EMGM –The European Meningococcal Disease Society

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Statement of the EMGM Society on meningococcal disease surveillance after licensure and implementation of vaccination with Bexsero™ in European countries

The European Meningococcal Disease Society (EMGM Society, www.emgm.eu) was founded in June 2005 as a forum for collaboration between the European Reference Laboratories for Meningococci and infectious disease epidemiologists. The EMGM society succeeded the previous European Monitoring Group on Meningococci, which for many years provided Europe with epidemiological data on meningococcal disease.

The EMGM Society has been following the development of protein based vaccines directed against meningococcal group B disease with great interest. Novartis very recently received a positive opinion of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) for its multicomponent protein vaccine Bexsero™. Market authorisation of Bexsero has recently been granted by the European Commission. To our knowledge National immunization technical advisory Groups (NITAG) in many countries have started the evaluation process towards a possible recommendation. Other manufacturers are continuing to develop further meningococcus B vaccines.

It is not the task of the EMGM Society to offer a particular position on the use of Bexsero™. However, Bexsero™ is a new generation vaccine based on several bacterial proteins and as such provides particular challenges to laboratory surveillance. The presence and/or expression of vaccine antigens are variable in the meningococcus, and not all invasive meningococcal serogroup B strains will be covered by the vaccine. Furthermore, vaccine pressure might have considerable effects on the composition of meningococcal clones and lineages, hypothetically to the extent that variants not covered by the vaccine might emerge and spread.

Thus, while the development of Bexsero™ is a major achievement towards the goal of preventing invasive meningococcal disease due to the predominant serogroup in Europe, we believe that for this particular vaccine, detailed post-licensure laboratory surveillance must be assured. This surveillance should ideally be implemented according to uniform standards throughout Europe. The EMGM board and working groups wish to bring to the attention of decision makers in Europe that countries should in particular address the following three aspects:

1. **Molecular Typing**: To monitor vaccine induced changes in invasive meningococcal strains, molecular typing of vaccine antigen encoding genes must be provided by reference laboratories [1]. Furthermore, to detect potential changes in the bacterial population, the multilocus sequence type of invasive isolates must be determined for a representative sample of strains [2]. Countries planning to introduce the vaccine should provide financial resources to ensure molecular typing for at least five years following broad introduction of the vaccine. Whole genome sequencing is now an option to obtain the necessary data by a single sequencing approach that may be considered [3,4], although it is only available at specialized laboratories to date.
2. **Antigen Expression Analysis:** The Meningococcal Antigen Typing System (MATS) provided by Novartis is currently the sole validated and reliable instrument to obtain expression data for three antigens (fHbp, NhbA, and NadA), which is of pivotal importance for assessment of vaccine strain coverage [5–7]. Without this tool, harmonized assessment of strain coverage in European countries will not be possible. Therefore, the unrestricted availability of MATS for European countries must be guaranteed. The producer of the kit should be pledged to reliably deliver the assay to national reference laboratories for at least three years after implementation of the vaccine. Due to the fact that the assay is provided by the manufacturer of the vaccine, reference laboratories should develop alternative assays to secure assay supply.
3. **Serological analyses:** Possible vaccine failures, i.e. vaccinated cases suffering from meningococcal group B disease, may be caused either by insufficient antibody titers due to primary vaccine failure or waning immunity or by disease isolates that do not bind vaccine-induced bactericidal antibodies . Thus vaccine specific antibody titers need to be determined in acute sera of such patients. Only the serum bactericidal assay using human complement can provide reliable data serving as a surrogate of protection [8]. However, very few laboratories in Europe are able to conduct this delicate test. Thus countries implementing serogroup B meningococcal vaccination are strongly advised to establish an operating procedure for testing acute serum samples of vaccinated serogroup B cases either in a national laboratory or by shipping to a qualified laboratory in a neighbouring country.

The EMGM advises decision makers to consider these requirements during the process of evaluation.

Signed by

President: Ulrich Vogel, Germany; Vice President: Paola Stefanelli, Italy; Secretary: Georgina Tzanakaki, Greece; Treasurer: Steve Gray

Conveners of EMGM Working Groups: Arie van der Ende, the Netherlands; Ray Borrow, UK; Ian Feavers, UK; Martin Maiden, UK; Muhamed-Kheir Taha, France; Julio Vázquez, Spain; Caroline Trotter, UK; Ed Kaczmarski, UK; Sigrid Heuberger, Austria; Wiebke Hellenbrand, Germany; Germaine Hanquet, Belgium

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