18-21 | Stichting Thuiszorg Rotterdam |
| 22 | Nationaal Referentie Laboratorium Bacteriële Meningitis AMC/RIVM, Amsterdam |
| 23 | Depot Nederlandse Publikaties en Nederlandse Bibliografie |
| 24 | Directie RIVM |
| 25 | Directeur sector Vaccins |
| 26 | Directeur sector Volksgezondheidsonderzoek |
| 27-29 | Hoofd LVO |
| 30-31 | Hoofd LCB |
| 32-33 | Hoofd LPO |
| 34-35 | Hoofd LVR |
| 36-37 | Hoofd KRZ |
| 38 | Hoofd CIE |
| 39 | Hoofd LIS |
| 40 | Hoofd LIO |
| 41 | Prof. Juhani Eskola, Nat. Inst. Public Health, Helsinki Finland |
| 42 | Prof. Keith Cartwright, Public Health Laboratory Gloucester, UK |
| 43 | Dr. Ray Borrow, Public Health Laboratory, Manchester, UK |
| 44 | Dr. David Salisbury, Dept. of Health, London, UK |
| 45 | Dr M.A.E Conyn-van Spaendonck |
| 46 | H.E. de Melker |
| 47-58 | Leden IGZ infectieziektenoverleg |
| 59-73 | Auteurs |
| 74 | SBD/Voorlichting en Public Relations |
| 75 | Bureau Rapportenregistratie |
| 76 | Bibliotheek RIVM |
| 77-91 | Bureau Rapportenbeheer |
| 92-125 | Reserve |

Appendix 2 Tables

Table 1. Number of recruited participants

| | 5-6 years | 10-11 years | Total |
|------------------|-----------|-------------|-----------|
| 'low dose' MenB | 29 | 43 | 72 |
| 'high dose' MenB | 24 | 35 | 59 |
| HepB | 24 | 22 | 46 |
| Total | 77 | 100 | 177 |
| sexe | F=35 M=42 | F=52 M=48 | F=87 M=90 |

Table 2. Exclusion of participants for protocol violations

Exclusion Protocol analyses

| Reason exclusion | UTN's | Excluded for: |
|--|---------------------------|------------------------------|
| vaccine lot not filled out on CRF | 261 266 609 615 617 | all analyses |
| time blood sampling/vaccination on CRF not clear | 259 182 578 625 | all analyses |
| non PorA specific bactericidal activity | 241 406 | all serological analyses |
| observation day1 <18hours after vaccination | 241 571 612 | adverse events analyses day1 |

Exclusion Intention-to-treat analyses

| Reason exclusion | UTN's | Excluded for: |
|-----------------------------------|---------------------------|---------------|
| vaccine lot not filled out on CRF | 261 266 609 615 617 | all analyses |

Table 3. Number of evaluable participants for adverse reactions vaccination 1

| | 5-6 years | 10-11 years | Total |
|-------------------------|-----------|-------------|-----------|
| 'low dose' MenB | | | |
| day 1 | 28 | 41 | 69 |
| day 2-3 | 27 | 41 | 68 |
| day 4-7 | 27 | 41 | 68 |
| 'high dose' MenB | | | |
| day 1 | 24 | 35 | 59 |
| day 2-3 | 24 | 35 | 59 |
| day 4-7 | 24 | 35 | 59 |
| HepB | | | |
| Day 1 | 23 | 21 | 44 |
| Day 2-3 | 23 | 21 | 44 |
| Day 4-7 | 23 | 21 | 44 |
| Total | | | |
| Day 1 | 75 | 97 | 172 |
| Day 2-3 | 74 | 97 | 171 |
| Day 4-7 | 74 | 97 | 171 |
| Sexe | F=40 M=35 | F=47 M=50 | F=87 M=85 |

Table 4. Number of evaluable participants for serological analyses

| | 5-6 years | | 10-11 years | | Total | |
|----------------------------|-------------|--------------|-------------|--------------|-------------|--------------|
| | pre vacc | post vacc | pre vacc | post vacc | pre vacc | post vacc |
| 'low dose' MenB | | | | | | |
| P1.7 ^h ,4 (90%) | 28 | 27 | 41 | 41 | 69 | 68 |
| P1.7 ^h ,4 (50%) | 28 | 27 | 41 | 41 | 69 | 68 |
| P1.12,13 | 28 | 27 | 41 | 41 | 69 | 68 |
| P1.5 ^c ,10 | 27 | 27 | 41 | 41 | 68 | 68 |
| P1.5,2 | 27 | 27 | 41 | 41 | 68 | 68 |
| P1.7,16 | 27 | 27 | 41 | 41 | 68 | 68 |
| P1.19,15 | 28 | 27 | 41 | 41 | 69 | 68 |
| H1.5 | 28 | 27 | 41 | 41 | 69 | 68 |
| 'high dose' MenB | | | | | | |
| P1.7 ^h ,4 (90%) | 24 | 24 | 35 | 34 | 59 | 58 |
| P1.7 ^h ,4 (50%) | 24 | 24 | 35 | 34 | 59 | 58 |
| P1.12,13 | 24 | 24 | 35 | 34 | 59 | 58 |
| P1.5 ^c ,10 | 24 | 23 | 35 | 34 | 59 | 57 |
| P1.5,2 | 24 | 24 | 35 | 34 | 59 | 58 |
| P1.7,16 | 24 | 24 | 35 | 34 | 59 | 58 |
| P1.19,15 | 24 | 24 | 35 | 34 | 59 | 58 |
| H1.5 | 24 | 23 | 35 | 34 | 59 | 57 |
| HepB | | | | | | |
| P1.7 ^h ,4 (90%) | 22 | 23 | 21 | 21 | 43 | 44 |
| P1.7 ^h ,4 (50%) | 22 | 22 | 21 | 21 | 43 | 43 |
| P1.12,13 | 22 | 23 | 21 | 21 | 43 | 44 |
| P1.5 ^c ,10 | 22 | 23 | 21 | 21 | 43 | 44 |
| P1.5,2 | 22 | 23 | 21 | 21 | 43 | 44 |
| P1.7,16 | 22 | 23 | 21 | 21 | 43 | 44 |
| P1.19,15 | 22 | 23 | 21 | 21 | 43 | 44 |
| H1.5 | 22 | 23 | 21 | 21 | 43 | 44 |
| Total | | | | | | |
| P1.7 ^h ,4 (90%) | 74 | 74 | 97 | 96 | 171 | 170 |
| P1.7 ^h ,4 (50%) | 74 | 73 | 97 | 96 | 171 | 169 |
| P1.12,13 | 74 | 74 | 97 | 96 | 171 | 170 |
| P1.5 ^c ,10 | 73 | 73 | 97 | 96 | 170 | 169 |
| P1.5,2 | 73 | 74 | 97 | 96 | 170 | 170 |
| P1.7,16 | 73 | 74 | 97 | 96 | 170 | 170 |
| P1.19,15 | 74 | 74 | 97 | 96 | 171 | 170 |
| H1.5 | 74 | 73 | 97 | 96 | 171 | 169 |

Table 5A. Frequencies of systemic adverse reactions

| | day 1 | | | | day 2-3 | | | | day 4-7 | | | |
|--------------------------|----------------|-----|------------------|-----|----------------|-----|------------------|------|----------------|-----|------------------|-----|
| | 5-6 yr N=75 | | 10-11 yr N=97 | | 5-6 yr N=74 | | 10-11 yr N=97 | | 5-6 yr N=74 | | 10-11 yr N=97 | |
| Events | n | % | n | % | n | % | n | % | n | % | n | % |
| fever | 1 | 1.3 | 1 | 1.0 | 2 | 2.7 | 2 | 2.1 | 1 | 1.4 | 1 | 1.0 |
| headache | 1 | 1.3 | 1 | 1.0 | 4 | 5.4 | 8 | 8.2 | 1 | 1.4 | 3 | 3.1 |
| drowsiness | 1 | 1.3 | 6 | 6.2 | 3 | 4.1 | 11 | 11.3 | 1 | 1.4 | 3 | 3.1 |
| unusual crying | 0 | | 1 | 1.0 | 2 | 2.7 | 3 | 3.1 | 0 | | 0 | |
| less appetite | 0 | | 2 | 2.1 | 3 | 4.1 | 7 | 7.2 | 2 | 2.7 | 1 | 1.0 |
| nausea | 1 | 1.3 | 2 | 2.1 | 2 | 2.7 | 3 | 3.1 | 0 | | 0 | |
| joints complaints | 0 | | 1 | 1.0 | 0 | | 0 | | 0 | | 0 | |
| cutaneous symptoms | 0 | | 1 | 1.0 | 0 | | 0 | | 0 | | 0 | |
| absence school | 0 | | 6 | 6.2 | 2 | 2.7 | 4 | 4.1 | 1 | 1.4 | 1 | 1.0 |
| medication | 0 | | 1 | 1.0 | 1 | 1.4 | 6 | 6.2 | 1 | 1.4 | 1 | 1.0 |
| visit doctor or hospital | 0 | | 0 | | 1 | 1.4 | 0 | | 0 | | 0 | |
| illness in family | 0 | | 1 | 1.0 | 0 | | 3 | 3.1 | 1 | 1.4 | 0 | |
| other | 0 | | 0 | | 2 | 2.7 | 1 | 1.0 | 0 | | 0 | |

