Introduction

Invasive meningococcal disease (IMD) is caused by infection with the bacterium *Neisseria meningitidis*. Clinically, meningococcal disease is most frequently observed as meningitis or septicemia; IMD is associated with significant levels of mortality; those who survive can experience disabling, long-term sequelae such as neurologic and hearing impairments and amputation. Disease incidence is highest in infants and toddlers, with a second peak often occurring among adolescents and young adults. Because of the sudden onset and rapid progression of the disease, preventive vaccination is considered the most effective strategy to protect against IMD.

Of the 12 identified serogroups of *N meningitidis*, 5 have historically predominated as the main cause of IMD globally (i.e., A, B, C, W, and Y); all are currently preventable with available monovalent and polyvalent meningococcal vaccine formulations. Specifically, several monovalent conjugate vaccines have been developed for protection against meningococcal serogroup C (MenC) disease, and a monovalent conjugate vaccine has been developed against serogroup A (MenA) disease. Vaccines that combine *Haemophilus influenzae* type b (Hib) and meningococcal antigens (i.e., serogroups Y and/or C) were available in some countries. Two vaccines based on subcapsular antigens are also available for the prevention of meningococcal serogroup B (MenB) disease. The availability of quadrivalent vaccines targeting meningococcal serogroups A, C, W, and Y (MenACYW) has led to broader serogroup coverage against disease-causing strains. The implementation of immunization programs using these various meningococcal vaccine formulations has substantially contributed to reductions in IMD disease burden.

Four quadrivalent meningococcal vaccines are currently licensed and differ according to carrier protein, posology, and availability (Table 1). One such quadrivalent vaccine is MenACYW-TT (Nimenrix®, Pfizer Ltd,Kent, UK), which is conjugated to tetanus toxoid (TT) and is indicated for use in individuals from age 6 weeks. MenACYW-TT, the focus of this review, is administered to infants as a 2-dose (6 weeks–<6 months) or 1-dose (6–<12 months) primary series plus a 1-dose booster in the second year of life. In individuals aged 12 months and older, MenACYW-TT is given as a single dose. Booster dosing can be given to individuals from age 12 months who were previously vaccinated with a conjugated or plain polysaccharide meningococcal vaccine.

The distribution of meningococcal serogroups causing disease varies geographically and over time. Therefore, to ensure adequate protection against IMD, national vaccination strategies have adapted to temporal changes in epidemiology. This is exemplified by the experience with the introduction of MenC vaccination programs. During the late 1990s, the incidence of
MenC disease increased in many European countries, mainly due to a hypervirulent ST-11 clone. In response, several countries added monovalent MenC vaccination to their routine infant immunization schedule, usually with catch-up programs in toddlers, children, and adolescents and, in some countries, young adults. Subsequent to the implementation of these strategies, decreases in MenC disease were observed. In contrast, during the past decade, the incidence of IMD caused by meningococcal serogroup W (MenW) and serogroup Y (MenY) has increased across multiple age groups in many countries within Europe. MenW cases have frequently been associated with a hypervirulent ST-11 strain and, more recently, an emergent ST-9316 strain predominantly affecting children aged <4 years. A proportion of these MenW cases have presented with atypical clinical features, such as septic arthritis, gastrointestinal symptoms, and severe respiratory tract infections, such as pneumonia, epiglottitis, and supraglottitis. MenY cases have shown variability in the most commonly affected age group; MenY cases have also shown increased manifestation as septicemia and decreased susceptibility to penicillin. In response to this serogroup shift, several countries introduced quadrivalent MenACWY vaccination to their immunization programs, in many instances as replacement for the existing monovalent MenC vaccine (Figure 1).

To ensure optimal protection against MenC disease is maintained in countries switching to MenACWY vaccines, it is important that the immune response elicited to serogroup C is comparable to that achieved with monovalent MenC vaccines. This article reviews key clinical studies that compared MenC immune responses induced by MenACWY-TT with those of monovalent MenC conjugate vaccines.

Methods

Clinical studies evaluating the immunogenicity of MenACWY-TT were identified by searches of clinical trial registries for studies in which MenACWY-TT was compared with a MenC vaccine and in which serology was completed for the licensed posology. PubMed, ClinicalTrials.gov, and the EU Clinical Trials Register were searched using the keywords “MenACWY-TT”, “Nimenrix”, “ACWY-TT”, and “GSK134612”, without filters or limits. The GSK Study Register was searched using the same keywords and the limit of “Meningococcal Infections” as the search term.

