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Durability of immunogenicity and strain coverage of MenBvac, a meningococcal vaccine based on outer membrane vesicles: lessons of the Normandy campaign

Julien Sevestre^{a,b,c,1}, Eva Hong^{c,1}, Valérie Delbos^{a,b}, Aude Terrade^c, Eric Mallet^{a,b}, Ala-Eddine Deghmane^c, Ludovic Lemée^{a,b}, Muhamed-Kheir Taha^{c,2}, François Caron^{a,b,2}

^aCentre Hospitalier Universitaire, Rouen, France

^bUniversité de Rouen, France

^cInstitut Pasteur, Paris, France

¹Both authors contributed equally to this work.

²Both authors contributed equally to this work as senior authors

Corresponding author Muhamed-Kheir Taha

Email: mktaha@pasteur.fr

Running title: Response of OMV-containing meningococcal vaccines

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5 Julien Sevestre^{a,b,c,1}, Eva Hong^{c,1}, Valérie Delbos^{a,b}, Aude Terrade^c, Eric Mallet^{a,b}, Ala-Eddine
6 Deghmane^c, Ludovic Lemée^{a,b}, Muhamed-Kheir Taha^{c,2}, François Caron^{a,b,2}

7

8 ^aCentre Hospitalier Universitaire, Rouen, France

9 ^bUniversité de Rouen, France

10 ^cInstitut Pasteur, Paris, France

11

12

13

14 ¹Both authors contributed equally to this work.

15

16 ²Both authors contributed equally to this work as senior authors

17

18 Corresponding author Muhamed-Kheir Taha

19 Email: mktaha@pasteur.fr

20

21

22 Running title: Response of OMV-containing meningococcal vaccines

23 **Abstract**

24 **Objectives:** MenBvac® is an outer membrane vesicle (OMV)-based meningococcal vaccine.
25 From 2006 to 2012, it was used to control a clonal B outbreak in Normandy (France). We
26 aimed to analyse the durability of the response against the epidemic strain and coverage
27 beyond the vaccine strain. These data should help to optimize the use of OMV-containing
28 vaccines, such as the new 4CMenB/Bexsero® recombinant vaccine.

29 **Methods:** Serum bactericidal activity (SBA) was measured in two cohorts of children who
30 received their first dose of MenBvac® at 1-5 years of age and accepted to provide a blood
31 sample either one or four years after a 2+1+1 schedule. All sera were tested against the
32 outbreak strain. Sera from responder subjects were also tested against 12 additional B or C
33 strains which were chosen to entirely, partially, or not at all match the two variable regions
34 (VR1 and VR2) of the PorA vaccine strain.

35 **Results:** Only 47.9% and 31.3% of subjects showed an SBA titre consistent with protection
36 one and four years, respectively, after the last boost. Protective SBA titres were observed in
37 all sera against B or C strains that entirely matched P1.7,16, and was high (75-100%) for all
38 but one strain that partially matched VR1 or VR2. Extrapolating our data to the OMV
39 component of 4CMenB/Bexsero® suggests that 14.5% of the current B strains would be
40 covered based on PorA matching to the OMV component of 4CMenB/Bexsero® (regardless
41 of the coverage of the three other vaccine components).

42 **Conclusions:** Our data confirm that OMV-based vaccines elicit short-lasting SBA titres and
43 may require repeated booster injections. However, strain coverage may be greater than
44 expected.

45 **Keywords:** *Neisseria meningitidis* serogroup B; serum bactericidal activity; outbreak;
46 persistence of vaccine response; invasive meningococcal disease; PorA; vaccination

47 The Authors declare no conflict of interest.

48 **Highlights**

- 49 • Meningococcal outbreaks can be controlled by OMV-based vaccines, such as
- 50 MenBvac
- 51 • Serum bactericidal activity of sera from vaccinated subjects was evaluated
- 52 • Serum bactericidal activity rapidly declined
- 53 • Meningococcal strains expressing partially matching PorA were covered
- 54 • OMV-containing vaccines may offer broader protection than originally expected.

