PUBLIC ASSESSMENT REPORT

FOR

PERTAGEN

Common Name: Recombinant acellular pertussis vaccine

Application No. 2A 90002/59 (NB)

Assessment Report as adopted by the Thai FDA with
all information of a commercially confidential nature deleted

TABLE OF CONTENTS

1. BACKGROUND INFORMATION ON THE PROCEDURE

1.1 Submission of the dossier

The applicant **BioNet-Asia Co., Ltd.** (BioNet) submitted an application of **PERTAGEN** (acellular Pertussis (aP) vaccine) for Marketing Authorization to the Thai Food and Drug Administration (Thai FDA) on April 22nd, 2016. At the time of submission and validation, PERTAGEN was designated as medicinal product for the following indication: active booster immunization against pertussis in individuals from the age of 11 years onwards.

The legal basis for this application refers to: Drug Act 2510 B.E.

The submitted application was a complete dossier composed of administrative information, complete quality data, non-clinical and clinical data based on applicant's own tests and studies and bibliographic literature substituting/supporting certain tests or studies.

Licensing status: The product was not licensed in any country at the time of submission of the application.

Thai FDA Product Team Leader (PTL): Mr. Pramote Akarapanon

Thai FDA External Experts: Quality, Non-clinical, Clinical

1.2 Steps taken for the assessment of the product

- The application was received by the Thai FDA on April 22nd, 2016.
- The procedure started on April 22nd, 2016.
- A list of questions, the overall conclusion and review of the scientific data were prepared by the Thai FDA's PTL and sent to the applicant on …
- The applicant submitted of the responses including revised Summary of Product Characteristic (SPC), labeling and package leaflet texts in English and/or Thai (where required by the Drug Act) on ….
- Thai FDA prepared preliminary Assessment Report based on the responses from the applicant and dispatched the assessment report to external experts for their consideration and comments on May 11th, 2016.
- During the assessment, the external experts agreed on the consolidated list of questions to be sent to the applicant.
  - Quality August 30th, 2016
  - Non-clinical September 8th, 2016
  - Clinical August 23rd, 2016
- Thai FDA considered the consolidated list of questions identifying either "major objections" and/or "other concerns" may be adopted. These were sent to the applicant together with the Thai FDA recommendation and scientific discussion.
- Final draft of English SPC, labeling and package leaflet was sent by the applicant to the Thai FDA on September 9th, 2016.

- Thai FDA adopted the decision for marketing authorization on September 30th, 2016.

2. SCIENTIFIC DISCUSSION

2.1 Introduction

Pertussis (whooping cough) is a bacterial respiratory infection caused by *Bordetella pertussis*, a gram-negative bacillus, which is transmitted through droplets from infected to susceptible individuals. This disease is a significant cause of infant mortality worldwide and continues to be a public health concern even in countries with high vaccination coverage. Recent estimates from WHO suggest that, in 2008, about 16 million cases of pertussis occurred worldwide, 95% of which were in developing countries, and that about 195,000 children died from this disease.

Currently, there are 2 types of pertussis vaccines used in the market.

1. Whole-cell (wP) pertussis vaccine
   It has been shown to provide protection against pertussis and still serve as the foundation of global pertussis control since 1940s. However, vaccination with wP has been frequently associated with adverse reactions.
2. Acellular pertussis vaccine
   The aP vaccines were developed in the early 1980's. The currently available aP vaccines contain 1 – 5 purified components of *B. pertussis*; chemically inactivated pertussis toxin (cPT), Filamentous Haemagglutinin (FHA), Pertactin (PRN), Fimbriae (Fim) type 2 and 3 in different amount and compositions. The cPT is inactivated by formaldehyde, glutaraldehyde or hydrogen peroxide. These aP vaccines have been successfully introduced into many national immunization programs.

Both types of pertussis vaccines are presented in a combined formulation with other antigens; at least with tetanus toxoid and diphtheria toxoid.

The resurgence of pertussis has been recently reported in many countries, especially in aP vaccine using countries. One of the major concerns is age-related waning immunity so that older children and adults may again become susceptible. The insufficient immune response could be explained by a dramatic change in protein structure of cPT following chemical inactivation, resulting in a great reduction (80%) of T-cell binding epitope.

A call for new pertussis vaccine containing genetically-detoxified Pertussis Toxin (rPT) and a vaccination strategy using more booster immunizations have been proposed to improve the immune response and increase its duration compared to aP vaccine containing cPT.