Figure 1. Countries with recent MenACWY vaccine recommendations. *In all provinces apart from Quebec. †Malta is not shown to scale or to shape.
condition/disease. The inclusion criteria were studies directly comparing the immunogenicity of MenACWY-TT with that of ≥1 monovalent MenC conjugate vaccine (MenC-TT, MenC-CRM₁₉₇/Al(OH)$_3$ or MenC-CRM₁₉₇/AlPO$_4$ [Table 1]). Immune responses in these studies were evaluated in serum bactericidal antibody assays using human (hSBA) or baby rabbit complement (rSBA). Imunogenicity assessments evaluated in the current review include percentage of subjects with rSBA titers ≥1:8, rSBA geometric mean titer (GMT), percentage of subjects with hSBA titers ≥1:8, and hSBA GMT at 1 month/42 days after primary or booster vaccination. Only data relevant to the licensed MenACWY-TT schedule are presented (i.e., 2 + 1 schedule in infants aged 6 weeks–<6 months; 1 + 1 schedule in infants aged 6–<12 months; single dose in individuals aged ≥12 months). Preimmune and persistence data were not considered. This article is based entirely on previously published studies and does not contain data from any new studies using human or animal subjects.

**Results**

**Studies included**

Eight studies met the criteria for inclusion in the review, comprising one study in infants, four in toddlers, and three in children and adolescents. The designs of these studies are summarized in Table 2. No studies carried out in adults met the inclusion criteria.

**Studies in infants**

Only 1 infant study met the inclusion criteria. Conducted in Spain, Germany, and Estonia, this noninferiority study compared 1567 infants who received MenACWY-TT, MenC-TT, or MenC-CRM₁₉₇/Al(OH)$_3$ at ages 2, 4, and 12 months. All subjects also received routine vaccinations as recommended. Immunogenicity was assessed at 1 month after the primary series and at 1 month after the booster dose. After primary vaccination, the percentage of subjects with rSBA titers ≥1:8 for MenC was high across the 3 vaccine groups, ranging from 98.7% (MenACWY-TT) to 100% (MenC-TT) (Figure 2A). The percentage of subjects with postbooster MenC rSBA titers ≥1:8 was also consistently high in all groups, varying from 98.4% in the MenC-CRM₁₉₇/Al(OH)$_3$ group to 99.8% and 100% in the MenACWY-TT and MenC-TT groups, respectively (Figure 2A). Comparisons of MenC rSBA GMT both after the primary series and the booster dose showed a <2-fold difference among vaccine groups (postprimary range, 612–1188; postbooster range, 1051–1960; Figure 2B). Postprimary and postbooster, the percentages of subjects with MenC hSBA titers ≥1:8 were 100% for the monovalent vaccines and ≥98.6% for MenACWY-TT (Figure 2C). MenC hSBA GMTs after primary vaccination were 1308 among MenACWY-TT recipients, 3188 among those who received MenC-CRM₁₉₇/Al(OH)$_3$, and 2627 among those who received MenC-TT. In contrast, after the booster vaccination, MenC hSBA GMTs ranged from 4992 to 5542 among the 3 vaccine groups (Figure 2D). These findings confirmed the noninferiority of an infant 2-dose primary series of MenACWY-TT with that of a 2-dose primary series of MenC-CRM₁₉₇/Al(OH)$_3$ or MenC-TT with respect to the immune response against MenC. Additionally, immune responses with a MenACWY-TT booster dose supported the induction of immune memory after receipt of a 2-dose primary infant series.