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73 **Introduction**

74 Capsular polysaccharide vaccines have been successfully developed against *Neisseria*
75 *meningitidis* of serogroup A, C, W, and Y. Such an approach is not possible for serogroup B
76 strains due to the homology between the group B capsule and the human neural cellular
77 adhesion molecule, leading to poor immunogenicity and a potential risk of autoimmunity.
78 This is particularly problematical because most invasive meningococcal disease in developed
79 countries is caused by serogroup B strains. Since the 1980s, tailor-made meningococcal B
80 vaccines, based on outer membrane vesicles (OMV), have been developed in response to
81 outbreaks, with campaigns in South Africa, Cuba, Norway, Brazil, Chile, and New Zealand
82 [1]. OMV vaccines elicit an immune response that is mainly directed against the protein porin
83 A (PorA) of the outer membrane which includes two variable regions, VR1 and VR2, with a
84 large diversity for both of them. The response is **generally** “strain specific” and is not cross-
85 reactive with divergent PorA variants. The last application of an OMV alone-based
86 meningococcal B vaccine was reported in Normandy, France, from 2006 to 2012, where a
87 clonal meningococcal outbreak, due to a strain of serotype 14, sero-subtype P1.7,16 and
88 clonal complex 32 (B:14:P1.7,16/cc32), was controlled using MenBvac®, a Norwegian
89 vaccine designed in the 1980s against a strain expressing the same PorA variant
90 (B:15:P1.7,16/cc32) [2].

91 Since then, multi-component protein-based vaccines that offer broad coverage against group
92 B *N. meningitidis* have been developed. Such new vaccines do not necessarily make former
93 OMV meningococcal vaccines obsolete [3]. The new multi-component protein-based
94 vaccines do not cover all circulating serogroup B isolates. Indeed, 4CMenB/Bexsero®, the
95 only meningococcal B vaccine available in Europe, **has been first evaluated to** cover 73–87%
96 of the B strains circulating in different European countries [4]. **More recent data have**
97 **predicted a 66% coverage in the UK [5]. These data imply** that a tailor-made OMV vaccine

98 might be requested in the future to control an outbreak due to an uncovered strain. Moreover,
99 OMV have adjuvant properties [6]. They have therefore been included in 4CMenB/Bexsero®
100 (using the preparation developed for MenZB, the OMV vaccine used in New Zealand) to
101 increase both the immunogenicity and persistence of the immune response against the other
102 vaccine components. Also, OMV vaccines may provide cross protection against strains that
103 do not express perfectly matching PorA proteins [7-9]. Importantly, antibodies generated by
104 OMV are independent of those targeting the capsule; thus OMV should work against
105 meningococcal strains from different serogroups, providing that they partially or entirely
106 share the PorA of the vaccine strain. Finally, animal experimentation, as well as several
107 clinical studies, suggest that the Norwegian OMV-based vaccine reduces meningococcal
108 carriage and may hence confer herd protection [10, 11].

109 During the Normandy outbreak, we performed two immunogenicity studies [11, 12] to
110 evaluate different schedules of MenBvac®. Several volunteers accepted to provide blood five
111 years after the first dose to evaluate the durability of the response and the spectrum of
112 coverage by measuring serum bactericidal titres (SBA), not only against the epidemic strain,
113 but also against other B and non-B strains which are currently endemic in the country.

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123 **Methods**

124 *Serum bactericidal activity*

125 SBA assays were performed using human serum, devoid of meningococcal lysis activity, as a
126 complement source (hSBA) for serogroup B isolates. Baby rabbit complement (rSBA) was
127 used for serogroup C isolates as previously described [2, 12]. The serum bactericidal activity
128 titres corresponded to the inverse of the final serum dilution causing 50% killing of the
129 inoculum after 1 h of incubation. A protective immune response was defined by an hSBA titre
130 ≥ 4 or a rSBA titre ≥ 8 , as these titres have been suggested as a surrogate for protection [13,
131 14].