Table 5B. Frequencies of local adverse reactions

| | day 1 | | | | day 2-3 | | | | day 4-7 | | | |
|---------------|----------------|------|------------------|------|----------------|------|------------------|------|----------------|-----|------------------|------|
| | 5-6 yr N=75 | | 10-11 yr N=97 | | 5-6 yr N=74 | | 10-11 yr N=97 | | 5-6 yr N=74 | | 10-11 yr N=97 | |
| Events | n | % | n | % | n | % | n | % | n | % | n | % |
| redness | | | | | | | | | | | | |
| <2.5cm | 12 | 16.0 | 15 | 15.5 | 13 | 17.6 | 17 | 17.5 | 1 | 1.4 | 4 | 4.1 |
| 2.5-5cm | 1 | 1.3 | 1 | 1.0 | 3 | 4.1 | 4 | 4.1 | 0 | | 3 | 3.1 |
| >5cm | 0 | | 0 | | 0 | | 7 | 7.2 | 0 | | 1 | 1.0 |
| swelling | | | | | | | | | | | | |
| <2.5cm | 7 | 9.3 | 15 | 15.5 | 6 | 8.1 | 8 | 8.2 | 1 | 1.4 | 3 | 3.1 |
| 2.5-5cm | 1 | 1.3 | 1 | 1.0 | 4 | 5.4 | 6 | 6.2 | 1 | 1.4 | 1 | 1.0 |
| >5cm | 0 | | 0 | | 0 | | 5 | 5.2 | 0 | | 1 | 1.0 |
| itching | | | | | | | | | | | | |
| mild | 1 | 1.3 | 2 | 2.1 | 3 | 4.1 | 7 | 7.2 | 0 | | 2 | 2.1 |
| serious | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | |
| very serious | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | |
| pain | | | | | | | | | | | | |
| mild | 54 | 72.0 | 76 | 78.4 | 26 | 34.7 | 50 | 51.5 | 4 | 5.4 | 12 | 12.4 |
| serious | 2 | 2.7 | 5 | 5.2 | 0 | | 6 | 6.2 | 0 | | 1 | 1.0 |
| very serious | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | |
| not using arm | | | | | | | | | | | | |
| mild | 2 | 2.7 | 2 | 2.1 | 7 | 9.5 | 18 | 18.6 | 0 | | 7 | 7.2 |
| serious | 0 | | 1 | 1.0 | 0 | | 1 | 1.0 | 0 | | 0 | |
| very serious | 0 | | 0 | | 0 | | 0 | | 0 | | 0 | |

Table 6A. Serum Bactericidal Antibody titre $\geq 1:4$ in 5-6 years old before and after vaccination with MonoMen

'low dose' MenB

| strain | Pre vaccination | | | Post vaccination | | |
|----------------------------|-----------------|----|----|------------------|----|----|
| | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 3 | 28 | 11 | 12 | 27 | 44 |
| P1.7 ^h ,4 (50%) | 5 | 28 | 18 | 20 | 27 | 72 |
| P1.12,13 | 1 | 28 | 4 | 3 | 27 | 11 |
| P1.5 ^c ,10 | 21 | 27 | 78 | 25 | 27 | 93 |
| P1.5,2 | 4 | 27 | 15 | 12 | 27 | 44 |
| P1.7,16 | 2 | 27 | 7 | 6 | 27 | 22 |
| P1.19,15 | 2 | 28 | 7 | 4 | 27 | 15 |
| H1.5 | 1 | 28 | 4 | 1 | 27 | 4 |

'high dose' MenB

| strain | Pre vaccination | | | Post vaccination | | |
|----------------------------|-----------------|----|----|------------------|----|-----|
| | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 0 | 24 | 0 | 18 | 24 | 75 |
| P1.7 ^h ,4 (50%) | 5 | 24 | 21 | 22 | 24 | 92 |
| P1.12,13 | 0 | 24 | 0 | 4 | 24 | 17 |
| P1.5 ^c ,10 | 18 | 24 | 75 | 23 | 23 | 100 |
| P1.5,2 | 6 | 24 | 25 | 17 | 24 | 71 |
| P1.7,16 | 0 | 24 | 0 | 7 | 24 | 29 |
| P1.19,15 | 0 | 24 | 0 | 1 | 24 | 4 |
| H1.5 | 0 | 24 | 0 | 0 | 23 | 0 |

HepB

| strain | Pre vaccination | | | Post vaccination | | |
|----------------------------|-----------------|----|---|------------------|----|----|
| | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 0 | 22 | 0 | 0 | 23 | 0 |
| P1.7 ^h ,4 (50%) | 0 | 22 | 0 | 3 | 22 | 14 |
| P1.12,13 | 0 | 22 | 0 | 0 | 23 | 0 |
| P1.5 ^c ,10 | 1 | 22 | 5 | 2 | 23 | 9 |
| P1.5,2 | 0 | 22 | 0 | 2 | 23 | 9 |
| P1.7,16 | 0 | 22 | 0 | 0 | 23 | 0 |
| P1.19,15 | 0 | 22 | 0 | 0 | 23 | 0 |
| H1.5 | 0 | 22 | 0 | 0 | 23 | 0 |

Table 6B. Serum Bactericidal Antibody titre $\geq 1:4$ in 10-11 years old before and after vaccination with MonoMen

'low dose' MenB

| strain | Pre vaccination | | | Post vaccination | | |
|----------------------------|-----------------|----|----|------------------|----|----|
| | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 3 | 41 | 7 | 19 | 41 | 46 |
| P1.7 ^h ,4 (50%) | 8 | 41 | 20 | 29 | 41 | 71 |
| P1.12,13 | 3 | 41 | 7 | 7 | 41 | 17 |
| P1.5 ^c ,10 | 26 | 41 | 63 | 35 | 41 | 85 |
| P1.5,2 | 12 | 41 | 29 | 20 | 41 | 49 |
| P1.7,16 | 2 | 41 | 5 | 8 | 41 | 19 |
| P1.19,15 | 3 | 41 | 7 | 9 | 41 | 22 |
| H1.5 | 0 | 41 | 0 | 0 | 41 | 0 |

'high dose' MenB

| strain | Pre vaccination | | | Post vaccination | | |
|----------------------------|-----------------|----|----|------------------|----|----|
| | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 1 | 35 | 3 | 14 | 34 | 41 |
| P1.7 ^h ,4 (50%) | 4 | 35 | 11 | 27 | 34 | 79 |
| P1.12,13 | 2 | 35 | 6 | 4 | 34 | 12 |
| P1.5 ^c ,10 | 26 | 35 | 74 | 30 | 34 | 88 |
| P1.5,2 | 8 | 35 | 23 | 17 | 34 | 50 |
| P1.7,16 | 3 | 35 | 9 | 11 | 34 | 32 |
| P1.19,15 | 3 | 35 | 9 | 9 | 34 | 26 |
| H1.5 | 1 | 35 | 3 | 0 | 33 | 0 |

HepB

| strain | Pre vaccination | | | Post vaccination | | |
|----------------------------|-----------------|----|----|------------------|----|----|
| | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 1 | 21 | 5 | 4 | 21 | 19 |
| P1.7 ^h ,4 (50%) | 4 | 21 | 19 | 8 | 21 | 38 |
| P1.12,13 | 0 | 21 | 0 | 0 | 21 | 0 |
| P1.5 ^c ,10 | 0 | 21 | 0 | 1 | 21 | 5 |
| P1.5,2 | 0 | 21 | 0 | 0 | 21 | 0 |
| P1.7,16 | 0 | 21 | 0 | 1 | 21 | 5 |
| P1.19,15 | 0 | 21 | 0 | 1 | 21 | 5 |
| H1.5 | 0 | 21 | 0 | 0 | 21 | 0 |

Table 7A. SBA GMT's in 5-6 years old after primary vaccination series

| Strain | 'low dose' MenB | | | 'high dose' MenB | | | HepB | | |
|----------------------------|-----------------|-------|-----------------|------------------|-------|-----------------|------|-----|-------------|
| | N | GMT | [95%CI] | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 | 28 | 2.7 | [1.6 - 4.7] | 24 | 4.1 | [2.2 - 7.9] | 23 | 1.0 | - - |
| P1.12,13 | 28 | 8.6 | [4.8 - 15.4] | 24 | 8.8 | [4.7 - 16.3] | 23 | 1.0 | - - |
| P1.5^c,10 | 28 | 221.3 | [186.1 - 261.4] | 24 | 249.0 | [233.9 - 263.2] | 23 | 1.3 | [0.8 - 2.1] |
| P1.5,2 | 28 | 39.1 | [22.6 - 67.2] | 24 | 70.0 | [38.6 - 126.2] | 23 | 1.0 | - - |
| P1.7,16 | 28 | 2.8 | [1.6 - 4.8] | 24 | 6.9 | [3.3 - 14.7] | 23 | 1.0 | - - |
| P1.19,15 | 28 | 2.0 | [1.3 - 2.9] | 24 | 2.3 | [1.4 - 3.7] | 23 | 1.0 | - - |