**Studies in toddlers**

Four toddler studies were reviewed, all of which compared the immunogenicity of a single dose of MenACWY-TT with that of MenC-CRM₁₉₇/AlPO$_4$ in unprimed subjects. Three studies were conducted in toddlers aged 12 to 23 months and 1 in toddlers aged 12 to 14 months; overall, 1246 subjects in directly comparable groups were vaccinated with MenACWY-TT or MenC-CRM₁₉₇/AlPO$_4$. In all studies, immunogenicity against MenC was measured by the rSBA assay at 1 month/42 days postvaccination, whereas hSBA titers were assessed in 2 studies. In 3 studies, the percentage of vaccinated subjects with MenC rSBA titers ≥1:8 was higher in the MenACWY-TT group compared with that in the MenC-CRM₁₉₇/AlPO$_4$ group (99.7%–100% vs 97.5%–98.5%), in the fourth study (toddlers aged 12–23 months), the percentages in

| Vaccine               | Type           | Meningococcal serogroups (other antigens) | European indication, age* |
|-----------------------|----------------|------------------------------------------|---------------------------|
| Monovalent            |                |                                          |                           |
| MenAfriVac (PsA-TT)   | TT conjugate   | A                                        | Not licensed in Europe    |
| Menjugate (MenC-CRM₁₉₇ adsorbed to aluminum hydroxide) | CRM₁₉₇ conjugate | C | ≥2 mo |
| Meningitec (Men-CRM₁₉₇ adsorbed to aluminum phosphate) | CRM₁₉₇ conjugate | C | Discontinued in Europe |
| NeisVac-C (Men-TT)    | TT conjugate   | C                                        | ≥2 mo                     |
| Bexsero (MenB-4C)     | Recombinant protein | B | ≥2 mo |
| Trumena (MenB-Fhbo)   | Recombinant protein | B | ≥10 y |
| Combination           |                |                                          |                           |
| MenHibrix (HibMenCY-TT) | TT conjugate | C, Y (Hib) | Not licensed in Europe |
| Menitorix (Hib-Men-TT) | TT conjugate | C (Hib) | ≥2 mo |
| Quadrivalent          |                |                                          |                           |
| Nimenex (MenACWY-TT)  | TT conjugate   | A, C, W, Y                               | ≥6 wk                     |
| Meneocio (MenACWY-CRM₁₉₇) | CRM₁₉₇ conjugate | A, C, W, Y | ≥2 y |
| Menactra (MenACYW-D)  | D conjugate    | A, C, W, Y                               | Not licensed in Europe    |
| MenQuadrif (MenACYW-TT) | TT conjugate | A, C, W, Y | Not licensed in Europe |

CRM₁₉₇, diphtheria protein cross-reactive material 197; D, diphtheria toxin; Hib, Haemophilus influenzae type b; TT, tetanus toxoid.

*For currently available vaccines.
the MenACWY-TT group were 97.3% and 98.2% in the MenC-CRM$_{197}$/AlPO$_4$ group (Figure 3A). Evaluation of MenC rSBA GMTs showed that postvaccination levels in 3 studies were ≥2-fold higher in toddlers vaccinated with MenACWY-TT compared with those in the corresponding MenC-CRM$_{197}$/AlPO$_4$ group (range, 212–984). In the remaining study, MenC rSBA GMTs were similar across both vaccine groups in toddlers aged 12 to 23 months of age, albeit slightly higher in those who received MenACWY-TT (MenACWY-TT recipients, 829; MenC-CRM$_{197}$/AlPO$_4$ recipients, 691; Figure 3B). Two of the toddler studies also used the hSBA assay to assess MenC immunogenicity. In both studies, the percentage of subjects with postvaccination MenC hSBA titers ≥1:8 was considerably higher in the MenACWY-TT group compared with the MenC-CRM$_{197}$/AlPO$_4$ group (98.5% vs 81.9% and 99.1% vs 72.1%, respectively; Figure 3C). Correspondingly, hSBA GMTs were approximately 5- and 10-fold higher in the MenACWY-TT groups compared with their MenC-CRM$_{197}$/AlPO$_4$ counterparts (196 vs 40 and 190 vs 21, respectively; Figure 3D).

