

**Public Assessment Report
for paediatric studies submitted in accordance
with Article 46 of Regulation (EC) No1901/2006, as
amended**

**Covaxis
(Triaxis/Adacel)**

DE/W/0034/pdWS/004

**Marketing Authorisation Holder:
Sanofi Pasteur MSD GmbH**

Rapporteur:	Germany (PEI)
Finalisation procedure (day 90):	7 February 2016

ADMINISTRATIVE INFORMATION

Invented name of the medicinal product:	Covaxis (Triaxis/Adacel)
INN (or common name) of the active substance(s):	Diphtheria, Tetanus, Pertussis (acellular, component) Vaccine (adsorbed, reduced antigen(s) content)
MAH:	Sanofi Pasteur MSD GmbH
Currently approved Indication(s):	Covaxis is indicated for active immunization against tetanus, diphtheria, and pertussis in persons from 4 years of age as a booster following primary immunization. The use of Covaxis should be determined based on official local recommendations.
Pharmaco-therapeutic group (ATC Code):	J07AJ52
Pharmaceutical form(s) and strength(s):	Suspension for Injection

I. EXECUTIVE SUMMARY

No SmPC and PL changes are proposed.

II. RECOMMENDATION

No further action required.

III. INTRODUCTION

The MAH submitted completed paediatric studies for Covaxis/Adacel, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, on medicinal products for paediatric use.

A short critical expert overview has also been provided.

The MAH stated that the submitted paediatric studies do not influence the benefit risk for Covaxis/Adacel and that there is no consequential regulatory action.

IV. SCIENTIFIC DISCUSSION

IV.1 Information on the pharmaceutical formulation used in the study(ies)

The commercially available formulation of Covaxis (Triaxis/Adacel) was used in the study.

IV.2 Clinical aspects

1. Introduction

The MAH submitted final reports for:

- **3 Booster studies:**
 - **Td517:** US study that compared Adacel to Daptacel (DTaP) as 5th dose in children 4-6 years of age. Concomitant use of MMR, V and IPV
 - **Td528:** Chinese study that compared a single dose of Adacel to a DT vaccine in children 4-11 years of age or to a Td vaccine adolescents and adults 12-64 years of age. No concomitant use.
 - **Td527:** Chinese study that used a single dose of Adacel in children 4-8 years of age and adults 18-64 years of age. No comparator, no concomitant use; safety data only.
- **1 safety surveillance study Td512 (US)**

2. Clinical studies

Td517

“Safety and Immunogenicity of Tdap Vaccine Compared to DTaP vaccine as Fifth Dose Booster in Children 4 to 6 Years of Age”

➤ Description

“Phase 3, controlled, multi-center, randomized, modified double-blind, 2-arm, parallel-group study conducted in the US and Canada.”

➤ Methods

- Objectives:

Compare the immunogenicity of Tdap and DTaP vaccines administered as a 5th dose to DTaP- or DTaP-IPV/Hib -primed subjects, given concurrently but in a separate arm from MMR, polio, and varicella vaccines.

The secondary objective was the percentage of subjects with a ≥ 4 -fold increase in antibody geometric mean concentration (GMC) to pertussis antigens (pertussis toxoid [PT], filamentous haemagglutinin [FHA], pertactin [PRN], and fimbriae types 2 and 3 [FIM]) at Day 30 post-vaccination compared with pre-vaccination GMC.

Observational objectives included anti-diphtheria and anti-tetanus seroprotection rates (≥ 0.01 international units [IU]/mL) and antibody GMC pre-(Day 0) and post-vaccination (Day 30); the percentage of subjects with a 4-fold increase in antidiaphtheria and anti-tetanus antibody concentration at Day 30 post-vaccination compared with prevaccination (Day 0); and the percentage of subjects with anti-pertussis (PT, FHA, PRN, and FIM) antibody concentrations \geq lower limit of quantitation (LLOQ), $\geq 2 \times \text{LLOQ}$, and $\geq 4 \times \text{LLOQ}$ pre- (Day 0) and post-vaccination (Day 30).

- Study design

Randomized, modified double-blind, 2-arm, parallel-group, multi-center study with 2 acellular 5-component pertussis vaccines given as the 5th dose booster to children ages 4 to 6 years. Subjects who met the eligibility criteria, including having a background of 4 doses of Pentacel or DAPTACEL were assigned in a 1:1 ratio to one of the following 2 study groups described:

Group	Visit 1/Day 0
A	Tdap vaccine (left arm) Polio, MMR and varicella vaccines (right arm)
B	DTaP vaccine (left arm) Polio, MMR and varicella vaccines (right arm)

Subjects were monitored at the sites for 30 minutes after vaccination and followed for safety for 180 days after vaccination.

Blood samples were collected on Visit 1 (Day 0 [prior to vaccination]) and Visit 2 (Day 30) for immunogenicity testing. For the long-term immunogenicity (LTI) follow-up study, subjects will be invited to provide blood samples at 1 year (± 1 month) and 5 years (± 1 month) after Visit 1. The LTI follow-up study is ongoing and will be presented in a separate report.