Table 7B. SBA GMT's in 10-11 years old after primary vaccination series

| Strain | 'low dose' MenB | | | 'high dose' MenB | | | HepB | | |
|----------------------------|-----------------|-------|----------------|------------------|-------|-----------------|------|-----|-------------|
| | N | GMT | [95%CI] | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 | 38 | 2.5 | [1.5 - 3.9] | 35 | 1.5 | [1.0 - 2.1] | 22 | 1.1 | [0.9 - 1.3] |
| P1.12,13 | 38 | 4.5 | [2.6 - 7.9] | 35 | 3.8 | [2.4 - 6.2] | 22 | 1.0 | - - |
| P1.5^c,10 | 38 | 114.6 | [79.3 - 165.4] | 35 | 153.3 | [111.4 - 210.8] | 22 | 1.3 | [0.8 - 1.9] |
| P1.5,2 | 38 | 19.2 | [11.2 - 33.1] | 35 | 32.0 | [20.4 - 50.2] | 22 | 1.0 | [1.0 - 1.1] |
| P1.7,16 | 38 | 3.1 | [1.9 - 4.8] | 35 | 3.3 | [2.0 - 5.8] | 22 | 1.0 | - - |
| P1.19,15 | 38 | 1.9 | [1.2 - 2.9] | 35 | 2.0 | [1.3 - 3.1] | 22 | 1.0 | - - |

Table 8A. SBA GMT's in 5-6 years old before and after vaccination MonoMen

| 'low dose' MenB | | | | | | |
|---------------------------------|----------|------------|----------------|-------------------------|------------|----------------|
| Pre vaccination | | | | Post vaccination | | |
| Strain | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 (90%) | 28 | 1.3 | [0.9 - 1.9] | 27 | *3.3 | [1.8 - 5.9] |
| P1.7^h,4 (50%) | 28 | 1.7 | [1.1 - 2.6] | 27 | *9.9 | [5.2 - 18.5] |
| P1.12,13 | 28 | 1.2 | [0.9 - 1.7] | 27 | 1.4 | [0.9 - 2.1] |
| P1.5^c,10 | 27 | *7.4 | [4.2 - 13.0] | 27 | *16.5 | [9.9 - 27.1] |
| P1.5,2 | 27 | 1.7 | [1.0 - 2.8] | 27 | *3.5 | [2.0 - 6.2] |
| P1.7,16 | 27 | 1.4 | [0.9 - 2.2] | 27 | *1.7 | [1.1 - 2.5] |
| P1.19,15 | 28 | 1.3 | [0.9 - 2.0] | 27 | 1.6 | [1.0 - 2.5] |
| H1.5 | 28 | 1.2 | [0.9 - 1.6] | 27 | 1.1 | [0.9 - 1.5] |

| 'high dose' MenB | | | | | | |
|---------------------------------|----------|------------|----------------|-------------------------|------------|----------------|
| Pre vaccination | | | | Post vaccination | | |
| Strain | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 (90%) | 24 | 1.0 | [1.0 - 1.1] | 24 | *10.1 | [4.9 - 20.7] |
| P1.7^h,4 (50%) | 24 | *1.6 | [1.2 - 2.1] | 24 | *30.3 | [15.1 - 60.1] |
| P1.12,13 | 24 | 1.0 | [- -] | 24 | *1.4 | [1.1 - 1.9] |
| P1.5^c,10 | 24 | *9.5 | [5.0 - 18.1] | 23 | *26.0 | [16.1 - 41.6] |
| P1.5,2 | 24 | *2.0 | [1.2 - 3.3] | 24 | *5.0 | [3.0 - 8.6] |
| P1.7,16 | 24 | 1.0 | [- -] | 24 | *1.8 | [1.2 - 2.6] |
| P1.19,15 | 24 | 1.0 | [- -] | 24 | 1.1 | [1.0 - 1.2] |
| H1.5 | 24 | 1.0 | [- -] | 23 | 1.0 | [- -] |

| HepB | | | | | | |
|---------------------------------|----------|------------|----------------|-------------------------|------------|----------------|
| Pre vaccination | | | | Post vaccination | | |
| Strain | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 (90%) | 22 | 1.0 | [- -] | 23 | 1.0 | [1.0 - 1.1] |
| P1.7^h,4 (50%) | 22 | 1.1 | [1.0 - 1.2] | 22 | 1.5 | [1.1 - 2.1] |
| P1.12,13 | 22 | 1.0 | [- -] | 23 | 1.0 | [1.0 - 1.0] |
| P1.5^c,10 | 22 | 1.3 | [0.8 - 2.3] | 23 | 1.6 | [0.8 - 3.2] |
| P1.5,2 | 22 | 1.0 | [1.0 - 1.1] | 23 | 1.3 | [0.9 - 2.0] |
| P1.7,16 | 22 | 1.0 | [1.0 - 1.0] | 23 | 1.0 | [1.0 - 1.0] |
| P1.19,15 | 22 | 1.0 | [- -] | 23 | 1.1 | [1.0 - 1.2] |
| H1.5 | 22 | 1.0 | [- -] | 23 | 1.0 | [- -] |

* significant difference in GMT between MenB and HepB (p<0.05; Mann-Whitney U)

Table 8B. SBA GMT's in 10-11 years old before and after vaccination MonoMen

| 'low dose' MenB | | | | | | |
|---------------------------------|----------|------------|----------------|-------------------------|------------|----------------|
| Pre vaccination | | | | Post vaccination | | |
| Strain | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 (90%) | 41 | 1.2 | [1.0 - 1.4] | 41 | *3.2 | [2.0 - 5.0] |
| P1.7^h,4 (50%) | 41 | 1.8 | [1.3 - 2.6] | 41 | *8.3 | [5.0 - 13.7] |
| P1.12,13 | 41 | 1.2 | [1.0 - 1.5] | 41 | *1.7 | [1.2 - 2.4] |
| P1.5^c,10 | 41 | *4.9 | [3.2 - 7.6] | 41 | *12.6 | [8.1 - 19.7] |
| P1.5,2 | 41 | *1.8 | [1.3 - 2.5] | 41 | *3.7 | [2.3 - 5.9] |
| P1.7,16 | 41 | 1.1 | [1.0 - 1.2] | 41 | 1.8 | [1.3 - 2.5] |
| P1.19,15 | 41 | 1.2 | [1.0 - 1.5] | 41 | *1.9 | [1.3 - 2.8] |
| H1.5 | 41 | 1.0 | [- -] | 41 | 1.0 | [- -] |

| 'high dose' MenB | | | | | | |
|---------------------------------|----------|------------|----------------|-------------------------|------------|----------------|
| Pre vaccination | | | | Post vaccination | | |
| Strain | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 (90%) | 35 | 1.1 | [1.0 - 1.2] | 34 | *3.1 | [2.0 - 5.0] |
| P1.7^h,4 (50%) | 35 | 1.4 | [1.1 - 1.8] | 34 | *12.3 | [7.1 - 21.3] |
| P1.12,13 | 35 | 1.2 | [0.9 - 1.6] | 34 | *1.4 | [1.1 - 1.7] |
| P1.5^c,10 | 35 | *6.5 | [4.1 - 10.0] | 34 | *14.7 | [9.2 - 23.6] |
| P1.5,2 | 35 | *1.7 | [1.2 - 2.5] | 34 | *3.8 | [2.3 - 6.5] |
| P1.7,16 | 35 | 1.2 | [1.0 - 1.5] | 34 | *2.4 | [1.5 - 3.8] |
| P1.19,15 | 35 | 1.4 | [0.9 - 1.9] | 34 | *2.2 | [1.4 - 3.7] |
| H1.5 | 35 | 1.1 | [0.9 - 1.4] | 34 | 1.0 | [- -] |

| HepB | | | | | | |
|---------------------------------|----------|------------|----------------|-------------------------|------------|----------------|
| Pre vaccination | | | | Post vaccination | | |
| Strain | N | GMT | [95%CI] | N | GMT | [95%CI] |
| P1.7^h,4 (90%) | 21 | 1.1 | [0.9 - 1.2] | 21 | 1.6 | [1.0 - 2.4] |
| P1.7^h,4 (50%) | 21 | 1.6 | [1.1 - 2.6] | 21 | 2.9 | [1.6 - 5.3] |
| P1.12,13 | 21 | 1.0 | [- -] | 21 | 1.0 | [1.0 - 1.1] |
| P1.5^c,10 | 21 | 1.0 | [- -] | 21 | 1.1 | [0.9 - 1.2] |
| P1.5,2 | 21 | 1.0 | [- -] | 21 | 1.0 | [1.0 - 1.1] |
| P1.7,16 | 21 | 1.0 | [1.0 - 1.1] | 21 | 1.1 | [0.9 - 1.4] |
| P1.19,15 | 21 | 1.0 | [- -] | 21 | 1.1 | [0.9 - 1.2] |
| H1.5 | 21 | 1.0 | [- -] | 21 | 1.0 | [- -] |

* significant difference in GMT between MenB and HepB (p<0.05; Mann-Whitney U)