132 Titres were compared using the percentage of subjects achieving the threshold for protection
133 and by calculating the geometric means of titres (GMT). Data were analyzed using the Chi-
134 squared test, Student's *t*-test, and analysis of variance (ANOVA). A *P* value of < 0.05 was
135 considered to be statistically significant. The Bonferroni correction was applied when the Chi-
136 squared test involved several comparisons.

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138 *Durability of immunogenicity against the targeted epidemic strain*

139 The SBA titres against the epidemic clone were analyzed for the two previously assembled
140 cohorts, the first in 2006 from subjects living in the Dieppe area and the second in 2009 from
141 subjects living in the Neufchâtel-en-Bray area [2, 12]. Briefly, children were aged 1-5 years at
142 the time of the first MenBvac® dose. They were selected by random sampling from all
143 subjects of the same age-range of the area eligible to receive MenBvac®. Both cohorts had
144 received a 2+1+1 schedule. The time of administration of the second boost (i.e., the last dose)
145 differed slightly between the two cohorts due to a production shortage of the vaccine that
146 required several adaptations of the initially planned scheme [2]. Thus, subjects received
147 MenBvac® at D0, W6, M8, and M23 in the Dieppe area, and at D0, W6, M8, and M36 in the

148 Neufchâtel-en-Bray area. Previously enrolled subjects were asked to provide a blood sample
149 four years after the last boost (i.e., at M71) for the Dieppe area [2] and one year after the last
150 boost (i.e., at M50) for the Neufchâtel-en-Bray area [12]. The extension of the former study
151 was approved for both cohorts by the regional ethics committee (Comité de Protection des
152 Personnes Nord-Ouest-1) and written informed consent was obtained from parents or legal
153 guardians of every participant.

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155 *Strain coverage*

156 We evaluated the range of strain coverage by MenBvac® by testing a subset of frozen serum
157 samples (collected six weeks after the second boost) of 12 subjects from the Neufchâtel-en-
158 Bray area cohort. The sera came from subjects who responded against strain LNP21362
159 (B:14:P1.7,16/cc32), which was previously used as a reference strain for SBA assays for the
160 Normandy outbreak [2]. These subjects did not show protective SBA titres before vaccination
161 (D0). Sera were tested against the reference strain (LNP21362), as well as 13 other strains of
162 serogroup B or C harbouring different PorA variable regions (14 SBA tests being the
163 maximal possible due to the low volume of residual serum available for each of these sera).
164 The other 13 strains were selected from B- and C-subgroup strains analysed in 2015 by the
165 National Reference Centre (NRC) for meningococci. In France, almost all cases of invasive
166 meningococcal disease are biologically confirmed by culture and/or PCR at the NRC. The
167 NRC performs complete genotyping of all strains by multi-sequence locus typing (clonal
168 complex) of PorA and FetA [15]. The 13 strains were selected to represent the different
169 combinations of variable regions, VR1 and VR2, partially matching PorA P1.7,16, that are
170 currently circulating in the country. When the same PorA profile was shared by several strains
171 belonging to different clonal complexes, one strain per clonal complex was selected. Human
172 complement was used for the SBA assay of serogroup B isolates. Baby rabbit complement

173 was used for serogroup C isolates due to the intrinsic meningococcal lysis against these
174 serogroup C strains in all human sera that were used as complement sources.

175 Finally, the results were extrapolated to the 2015 NRC data to determine the percentage of
176 invasive meningococcal strains currently endemic in the country that completely or partially
177 match the OMV component of MenBvac® (P1.7,16) or 4CMenB/Bexsero® (P1.7-2, 4).

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198 **Results**

199 *Durability of immunogenicity against the targeted epidemic strain*

200 Table 1 shows the long-term SBA titres for the two cohorts (last line) and compares them to
201 the results previously reported for each scheme [2, 11].

202 For the Dieppe area cohort, 115 children among the 243 initially included (47%) agreed to
203 participate in the final phase of the study four years after the second boost, amongst which
204 only 31.3% (95% CI 22.8 to 39.8) had an hSBA titre consistent with protection, whereas the
205 geometric mean hSBA was only 3.3 (95% CI 2.8-3.9). These data are in accordance with the
206 marked decline of hSBA titres previously observed 15 months after the first boost, for which
207 only 56% of subjects showed protective titres.