**Studies in children and adolescents**

Three studies investigating the immune response to MenACWY-TT in subjects aged ≥2 years were included in the review. A study conducted in 414 children aged 2 to 10 years compared a single dose of MenACWY-TT and MenC-CRM$_{197}$/Al(OH)$_3$. Two studies assessed the vaccines as a booster: 501 adolescents aged 10, 12, or 15 years who were previously vaccinated with a single dose of MenC-TT as toddlers received a booster dose of MenACWY-TT or MenC-TT; 293 children aged 50 to 69 months who had previously received 1 primary dose of MenACWY-TT or MenC-CRM$_{197}$/AlPO$_4$ as toddlers were administered the same vaccine as a booster dose. The percentage of subjects with postvaccination MenC rSBA titers ≥1:8 was high across all 3 studies (Figure 4A). In both the primary vaccination and the booster study conducted in children, all subjects in the MenACWY-TT and MenC-CRM$_{197}$ groups had rSBA titers ≥1:8 at 1 month. In the adolescent study, postbooster rSBA titers ≥1:8 against MenC were observed in all subjects aged 12 and 15 years and in 98.6% and 100% of subjects vaccinated with MenACWY-TT and MenC-TT, respectively, aged 10 years. Overall, MenC rSBA GMTs were also similar in MenACWY-TT and monovalent vaccine groups (Figure 4B). In both studies conducted in children, there was a ≥2-fold difference in GMT between the MenACWY-TT and MenC-CRM$_{197}$ groups, and in the adolescent study, postbooster GMTs were comparably high across all ages and vaccines. A single study reported hSBA titers. All children administered a booster dose of MenACWY-TT or MenC-CRM$_{197}$/AlPO$_4$ after receiving the same vaccine as toddlers had MenC hSBA titers ≥1:8 at 1 month (Figure 4C), whereas the postbooster hSBA GMT in subjects vaccinated with MenACWY-TT was approximately 2-fold higher than that in subjects vaccinated with MenC-CRM$_{197}$/AlPO$_4$ (Figure 4D).
Discussion

The current review of clinical studies comparing MenC immunogenicity between MenACWY-TT and monovalent MenC conjugate vaccines consistently showed that rSBA and hSBA immune response to MenC elicited by MenACWY-TT is comparable to that of monovalent MenC conjugate vaccines. The reviewed studies measured the percentage of subjects with rSBA titers ≥1:8 at approximately 1 month postvaccination.  

The dynamic nature of meningococcal disease, which varies geographically and temporally, has necessitated that vaccination programs adapt to provide rational recommendations for vaccines that address current epidemiologic trends in a given region. As shown in several countries, recent changes in the recommendations were modified from use of monovalent MenC vaccines to MenACWY vaccines in response to increased risk of MenW and MenY disease (Figure 1). Although quadrivalent vaccines provide broader serogroup coverage than monovalent vaccines against disease-causing strains including against increasingly prevalent MenW and MenY disease, it is important to confirm that optimal protection against MenC is maintained. This is particularly pertinent as vaccination programs using monovalent MenC vaccines have shown sizable decreases in the number of cases of MenC disease.

In the infant study, criteria based on the percentage of subjects with rSBA titers ≥1:8 at 1 month after a 2-dose primary schedule showed the noninferiority of MenACWY-TT to the monovalent vaccines MenC-TT and MenC-CRM197/Al(OH)3. The booster response after a further MenACWY-TT dose at age 12 months was similarly robust, with 99.8% of subjects reaching the ≥1:8 threshold. Notably, although hSBA and rSBA
The percentage of toddlers with rSBA titers ≥1:8 and hSBA GMTs, percentage of toddlers with hSBA titers ≥1:8, and hSBA GMTs. Subject had blood samples collected at 1 month (range, 21–48 days) after the second primary dose (primary ATP cohort) and booster dose (booster ATP cohorts). Panel A. Postprimary, n = 455–457; postbooster, n = 464–467. Panel B. Postprimary, n = 455–457; postbooster, n = 446–466. Panel C. Postprimary, n = 202–226; postbooster, n = 216–221. Panel D. Postprimary, n = 64–67; postbooster, n = 61–63. GMT = geometric mean titer; hSBA = serum bactericidal antibody using human complement; MenACWY-TT = meningococcal serogroups A, C, W, and Y vaccine conjugated to tetanus toxoid as a carrier protein; MenC-CRM197/Al(OH)3 = meningococcal serogroup C vaccine conjugated to the nontoxic form of diphtheria protein cross-reactive material 197 and adsorbed onto alum hydroxide; MenC-TT = meningococcal serogroup C vaccine conjugated to tetanus toxoid; rSBA = serum bactericidal antibody using baby rabbit complement.

GMTs were lower in the MenACWY-TT group at 1 month after primary vaccination, declines during the post-primary period were sharper in infants who received MenC-TT or MenC-CRM197/Al(OH)3 so that GMTs were similar among all 3 vaccine groups by the prebooster time point.

