Clinical Development of a Meningococcal Group A, C, W, and Y Tetanus Toxoid Conjugate Vaccine

Lidia C. Serra,[1] Laura J. York,[2,*] Paul Balmer,[1] John L. Perez,[3] France Laudat,[4] Susan Mather,[5] Matthew Marsden,[6] Chris Webber[7]

[1]Pfizer Global Medical Development and Scientific/Clinical Affairs, Vaccines, Pfizer Inc, Collegeville, PA, USA; [2]Pfizer Vaccine Medical Development, Scientific & Clinical Affairs, Collegeville, PA, USA; [3]Pfizer Vaccines Clinical Research, Collegeville, PA, USA; [4]Pfizer Clinical Research and Development, Paris, France; [5]Worldwide Safety and Regulatory, Pfizer Inc, Collegeville, PA, USA; [6]Worldwide Safety and Regulatory, Pfizer Ltd, Sandwich, UK; [7]Pfizer Vaccine Clinical Research and Development, Pearl River, NY, USA

*Presenting author

For more information please contact:
Laura J. York
Pfizer Vaccine Medical Development, Scientific & Clinical Affairs
Collegeville, PA, USA
Laura.York@pfizer.com

INTRODUCTION

- Meningococcal disease is a global concern, with a high risk of mortality and morbidity even in previously healthy individuals.[1,2]
- The majority of invasive meningococcal disease is caused by groups A, B, C, W, X, and Y[3]; however, group prevalence varies temporally, geographically, and by age group.[4]
- Although the majority of meningococcal disease in Europe is currently caused by groups B and C (collectively accounting for 75% of cases in 2015), an increase in group W disease has been observed since 2011 (2.3% and 11.4% of cases in 2011 and 2015, respectively).[5]
- Quadrivalent meningococcal vaccines can provide protection in countries where several groups predominate or if new vaccine-type groups emerge.[6,7]
- MenACWY-TT (Nimenrix®; Pfizer Ltd; Sandwich, Kent, UK) is a meningococcal group A, C, W, and Y tetanus toxoid conjugate vaccine[8] and the only quadrivalent conjugate vaccine licensed in the European Union in children <2 years old.

METHODS

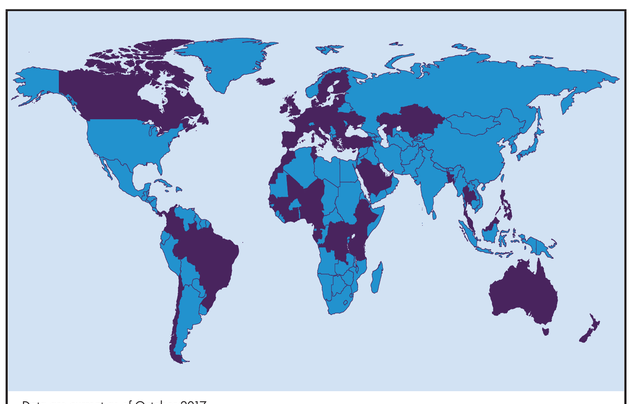
- The clinical study programme supporting licensure of MenACWY-TT is summarised based on the Summary of Product Characteristics.[8]

RESULTS

Licensure and Dosing

- MenACWY-TT is licensed in the European Union and 43 additional countries, including those in Africa, the Americas, Asia, Eastern Europe, the Middle East, and Oceania **(Figure 1)**.
- In the European Union and other countries, MenACWY-TT is administered intramuscularly in a 2+1 schedule in infants beginning vaccination from 6–12 weeks of age. MenACWY-TT is also licensed as a single dose in children (aged ≥12 months), adolescents, and adults.
- A booster MenACWY-TT dose may be given at ≥12 months of age in those previously vaccinated with a conjugated or polysaccharide meningococcal vaccine.