- Study population /Sample size
The per-protocol (PP) population was the primary analytical population for the evaluation of immunogenicity, and included 442 Tdap recipients and 426 DTaP recipients.

➤ Results

- Immunogenicity results

For diphtheria and tetanus, Tdap was non-inferior to DTaP when administered as a 5th dose booster based on the seroprotection, serothreshold, and booster response rates criteria at 30-days post-vaccination. Similar high post-vaccination rates of seroprotection, serothreshold and booster response ($\geq 96.7\%$) were observed in subjects who received either Tdap or DTaP. Details can be found in Table 1.

Table 1 Number and proportion of subjects who achieved serothreshold at baseline and 30 days post-vaccination for diphtheria and tetanus at level ≥ 1.0 IU/mL (PP population) (source: Table 5.3, study report)

Antigen strain	Time point	DAPTACEL-primed						Pentacel-primed						Total					
		n/M	Tdap (N=328) %	(95% CI)	n/M	DTaP (N=320) %	(95% CI)	n/M	Tdap (N=114) %	(95% CI)	n/M	DTaP (N=106) %	(95% CI)	n/M	Tdap (N=442) %	(95% CI)	n/M	DTaP (N=426) %	(95% CI)
Diphtheria (IU/mL)	Pre	15/328	4.6	(2.6; 7.4)	22/319	6.9	(4.4; 10.3)	4/114	3.5	(1.0; 8.7)	8/106	7.5	(3.3; 14.3)	19/442	4.3	(2.6; 6.6)	30/425	7.1	(4.8; 9.9)
	Post	326/328	99.4	(97.8; 99.9)	318/320	99.4	(97.8; 99.9)	113/114	99.1	(95.2; 100.0)	106/106	100.0	(96.6; 100.0)	439/442	99.3	(98.0; 99.9)	424/426	99.5	(98.3; 99.9)
Tetanus (IU/mL)	Pre	37/328	11.3	(8.1; 15.2)	41/320	12.8	(9.4; 17.0)	10/114	8.8	(4.3; 15.5)	8/106	7.5	(3.3; 14.3)	47/442	10.6	(7.9; 13.9)	49/426	11.5	(8.6; 14.9)
	Post	320/328	97.6	(95.3; 98.9)	317/320	99.1	(97.3; 99.8)	109/114	95.6	(90.1; 98.6)	100/106	94.3	(88.1; 97.9)	429/442	97.1	(95.0; 98.4)	417/426	97.9	(96.0; 99.0)

N is the total number of subjects per group in the Per Protocol Population.

n is the number of subjects who achieved serothreshold at level ≥ 1.0 IU/mL.

M is the number of subjects per group in the Per Protocol Population with available data for the antigen.

For Pertussis, Tdap was non-inferior to DTaP in booster response rates to each of the 4 pertussis antigens (PT, FHA, PRN, and FIM) and in antibody GMC to FHA and FIM at Day 30 post-vaccination.

Statistically significant differences in GMTs can be seen for anti-FHA and anti-FIM post vaccination (Pentacel primed subjects show higher GMTs), anti-PRN pre vaccination (Daptacel primed subjects show higher GMTs) and anti-PT (Daptacel booster effects higher GMTs regardless of priming).

Details can be found in Table 2 and Table 3.

Table 2 Number and proportion of subjects who demonstrated booster response at 30 days post-vaccination for pertussis (PP population) (source: Table 5.6, study report)

Antigen strain	DAPTACEL-primed						Pentacel-primed						Total					
	n/M	Tdap (N=328) %	(95% CI)	n/M	DTaP (N=320) %	(95% CI)	n/M	Tdap (N=114) %	(95% CI)	n/M	DTaP (N=106) %	(95% CI)	n/M	Tdap (N=442) %	(95% CI)	n/M	DTaP (N=426) %	(95% CI)
PT (EU/mL)	264/301	87.7	(83.5; 91.2)	278/297	93.6	(90.2; 96.1)	88/100	88.0	(80.0; 93.6)	84/90	93.3	(86.1; 97.5)	352/401	87.8	(84.2; 90.8)	362/387	93.5	(90.6; 95.8)
FHA (EU/mL)	289/320	90.3	(86.5; 93.3)	272/306	88.9	(84.8; 92.2)	108/112	96.4	(91.1; 99.0)	91/101	90.1	(82.5; 95.1)	397/432	91.9	(88.9; 94.3)	363/407	89.2	(85.8; 92.0)
PRN (EU/mL)	301/327	92.0	(88.6; 94.7)	300/317	94.6	(91.6; 96.8)	105/114	92.1	(85.5; 96.3)	100/106	94.3	(88.1; 97.9)	406/441	92.1	(89.1; 94.4)	400/423	94.6	(92.0; 96.5)
FIM (EU/mL)	305/321	95.0	(92.0; 97.1)	296/315	94.0	(90.7; 96.3)	105/111	94.6	(88.6; 98.0)	98/103	95.1	(89.0; 98.4)	410/432	94.9	(92.4; 96.8)	394/418	94.3	(91.6; 96.3)

Booster response is defined as post titer $\geq 4 \times \text{LLOQ}$ and pre titer $< \text{LLOQ}$, or

Post/Pre titer ≥ 4 increase and pre titer $\geq \text{LLOQ}$ but $< 4 \times \text{LLOQ}$, or Post/Pre titer ≥ 2 increase and pre titer $\geq 4 \times \text{LLOQ}$.

