GSK Response on IFG Inquiry 09/18 Tolzin: Immunogenicity data for licensure of Priorix and Priorix-Tetra

In all studies mentioned below, immune response to measles was measured by Enzmye Linked Immunosorbent Assay (ELISA) and the seroresponse threshold for anti-measles antibodies was defined as $\geq$ 150 mIU/mL.

Priorix

For initial licensure of Priorix, 7 clinical studies comparing the human serum albumin (HSA)-containing formulation of Priorix and already registered MMR vaccines were conducted in more than 1.000 subjects. In 2 of these studies, antibody persistence was evaluated up to 12 months. The conclusions on the immunogenicity results from these studies are reflected in the Company's Global Data Sheet, and can be summarized in terms of immune response to measles as follows:

In clinical studies, Priorix has been demonstrated to be highly immunogenic.

Antibodies against measles were detected in 98.0% of previously seronegative vaccinees.

In comparative studies, antibodies against measles were detected in 98.7% of previously seronegative vaccinees who received Priorix compared to 96.9% in the group receiving a commercially available MMR combined vaccine.*

Subjects followed up to 12 months following vaccination all remained seropositive for anti-measles antibodies.

* The corresponding GMTs were 2.958 mIU/mL for anti-measles antibodies in the Priorix group and 3.270 mIU/mL in the group receiving a commercially available MMR vaccine, respectively.

The currently marketed formulation of Priorix worldwide is the HSA-free formulation. Therefore, the immunogenicity data from the pivotal studies conducted with this formulation are the most representative data for immunogenicity of the vaccine. Two studies were specifically performed in children aged 12-24 months to demonstrate non-inferiority of the immune response elicited by an HSA-free formulation as compared to an HSA-containing formulation of Priorix. In addition, antibody persistence was evaluated up to 2 years in these studies. The immunogenicity results of these studies were submitted to EU MRP at the time of the Article 30 procedure. Consequently, the Priorix EU Summary of Product Characteristics (SmPC) was updated (bold italics text) with immunogenicity results from these studies, and can be summarized in terms of immune response to measles as follows:

In clinical studies in children aged from 12 months to 2 years Priorix has been demonstrated to be highly immunogenic.

Vaccination with a single dose of Priorix induced antibodies against measles in 98.1% of previously seronegative vaccinees.°

Two years after primary vaccination seroconversion rates were 93.4% for measles.

These data are consistent with all the immunogenicity data collected in previous studies of Priorix.

° The corresponding GMTs were 3068.3 mIU/ml in the pooled *Priorix* HSA-free group for anti-measles antibodies as compared to 3040.7 mIU/ml in the *Priorix* HSA-containing group (pooled studies, ATP cohort for immunogenicity).

Data source: These data have been taken from the registration file of the company (at time of registration SmithKline Beecham), Part 1, Vol 1/1, Part I.C.3, Section 5.3, Table 8, Section 5.4, Table

10, and the Article 30 Clinical Overview, Section 2.5.4.2, Table 1 and Summary of Clinical Efficacy, Section 2.7.3.5.1, Table 21.

Priorix-Tetra

A total of 7 clinical studies comparing Priorix-Tetra and already registered MMR and Varicella vaccines were conducted in more than 3.800 subjects (Knuf, 2008)[1].

For licensure of Priorix-Tetra, 3 clinical trials were conducted in Europe (Austria, Finland, Germany, Greece, Poland), in which approx. 2.000 previously unvaccinated subjects from 11 to 23 months of age were vaccinated with 2 doses of the commercial formulation of Priorix-Tetra with an interval between doses of 6 weeks. Immunogenicity results of the 3 studies were pooled, and the seroconversion rates (SC) and geometric mean antibody concentrations/titres (GMC/GMT) for measles are summarized in the table below:

Seroconversion rates for MMRV Commercial Formulation (pooled results of 3 studies; ATP immunogenicity cohort)

Antibody Test (cut-off)	**Post dose 1**		**Post dose 2**	
	SC (95 % CI)	GMC/GMT (95 % CI)	SC (95 % CI)	GMC/GMT (95 % CI)
Measles ELISA (150 mIU/ml)	96.4% (CI: 95.5;97.2)	3184.5 (CI: 3046.5;3328.7)	99.1% (CI: 98.6;99.5)	4828.6 (CI: 4644.3;5020.1)

Data Source: Priorix-Tetra EU SmPC, Section 5.1 (Pharmacodynamic properties), Immune response

Seroconversion rates and geometric mean antibody concentrations/titres were similar to those observed after vaccination with Priorix co-administered with Varilrix.

Data source: These data have been taken from the registration file of the company GlaxoSmithKline Biologicals, CTD Module 2, Volume 1, Section 2.5: „Clinical overview“, Section 2.5.4.4, Table 5.

[1] Knuf M, Faber J, Barth I, Habermehl P. A combination vaccine against measles, mumps, rubella and varicella. Drugs Today (Barc). 2008; 44(4): 279-92.