208 For the Neufchâtel-en-Bray area cohort, 96 children among the 213 initially included (45%)
209 agreed to participate in the final phase of the study one year after the second boost, amongst
210 which only 47.9% (95% CI 37.9 to 57.9) showed protective hSBA titres. This percentage, as
211 well as the geometric mean hSBA value (4.4; 95% CI 3.5-5.5), were not significantly
212 different from those previously achieved one year after the first boost (i.e., at M20).

213

214 *Strain coverage*

215 The characteristics of the 14 strains studied and the hSBA or rSBA titres achieved against
216 each of them in the sera from 12 (10 for serogroup C due to a limited amount of sera) high
217 responders to MenBvac are presented Table 2.

218 Among the 14 strains, two (one of serogroup B used as a control and one of serogroup C)
219 completely matched the PorA of MenBvac (P1.7,16) and both belonged to cc32. Nine strains
220 (seven of serogroup B and two of serogroup C) shared either VR1 or VR2 with the vaccine
221 strain or were variants of the P1.7 (VR1) or P1.16 (VR2) family. The last three serogroup B

222 strains had PorA which completely differed from that of the strain vaccine (P1.22, 9, P1.19-2,
223 13-1 and P1.19-1, 15-11). Ten of the 14 strains (71%) belonged to major hyperinvasive clonal
224 complexes (cc11, cc32, cc41/44, cc269).

225 As expected, hSBA titres against the serogroup B isolate (LNP21362) that matched the
226 vaccine strain (P1.7,16) were significantly higher than the threshold of 4 for all 12 sera tested,
227 with a lower limit of the 95% CI > 4.

228 In contrast, the lower limit of the 95% CI of the GMT was lower than the threshold of 4 for
229 the SBA titres against the three isolates (LNP27143, LNP27050 and LNP27000) that did not
230 at all match PorA. One of these strains (LNP27000) did not show coverage in any tested
231 serum. However, 25% and 42% of the volunteers had hSBA titres of 4 and 8 against the other
232 two strains LNP27143 and LNP27050, respectively. Additionally, strain LNP27200, a non-
233 cc32 strain with a partial PorA match (P.21,16-36), also showed a low GMT, with 25% of
234 tested sera displaying hSBA titres of 4.

235 The GMT and the lower limits of the 95% CI were above 4 for the remaining six B strains.
236 The SBA titres were high in all 12 tested sera for three of the six strains (LNP27338,
237 LNP27087 and LNP27386 all belonged to the cc32) and were not significantly different from
238 those achieved against the reference strain (LNP21362). The hSBA titres differed greatly
239 (depending on the strain) for the three remaining strains (LNP27372, LNP27010 and
240 LNP27114). However, the lower limit of the 95% CI remained higher than 4, although the
241 GMT were significantly lower than those obtained against the reference strain LNP21362.

242 We also studied three strains of serogroup C, amongst which one entirely matched PorA of
243 MenBvac (LNP25514) and two partially matched (LNP25553 and LNP26251). The rSBA
244 threshold of 8 was achieved against the three C strains in all tested sera. A hierarchy of

245 responses was however observed, with the rSBA titres being significantly higher against the
246 strain which entirely matched the vaccine PorA than the other two serogroup C strains.

247 The percentages of invasive meningococcal strains predicted to be covered by either
248 MenBvac® or 4CMenB/Bexsero® based on their PorA variable regions, and regardless their
249 serogroups, are shown in Table 3. For MenBvac®, only 2.6% of the current French strains
250 totally matched PorA. This putative coverage increased to 16.9% when considering both
251 complete and partially matching (i.e. strains with family 7 VR1 and/or strains with family 16
252 VR2). For 4CMenB/Bexsero®, the respective percentages were 8.1% and 14.5%.