Genetically-inactivated PT mutants were developed simultaneously in Italy and US at the National Institute of Allergy and Infectious Diseases (NIAID). The rPT contains two mutations of R9K and E129G in the S1 subunit resulting in loss of catalytic toxicity of PT. Studies of aP vaccine containing 5 µg rPT, 2.5 µg FHA and 2.5 µg PRN in combination

with diphtheria and tetanus conducted in infants showed similar safety profile and efficacy [84%, 95%CI (76 – 90)] compared to aP containing cPT at 5-time higher pertussis toxoid content. The protective efficacy was sustained for 6 years after primary immunization. This vaccine was launched in many countries but was withdrawn from the market due to commercial reasons.

BioNet-Asia Co., Ltd. (BioNet), a Thai vaccine company, has developed a new recombinant *B. pertussis* strain expressing a genetically detoxified PT for manufacture of recombinant aP vaccine (Patent US 9,187,754 B2). The recombinant aP vaccines containing purified pertussis antigens adsorbed onto aluminum hydroxide are produced as standalone vaccine and in combination with tetanus and diphtheria toxoids for booster use according to international standards including World Health Organization (WHO) guidelines, European Pharmacopoeia (Ph. Eur.) and Thai regulations.

2.2 Quality aspects

Introduction

PERTAGEN, a recombinant aP vaccine, is a monovalent (standalone) aP vaccine which belongs to the pharmaco-therapeutic group of Bacterial vaccines, Pertussis, purified antigen (ATC code: J07AJ02). PERTAGEN is a sterile, whitish, turbid and uniform suspension for injection. This vaccine contains purified *B. pertussis* antigens (rPT and FHA) which are adsorbed on aluminum hydroxide. The rPT is a genetically-detoxified PT obtained by recombinant DNA technology. PERTAGEN meets the World Health Organisation requirements for the manufacture of biological substances and acellular pertussis vaccines.

This recombinant aP vaccine is indicated for active booster immunization for the prevention of pertussis in individuals from the age of 11 years onwards. As a booster, a single dose (0.5 mL) is given.

The production and quality control testing of PERTAGEN are performed under Good Manufacturing Practice (GMP). Purified *B. pertussis* antigens were obtained from GMP working seed of recombinant *B. pertussis* strain which has been well characterized for genetic sequence, genetic stability, protein sequence and protein structure. The purified *B. pertussis* antigens are then formulated by adsorption onto aluminum hydroxide. The final vaccine lot is filled into a pre-filled syringe.

Raw materials and reagents used in the production process are controlled in compliance with USP/NF, Ph. Eur. or in-house specification for materials with no compendial reference. Impurity tests are performed to determine the manufacturing process related impurities or residuals. The production process including upstream, downstream, formulation and filling as well as aseptic process and cleaning were validated. The consistency of the process was demonstrated. The in-process control and controls of drug substance and drug product are performed using validated analytical methods. Stability of

drug substance and drug product is evaluated according to in-house protocols which comply with ICH guidelines. The stability data for PERTAGEN support a shelf-life of 24 months when stored at +2°C to +8°C (recommended storage condition).

Active Substance

Each single dose (0.5 mL) of PERTAGEN contains 5 µg rPT and 5 µg FHA adsorbed onto aluminum hydroxide.

Manufacturer(s)

Manufacturing process and testing are performed at BioNet-Asia Co., Ltd. located at 81 Moo 1, Hi-Tech Industrial Estate, Baan-Lane, Bang Pa-In Ayutthaya, 13160 Thailand.

Quality assessment:

I. The Thai FDA comments and recommendation

1. SOPs of analytical procedures according to section S.4.2 (Analytical procedure) and P.5.2 (Analytical procedure) should be additionally provided.
2. Details of preparation, calibration, shelf-life, storage condition, CoA and stability study of reference materials used for QC testing should be additionally submitted.
3. A justification or guidelines to set the acceptance criteria of validation parameters in analytical method validation should be defined.
4. Determination of specification of aP components should be explained.
5. A plate location of ELISA testing in the analytical method validation for identification and quantitation of aP antigens should be provided.
6. The results of some on-going tests in process validation section should be updated.
7. CoA of all seed banks and vaccine batches in batch analysis should be additionally provided.
8. Raw data of growth inhibitory effect and growth promotion test of sterility study should be additionally provided.
9. According to WHO TRS 979, 2013 Annex 4, acellular pertussis vaccine should be tested for residual activity of pertussis toxin by histamine sensitization and specific CHO cell assay. The test rationale should be explained.
10. As far as reversion to toxicity is concerned, a confirmation of genetic stability should be evaluated for at least 3 batches.
11. A rationale and justification for purification process to remove impurity and the test methods used should be additionally described.
12. A validation report of reusability of chromatographic resins should be provided.
13. Shelf-life or holding time of drug product and drug substance should be clearly mentioned.

