

****New release March 2009****

DiseaseINFOPACK: Non-typeable *Haemophilus influenzae* (CAT: VADIP011)

Proposal No/#PO	:	[Enter client specific #PO]
Product Name	:	Comprehensive review/analysis of Non-typeable <i>Haemophilus influenzae</i> in AOM
Project Initiation Date	:	n/a
Billable days	:	n/a
Initiator(s)	:	[Enter client name, function and address]
Therapeutic Area	:	<i>Non-typeable Haemophilus influenzae (NTHi), Acute Otitis Media (AOM)</i>
Product (if applicable)	:	CAT No: VADIP011, published March 2009

Background

Non-typeable *Haemophilus influenzae* (NTHi) is a gram-negative bacterium which is a major cause of acute otitis media (AOM) and invasive infections such as bacteremia and pneumonia. The pathogen can also cause meningitis in children and adults. In the US, the Centers For Disease Control (CDC) and Prevention estimates that *H. influenzae* caused greater than 4,500 cases of invasive disease resulting in 405 deaths in 2007 of which around 60% of case were due to NTHi¹. For AOM, current knowledge of the natural infection and pathogenesis of NTHi is limited but becoming an important new research area for vaccine manufacturers.

This **DiseaseINFOPACK** report is an expert secondary review of the current literature (March 2008) providing the reader with a detailed overview of the pathogen, its epidemiology, through to its clinical impact in major clinical manifestations. The report also includes a focus on the changing microbiology of AOM and the relative importance of NTHi according to currently available journal literature per country. An assessment of the AOM/NTHi dynamics with regard to current and new *pneumococcal* vaccines e.g. GSK Biological's Synflorix is also included.

¹ Centers for Disease Control and Prevention. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *H. influenzae*, 2007. Available at: <http://www.cdc.gov>. Accessed: March 2009

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PAGES: 31 detailed MS PowerPoint slides, fully referenced/sourced. Available in .pdf form

PROJECT METHODOLOGY:

VacZine Analytics has conducted a comprehensive secondary research to review all available information regarding pre-pandemic and pandemic specific vaccines in major EU/Canada and US markets. Source materials used are literature articles, government websites, medical bodies and associations, conference proceedings etc.

Published research from **VacZine Analytics** has also been utilised.