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270 **Discussion**

271 This study was performed in an area of Normandy recently affected by a clonal
272 meningococcal B outbreak that was controlled using MenBvac, an OMV vaccine [2]. The two
273 major results of this study were: (i) the short durability of protection against the targeted
274 strain, despite a four dose vaccination scheme and (ii) an extension of the strain coverage to
275 other B and non-B strains that at least partially shared the PorA of the vaccine strain.

276 The short persistence of protection was observed even after a second booster dose, although
277 the absence of samples from six weeks after the second booster dose in the Dieppe cohort
278 limits the extrapolation of this conclusion. Several previous studies on OMV vaccines have
279 also reported the rapid decline of SBA titres elicited against the targeted strain [16]. This is
280 not necessarily a major drawback, as such “tailor-made” vaccines are aimed to control an
281 outbreak rather than to offer persistent protection against sporadic events. For the control of a
282 clonal outbreak, two doses of a targeted OMV vaccine given at a 4-6 week interval can be
283 sufficient to “put the fire out” as reported during the first application of MenBvac® in
284 Norway [17]. However, because clonal B outbreaks might naturally persist for up to two
285 decades, obtaining immunity for several years in an affected area is probably pertinent. The
286 four-dose MenBvac® regimen applied during a two-year period in Normandy resulted in
287 limited persistence of the SBA titres against the outbreak strain (B:14:P1.7,16/cc32) which
288 was observed in less than one third of vaccinated 1-5 year-old children 5 years after the first
289 dose. Such poor results do not necessarily exclude a better response in adolescents and young
290 adults, as shown for other OMV vaccines [18]. The short observed persistence of bactericidal
291 antibodies against B:14:P1.7,16/cc32 (even in the Dieppe area, epicentre of the outbreak) may
292 be due to the rapid decline of the response to the vaccine and the lack of natural immunity
293 favoured by a very low rate of pharyngeal carriage of the epidemic strain in the population, as
294 reported by a carriage study performed at the height of the outbreak [10].

295 The broader strain coverage of MenBvac® is relevant in meningococcal vaccinology as the
296 4CMenB/Bexsero® vaccine includes an OMV component. OMV-based vaccines elicit an
297 immune response that is mainly directed against the PorA outer membrane protein. Due to the
298 high variability of PorA among isolates, this type of vaccine is classically considered strain-
299 specific [19]. However, several previous studies with MenBvac® [8, 9, 18, 20] and other
300 OMV vaccines [7, 9, 18, 20] have reported protection beyond the vaccine strain. Rosenqvist
301 *et al.* have shown that MenBvac® induced in adult volunteers significant SBA response
302 against variants of the vaccine strain lacking some outer membrane proteins [8]. The
303 Norwegian Institute of Public Health team had performed a study in adult volunteers
304 comparing the immunogenicity of MenBvac® (P1.7,16 strain) and MeNZB® (P1.7-2,4
305 strain) showing that SBA titres were better against the homologous strain than with the
306 heterologous strain [9, 20]. Tappero *et al* have reported that both MenBvac (P1.7,16 strain)
307 and the Finlay Institute OMV vaccine (P1.15 strain) did not induce significant response in
308 infants while children and adults showed SBA titres against a heterologous strain but to a
309 lesser extent than to the vaccine homologous strain[18]. Boutriau *et al* have analyzed a
310 bivalent OMV vaccine designed to cover a large proportion of B strains circulating in Europe
311 that induced increased SBA titres against the two vaccine strains as well as against three
312 heterologous strains but this vaccine did not reach the market [7]. Our study provides
313 additional data, suggesting that strain coverage can be larger than initially expected.
314 Completely or partially matching one of the two variable regions of PorA (VR1 and VR2)
315 may lead to coverage by the MenBvac® irrespective of the serogroup. However, SBA titres
316 were significantly higher when both VR1 and VR2 matched the vaccine, suggesting
317 synergism of serum bactericidal activity against these variable regions. Further studies may be
318 needed to explore how the alterations of VR regions affect serum bactericidal activity.
319 Moreover, other minor proteins in the OMV can confer protection, as suggested by the SBA