In the 4 toddler studies, the percentage of subjects vaccinated with MenACWY-TT with rSBA titers ≥1:8 at 1 month (42 days for 1 study) after a single primary dose was comparable to, and in some studies potentially higher than, that observed in the corresponding MenC-CRM197/Al(OH)3 group.61–63,67 Two of these toddler studies assessed the non-inferiority of MenACWY-TT to MenC-CRM197/Al(OH)3 for MenC immunogenicity based on group differences in the percentages of subjects with MenC rSBA titers ≥1:8; in both studies, noninferiority of MenACWY-TT was confirmed.61,67 A strong immune response against MenC was observed in children aged 2 to 10 years after a single primary MenACWY-TT or MenC-CRM197/Al(OH)3 dose, with all subjects reaching the ≥1:8 rSBA threshold.54 Noninferiority of MenACWY-TT to MenC-CRM197/Al(OH)3 for immunogenicity against MenC was confirmed by comparison of a predefined vaccine response based on rSBA titer increases.

The booster response to MenACWY-TT in older children and adolescents was compared with monovalent MenC vaccines in two studies.65,66 When children aged 5 years received a booster dose with the same vaccine used for primary vaccination as toddlers, 100% of subjects in the MenACWY-TT and MenC-CRM197/Al(OH)3 groups had an rSBA titer ≥1:8 at 1 month postbooster.65 In the adolescent study, subjects vaccinated with MenC-TT as toddlers received a booster dose of either MenC-TT or MenACWY-TT; booster rSBA responses to both vaccines were robust, with 98.6% to 100% of subjects aged 10 years and all subjects aged 12 and 15 years showing an rSBA titer ≥1:8 at 1 month.66
The reviewed studies also reported rSBA GMTs.\textsuperscript{60–67} Within each study, the magnitude of rSBA GMT against serogroup C in the MenACWY-TT compared with monovalent MenC vaccine groups varied by <3-fold. There was no apparent pattern regarding which vaccine type gave rise to higher MenC rSBA GMTs: in 5 studies, levels were higher in the MenACWY-TT–vaccinated groups (i.e., all toddler studies and the study in 5-year-olds),\textsuperscript{61–63,65,66} and in 3 studies, levels were higher in the monovalent vaccinated groups (i.e., the infant study, the adolescent study, and the study in 2–10-year-olds).\textsuperscript{60,64,66} The study in adolescents used MenC rSBA GMT ratio to assess noninferiority of MenACWY-TT to MenC-TT at 1 month;
noninferiority was shown for the 12-year-olds (GMT ratio, 0.88 [95% CI: 0.67–1.15]) but not for the 10- (GMT ratio, 0.80 [95% CI: 0.54–1.18]) or 15-year (GMT ratio, 0.81 [95% CI: 0.61--1.06]) age group. However, these differences are minor and not likely to be of clinical significance.

The hSBA assessments were reported in four of the reviewed studies, supporting the similar trends observed with MenC rSBA assessments. In the infant study, the percentage of subjects with MenC hSBA titers ≥1:8 after primary vaccination generally reflected the corresponding rSBA percentages, whereas that of postbooster hSBA titers ≥1:8 appeared to be slightly more uniform across vaccine groups. Similarly, the pattern of variation in hSBA GMTs among infant vaccine groups at the post-primary time point was consistent with that observed in rSBA GMTs, whereas postbooster hSBA GMTs were more uniform than their rSBA counterparts. In both toddler studies that assessed hSBA titers, the magnitude of difference between MenACWY-TT and MenC-CRM49/AlPO4 in the percentages of subjects with titers ≥1:8 was notably larger in hSBA compared with rSBA assays (hSBA 16.6% vs rSBA 2.2%, and hSBA 27.0% vs rSBA 1.5%, respectively). However, the ranking of vaccine groups did not differ between SBA assay types; in each study, both assays consistently resulted in higher percentages for the MenACWY-TT cohorts.

Monovalent MenC conjugate vaccines were initially licensed based on strong postvaccination immune responses shown in the rSBA assay. Subsequent postlicensure data from the United Kingdom indicated that the percentages of subjects with rSBA titers ≥1:8 were more consistent with observed effectiveness than the percentages with titers ≥1:128. Accordingly, rSBA titers ≥1:8 have been widely accepted as correlate of protection for MenC conjugate vaccines. Although studies have generally found that higher titers are measured by rSBA compared with hSBA assays, reasonable correlations between rSBA and hSBA titers have been shown for MenC vaccines. However, the licensure of MenACWY-TT was primarily based on rSBA assay results, although some hSBA assay data were included. Data, including that from postlicensure effectiveness studies, support the use of rSBA for this vaccine, and data from recent MenACWY-TT clinical studies suggest that hSBA assays may be less relevant.