Figure 1. Global Registration Status of MenACWY-TT



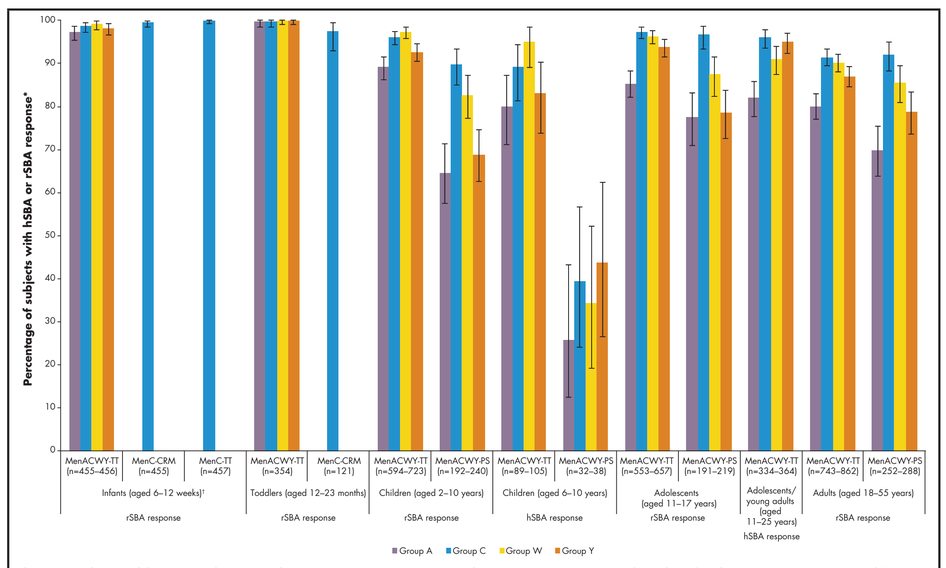
Data are current as of October 2017.
MenACWY-TT is licensed for use in infants as a 2+1 dose series in the European Union, Hong Kong, Kuwait, Qatar, United Arab Emirates, Ghana, and Nigeria. In the clinical study in infants, MenACWY-TT was administered at 6–12 weeks of age, the second dose was given after an interval of 2 months, and the booster dose was administered at approximately 12 months of age. Purple indicates country in which MenACWY-TT is licensed.

Immunogenicity

- Across studies and age groups, MenACWY-TT elicited comparable antibody responses against all groups compared with other meningococcal vaccines (meningococcal C vaccines in infants/toddlers and quadrivalent meningococcal vaccines in other age groups; **Figure 2**).
- Robust antibody responses against all 4 meningococcal groups are observed following administration of a booster dose of MenACWY-TT at approximately 12 months of age in infants previously vaccinated with 2 MenACWY-TT doses beginning at 6–12 weeks of age.
  - Booster doses of MenACWY-TT in individuals ≥12 months of age who previously received a monovalent or quadrivalent conjugate meningococcal vaccine resulted in robust anamnestic responses to the antigens in the priming vaccine.
- Persistence of antibody responses up to 5 years after administration of the MenACWY-TT primary series has been demonstrated across age groups **(Figure 3)**.
  - Waning of serum bactericidal titers against meningococcal group A is observed when assessed with serum bactericidal assay using human complement (hSBA); the clinical relevance of this observation is unknown, but consideration should be made to administering a booster dose of MenACWY-TT in individuals at risk of meningococcal group A exposure who received a MenACWY-TT dose >1 year prior.