BIBLIOGRAPHY

1. Barbosa-Cesnik C et al. Predictors for *Haemophilus influenzae* colonization, antibiotic resistance and for sharing an identical isolate among children attending 16 licensed day-care centers in Michigan. *Pediatr Infect Dis J.* 2006 Mar;25(3):219-23
2. Wang SR et al. Low rate of nasopharyngeal carriage and high rate of ampicillin resistance for *Haemophilus influenzae* among healthy children younger than 5 years old in northern Taiwan. *J Microbiol Immunol Infect.* 2008 Feb;41(1):32-40
3. Casey JR & Pichichero ME. Changes in frequency and pathogens causing acute otitis media in 1995-2003. *Pediatr Infect Dis J.* 2004 Sep;23(9):824-8
4. Block SL et al. Community-wide vaccination with the heptavalent pneumococcal conjugate significantly alters the microbiology of acute otitis media. *Pediatr Infect Dis J.* 2004 Sep;23(9):829-33.
5. Centers for Disease Control and Prevention. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *H. influenzae*, 2007. Available at: <http://www.cdc.gov>. Accessed: March 2009
6. German Federal Health Monitoring. Diagnostic data of the hospitals starting from 2000. Available at: <http://www.gbe-bund.de>. Accessed: March 2009
7. EU-IBIS Network. *Haemophilus influenzae* in Europe 2006. Available at: www.euibis.org. Accessed: March 2009
8. Nigrovic LE et al. Children with bacterial meningitis presenting to the emergency department during the pneumococcal conjugate vaccine era. *Acad Emerg Med.* 2008 Jun;15(6):522-8.
9. Moxon ER et al. *Haemophilus influenzae* biofilms: hypothesis or fact? *Trends Microbiol.* 2008 Mar;16(3):95-100
10. Moriyama S et al. Formation of biofilm by *Haemophilus influenzae* isolated from pediatric intractable otitis media. *Auris Nasus Larynx.* 2009 Jan 7
11. Eskola J et al. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. *N Engl J Med.* 2001 Feb 8;344(6):403-9
12. Number of People with Care for Selected Conditions by Type of Service: United States, 2006. Agency for Healthcare Research and Quality, Rockville. Available at: <http://www.meps.ahrq.gov/>. Accessed: 5 March 2009
13. Soni, A. Ear Infections (Otitis Media) in Children (0-17): Use and Expenditures, 2006. Statistical Brief #228. December 2008. Agency for Healthcare Research and Quality, Rockville.
14. Schnabel E. Burden of otitis media and pneumonia in children up to 6 years of age: results of the LISA birth cohort. *Eur J Pediatr.* 2009 Jan 23.
15. Garcés-Sánchez M et al. [Epidemiology and burden of acute otitis media in Valencia (Spain)] *An Pediatr (Barc).* 2004 Feb;60(2):125-32.
16. Number of People with Care for Selected Conditions by Type of Service: United States, 1997-2006. Agency for Healthcare Research and Quality, Rockville. Available at: <http://www.meps.ahrq.gov/>. Accessed: 5 March 2009
17. Sox CM et al. Trends in otitis media treatment failure and relapse. *Pediatrics.* 2008 Apr;121(4):674-9.
18. Dowell SF et al. Otitis media—principles of judicious use of antimicrobial agents. *Pediatrics.* 1998; 101(suppl) :165
19. Pichichero ME et al. Pathogens causing recurrent and difficult-to-treat acute otitis media, 2003-2006. *Clin Pediatr (Phila).* 2008 Nov;47(9):901-6.
20. Zielnik-Jurkiewicz B and Bielicka A. [Evaluation of antibiotic resistance in material isolated from the middle ear in children with acute otitis media not responding to standard antibiotic treatment.] *Otolaryngol Pol.* 2007;61(5):892-7
21. Pichichero ME and Casey JR. Emergence of a multiresistant serotype 19A pneumococcal strain not included in the 7-valent conjugate vaccine as an otopathogen in children. *JAMA.* 2007 Oct 17;298(15):1772- 8
22. Mahjoub-Messai F et al. [Epidemiology of acute otitis media caused by *Streptococcus pneumoniae*: emergence of serotype 19A]. *Arch Pediatr.* 2008 Nov;15(11):1713-6
23. Kvaerner KJ and Helgaker AB. Otitis media referrals - the general practitioner perspective. *Int J Pediatr Otorhinolaryngol.* 2007 Aug;71(8):1219-24.
24. Prymula R et al. Pneumococcal capsular polysaccharides conjugated to protein D for prevention of acute otitis media caused by both *Streptococcus pneumoniae* and non-typable *Haemophilus influenzae*: a randomised double-blind efficacy study. *Lancet.* 2006 Mar 4;367(9512):740-8.
25. Sakran W et al. Acute otitis media in infants less than three months of age: clinical presentation, etiology and concomitant diseases. *Int J Pediatr Otorhinolaryngol.* 2006 Apr;70(4):613-7.
26. Arguedas A et al. A randomized, multicenter, double blind, double dummy trial of single dose azithromycin versus high dose amoxicillin for treatment of uncomplicated acute otitis media. *Pediatr Infect Dis J.* 2005 Feb;24(2):153-61
27. Rosenblüt A et al. Penicillin resistance is not extrapolable to amoxicillin resistance in *Streptococcus pneumoniae* isolated from middle ear fluid in children with acute otitis media. *Ann Otol Rhinol Laryngol.* 2006 Mar;115(3):186-90.
28. Gené A et al. [Etiology of acute otitis media in a children's hospital and antibiotic sensitivity of the bacteria involved]. *Enferm Infecc Microbiol Clin.* 2004 Aug-Sep;22(7):377-80.
29. Minnesota surveillance statistics. *Haemophilus influenzae* Invasive Disease, 2007. Available at: <http://www.health.state.mn.us/>. Accessed March 2009.

30. Tsang RS. Characterization of invasive Haemophilus influenzae disease in Manitoba, Canada, 2000-2006: invasive disease due to non-type b strains. Clin Infect Dis. 2007 Jun 15;44(12):1611-4.
31. Continued Shortage of Haemophilus influenzae Type b (Hib) Conjugate Vaccines and Potential Implications for Hib Surveillance --- United States, 2008. MMWR November 21, 2008 / 57(46);1252-1255
32. Satola SW et al. Association of IS1016 with the hia adhesin gene and biotypes V and I in invasive non-typeable Haemophilus influenzae. Infect Immun. 2008 Nov;76(11):5221-7.
33. European Medicines Agency. Committee for medicinal products for human use summary of positive opinion for Synflorix. Available at: <http://www.emea.europa.eu>. Accessed: March 2009.
34. NCT00466947: COMPAS (Clinical Otitis Media & Pneumonia Study): Pneumonia & AOM Efficacy Study of the Pneumococcal Conjugate Vaccine. Available at: clinicaltrials.gov. Accessed: March 2009.
35. NCT00839254: Impact on Carriage, Acute Otitis Media, Immuno & Safety of GSK Biologicals' Pneumococcal Conjugate Vaccine 1024850A. Available at: clinicaltrials.gov. Accessed: March 2009.

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About VacZine Analytics:

VacZine Analytics is a new strategic research agency based in the United Kingdom. Its aim is to provide disease and commercial analysis for the vaccine industry and help build the case for developing new vaccines and biologics.

For more information please visit our website www.vacZine-analytics.com

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