14. Stability of the product based on monitoring the quality parameters (especially potency) for each antigen in aP vaccines can support the shelf-life of 24 months at 2-8°C for PERTAGEN. The manufacturer has to complete the stability study of the vaccine lots up to 36 months according to the submitted stability protocol and officially inform the responsible authorities in case of any deviations from approved specifications. If such deviations occur, a re-evaluation to establish for the new shelf-life should be done.

Suggestion for Post-approval Stability Commitment

The frequency of stability testing for commercial lots of PERTAGEN is at least one lot annually per each presentation (0.5 mL pre-filled syringe) if lots for that configuration are manufactured during the year.

II. Response from the applicant

1. All the SOPs requested according to section S.4.2 (Analytical procedure) and P.5.2 (Analytical procedure) were submitted.
2. The details of preparation, calibration, shelf-life, storage condition, CoA and stability study of in-house reference materials were submitted. The available document of international reference standard or commercial materials obtained from suppliers were provided.
3. The applicant explained that the acceptance criteria were set based on specific type of analytical method used according to ICH and EMA guidelines for analytical method validation. A justification of each validation parameters and its references were submitted.
4. The rationale and historical data to set the specification of aP components were submitted.
5. A plate location of ELISA testing used in the analytical method validation for identification and quantitation of aP antigens was provided.
6. All results of on-going tests in process validation section were updated.
7. The CoA of all seed banks and vaccine batches in batch analysis were submitted.
8. Raw data of growth inhibitory effect and growth promotion test of sterility study were provided.
9. The applicant explained that the residual activity of pertussis toxin for recombinant pertussis toxin antigen was performed according to WHO TRS 979, 2013 Annex 4, acellular pertussis vaccine which describes "*The residual activity of pertussis toxin (PT) in pertussis antigen bulk material and final bulk containing chemically detoxified antigens should be estimated after detoxification by means of a sufficient sensitive test such as HIST or the CHO cell assay. However, the HIST test may not be necessary for the product containing genetically detoxified Pertussis Toxin.*"
10. The applicant confirmed that the reversion to toxicity was evaluated in molecular characterization and genetic stability study for at least 3 batches. Additional documents were submitted.
11. A rationale for each purification process used to remove impurity and its references were submitted. The test methods used for impurity testing were described by

referring to the Analytical Procedures in the dossier. Additional information of some methods was provided.

12. The applicant explained the on-going validation of reusability to identify the column life-cycle or maximum number of use.
13. The applicant informed that the shelf-life or holding time of drug product and drug substance were described in the dossier/application. However, it was clearly mentioned in the response document.
14. Some on-going stability data were updated. The applicant committed to perform the stability study of the vaccine lots (clinical and process validation batches) up to 36 months at 2-8°C according to the submitted stability protocol. In case of any deviations from approved specifications, the applicant will inform the responsible authorities. If such deviations occur, a re-evaluation to establish for the new shelf-life will be performed.

    The applicant also committed to include one new batch per year into stability program as submitted.

Thai FDA PTL and external expert's overall conclusions on Quality aspects

xxx

Proposal for pre-authorization testing

Samples for testing the proposed vaccine are not required at time of submission of the application. However, the Thai FDA requests the applicants to submit their vaccines for testing of samples of the vaccines and/or its constituents at the Division of Biological, Department of Medical Sciences as early as possible in order to obtain test in due course.

The NCL (Division of Biological, Department of Medical Sciences) in close collaboration with the Thai FDA will specify a test protocol (type of samples, number of samples, number of batches, testing to be performed and methods and specifications to be used). The results of the tests are reported to the Thai FDA PTL for consideration in finalizing the Thai FDA Assessment Report.