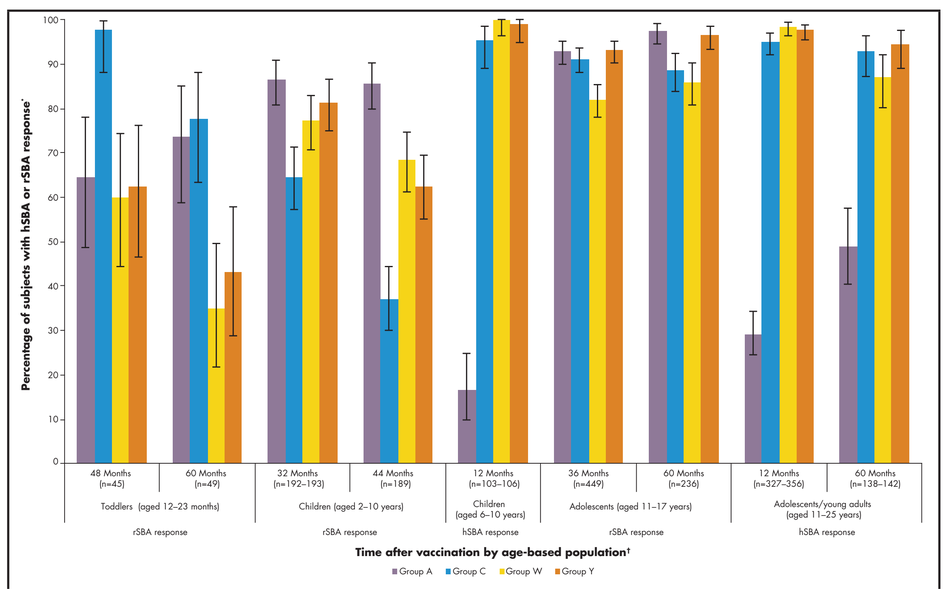
RESULTS (continued)

Figure 2. Immune Response to MenACWY-TT Across Clinical Studies and Age Groups[8]



hSBA=serum bactericidal assay using human complement; MenACWY-PS=meningococcal A, C, W, Y vaccine conjugated to polysaccharide; MenC-CRM=meningococcal C vaccine conjugated to CRM; MenC-TT=meningococcal C vaccine conjugated to tetanus toxoid; rSBA=serum bactericidal assay using rabbit complement.
*hSBA response=hSBA titres ≥1:8; rSBA response=rSBA titres ≥1:32 for initially seronegative subjects (rSBA titre <1:8) or ≥4-fold increase in rSBA titres from pre- to postvaccination for initially seropositive subjects (rSBA titre ≥1:8).
†Data for 1 month after vaccination 2 are shown.

Figure 3. Persistence of Antibody Response to MenACWY-TT Across Age Groups[8]



hSBA=serum bactericidal assay using human complement; MenACWY-PS=meningococcal A, C, W, Y vaccine conjugated to polysaccharide; MenC-CRM=meningococcal C vaccine conjugated to CRM; MenC-TT=meningococcal C vaccine conjugated to tetanus toxoid; rSBA=serum bactericidal assay using rabbit complement.
*hSBA response=hSBA titres ≥1:8; rSBA response=rSBA titres ≥1:32 for initially seronegative subjects (rSBA titre <1:8) or ≥4-fold increase in rSBA titres from pre- to postvaccination for initially seropositive subjects (rSBA titre ≥1:8).
†Age at vaccination indicated in parentheses.

Concomitant Administration With Other Vaccines

- MenACWY-TT can be concomitantly administered with other commonly administered vaccines across age groups **(Table 1)**.

Table 1. Administration of MenACWY-TT With Concomitant Vaccines

	Infants	≥1 Year Old	Second Year of Life
HAV		•	
HBV		•	
MMR		•	
MMR/varicella		•	
PCV10	•	•	
PCV13			•
Tdap*			•
Tdap/HBV/IPV/Hib	•		
Influenza vaccine†		•	

HAV=hepatitis A vaccine; HBV=hepatitis B vaccine; MMR=mumps/measles/rubella vaccine; PCV10=10-valent pneumococcal conjugate vaccine; PCV13=13-valent pneumococcal conjugate vaccine; Tdap=diphtheria/tetanus/acellular pertussis vaccine; Tdap/HBV/IPV/Hib=combined diphtheria, tetanus, acellular pertussis/hepatitis B/inactivated polio virus/*Haemophilus influenzae* type B vaccine.
*Also includes Tdap combination vaccines.
†Unadjuvanted seasonal vaccine.