Table 9. Percentages participants with 4-fold rise in SBA titre after vaccination MonoMen

| Strain | 'low dose' MenB | | | | | | 'high dose' MenB | | | | | | HepB | | | | | |
|----------------------------|-----------------|----|----|----------|----|----|------------------|----|----|----------|----|----|--------|----|----|----------|----|----|
| | 5-6yrs | | | 10-11yrs | | | 5-6yrs | | | 10-11yrs | | | 5-6yrs | | | 10-11yrs | | |
| | n | N | % | n | N | % | n | N | % | n | N | % | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 11 | 27 | 41 | 18 | 41 | 44 | 18 | 24 | 75 | 14 | 34 | 41 | 0 | 22 | 0 | 4 | 21 | 19 |
| P1.7 ^h ,4 (50%) | 19 | 27 | 70 | 24 | 41 | 59 | 22 | 24 | 92 | 26 | 34 | 76 | 3 | 21 | 14 | 5 | 21 | 24 |
| P1.12,13 | 1 | 27 | 4 | 6 | 41 | 15 | 4 | 24 | 17 | 3 | 34 | 9 | 0 | 22 | 0 | 0 | 21 | 0 |
| P1.5 ^c ,10 | 9 | 26 | 35 | 16 | 41 | 39 | 10 | 23 | 43 | 14 | 34 | 41 | 1 | 22 | 5 | 1 | 21 | 5 |
| P1.5,2 | 8 | 26 | 31 | 13 | 41 | 32 | 12 | 24 | 50 | 12 | 34 | 35 | 2 | 22 | 9 | 0 | 21 | 0 |
| P1.7,16 | 4 | 26 | 15 | 8 | 41 | 20 | 7 | 24 | 29 | 9 | 34 | 26 | 0 | 22 | 0 | 1 | 21 | 5 |
| P1.19,15 | 2 | 27 | 7 | 8 | 41 | 20 | 1 | 24 | 4 | 7 | 34 | 21 | 0 | 22 | 0 | 1 | 21 | 5 |
| H1.5 | 0 | 27 | 0 | 0 | 41 | 0 | 0 | 23 | 0 | 0 | 34 | 0 | 0 | 22 | 0 | 0 | 21 | 0 |

*Table 10. Percentages participants with 4-fold rise in SBA after vaccination MonoMen
In a subpopulation showing also a 4-fold rise after primary series with the hexavalent vaccine*

| Strain | 'low dose' MenB | | | | | | 'high dose' MenB | | | | | |
|----------------------------|-----------------|----|----|----------|----|----|------------------|----|-----|----------|----|----|
| | 5-6yrs | | | 10-11yrs | | | 5-6yrs | | | 10-11yrs | | |
| | n | N | % | n | N | % | n | N | % | n | N | % |
| P1.7 ^h ,4 (90%) | 7 | 9 | 78 | 8 | 12 | 67 | 12 | 12 | 100 | 2 | 4 | 50 |
| P1.12,13 | 1 | 20 | 5 | 4 | 20 | 20 | 4 | 17 | 24 | 1 | 18 | 6 |
| P1.5 ^c ,10 | 9 | 26 | 35 | 16 | 38 | 42 | 10 | 23 | 43 | 14 | 34 | 41 |
| P1.5,2 | 7 | 25 | 28 | 11 | 32 | 34 | 12 | 23 | 52 | 12 | 34 | 35 |
| P1.7,16 | 2 | 9 | 22 | 5 | 16 | 31 | 6 | 14 | 43 | 4 | 13 | 31 |
| P1.19,15 | 2 | 9 | 22 | 6 | 8 | 75 | 1 | 9 | 11 | 2 | 10 | 20 |

*Table 11A. Monovalent ELISA GMT's in 5-6 years old before and after vaccination
MonoMen*

| Study group | Pre vaccination | | | Post vaccination | | |
|------------------|-----------------|-----|-------------|------------------|------|---------------|
| | N | GMT | [95%CI] | N | GMT | [95%CI] |
| 'low dose' MenB | 28 | 249 | [177 - 350] | 27 | 3915 | [2899 - 5287] |
| 'high dose' MenB | 24 | 264 | [187 - 373] | 24 | 5444 | [4254 - 6966] |
| HepB | 22 | 28 | [24 - 33] | 23 | 289 | [209 - 399] |

*Table 11B. Monovalent ELISA GMT's in 10-11 years old before and after vaccination
MonoMen*

| Study group | Pre vaccination | | | Post vaccination | | |
|------------------|-----------------|-----|-------------|------------------|------|---------------|
| | N | GMT | [95%CI] | N | GMT | [95%CI] |
| 'low dose' MenB | 41 | 270 | [207 - 352] | 41 | 2891 | [2353 - 3551] |
| 'high dose' MenB | 35 | 213 | [154 - 295] | 34 | 3980 | [3131 - 5059] |
| HepB | 21 | 33 | [24 - 45] | 21 | 335 | [228 - 492] |

Appendix 3 Individual line listings

| UTN | age group | vaccination study 1995-'96 | P1.7h,4 90% pre serum | P1.7h,4 90% blood 1 | P1.7h,4 90% blood 2 | P1.7h,4 50% blood 1 | P1.7h,4 50% blood 2 |
|-----|-----------|----------------------------|-----------------------|---------------------|---------------------|---------------------|---------------------|
| 102 | 5-6 yr | 'low dose' MenB | 1 | 1 | 16 | 1 | 64 |
| 103 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 105 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 112 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 113 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 114 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 124 | 5-6 yr | 'low dose' MenB | 8 | 1 | 1 | 1 | 4 |
| 125 | 5-6 yr | 'high dose' MenB | 8 | 1 | 8 | 4 | 32 |
| 126 | 5-6 yr | 'high dose' MenB | 1 | 1 | 1 | 2 | 1 |
| 127 | 5-6 yr | HepB | 1 | 1 | 2 | 1 | 16 |
| 132 | 5-6 yr | 'high dose' MenB | 4 | 1 | 64 | 8 | 128 |
| 133 | 5-6 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 138 | 5-6 yr | 'low dose' MenB | 16 | 1 | 4 | 1 | 16 |
| 143 | 5-6 yr | 'high dose' MenB | 16 | 1 | 256 | 1 | 512 |
| 145 | 5-6 yr | 'high dose' MenB | 2 | 1 | 2 | 1 | 16 |
| 147 | 5-6 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 16 |
| 149 | 5-6 yr | 'high dose' MenB | 8 | 1 | 8 | 1 | 32 |
| 150 | 5-6 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 8 |
| 151 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 152 | 5-6 yr | HepB | 1 | 1 | 1 | 2 | 1 |
| 153 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 155 | 5-6 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 16 |
| 156 | 5-6 yr | HepB | 1 | missing | 1 | missing | 2 |
| 157 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 162 | 5-6 yr | 'high dose' MenB | 32 | 1 | 64 | 1 | 128 |
| 167 | 5-6 yr | 'low dose' MenB | 2 | 1 | 1 | 1 | 8 |
| 169 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 173 | 5-6 yr | 'low dose' MenB | 2 | 1 | 1 | 1 | 1 |
| 174 | 5-6 yr | 'low dose' MenB | 4 | 1 | 8 | 4 | 32 |
| 176 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 2 |
| 182 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 2 |
| 183 | 5-6 yr | 'high dose' MenB | 1 | 1 | 2 | 1 | 8 |
| 184 | 5-6 yr | 'low dose' MenB | 1 | 1 | 2 | 1 | 8 |
| 185 | 5-6 yr | 'low dose' MenB | 1 | 1 | 2 | 1 | 8 |
| 186 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 187 | 5-6 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 189 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 2 |
| 193 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 198 | 5-6 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 16 |
| 202 | 5-6 yr | 'high dose' MenB | 8 | 1 | 8 | 1 | 32 |
| 206 | 5-6 yr | 'low dose' MenB | 32 | 1 | 4 | 2 | 32 |
| 208 | 5-6 yr | 'high dose' MenB | 1 | 1 | 2 | 2 | 8 |
| 210 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 211 | 5-6 yr | 'high dose' MenB | 256 | 2 | 256 | 8 | 512 |
| 213 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 216 | 5-6 yr | 'high dose' MenB | 8 | 1 | 32 | 1 | 64 |
| 222 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 223 | 5-6 yr | 'low dose' MenB | 8 | 1 | 16 | 2 | 32 |
| 225 | 5-6 yr | 'low dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 226 | 5-6 yr | 'high dose' MenB | 8 | 1 | 16 | 1 | 64 |
| 227 | 5-6 yr | 'low dose' MenB | 256 | 4 | 256 | 16 | 512 |
| 231 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 8 |
| 232 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 233 | 5-6 yr | 'high dose' MenB | 16 | 1 | 256 | 4 | 512 |