320 titres against the strain LNP27050 that did not match variable regions of PorA P1.7,16. This
321 part of the study had however three limitations. (i) Due to low volumes of residual serum
322 available, it was impossible for a given strain to test all subvariants in terms of VRs; all sub-
323 variants of P1.7,16 may not be covered and testing several other strains may be required. (ii)
324 It was also impossible to evaluate the protection at baseline against the tested strains.
325 However, we have previously reported low level of protective SBA titres against the stain
326 with P1.7,16 before the first dose of MenBvac®) [12].
327 (iii) The broader of coverage has been studied only for MenBvac®; it is not excluded that
328 results may differ for other OMV based vaccines.
329 The strain coverage by 4CMenB/Bexsero® has been extensively studied for the three proteins
330 NadA, fHbp, and NHBA, but much less for its fourth component, corresponding to PorA
331 P1.7-2, 4 from MeNZB® [21]. Previous reports have suggested that the VR1 region (7-2) of
332 PorA was poorly recognised by a monoclonal antibody against subtype P1.7 due to an internal
333 deletion, leading to masking of this region [22]. However, our study shows that polyclonal
334 anti-PorA antibodies, obtained after vaccination in several subjects, achieved SBA titres
335 against the two strains (LNP27010 and LNP27114) that only had VR1 7-2. The potential
336 protection against non-B strains, as suggested by our data, is of interest, as this is expected to
337 enlarge strain converge. Such protection was suggested in reports on the use of 4CmenB®
338 against serogroups W and X [23, 24]. The subjects of our study were not vaccinated against
339 serogroup C meningococci when MenBvac® vaccination started. Indeed, the
340 recommendation for vaccination against MenC only started in France in 2010. The uptake of
341 the vaccine remains very low in France and vaccine coverage in 1-4 year olds was only 50%
342 by the end of 2013 [25].
343 Based on the 2015 database from the NRC, 14.5% of the current serogroup B strains are
344 predicted to be covered by the OMV component of 4CMenB/Bexsero® (regardless of the

345 coverage by the three other components of the vaccine). The Meningococcal Antigen Typing
346 system (MATS) predicted 85% coverage of the serogroup B isolates in France. Importantly,
347 among the 15% (n = 30) of uncovered strains, 13% (n = 4) could be covered on the basis of
348 partial matching with PorA [4]. Thus, strain coverage could be higher than that predicted
349 solely by MATS.

350 In conclusion, the results of the current study show that OMV-containing vaccines induce
351 immunity, although of short duration, far below that of the vaccine strain. This argues for
352 adapting the OMV component from new meningococcal vaccines to improve the coverage of
353 local strains, particularly in the event of outbreaks that may not be covered by the other
354 components of the vaccines.

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Table 1

Immunogenicity of MenBvac® vaccine and persistence of the response against B:14:P1.7,16 (strain LNP21362) in two cohorts of children of 1-5 years of age at first dose and previously analyzed at short term.

Dieppe cohort MenBvac at D0-W6-M8-M23				Neufchâtel-en-Bray cohort MenBvac at D0-W6-M8-M36			
Time of sampling	Number	% of subjects with hSBA ≥ 4 [95% CI]	GMT of hSBA titres [95% CI]	Time of sampling	Number	% of subjects with hSBA ≥ 4 [95% CI]	GMT of hSBA titers [95% CI]
-	-	-	-	D0*	213	10.8 (6.6-15)	2.3 (2.1-2.5)
-	-	-	-	M3	172	41.3 (33.9-48.7)	3.3 (2.9-3.7)
M8*	243	37.0 (30.9-39.8)	2.8 (2.6-2.9)	M8*	159	25.5 (19-32.6)	2.8 (2.5-3.1)
M9.5	235	87.7 (83.5-91.9)	11.3 (9.5-13.4)	M9.5	126	84.1 (77.7-90.5)	10.9 (8.7-13.6)
-	-	-	-	M20	126	39.7 (31.2-48.2)	4.1 (3.4-5)
M23*	193	56.3 (49.2-63.3)	3.9 (3.5-4.5)	-	-	-	-
-	-	-	-	M36*	117	21.4 (14-21.4)	2.7 (2.4-3.1)
-	-	-	-	M37.5	99	86.9 (80.3-93.5)	17.5 (13.2-23.2)
-	-	-	-	M50	96	47.9 (37.9-57.9)	4.4 (3.5-5.5)
M71	115	31.3 (22.8-39.8)	3.28 (2.8-3.9)	-	-	-	-

*Sample collected before dose.