2.3 Non-clinical aspects

Introduction

The non-clinical studies have been conducted in compliance with WHO guideline on non-clinical evaluation of vaccine (Annex 1 of WHO TRS No 927, 2005) and were performed under Good Laboratory Practice (GLP) according to Council of the Organisation of Economic Cooperation and Development (OECD) Principles on Good Laboratory Practices ENV/MC/CHEM(98) 17, 1998.

Pharmacology

I. Pharmacodynamic studies (Immunogenicity of the vaccine)

To ensure the safety and efficacy, several immunogenicity and toxicity studies of PERTAGEN were conducted.

The immunogenicity or aP potency of PERTAGEN was evaluated in mice based on mouse immunogenicity test (MIT) according to WHO TRS 979, 2013 Annex 4 for acellular pertussis vaccine and in rats (obtained from toxicity studies). The antibody titers to PT and FHA are measured by ELISA method. PT-neutralizing titer is determined by CHO cell assay.

Based on MIT in mice, the relative potency to PT and FHA, and PT-neutralizing titer of PERTAGEN met the specifications. In the immune response study in rats, PERTAGEN showed higher antibodies to PT and FHA and PT-neutralization than a licensed Tdap vaccine.

Comparability studies of the immune response between PERTAGEN and other vaccine formulations containing PERTAGEN antigens were assessed in mice and rats after single injection. The relative potency to PT and FHA, anti-pertussis antibodies and PT-neutralizing titer in all vaccines were comparable.

In a maternal immunization study in rats, the PERTAGEN antigens in combined formulation with tetanus and diphtheria toxoids elicited high anti-PT and anti-FHA antibodies in dams during pregnancy and lactation. Maternal antibody transfer was observed in offspring.

II. Pharmacodynamic studies of adjuvant(s) (if applicable)

Not applicable.

Pharmacokinetics

Not applicable.

Toxicology

I. General toxicity

Single-dose toxicity

The single-dose toxicity study of PERTAGEN was performed in rats under OECD GLP. The results showed that PERTAGEN did not cause death nor induce any adverse effects on systemic and local reactions.

Repeat-dose toxicity

The repeat-dose toxicity of BioNet aP vaccine containing PERTAGEN antigens and PRN was studied in rats in comparison to a licensed Tdap vaccine under OECD GLP. This study aimed to evaluate the potential adverse reaction after multiple administration. The aP vaccine did not induce any adverse effects in the treated rats under the experimental conditions of the study. The aP vaccine was well tolerated at the injection sites with respect to its local effect and in comparison with the comparator vaccine.

II. Special toxicity for vaccines, when applicable

Toxicity studies in special populations

Not applicable.

Genotoxicity and carcinogenicity studies, when applicable

Not applicable.

Reproductive and developmental toxicity studies

The prenatal and postnatal developmental toxicity of PERTAGEN antigens (rPT and FHA) in combined formulation with tetanus and diphtheria toxoids was studied in pregnant rats. No adverse effects on pregnancy, parturition, lactation or prenatal and postnatal development were observed. There was no vaccine related postnatal anomalies or teratogenic effect noted in this study. These findings confirm the safety of PERTAGEN antigens in combined formulation with tetanus and diphtheria toxoids during pregnancy and lactation.

Non-clinical assessment:

I. The Thai FDA comments and recommendation

1. In Thai package leaflet, some of Thai translation should be revised. Correction was suggested.
2. Data of pharmacodynamic studies (immunogenicity of the vaccine) of PERTAGEN are sufficient to demonstrate the immunogenicity of each immunogenic factor of PERTAGEN (rPT and FHA) and could support the efficacy of the vaccine when it is administered to human subjects.
3. Data from acute single-dose toxicity and one repeat-dose toxicity study are acceptable and PERTAGEN can be considered for use in the intended human population.

II. Response from the applicant

1. The revised Thai package leaflet according to Thai FDA and external expert's comments was submitted.
2. No response is required for this comment.
3. No response is required for this comment.

Thai FDA PTL and external expert's comments on the SPC, labels and package leaflet

Package leaflet should be revised according to comments and Thai FDA regulations.

Thai FDA PTL and external expert's overall conclusions on Non-clinical aspects

Based on all immunogenicity and toxicity studies, PERTAGEN has acceptable immunogenicity and safety profile.

2.4 Clinical aspects

Introduction

The clinical studies of PERTAGEN developed by BioNet-Asia were conducted in compliance with ICH-GCP and WHO Recommendation to assure the quality, safety and efficacy of acellular pertussis vaccine (Annex 4 of WHO TRS No. 979, 2013).