| UTN | age group | vaccination study 1995-'96 | P1.7h,4_90% pre serum | P1.7h,4_90% blood 1 | P1.7h,4_90% blood 2 | P1.7h,4_50% blood 1 | P1.7h,4_50% blood 2 |
|-----|-----------|----------------------------|-----------------------|---------------------|---------------------|---------------------|---------------------|
| 234 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 235 | 5-6 yr | 'high dose' MenB | 4 | 1 | 16 | 1 | 64 |
| 237 | 5-6 yr | 'low dose' MenB | 8 | 8 | 64 | 16 | 128 |
| 238 | 5-6 yr | 'low dose' MenB | 4 | 1 | 16 | 1 | 16 |
| 241 | 5-6 yr | 'low dose' MenB | 1 | 64 | 16 | 64 | 128 |
| 247 | 5-6 yr | 'low dose' MenB | 4 | 1 | 1 | 1 | 2 |
| 248 | 5-6 yr | 'high dose' MenB | 1 | 1 | 16 | 1 | 64 |
| 249 | 5-6 yr | 'low dose' MenB | 2 | 1 | 1 | 1 | 2 |
| 250 | 5-6 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 16 |
| 257 | 5-6 yr | HepB | 1 | 1 | 1 | 2 | 2 |
| 258 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 259 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | missing |
| 260 | 5-6 yr | 'high dose' MenB | 2 | 1 | 4 | 2 | 16 |
| 261 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 262 | 5-6 yr | 'high dose' MenB | 64 | 1 | 4 | 4 | 16 |
| 263 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 264 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 2 |
| 265 | 5-6 yr | 'high dose' MenB | 2 | 1 | 4 | 1 | 16 |
| 266 | 5-6 yr | 'low dose' MenB | 1 | 1 | 2 | 1 | 64 |
| 271 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 4 |
| 275 | 5-6 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 278 | 5-6 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 2 |
| 284 | 5-6 yr | 'low dose' MenB | 32 | 1 | missing | 8 | missing |
| 401 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 402 | 10-11 yr | 'low dose' MenB | 16 | 1 | 128 | 16 | 512 |
| 403 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 2 |
| 404 | 10-11 yr | HepB | 1 | 1 | 8 | 1 | 32 |
| 405 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 406 | 10-11 yr | 'high dose' MenB | 1 | 8 | 1 | 32 | missing |
| 407 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 408 | 10-11 yr | 'high dose' MenB | 32 | 2 | 2 | 8 | 16 |
| 410 | 10-11 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 411 | 10-11 yr | HepB | 1 | 1 | 1 | 16 | 8 |
| 413 | 10-11 yr | 'low dose' MenB | 16 | 1 | 32 | 1 | 64 |
| 414 | 10-11 yr | 'high dose' MenB | 1 | 1 | 4 | 1 | 32 |
| 415 | 10-11 yr | 'low dose' MenB | 4 | 8 | 32 | 64 | 64 |
| 416 | 10-11 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 16 |
| 417 | 10-11 yr | 'high dose' MenB | 1 | 1 | 4 | 1 | 32 |
| 418 | 10-11 yr | 'low dose' MenB | 1 | 1 | 8 | 1 | 16 |
| 420 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 421 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 2 |
| 443 | 10-11 yr | 'low dose' MenB | 128 | 1 | 64 | 4 | 128 |
| 445 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 2 | 2 |
| 447 | 10-11 yr | 'high dose' MenB | 1 | 1 | 16 | 1 | 32 |
| 453 | 10-11 yr | HepB | 8 | 4 | 16 | 32 | 64 |
| 454 | 10-11 yr | 'low dose' MenB | 8 | 1 | 1 | 4 | 4 |
| 455 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 8 |
| 458 | 10-11 yr | HepB | 1 | 1 | 2 | 2 | 4 |
| 460 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 2 | 2 |
| 461 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 2 |
| 464 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 482 | 10-11 yr | 'low dose' MenB | 16 | 1 | 1 | 2 | 8 |
| 487 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 489 | 10-11 yr | 'low dose' MenB | 4 | 1 | 4 | 2 | 8 |
| 494 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 2 | 8 |
| 495 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 4 | 2 |
| 496 | 10-11 yr | HepB | 1 | 1 | 4 | 1 | 8 |

| UTN | age group | vaccination study 1995-'96 | P1.7h,4_90% pre serum | P1.7h,4_90% blood 1 | P1.7h,4_90% blood 2 | P1.7h,4_50% blood 1 | P1.7h,4_50% blood 2 |
|-----|-----------|----------------------------|-----------------------|---------------------|---------------------|---------------------|---------------------|
| 498 | 10-11 yr | 'low dose' MenB | 32 | 1 | 8 | 2 | 32 |
| 499 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 500 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 2 |
| 501 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 64 |
| 502 | 10-11 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 505 | 10-11 yr | 'high dose' MenB | 1 | 1 | 2 | 1 | 16 |
| 506 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 508 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 509 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 2 |
| 526 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 527 | 10-11 yr | 'high dose' MenB | 1 | 1 | 2 | 1 | 8 |
| 528 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 2 | 2 |
| 529 | 10-11 yr | 'low dose' MenB | 2 | 1 | 2 | 1 | 16 |
| 532 | 10-11 yr | 'high dose' MenB | 1 | 1 | 16 | 1 | 64 |
| 533 | 10-11 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 16 |
| 534 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 535 | 10-11 yr | 'low dose' MenB | 1 | 1 | 16 | 2 | 64 |
| 536 | 10-11 yr | HepB | 1 | 1 | 16 | 4 | 32 |
| 537 | 10-11 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 16 |
| 538 | 10-11 yr | 'low dose' MenB | 128 | 4 | 8 | 16 | 16 |
| 540 | 10-11 yr | 'high dose' MenB | 16 | 1 | 1 | 1 | 2 |
| 541 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 543 | 10-11 yr | 'low dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 544 | 10-11 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 545 | 10-11 yr | 'low dose' MenB | 1 | 1 | 2 | 1 | 8 |
| 546 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 548 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 561 | 10-11 yr | HepB | 1 | 1 | 1 | 2 | 8 |
| 562 | 10-11 yr | 'low dose' MenB | 16 | 1 | 4 | 1 | 16 |
| 564 | 10-11 yr | 'low dose' MenB | missing | 1 | 4 | 1 | 32 |
| 565 | 10-11 yr | 'low dose' MenB | missing | 1 | 1 | 1 | 1 |
| 568 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 569 | 10-11 yr | 'high dose' MenB | 32 | 1 | 128 | 4 | 512 |
| 571 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 572 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 573 | 10-11 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 8 |
| 574 | 10-11 yr | 'high dose' MenB | 1 | 1 | 2 | 1 | 16 |
| 575 | 10-11 yr | 'high dose' MenB | 1 | 1 | 8 | 1 | 32 |
| 577 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 8 |
| 578 | 10-11 yr | 'high dose' MenB | 2 | 1 | 64 | 1 | 256 |
| 580 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 581 | 10-11 yr | 'low dose' MenB | 1 | 1 | 16 | 1 | 64 |
| 583 | 10-11 yr | 'low dose' MenB | missing | 16 | 128 | 64 | 128 |
| 584 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 4 |
| 588 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 589 | 10-11 yr | 'high dose' MenB | 1 | 1 | 16 | 1 | 32 |
| 601 | 10-11 yr | 'high dose' MenB | 1 | 1 | 4 | 2 | 16 |
| 602 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 603 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 2 |
| 605 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 4 | 4 |
| 606 | 10-11 yr | 'high dose' MenB | 16 | 1 | 8 | 4 | 32 |
| 609 | 10-11 yr | HepB | 1 | 1 | 1 | 2 | 4 |
| 611 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 612 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 615 | 10-11 yr | 'low dose' MenB | 2 | 1 | 32 | 1 | 64 |
| 616 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 617 | 10-11 yr | 'low dose' MenB | 1 | 1 | 4 | 1 | 16 |

| UTN | age group | vaccination study 1995-'96 | P1.7h,4_90% pre serum | P1.7h,4_90% blood 1 | P1.7h,4_90% blood 2 | P1.7h,4_50% blood 1 | P1.7h,4_50% blood 2 |
|-----|-----------|----------------------------|--------------------------|------------------------|------------------------|------------------------|------------------------|
| 618 | 10-11 yr | 'low dose' MenB | 1 | 1 | 1 | 1 | 1 |
| 619 | 10-11 yr | 'high dose' MenB | 1 | 1 | 1 | 1 | 4 |
| 620 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 625 | 10-11 yr | HepB | 1 | 1 | 1 | 1 | 1 |
| 627 | 10-11 yr | 'high dose' MenB | 2 | 1 | 2 | 1 | 8 |
| 628 | 10-11 yr | 'high dose' MenB | 1 | 1 | 32 | 2 | 128 |
| 629 | 10-11 yr | 'low dose' MenB | 16 | 1 | 4 | 2 | 8 |
| 630 | 10-11 yr | HepB | 1 | 1 | 1 | 4 | 1 |
| 631 | 10-11 yr | 'low dose' MenB | 4 | 1 | 1 | 1 | 2 |

