

Record of Telephone Conversation - July 17, 2009 - Prevnar 13

System Info - 99909 SMITH, MICHAEL J 17-Jul-2009 14:20:52 SMITHM

RECORD OF TELEPHONE CONVERSATION

Submission Type: Original Application Submission ID: 125324/0 Office: OVR

Product:

Pneumococcal 13-valent Conjugate Vaccine (Diphtheria CRM197 Protein)

Applicant:

Wyeth Pharmaceuticals Inc.

Telecon Date/Time: 17-JUL-2009 12:23 PM Initiated by FDA? Yes

Telephone Number:

Communication Category(ies):

Information Request

Author: MICHAEL SMITH

Telecon Summary:

Toxicology IR for historical reference data and background information regarding pathology data.

FDA Participants: Michael Smith, Julie Vaillancourt and Claudia Wrzesinski

Non-FDA Participants: Jack Love and Carmel Devlin

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

Email: I emailed Jack Love and Carmel Devlin a request on behalf of Claudia Wrzesinski for information regarding historical reference data and background information regarding pathology data.

From: Smith, Michael (CBER)
Sent: Friday, July 17, 2009 12:23 PM
To: Jack Love; 'Carmel Devlin'
Cc: Vaillancourt, Julianne; Wrzesinski, Claudia
Subject: RE: Request for clarification/information from toxicologist Jack and Carmel,

Dr. Claudia Wrzesinski, the toxicologist on the BLA, has the following requests for historic reference data and background information regarding some pathology data. Please note that she does not consider this information to be critical for her recommendation. Please submit the requested information to CBER as an amendment to the BLA.

We noted that the following pathological findings of the intestinal system were observed with greater incidence in the vaccine treatment group relative to the saline control group in 3 independent toxicity studies in various species using the subcutaneous route of injection for the investigational vaccine. In toxicity study number 900742 with group sizes of 20 animals per group, juvenile rats given vaccine and adjuvant (30.8 µg polysaccharide (4.4 µg/mL of each of the serotypes except for serotype 6B at 8.8 µg/mL) 66.05 µg/mL CRM197 carrier

protein, 5mM succinate buffer containing 0.02% Polysorbate 80 in -----(b)(4)----- aluminum phosphate at 0.25 mg aluminum/mL), two animals experienced a hemorrhage of the stomach: one male animal on study day 23 and on study day 65; an erosion of the glandular mucosa in the stomach in one female animal was also observed on study day 23. Additionally, an inflammation of the stomach was observed in four male animals and one female animal of the treatment group given vaccine and adjuvant, but only in one animal of the control group. In another toxicity study numbered 501297 which used nonhuman primates, hemorrhage of the cecum was observed in one out of three animals in the male treatment group, but in none of the control groups. Lastly, in toxicity study number 6617-282A which was conducted using rats one out of 10 animals was diagnosed with either a squamous stomach cyst, mixed cell infiltration of the cecum or a mixed cell inflammation in the stomach. These observations are suggestive of a non-specific stress response which might be increased by the vaccine application. Please provide any available background information or comment on these findings. If you consider these findings to be incidental, please provide some historic reference data for animals of the same species of comparable age and weight.

We also noted that the following thyroid pathologies were observed with greater incidence in the vaccine/adjuvant group ((4.4 µg/mL of each of the serotypes except for serotype 6B at 8.8 µg/mL) 66.05 µg/mL CRM197 carrier protein, 5mM succinate buffer containing 0.02% Polysorbate 80 in -----(b)(4)----- aluminum phosphate at 0.25 mg aluminum/mL) and adjuvant alone group (5 mM succinate buffer at -----(b)(4)----- and 0.02% Polysorbate 80 as excipients and aluminum phosphate at 0.25 mg aluminum/mL) group relative to the saline control group (0.9% sodium chloride) in 3 independent toxicity studies in various species using the intramuscular or subcutaneous route of injection for the investigational vaccine. In the toxicity study number 501297, two out of three female monkeys, and one out of three male monkeys showed thyroid cysts after the subcutaneous injection of the vaccine at day 87. Additionally on day 115, one male animal in the treatment group developed a thyroid cyst. After intramuscular injection of the vaccine in the toxicity study number 07_2483, mixed cell inflammation of the thyroid was seen in one out of five rabbits of the male treatment group as well as C-cell hyperplasia and a squamous cyst in the thyroid in one male rabbit in the adjuvant group. In the toxicity study number 6617-282 (subcutaneous injection), C-cell hyperplasia was also observed in one out of ten male rats in the treatment group. None of the observations described in the vaccine group were made in the saline control group. Please provide any available background information or comment on these findings. If you consider these findings to be incidental, please provide some historic reference data for animals of the same species of comparable age and weight.

Thank you,

Mike

Mike Smith, Ph.D.

Lieutenant Commander (LCDR), U.S. Public Health Service
Regulatory Reviewer

Division of Vaccines and Related Products Applications

Office of Vaccines Research and Review

Center for Biologics Evaluation and Research

US Food and Drug Administration

Phone: 301-827-9047

Fax: 301-827-3532

E-mail: michael.smith2@fda.hhs.gov

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