D=day. W=week. M=month.

Table 2 Immunogenicity of MenBvac® vaccine against strains of serogroups B or C in 12 responder subjects. Results are expressed in comparison to reference strains that completely match PorA of the vaccine strain.

Study strain number (LNP)	Genotyping					SBA			p-value
	Group	PorA VR1	PorA VR2	cc	FetA	Range of SBA titres (Proportions of sera with protective titres)	GMT of hSBA titres [95% CI]	GMT [95% CI]	
Serogroup B strains; SBA using human complement (hSBA); protective response for hSBA ≥ 4									
Complete match with the vaccine strain									
LNP21362	B	7	16	32	F3-3	16-128 (100%)	107.6	73.5-157.6	Ref*
Partial match with the vaccine strain									
LNP27010	B	7-2	4	41/44	F1-5	2-16 (92%)	6.4	4.3-9.4	0.0005
LNP27087	B	7	16-26	32	F3-3	32-128 (100%)	114	88.4-147.1	>0.99
LNP27114	B	7-2	4	162	F5-9	2-128 (75%)	15.1	5.9-39	0.002
LNP27338	B	7-2	16-26	32	F3-3	128-128 (100%)	128	128-128	>0.99
LNP27372	B	7-1	1	32	F3-3	2-128 (92%)	24	9.7-59.5	0.00195
LNP27200	B	21	16-36	865	F5-8	2-4 (25%)	2.4	1.9-2.9	0.0005
LNP27386	B	21	16	41/44	F1-7	128-128 (100%)	128	128-128	>0.99
No match with the vaccine strain									
LNP27000	B	19-1	15-11	269	-	2-2 (0%)	2	2-2	0.0005
LNP27050	B	19-2	13-1	461	-	2-8(42%)	4	2.1-7.5	<0.0001
LNP27143	B	22	9	269	F1-5	2-8 (25%)	2.7	1.9-3.8	0.0005
Serogroup C strains; SBA using rabbit complement (rSBA); protective response for rSBA ≥ 8									
Complete match with the vaccine strain									
LNP25514	C	7	16	32	F3-3	16-512 (100%)	64	26.7-153.2	Ref**
Partial match with the vaccine strain									
LNP25553	C	17	16-3	11	F1-1	16-32 (100%)	18.4	14.9-22.7	0.016
LNP26251	C	21-7	16	1157	F5-36	64-512 (100%)	161.3	59.7-435.8	0.019

* Significance level $p < 0.005$ after Bonferroni correction for 10 comparisons

** Significance level $p < 0.025$ after Bonferroni correction for 2 comparisons

Table 3

Percentage of current invasive meningococcal strains in France that are expected be covered by either MenBvac® or 4CMenB/Bexsero® based on their PorA domain (for 4CMenB/Bexsero® the coverage is largely enhanced by the three other components of the vaccine).

2015 French <i>N. meningitidis</i> isolates with complete typing available (n=344)						
	Matching with the P1.7,16 PorA antigen of MenBvac			Matching with the P1.7-2,4 PorA antigen of 4CMenB/Bexsero		
	Complete	Incomplete	Null	Complete	Incomplete	Null
B strains (n=170)	8 (4.7%)	45 (26.5%)	117 (68.8%)	28 (16.5%)	21 (12.4%)	121 (71.1%)
Strains of other groups (n=174)	1 (0.6%)	4 (2.3%)	169 (97.1%)	0 (0%)	1 (0.6%)	173 (99.4%)
Total (n=344)	9 (2.6%)	49 (14.3%)	286(83.1)	28 (8.1%)	22 (6.4%)	294 (85.5%)