| UTN | P1.12,13 pre serum | P1.12,13 blood 1 | P1.12,13 blood 2 | P1.5c,10 pre serum | P1.5c,10 blood 1 | P1.5c,10 blood 2 | P1.5,2 pre serum | P1.5,2 blood 1 | P1.5,2 blood 2 |
|-----|-----------------------|---------------------|---------------------|-----------------------|---------------------|---------------------|---------------------|-------------------|-------------------|
| 102 | 32 | 1 | 16 | 256 | 16 | 64 | 64 | 1 | 64 |
| 103 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 105 | 2 | 1 | 1 | 64 | 8 | 16 | 8 | 1 | 1 |
| 112 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 113 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 114 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 124 | 16 | 1 | 1 | 256 | 8 | 8 | 32 | 1 | 1 |
| 125 | 16 | 1 | 1 | 256 | 64 | 256 | 256 | 16 | 16 |
| 126 | 1 | 1 | 1 | 256 | 4 | 8 | 1 | 1 | 1 |
| 127 | 1 | 1 | 1 | 1 | 1 | 256 | 1 | 1 | 16 |
| 132 | 16 | 1 | 1 | 256 | 16 | 32 | 256 | 16 | 32 |
| 133 | 32 | 1 | 1 | 256 | 16 | 32 | 256 | 2 | 1 |
| 138 | 32 | 1 | 1 | 256 | 1 | 16 | 64 | 1 | 8 |
| 143 | 64 | 1 | 4 | 256 | 16 | 128 | 256 | 8 | 32 |
| 145 | 16 | 1 | 1 | 256 | 1 | 16 | 32 | 1 | 1 |
| 147 | 1 | 1 | 1 | 256 | 2 | 4 | 32 | 1 | 4 |
| 149 | 128 | 1 | 4 | 256 | 32 | 64 | 256 | 16 | 16 |
| 150 | 16 | 1 | 1 | 256 | 16 | 16 | 256 | 1 | 8 |
| 151 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 152 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 153 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 155 | 8 | 1 | 1 | 256 | 1 | 32 | 256 | 1 | 4 |
| 156 | 1 | missing | 1 | 1 | missing | 1 | 1 | missing | 1 |
| 157 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 162 | 4 | 1 | 1 | 256 | 16 | 32 | 64 | 1 | 8 |
| 167 | 32 | 1 | 1 | 256 | 4 | 4 | 64 | 1 | 1 |
| 169 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 173 | 256 | 1 | 1 | 256 | 1 | 1 | 32 | 1 | 1 |
| 174 | 16 | 1 | 1 | 256 | 8 | 8 | 32 | 1 | 1 |
| 176 | 1 | 1 | 1 | 256 | 256 | 256 | 1 | 2 | 32 |
| 182 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 |
| 183 | 16 | 1 | 1 | 256 | 8 | 16 | 16 | 1 | 1 |
| 184 | 8 | 1 | 1 | 256 | 8 | 32 | 64 | 1 | 8 |
| 185 | 8 | 1 | 1 | 256 | 4 | 8 | 64 | 1 | 1 |
| 186 | 4 | 1 | 1 | 256 | 8 | 64 | 64 | 1 | 8 |
| 187 | 8 | 1 | 1 | 256 | 32 | 16 | 64 | 1 | 4 |
| 189 | 16 | 1 | 1 | 256 | missing | 16 | 16 | missing | 2 |
| 193 | 1 | 1 | 1 | 256 | 1 | 2 | 8 | 1 | 1 |
| 198 | 1 | 1 | 1 | 256 | 4 | 8 | 8 | 1 | 1 |
| 202 | 1 | 1 | 1 | 256 | 32 | 128 | 8 | 1 | 1 |
| 206 | 64 | 1 | 1 | 256 | 8 | 16 | 64 | 1 | 4 |
| 208 | 1 | 1 | 1 | 256 | 16 | 16 | 32 | 1 | 4 |
| 210 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 211 | 1 | 1 | 1 | 256 | 1 | 8 | 32 | 1 | 1 |
| 213 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 216 | 16 | 1 | 16 | 256 | 256 | 128 | 64 | 1 | 32 |
| 222 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 223 | 16 | 1 | 1 | 256 | 1 | 16 | 16 | 1 | 8 |
| 225 | 8 | 1 | 1 | 256 | 8 | 8 | 4 | 1 | 1 |
| 226 | 64 | 1 | 2 | 256 | 4 | 16 | 256 | 1 | 8 |
| 227 | 64 | 2 | 4 | 256 | 64 | 16 | 256 | 32 | 64 |
| 231 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 232 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 233 | 32 | 1 | 2 | 256 | 64 | 64 | 256 | 8 | 16 |
| 234 | 1 | 1 | 1 | 64 | 1 | 8 | 32 | 1 | 1 |
| 235 | 16 | 1 | 1 | 256 | 2 | missing | 256 | 1 | 4 |

[illegible]

| UTN | P1.12,13 pre serum | P1.12,13 blood 1 | P1.12,13 blood 2 | P1.5c,10 pre serum | P1.5c,10 blood 1 | P1.5c,10 blood 2 | P1.5,2 pre serum | P1.5,2 blood 1 | P1.5,2 blood 2 |
|-----|-----------------------|---------------------|---------------------|-----------------------|---------------------|---------------------|---------------------|-------------------|-------------------|
| 500 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 501 | 1 | 1 | 1 | 256 | 32 | 32 | 256 | 1 | 1 |
| 502 | 4 | 1 | 1 | 256 | 2 | 4 | 8 | 1 | 2 |
| 505 | 1 | 1 | 1 | 64 | 1 | 16 | 16 | 1 | 1 |
| 506 | 4 | 1 | 1 | 32 | 1 | 1 | 16 | 1 | 1 |
| 508 | 1 | 1 | 1 | 256 | 16 | 16 | 32 | 1 | 1 |
| 509 | 8 | 1 | 8 | 16 | 1 | 8 | 256 | 8 | 16 |
| 526 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 527 | 8 | 1 | 1 | 256 | 8 | 32 | 32 | 1 | missing |
| 528 | 1 | 1 | 1 | 64 | 8 | 16 | 8 | 1 | 2 |
| 529 | 16 | 1 | 1 | 256 | 1 | 2 | 64 | 1 | 1 |
| 532 | 8 | 1 | 1 | 256 | 16 | 32 | 8 | 1 | 4 |
| 533 | 16 | 1 | 1 | 32 | 1 | 1 | 32 | 1 | 1 |
| 534 | 1 | 1 | 1 | 256 | 1 | 1 | 32 | 1 | 1 |
| 535 | 8 | 1 | 16 | 256 | 32 | 64 | 256 | 8 | 64 |
| 536 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 537 | 1 | 1 | 1 | 64 | 1 | 16 | 8 | 1 | 4 |
| 538 | 32 | 1 | 1 | 256 | 32 | 32 | 256 | 64 | 64 |
| 540 | 1 | 1 | 1 | 256 | 4 | 2 | 256 | 8 | 4 |
| 541 | 1 | 1 | 1 | 256 | 32 | 16 | 32 | 4 | 8 |
| 543 | 1 | 1 | 1 | 256 | 1 | 8 | 4 | 1 | 4 |
| 544 | 8 | 1 | 1 | 256 | 4 | 256 | 64 | 1 | 64 |
| 545 | 256 | 1 | 2 | 256 | 2 | 32 | 64 | 4 | 32 |
| 546 | 1 | 1 | 1 | 64 | 2 | 4 | 4 | 1 | 1 |
| 548 | 1 | 1 | 1 | 64 | 16 | 32 | 8 | 1 | 1 |
| 561 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 562 | 256 | 16 | 64 | 128 | 8 | 64 | 64 | 16 | 64 |
| 564 | missing | 1 | 1 | missing | 8 | 16 | missing | 4 | 16 |
| 565 | missing | 1 | 1 | missing | 1 | 32 | missing | 1 | 8 |
| 568 | 1 | 1 | 1 | 64 | 1 | 1 | 1 | 1 | 1 |
| 569 | 1 | 1 | 4 | 256 | 64 | 256 | 256 | 32 | 256 |
| 571 | 4 | 1 | 1 | 32 | 4 | 16 | 8 | 1 | 1 |
| 572 | 16 | 2 | 2 | 256 | 16 | 16 | 8 | 1 | 8 |
| 573 | 1 | 1 | 2 | 256 | 32 | 64 | 64 | 1 | 4 |
| 574 | 16 | 1 | 2 | 256 | 8 | 16 | 32 | 4 | 32 |
| 575 | 1 | 1 | 1 | 256 | 4 | 8 | 16 | 1 | 4 |
| 577 | 4 | 1 | 1 | 256 | 2 | 8 | 32 | 2 | 4 |
| 578 | 8 | 1 | 4 | 256 | 16 | 64 | 64 | 1 | 32 |
| 580 | 4 | 1 | 1 | 256 | 1 | 8 | 1 | 1 | 4 |
| 581 | 8 | 1 | 1 | 128 | 8 | 4 | 2 | 1 | 1 |
| 583 | missing | 1 | 1 | missing | 4 | 8 | missing | 2 | 2 |
| 584 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 588 | 8 | 1 | 1 | 128 | 4 | 16 | 32 | 1 | 8 |
| 589 | 2 | 1 | 2 | 256 | 4 | 64 | 32 | 2 | 16 |
| 601 | 2 | 1 | 8 | 64 | 8 | 32 | 16 | 1 | 16 |
| 602 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 603 | 1 | 1 | 1 | 256 | 8 | 16 | 8 | 1 | 1 |
| 605 | 1 | 1 | 1 | 256 | 4 | 32 | 16 | 1 | 16 |
| 606 | 32 | 1 | 1 | 256 | 1 | 8 | 8 | 1 | 2 |
| 609 | 1 | 1 | 1 | 1 | 2 | 32 | 1 | 1 | 16 |
| 611 | 1 | 1 | 1 | 256 | 16 | 64 | 64 | 4 | 32 |
| 612 | 1 | 1 | 1 | 256 | 4 | 16 | 4 | 1 | 1 |
| 615 | 1 | 1 | 1 | 256 | 2 | 8 | 2 | 1 | 1 |
| 616 | 4 | 1 | 1 | 256 | 4 | 4 | 64 | 4 | 8 |
| 617 | 2 | 1 | 1 | 64 | 8 | 8 | 8 | 1 | 2 |
| 618 | 1 | 1 | 1 | 16 | 1 | 8 | 2 | 1 | 1 |
| 619 | 1 | 1 | 1 | 256 | 16 | 32 | 32 | 2 | 1 |

| UTN | P1.12,13 pre serum | P1.12,13 blood 1 | P1.12,13 blood 2 | P1.5c,10 pre serum | P1.5c,10 blood 1 | P1.5c,10 blood 2 | P1.5,2 pre serum | P1.5,2 blood 1 | P1.5,2 blood 2 |
|-----|-----------------------|---------------------|---------------------|-----------------------|---------------------|---------------------|---------------------|-------------------|-------------------|
| 620 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 625 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 627 | 16 | 1 | 1 | 256 | 4 | 64 | 256 | 1 | 2 |
| 628 | 1 | 1 | 1 | 8 | 1 | 1 | 4 | 1 | 1 |
| 629 | 32 | 4 | 1 | 256 | 16 | 32 | 32 | 4 | 2 |
| 630 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 631 | 16 | 1 | 4 | 64 | 1 | 8 | 4 | 1 | 4 |