The clinical development of PERTAGEN included 2 clinical studies.

1. Phase I/II study (TDA101) "A phase I/II randomized, observer-blind, controlled study to assess safety and immunogenicity of acellular Pertussis vaccine given alone or in

combination with Tetanus-diphtheria vaccine in healthy adults aged 18-35 years" in 60 subjects compared to Adacel®, a licensed Tdap vaccine in Thailand.

2. Phase II/III study (TDA202) "A phase II/III randomized, observer-blind, controlled study to demonstrate non-inferior immunogenicity of a combined Tetanus-diphtheria-acellular Pertussis vaccine as compared to Adacel® vaccine in healthy subjects aged 12-17 years".

Reports of clinical studies

I. Phase I study

The first-in-human study (Phase I/II, TDA101) aimed to evaluate the safety, tolerability and immunogenicity of BioNet aP vaccine containing PERTAGEN antigens (5 µg rPT, 5 µg FHA) and 2.5 µg PRN and BioNet TdaP vaccine containing PERTAGEN antigens (5 µg rPT, 5 µg FHA), 2.5 µg PRN, 7.5 Lf tetanus toxoid and 2 Lf diphtheria toxoid in comparison to Adacel®, a licensed Tdap vaccine, in 18-35 years old (total subjects of 60 healthy volunteers). Since the comparator vaccine was registered in Thailand, there was no ethical concern.

Each subject was intramuscularly injected with one of three vaccines (20 subjects per group). Subjects were followed at 7 days and 28 days after vaccination for safety and immunogenicity evaluation. Immune response to vaccine antigens for antibody response (anti-PT IgG, anti-FHA IgG and anti-PRN IgG) and PT-neutralizing antibody was measured by validated ELISA method and CHO cell assay, respectively.

Based on the study results,

1. BioNet aP vaccine containing PERTAGEN antigens and PRN elicited a good immunogenicity response to pertussis antigens with similar seroconversion rate to Adacel®. It showed significantly higher anti-PT and anti-FHA GMTs when compared to Adacel®.
2. BioNet aP vaccine containing PERTAGEN antigens and PRN showed similar safety profile to Adacel®.

II. Phase II study

See Phase I study.

III. Phase III study

The Phase II/III (TDA202) study was designed to evaluate non-inferior immunogenicity of PERTAGEN and BOOSTAGEN (TdaP vaccine containing 5 µg rPT, 5 µg FHA, 7.5 Lf tetanus toxoid and 2 Lf diphtheria toxoid) compared to Adacel® in 12-17 years old subjects. Since the comparator vaccine was registered in Thailand, there was no ethical concern. This study was a double-center, observer-blind randomized controlled vaccine trial in 12-17 years old healthy subjects. The

study was statistically powered with 150 subjects per vaccine groups enrolled (and a total of 450 subjects).

Each subject was intramuscularly injected with one of three vaccines (150 subjects per group). Safety assessment were conducted during the study. At 28 days after vaccination, immunogenicity was assessed. Immune response to vaccine antigens for antibody response (anti-PT IgG, anti-FHA IgG and anti-PRN IgG) and PT-neutralizing antibody was measured by validated ELISA method and validated CHO cell assay, respectively.

Based on the study results,

1. The study objective of demonstrating non-inferior immunogenicity of PERTAGEN as compared to Adacel® was met.
2. The seroconversion rates of ELISA anti-PT and anti-FHA antibody titers were statistically significant higher in subjects vaccinated with PERTAGEN (respectively 96.0% and 93.2%) than in subjects vaccinated with Adacel® (respectively 55.0% and 54.4%).
3. PERTAGEN showed significantly higher ELISA anti-PT and anti-FHA titers and PT-neutralizing antibody than those of Adacel®.
4. Superiority of ELISA anti-PT and anti-FHA seroconversion rates and GMTs was demonstrated according to EMEA guideline (CPMP/EWP/482/99, 2000).