The strengths of our review include the large number of studies, with >4000 subjects, and the range of age groups assessed. However, our review was limited to comparing SBA assay results within studies. As aspects of the protocols varied, comparison of SBA assay results across different laboratories is difficult. Even when a standardized method exists, such as the widely adopted rSBA assay standard for serogroups A and C published in 1997, interlaboratory variation remains significant. Additionally, this review did not consider the immunogenicity of the other serogroups in the vaccine (i.e., A, W, and Y). In the included studies, robust immune responses to serogroups A, W, and Y were observed following primary MenACWY-TT vaccination, similar to the serogroup C response, rSBA and hSBA antibody levels against A, W, and Y declined during the post-primary period and responded strongly post-booster. Differences in immune responses based on 1- versus 2-dose schedules were also not considered. Of note, MenACWY-TT was chosen for this comparison because of the availability of clinical data across age groups; however, this review did not consider comparative MenC responses to other quadrivalent vaccines.

Only short-term MenC antibody responses were considered in this current analysis. However, long-term antibody persistence following MenACWY-TT and MenC-CRM vaccination has been recently reported. Ten years after primary vaccination with 1 dose of MenACWY-TT or MenC-CRM as toddlers, 57% of MenACWY-TT recipients and 86% of MenC-CRM recipients had MenC rSBA titers ≥1:8. In the same study, subjects with a suboptimal serogroup C response to primary MenACWY-TT or MenC-CRM vaccination received a booster dose of MenC-CRM by Year 5; in these subjects, percentages with MenC rSBA titers ≥1:8 at Year 10 were 98% and 90%, respectively. Overall, the percentage of subjects with a MenC rSBA titer ≥1:8 at Year 10 was 83% in the MenACWY-TT primary vaccine group and 88% in the MenC-CRM primary vaccine group. Notably, all 4 subgroups showed a robust response to booster vaccination with MenACWY-TT at Year 10, with 100% of subjects having a MenC rSBA titer ≥1:8 at 1 month post-booster. In another persistence study, 6 years after booster vaccination of 5-year-old children with MenACWY-TT or MenC-CRM (i.e., 10 years after primary vaccination with the same vaccine), 72% of MenACWY-TT recipients and 65% of MenC-CRM recipients had MenC rSBA titers ≥1:8.

In conclusion, MenC immune responses induced by MenACWY-TT are robust and generally comparable to monovalent MenC conjugate vaccines, supporting changes from monovalent MenC to MenACWY vaccination recommendations. The broad serogroup protection provided by MenACWY-TT, as well as its licensure from 6 weeks of age, together suggest that MenACWY-TT is a suitable option to provide protection against many of the common disease-causing meningococcal serogroups across at-risk age-based populations.

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LS, JF, and KY are employees of Pfizer Inc and may have stock or stock options.

MK is a principal investigator for clinical studies and has been an advisor to and made presentations during industry symposia for GSK, Pfizer Inc, Baxter, Novartis, AstraZeneca, MedImmune, SPSM, Sanofi, MSD, and Janssen.

FM-T has received compensation from GSK, Pfizer Inc, Sanofi Pasteur, MSD, Seqirus, and Janssen for taking part in advisory boards and expert meetings and for acting as a speaker in congresses outside the scope of the submitted work. FM-T has also acted as principal investigator in randomized controlled trials of the above-mentioned companies as well as Ablynx, Regeneron, Roche, Abbott, Novavax, and MedImmune, with honoraria paid to his institution. FM-T received support for research activities from the Instituto de Salud Carlos III (Proyecto de Investigación en Salud, Acción Estratégica en Salud): Fondo de Investigación Sanitaria (FIS; PI070069/PI1000540/PI1601569/PI1901090) del plan nacional de I+D+i and ‘fondos FEDER’, and 2016-PG071 Consolidación e Estructuración REDES 2016GI-1344 G3VIP (Grupo Gallego de Genética Vacunas Infecciones y Pediatría, ED341D R2016/021).
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