| UTN | P1.7,16 pre serum | P1.7,16 blood 1 | P1.7,16 blood 2 | H1.5 blood 1 | H1.5 blood 2 | ELISA P1.4 blood 1 | ELISA P1.4 blood 2 | Exclusion PP analyses | Exclusion ITT analyses |
|-----|----------------------|--------------------|--------------------|-----------------|-----------------|-----------------------|-----------------------|--------------------------|---------------------------|
| 102 | 2 | 1 | 8 | 1 | 1 | 413 | 11676 | no | no |
| 103 | 1 | 1 | 1 | 1 | 1 | 25 | 217 | no | no |
| 105 | 1 | 1 | 1 | 1 | 1 | 329 | 4687 | no | no |
| 112 | 1 | 1 | 1 | 1 | 1 | 25 | 91 | no | no |
| 113 | 1 | 1 | 1 | 1 | 1 | 25 | 307 | no | no |
| 114 | 1 | 1 | 1 | 1 | 1 | 52 | 158 | no | no |
| 124 | 1 | 1 | 1 | 1 | 1 | 249 | 2977 | no | no |
| 125 | 8 | 1 | 1 | 1 | 1 | 876 | 3813 | no | no |
| 126 | 1 | 1 | 1 | 1 | 1 | 309 | 1581 | no | no |
| 127 | 1 | 1 | 1 | 1 | 1 | 25 | 348 | no | no |
| 132 | 16 | 1 | 1 | 1 | 1 | 673 | 7795 | no | no |
| 133 | 32 | 1 | 4 | 1 | 1 | 754 | 2684 | no | no |
| 138 | 64 | 1 | 4 | 1 | 1 | 232 | 6656 | no | no |
| 143 | 64 | 1 | 8 | 1 | 1 | 317 | 14474 | no | no |
| 145 | 1 | 1 | 1 | 1 | 1 | 102 | 3078 | no | no |
| 147 | 1 | 1 | 4 | 1 | 1 | 94 | 4581 | no | no |
| 149 | 256 | 1 | 4 | 1 | 1 | 388 | 8776 | no | no |
| 150 | 8 | 1 | 1 | 1 | 1 | 287 | 7066 | no | no |
| 151 | 1 | 1 | 1 | 1 | 1 | 25 | 356 | no | no |
| 152 | 1 | 1 | 1 | 1 | 1 | 25 | 1120 | no | no |
| 153 | 1 | 1 | 1 | 1 | 1 | 25 | 71 | no | no |
| 155 | 16 | 1 | 1 | 1 | 1 | 126 | 9791 | no | no |
| 156 | 1 | missing | 1 | missing | 1 | missing | 1173 | no | no |
| 157 | 1 | 1 | 1 | 1 | 1 | 25 | 360 | no | no |
| 162 | 16 | 1 | 1 | 1 | 1 | 130 | 6925 | no | no |
| 167 | 4 | 1 | 1 | 1 | 1 | 99 | 1863 | no | no |
| 169 | 1 | 1 | 1 | 1 | 1 | 25 | 485 | no | no |
| 173 | 8 | 1 | 1 | 1 | 1 | 430 | 2162 | no | no |
| 174 | 8 | 1 | 1 | 1 | 1 | 590 | 3513 | no | no |
| 176 | 1 | 1 | 1 | 1 | 1 | 25 | 489 | no | no |
| 182 | 1 | 1 | 1 | 1 | 1 | 53 | 363 | yes | no |
| 183 | 1 | 1 | 1 | 1 | 1 | 119 | 3159 | no | no |
| 184 | 1 | 1 | 2 | 1 | 1 | 133 | 17637 | no | no |
| 185 | 1 | 1 | 1 | 1 | 1 | 67 | 2706 | no | no |
| 186 | 1 | 1 | 1 | 1 | 1 | 224 | 7784 | no | no |
| 187 | 1 | 1 | 1 | 1 | 1 | 576 | 5890 | no | no |
| 189 | 1 | missing | 1 | 1 | 1 | 319 | 2238 | no | no |
| 193 | 1 | 1 | 1 | 1 | 1 | 83 | 2168 | no | no |
| 198 | 2 | 1 | 8 | 1 | 1 | 501 | 2484 | no | no |
| 202 | 1 | 1 | 1 | 1 | 1 | 97 | 4307 | no | no |
| 206 | 16 | 1 | 1 | 1 | 1 | 286 | 9552 | no | no |
| 208 | 2 | 1 | 1 | 1 | 1 | 513 | 3088 | no | no |
| 210 | 1 | 1 | 1 | 1 | 1 | 25 | 235 | no | no |
| 211 | 1 | 1 | 1 | 1 | 1 | 294 | 3548 | no | no |
| 213 | 1 | 1 | 1 | 1 | 1 | 25 | 222 | no | no |
| 216 | 32 | 1 | 32 | 1 | 1 | 853 | 8564 | no | no |
| 222 | 1 | 1 | 1 | 1 | 1 | 88 | 108 | no | no |
| 223 | 1 | 1 | 1 | 1 | 1 | 139 | 3682 | no | no |
| 225 | 1 | 1 | 1 | 1 | 1 | 302 | 5475 | no | no |
| 226 | 256 | 1 | 4 | 1 | 1 | 377 | 10571 | no | no |
| 227 | 256 | 16 | 8 | 1 | 1 | 630 | 4957 | no | no |
| 231 | 1 | 1 | 1 | 1 | 1 | 25 | 642 | no | no |
| 232 | 1 | 1 | 1 | 1 | 1 | 25 | 472 | no | no |
| 233 | 16 | 1 | 2 | 1 | 1 | 460 | 8597 | no | no |
| 234 | 1 | 1 | 1 | 1 | 1 | 97 | 1373 | no | no |
| 235 | 16 | 1 | 1 | 1 | missing | 135 | 6210 | no | no |

| UTN | P1.7,16 pre serum | P1.7,16 blood 1 | P1.7,16 blood 2 | H1.5 blood 1 | H1.5 blood 2 | ELISA P1.4 blood 1 | ELISA P1.4 blood 2 | Exclusion PP analyses | Exclusion ITT analyses |
|-----|----------------------|--------------------|--------------------|-----------------|-----------------|-----------------------|-----------------------|--------------------------|---------------------------|
| 237 | 16 | 1 | 8 | 1 | 1 | 986 | 8897 | no | no |
| 238 | 8 | 1 | 1 | 1 | 1 | 213 | 4580 | no | no |
| 241 | 4 | 256 | 32 | 64 | 32 | 1078 | 7105 | no | no |
| 247 | 2 | 1 | 1 | 1 | 1 | 25 | 1128 | no | no |
| 248 | 2 | 1 | 2 | 1 | 1 | 106 | 11040 | no | no |
| 249 | 2 | 1 | 1 | 1 | 1 | 192 | 2704 | no | no |
| 250 | 1 | 1 | 1 | 1 | 1 | 279 | 4821 | no | no |
| 257 | 1 | 1 | 1 | 1 | 1 | 25 | 159 | no | no |
| 258 | 1 | 1 | 1 | 1 | 1 | 113 | 1678 | no | no |
| 259 | 1 | 1 | 1 | 1 | 1 | 25 | 606 | yes | no |
| 260 | 8 | 1 | 1 | 1 | 1 | 187 | 2923 | no | no |
| 261 | 1 | 1 | 1 | 1 | 1 | 25 | 232 | yes | yes |
| 262 | 16 | 1 | 4 | 1 | 1 | 668 | 2812 | no | no |
| 263 | 1 | 1 | 1 | 1 | 1 | 25 | 177 | no | no |
| 264 | 1 | 1 | 1 | 1 | 1 | 165 | 13983 | no | no |
| 265 | 1 | 1 | 1 | 1 | 1 | 67 | 10984 | no | no |
| 266 | 1 | 1 | 1 | 1 | 1 | 2223 | 5143 | yes | yes |
| 271 | 1 | 1 | 1 | 1 | 1 | 25 | 345 | no | no |
| 275 | 1 | 1 | 1 | 1 | 1 | 25 | 115 | no | no |
| 278 | 1 | 1 | 1 | 1 | 1 | 887 | 1118 | no | no |
| 284 | 4 | 1 | missing | 1 | missing | 639 | missing | no | no |
| 401 | 1 | 1 | 1 | 1 | 1 | 25 | 381 | no | no |
| 402 | 32 | 1 | 1 | 1 | 1 | 266 | 5121 | no | no |
| 403 | 1 | 1 | 1 | 1 | 1 | 25 | 388 | no | no |
| 404 | 1 | 1 | 1 | 1 | 1 | 25 | 420 | no | no |
| 405 | 1 | 1 | 1 | 1 | 1 | 25 | 322 | no | no |
| 406 | 2 | 16 | missing | 32 | missing | 319 | missing | no | no |
| 407 | 4 | 1 | 1 | 1 | 1 | 192 | 1033 | no | no |
| 408 | 2 | 1 | 2 | 1 | 1 | 2228 | 3417 | no | no |
| 410 | 1 | 1 | 1 | 1 | 1 | 172 | 4442 | no | no |
| 411 | 1 | 1 | 1 | 1 | 1 | 50 | 402 | no | no |
| 413 | 4 | 1 | 64 | 1 | 1 | 127 | 3978 | no | no |
| 414 | 2 | 1 | 32 | 1 | missing | 118 | 9398 | no | no |
| 415 | 2 | 1 | 1 | 1 | 1 | 1236 | 2759 | no | no |
| 416 | 1 | 1 | 1 | 1 | 1 | 375 | 6235 | no | no |
| 417 | 2 | 1 | 16 | 1 | 1 | 126 | 7810 | no | no |
| 418 | 1 | 1 | 1 | 1 | 1 | 269 | 4542 | no | no |
| 420 | 1 | 1 | 1 | 1 | 1 | 25 | 357 | no | no |
| 421 | 1 | 1 | 1 | 1 | 1 | 25 | 1986 | no | no |
| 443 | 1 | 1 | 2 | 1 | 1 | 259 | 3861 | no | no |
| 445 | 32 | 1 | 1 | 1 | 1 | 143 | 1486 | no | no |
| 447 | 8 | 1 | 4 | 1 | 1 | 87 | 7292 | no | no |
| 453 | 1 | 1 | 1 | 1 | 1 | 266 | 981 | no | no |
| 454 | 8 | 1 | 2 | 1 | 1 | 1426 | 2129 | no | no |
| 455 | 1 | 1 | 1 | 1 | 1 | 94 | 4940 | no | no |
| 458 | 1 | 1 | 1 | 1 | 1 | 25 | 989 | no | no |
| 460 | 1 | 1 | 1 | 1 | 1 | 202 | 1325 | no | no |
| 461 | 1 | 1 | 1 | 1 | 1 | 25 | 421 | no | no |
| 464 | 1 | 1 | 1 | 1 | 1 | 378 | 1641 | no | no |
| 482 | 8 | 1 | 2 | 1 | 1 | 430 | 2437 | no | no |
| 487 | 1 | 1 | 1 | 1 | 1 | 1579 | 2383 | no | no |
| 489 | 64 | 1 | 8 | 1 | 1 | 318 | 5233 | no | no |
| 494 | 1 | 1 | 1 | 1 | 1 | 153 | 3524 | no | no |
| 495 | 1 | 1 | 1 | 1 | 1 | 1372 | 1991 | no | no |
| 496 | 1 | 1 | 1 | 1 | 1 | 25 | 542 | no | no |
| 498 | 1 | 1 | 1 | 1 | 1 | 96 | 2042 | no | no |
| 499 | 1 | 1 | 1 | 1 | 1 | 25 | 125 | no | no |