Non-inferiority test for anti-PT and anti-FHA GMTs as assessed by ELISA in Pertagen® *vs* a licensed Tdap vaccine in 12 – 17 years old adolescents

Geometric Mean	Pertagen® GMT [a] (IU/mL) (95% CI)	Licensed Tdap GMT [a] (IU/mL) (95% CI)	GMT Ratio [b] (95% CI)
PT	527.51 (435.57 – 638.87)	48.09 (36.99 – 62.50)	10.97 (8.39 – ∞)
FHA	836.13 (725.13 – 964.12)	178.19 (148.94 – 213.19)	4.69 (3.88 – ∞)

a: Geometric Mean Change from baseline at Day 28 after vaccination
b: Based on non-inferiority test with GMT Ratio > 0.67

5. The safety profile of PERTAGEN appeared similar to the safety profile of Adacel®.

IV. Special considerations

See Clinical assessment.

V. Adjuvant(s)

Adjuvant used is similar to other vaccines including Adacel®. No concern.

VI. Phase IV studies and/or pharmacovigilance plan (if applicable)

See Clinical assessment.

VII. Non-inferiority studies (for combined vaccines or approved vaccines prepared by new manufacturers)

Not applicable.

VIII. Co-administration study with other vaccines

Not applicable.

Clinical assessment:

I. The Thai FDA comments and recommendation

1. PERTAGEN showed higher immune response to PT and FHA than Adacel®. But the composition of pertussis components in PERTAGEN and Adacel® is different, therefore it is necessary to demonstrate the efficacy.
2. Current aP vaccines registered in Thailand contain 3 or more components which have been reported with better efficacy. A rationale on selection of pertussis components in PERTAGEN should be given.
3. Number of subjects for safety and tolerability assessment in Phase II/III study was less than the WHO recommendations. A detailed safety monitoring plan (Post-licensing safety plan) is recommended. Additional information on phase IV study protocol should be submitted.

II. Response from the applicant

1. The applicant explained that as per WHO TRS, efficacy study against pertussis is not required for licensure of new acellular pertussis vaccines if non-inferior immunogenicity is demonstrated against a licensed acellular pertussis vaccine. Superior immunogenicity of PERTAGEN was demonstrated according to EMEA guideline (2000). As per WHO guideline (2016), demonstration of a superior immunogenicity is likely predictive of superior efficacy. References were submitted.
2. As per WHO position paper (2015), *"Although some systematic reviews have favoured multi-component aP vaccines over vaccines with 1 or 2 aP components, taken together with the experience of vaccine use in countries, evidence is not sufficient to establish any significant difference in vaccine effectiveness of aP vaccines with differing numbers of components"*. The applicant provided reference of a study showing similar immunogenicity between Adacel® and 2-component aP pediatric vaccine (approved in Thailand and previously evaluated in efficacy study).
3. The applicant referred to the WHO 2016 guideline on clinical evaluation of vaccines with regards to new vaccine consisting *"only of antigenic components that are already licensed in other vaccines with which there is considerable experience in routine use"*. The applicant committed to perform post-licensing safety monitoring according to Thai FDA guidelines which was submitted in the

application. The risk management plan and pharmacovigilance plan were re-submitted.

Thai FDA PTL and external expert's comments on the SPC, labels and package leaflet

The age of individuals for vaccine use should be clearly specified in package leaflet.

Thai FDA PTL and external expert's overall conclusions on Clinical aspects

Based on clinical studies, PERTAGEN showed good immunogenicity response to the vaccine components which is non-inferior to Adacel®. The antibody response and seroconversion rates to PT and FHA were higher than Adacel®. PERTAGEN is safe. However, the sample size was limited and there is difference in antigenic components to comparator vaccine. Phase IV study should be planned.

2.5 Overall conclusion, risk/benefit assessment and recommendation

Efficacy

Immunogenicity data demonstrate that PERTAGEN is highly immunogenic as compared to a licensed Tdap vaccine. The non-inferiority criteria were met for licensure of new acellular pertussis vaccine according to WHO recommendation.

Safety

Local and systemic reactions of PERTAGEN are generally similar in nature, frequency, and severity as a licensed Tdap vaccine. There is no difference in the rate and severity of the other adverse events. Altogether, the safety profile of PERTAGEN appears comparable to the safety profile of a licensed Tdap vaccine.

Recommendations

Thai FDA and external experts have reviewed quality, safety, toxicology and clinical studies data and found them evidently supportive; therefore, positive opinion was given toward the approval of marketing authorization of PERTAGEN with one condition requesting the applicant to have a pharmacovigilance plan and closely monitor the safety and report to Thai FDA according to Thai FDA requirement under Safety Monitoring Program (SMP) for a period of two years.

The applicant submitted a safety monitoring program as part of the pharmacovigilance plan.