Safety

- The safety of single-dose MenACWY-TT has been evaluated in a clinical study population that included 3079 toddlers (aged 12–23 months), 1899 children (aged 2–10 years), 2317 adolescents (11–17 years old), 2326 adults (18–55 years old), and 274 older adults (≥56 years old).
- In subjects from 6 weeks to 55 years of age, MenACWY-TT had an acceptable and consistent safety and reactogenicity profile **(Table 2)**.
  - Very common adverse reactions (frequency of ≥1/10) included local (pain, redness, and swelling at the injection site) and systemic (drowsiness, fatigue, fever, headache, irritability, and lost appetite) events.
- The safety profile in adults aged >55 years was similar to that of younger adults.
- Safety has also been assessed in 1052 infants receiving ≥1 MenACWY-TT dose beginning at 6–12 weeks of age and in 1008 toddlers (aged 12–14 months) who received a booster dose.
  - In toddlers 12–14 months of age who received 2 doses given 2 months apart, the first and second MenACWY-TT dose were associated with similar reactogenicity.

Table 2. MenACWY-TT Safety Profile From Clinical Studies in Individuals Aged 6 Weeks to 55 Years and Postmarketing Experience

Adverse Reaction	Frequency
Metabolism and nutrition disorders	
Appetite lost	Very common
Psychiatric disorders	
Irritability	Very common
Insomnia	Uncommon
Crying	Uncommon
Nervous system disorders	
Drowsiness	Very common
Headache	Very common
Hypoaesthesia	Uncommon
Dizziness	Uncommon
Gastrointestinal disorders	
Diarrhoea	Common
Vomiting	Common
Nausea	Common*
Skin and subcutaneous tissue disorders	
Pruritus	Uncommon
Rash	Uncommon†
Musculoskeletal and connective tissue disorders	
Myalgia	Uncommon
Pain in extremity	Uncommon
General disorders and administration site conditions	
Fever	Very common
Swelling at injection site	Very common
Pain at injection site	Very common
Redness at injection site	Very common
Fatigue	Very common
Injection site haematoma	Common*
Malaise	Uncommon
Injection site induration	Uncommon
Injection site pruritus	Uncommon
Injection site warmth	Uncommon
Injection site anaesthesia	Uncommon
Extensive limb swelling at injection site‡	Unknown

Adverse reactions are reported according to the following frequency definitions: very common, ≥1/10; common, ≥1/100 to <1/10; uncommon, ≥1/1000 to <1/100.
*In infants, the frequency was uncommon.
†In infants, the frequency was common.
‡Identified through postmarketing reports and was frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb.

CONCLUSIONS

- The MenACWY-TT clinical study programme demonstrated the consistency of vaccine-induced immune responses and the safety and tolerability across age groups.
- These data support licensure and recommendations for use of MenACWY-TT to prevent disease due to meningococcal groups A, C, W, and Y across all ages.

FUNDING SOURCE

Pfizer Inc.

DISCLOSURES

All authors are employees of Pfizer Inc.

ACKNOWLEDGEMENTS

Editorial support was provided by Tricia Newell, PhD, of Complete Healthcare Communications, LLC (West Chester, PA, USA) and funded by Pfizer Inc.

REFERENCES

1. Pace D and Pollard AJ. *Vaccine*. 2012;30(suppl 2):B3-9.
2. McIntosh ED, et al. *Ther Adv Vaccines*. 2015;3(1):13-23.
3. Harrison OB, et al. *Emerg Infect Dis*. 2013;19(4):566-573.
4. Rouphael NG and Stephens DS. *Methods Mol Biol*. 2012;799:1-20.
5. European Centre for Disease Prevention and Control. Surveillance Atlas of Infectious Diseases. Available at: https://ecdc.europa.eu/en/surveillance-atlas-infectious-diseases. Accessed October 16, 2017.
6. Bermal N, et al. *Hum Vaccin*. 2011;7(2):239-247.
7. Cohn A and MacNeil *J. Infect Dis Clin North Am*. 2015;29(4):667-677.
8. NIMENRIX (meningococcal polysaccharide serogroups A, C, W-135 and Y conjugate vaccine). Summary of Product Characteristics, Pfizer Limited, Sandwich, Kent, UK, 2017.

Presented at Meningitis Research Foundation Conference 2017; 14–15 November, 2017; London, UK.