| UTN | P1.7,16 pre serum | P1.7,16 blood 1 | P1.7,16 blood 2 | H1.5 blood 1 | H1.5 blood 2 | ELISA P1.4 blood 1 | ELISA P1.4 blood 2 | Exclusion PP analyses | Exclusion ITT analyses |
|-----|----------------------|--------------------|--------------------|-----------------|-----------------|-----------------------|-----------------------|--------------------------|---------------------------|
| 500 | 1 | 1 | 1 | 1 | 1 | 25 | 161 | no | no |
| 501 | 1 | 1 | 1 | 1 | 1 | 111 | 1413 | no | no |
| 502 | 1 | 1 | 1 | 1 | 1 | 54 | 1966 | no | no |
| 505 | 1 | 1 | 32 | 1 | 1 | 151 | 2755 | no | no |
| 506 | 256 | 1 | 1 | 1 | 1 | 533 | 3630 | no | no |
| 508 | 1 | 1 | 4 | 1 | 1 | 185 | 2236 | no | no |
| 509 | 1 | 1 | 4 | 1 | 1 | 235 | 5140 | no | no |
| 526 | 1 | 1 | 1 | 1 | 1 | 25 | 92 | no | no |
| 527 | 4 | 1 | 1 | 1 | 1 | 190 | 2912 | no | no |
| 528 | 4 | 1 | 1 | 1 | 1 | 257 | 2211 | no | no |
| 529 | 1 | 1 | 1 | 1 | 1 | 120 | 2451 | no | no |
| 532 | 16 | 4 | 8 | 1 | 1 | 267 | 8934 | no | no |
| 533 | 1 | 1 | 1 | 1 | 1 | 113 | 646 | no | no |
| 534 | 1 | 1 | 1 | 1 | 1 | 57 | 944 | no | no |
| 535 | 32 | 4 | 32 | 1 | 1 | 538 | 6436 | no | no |
| 536 | 1 | 1 | 1 | 1 | 1 | 25 | 251 | no | no |
| 537 | 32 | 1 | 1 | 1 | 1 | 80 | 2336 | no | no |
| 538 | 8 | 1 | 1 | 1 | 1 | 952 | 3889 | no | no |
| 540 | 8 | 1 | 1 | 1 | 1 | 118 | 889 | no | no |
| 541 | 1 | 1 | 1 | 1 | 1 | 423 | 2707 | no | no |
| 543 | 1 | 1 | 1 | 1 | 1 | 207 | 7433 | no | no |
| 544 | 8 | 1 | 4 | 1 | 1 | 222 | 7989 | no | no |
| 545 | 16 | 1 | 8 | 1 | 1 | 313 | 8482 | no | no |
| 546 | 1 | 1 | 1 | 1 | 1 | 142 | 2700 | no | no |
| 548 | 1 | 1 | 1 | 1 | 1 | 501 | 1955 | no | no |
| 561 | 1 | 1 | 1 | 1 | 1 | 49 | 1882 | no | no |
| 562 | 64 | 8 | 64 | 1 | 1 | 579 | 4094 | no | no |
| 564 | missing | 1 | 2 | 1 | 1 | 363 | 2335 | no | no |
| 565 | missing | 1 | 1 | 1 | 1 | 567 | 4178 | no | no |
| 568 | 1 | 1 | 1 | 1 | 1 | 25 | 325 | no | no |
| 569 | 1 | 1 | 4 | 1 | 1 | 369 | 5863 | no | no |
| 571 | 4 | 1 | 1 | 1 | 1 | 518 | 1412 | no | no |
| 572 | 2 | 1 | 2 | 1 | 1 | 201 | 3084 | no | no |
| 573 | 1 | 1 | 4 | 1 | 1 | 279 | 9403 | no | no |
| 574 | 8 | 1 | 2 | 1 | 1 | 265 | 8187 | no | no |
| 575 | 1 | 1 | 1 | 1 | 1 | 277 | 2706 | no | no |
| 577 | 1 | 1 | 1 | 1 | 1 | 160 | 4337 | no | no |
| 578 | 32 | 1 | 128 | 1 | 1 | 261 | 11467 | yes | no |
| 580 | 1 | 1 | 1 | 1 | 1 | 120 | 7684 | no | no |
| 581 | 8 | 1 | 1 | 1 | 1 | 629 | 3034 | no | no |
| 583 | missing | 1 | 1 | 1 | 1 | 832 | 2711 | no | no |
| 584 | 1 | 2 | 2 | 1 | 1 | 213 | 1143 | no | no |
| 588 | 1 | 1 | 1 | 1 | 1 | 189 | 2086 | no | no |
| 589 | 8 | 1 | 4 | 1 | 1 | 849 | 12728 | no | no |
| 601 | 2 | 1 | 8 | 1 | 1 | 184 | 5306 | no | no |
| 602 | 1 | 1 | 1 | 1 | 1 | 25 | 93 | no | no |
| 603 | 1 | 1 | 1 | 1 | 1 | 66 | 1446 | no | no |
| 605 | 16 | 1 | 1 | 1 | 1 | 249 | 5564 | no | no |
| 606 | 256 | 16 | 32 | 1 | 1 | 594 | 5929 | no | no |
| 609 | 1 | 1 | 4 | 1 | 1 | 52 | 316 | yes | yes |
| 611 | 1 | 1 | 1 | 1 | 1 | 124 | 6243 | no | no |
| 612 | 2 | 1 | 1 | 1 | 1 | 161 | 1825 | no | no |
| 615 | 4 | 1 | 1 | 1 | 1 | 147 | 3517 | yes | yes |
| 616 | 32 | 1 | 1 | 1 | 1 | 186 | 4557 | no | no |
| 617 | 8 | 1 | 1 | 1 | 1 | 405 | 5633 | yes | yes |
| 618 | 1 | 1 | 1 | 1 | 1 | 102 | 1129 | no | no |
| 619 | 1 | 1 | 1 | 1 | 1 | 359 | 4913 | no | no |

| UTN | P1.7,16 pre serum | P1.7,16 blood 1 | P1.7,16 blood 2 | H1.5 blood 1 | H1.5 blood 2 | ELISA P1.4 blood 1 | ELISA P1.4 blood 2 | Exclusion PP analyses | Exclusion ITT analyses |
|-----|----------------------|--------------------|--------------------|-----------------|-----------------|-----------------------|-----------------------|--------------------------|---------------------------|
| 620 | 1 | 1 | 1 | 1 | 1 | 25 | 85 | no | no |
| 625 | 1 | 1 | 1 | 1 | 1 | 25 | 198 | yes | no |
| 627 | 8 | 1 | 1 | 1 | 1 | 367 | 9615 | no | no |
| 628 | 1 | 1 | 1 | 1 | 1 | 25 | 3865 | no | no |
| 629 | 16 | 1 | 1 | 1 | 1 | 763 | 3247 | no | no |
| 630 | 1 | 1 | 8 | 1 | 1 | 25 | 321 | no | no |
| 631 | 1 | 1 | 1 | 1 | 1 | 92 | 815 | no | no |