

Clostridium difficile vaccines: multipronged US-biased strategy to reduce economic burden

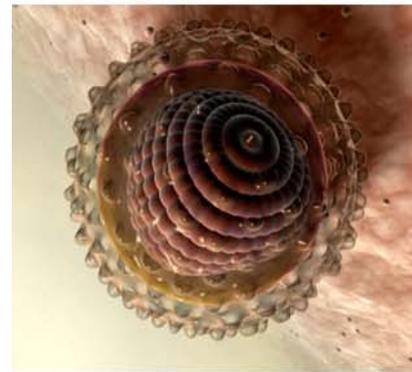
LONDON, UK----17th December 2013----ExpertREACT. With a 20% rise in US cases between 2006-2011 (AHRQ data) and an estimated 96% of costs attributed to prolongation of hospitalization, C.diff exerts a multibillion dollar economic burden (est \$4.8bn/yr in US alone). The case for vaccine adoption is strong but less so in the EU.

A vaccine to reduce the morbidity and economic burden associated with *Clostridium difficile* infection (**CDI**) is urgently required. In August 2013, Sanofi Pasteur announced the start of a Phase III trial “Cdiffense” (NCT01887912) evaluating the efficacy of a C.diff toxoid vaccine for the prevention of primary CDI. The vaccine, given as a series of three IM injections (0, 7, & 30 days), is a purified preparation of C.diff toxoids A and B which should confer antibody based protection against toxin mediated disease. Potential target populations for the vaccine are adults with planned hospitalization, LTCF residents and adults with co-morbidities requiring frequent/prolonged antibiotic use **(1)**. The trial is enrolling ~15,000 adults aged >50 yrs, at 200 sites across 17 countries, who are at increased risk of CDI due to planned or previous hospital in-patient admission with a stay of >=72 hours **(2)**. The trial will take approximately 4.5 years based on a primary completion date of December 2017, suggesting approval could be granted in early 2019. Pfizer and Valneva (formerly Intercell) also have C.diff vaccines in earlier clinical development.

The ideal C.diff vaccine should be cost-effective by reducing hospitalization costs, although this depends on C.diff epidemiology and hospital costs which vary by country, region and hospital. **VacZine Analytics** estimates that ~75% of the total CDI cases in the major markets 2013 occurred in the US, which has the greatest need for a vaccine given federally co-ordinated efforts to reduce the incidence of CDI appear to be failing **(3)**. US CDI incidence rates are now comparable to rates in the UK from 2004-2007, which triggered government mandated infection control policies such as cohort wards and antibiotic usage control. Although C.diff infection control has been successful in the UK, achieving a similar outcome may be more challenging in the fragmented US healthcare system. CDI, however, may become part of the Centers for Medicare & Medicaid Services (CMS) Hospital Value-Based Purchasing (VBP) Program in 2017, meaning financial penalties will be imposed on hospitals with high CDI incidence rates **(4)**. Financial penalties will likely increase hospital investment in CDI control programs and may also accelerate adoption of a vaccine. In Europe, CDI incidence rates are rising and recognizing the high burden of CDI, the EU Parliament adopted a resolution in October 2013 that calls for C.diff, which accounts for a ~5 percent of all healthcare-associated infections in Europe, to be placed near the top of the political agenda **(5)**. EU CDI incidence rates, however, appear to be lower than in the US and unless there is a substantial rise in incidence rates, it is possible European countries will not increase investment in C.diff infection control interventions, including vaccines. Demonstrating vaccine cost-effectiveness in Europe may also be more challenging especially for a vaccine that does not confer a “herd effect”.

In an updated **MarketVIEW** analysis **(6)**, **VacZine Analytics** has quantified the market for C.diff vaccines in five target populations. Elective hospital admissions, with patients vaccinated as part of pre-operative care, are modelled as the principal target population with commercial potential quantified based on detailed analysis of US and England hospital discharge data. However, vaccination of these elective patients alone may not significantly reduce the burden of CDI acquired in the community since persons admitted to hospital on an emergency basis will not be protected. Therefore vaccination of residents of LTCFs, also at risk of CDI due to advanced age, co morbidities, antibiotic use and high-level exposure present an additional opportunity to reduce CDI burden.

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Elderly persons living outside LTCFs may also be at risk of CDI due to multiple chronic conditions (e.g. diabetes and heart disease) or a single co morbidity (e.g. melanoma or lymphoma) which increase the likelihood of healthcare exposure and/or antibiotic use, which again are both major CDI risk-factors.

Overall, it appears that a multipronged vaccination strategy which targets multiple groups with an emphasis on the US is the way forward for Sanofi. With *Staphylococcal* and *Pseudomonal* vaccines suffering setbacks C.diff is more likely to become the first nosocomial vaccine.

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References and Notes:

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