N is the total number of subjects per group in the Per Protocol Population.

n is the number of subjects who demonstrated booster response.

M is the number of subjects per group in the Per Protocol Population with available data for the antigen.

Table 3 Geometric mean titers (GMTs) at baseline and 30 days post-vaccination for pertussis (PP population)

Antigen strain	Time point	DAPTACEL-primed						Pentacel-primed						Total					
		M	Tdap (N=328) GMT	(95% CI)	M	DTaP (N=320) GMT	(95% CI)	M	Tdap (N=114) GMT	(95% CI)	M	DTaP (N=106) GMT	(95% CI)	M	Tdap (N=442) GMT	(95% CI)	M	DTaP (N=426) GMT	(95% CI)
PT (EU/mL)	Pre	307	4.76	(4.26; 5.31)	299	4.97	(4.42; 5.59)	104	4.09	(3.33; 5.02)	91	5.00	(4.04; 6.18)	411	4.58	(4.16; 5.05)	390	4.98	(4.49; 5.51)
	Post	321	52.7	(48.3; 57.4)	318	85.5	(77.7; 94.1)	109	54.5	(47.4; 62.6)	105	89.3	(77.9; 102)	430	53.1	(49.3; 57.2)	423	86.4	(79.9; 93.5)
FHA (EU/mL)	Pre	323	7.21	(6.19; 8.39)	307	6.93	(5.88; 8.16)	112	8.70	(6.74; 11.2)	101	10.0	(7.51; 13.5)	435	7.56	(6.64; 8.61)	408	7.60	(6.59; 8.76)
	Post	325	93.1	(83.7; 104)	318	78.9	(70.4; 88.4)	114	131	(113; 152)	106	114	(93.6; 139)	439	102	(93.1; 111)	424	86.5	(78.3; 95.5)
PRN (EU/mL)	Pre	328	10.9	(9.70; 12.3)	318	13.0	(11.5; 14.7)	114	5.90	(4.88; 7.12)	106	7.00	(5.79; 8.45)	442	9.31	(8.40; 10.3)	424	11.1	(10.0; 12.4)
	Post	327	137	(121; 154)	319	205	(182; 231)	114	85.9	(71.3; 103)	106	104	(84.5; 128)	441	121	(109; 134)	425	173	(155; 193)
FIM (EU/mL)	Pre	322	23.7	(20.5; 27.4)	317	22.9	(19.6; 26.7)	112	24.3	(18.9; 31.1)	103	29.6	(23.8; 36.7)	434	23.8	(21.0; 27.0)	420	24.4	(21.4; 27.7)
	Post	326	384	(345; 428)	318	345	(310; 383)	113	570	(472; 688)	106	551	(464; 654)	439	425	(387; 467)	424	388	(354; 425)

N is the total number of subjects per group in the Per Protocol Population.

M is the number of subjects with available data for the particular antigen, including results reported as < LLOQ or > ULOQ.

For IPV there were no statistically significant differences seen between the groups and regarding priming.

- **Safety results**

The proportion of subjects reporting at least one injection-site reaction within 7 days of vaccination was 86.0% in the Tdap group and 91.1% in the DTaP group. Most injection-site reactions had an onset on Day 0 through Day 3 post-vaccination and resolved within 3 days.

The most frequently reported injection-site reaction in the total population was pain, which was reported in 60.1% of Tdap subjects and 67.5% of DTaP subjects.

The incidence of erythema (26.5% and 40.7%) and swelling (18.9% and 29.2%) was lower in the Tdap group compared to the DTaP group. The rate of increase in left limb circumference (the arm in which the Tdap or DTaP vaccines were administered) was lower in the Tdap group compared to the DTaP group (58.6% and 71.5%, respectively). A similar proportion of subjects in both vaccine groups experienced an increase in the circumference of the right limb, in which the concomitant vaccines were administered (45.7% and 49.4% of subjects in the Tdap and DTaP groups, respectively). No subjects in the Tdap group and 1.0% of subjects in the DTaP group reported extensive limb swelling.

Most solicited injection-site reactions were rated as mild or moderate in intensity (Grade 1 or 2) in both vaccine groups. Severe erythema and swelling (Grade 3) were less frequent among Tdap recipients. Overall, 4.3% of Tdap recipients and 14.5% of DTaP recipients reported at least one Grade 3 solicited injection-site reaction. The majority of subjects who experienced an injection-site reaction did not seek medical treatment nor was medication administered to treat the reaction.

A similar proportion of Tdap and DTaP recipients experienced at least one systemic reaction (48.4% and 52.5%, respectively). Most systemic reactions had an onset within the first 3 days of vaccination and resolved within 8 days.

Myalgia was the most frequently reported solicited systemic reaction in both the Tdap (35.0%) and DTaP (39.6%) groups. Additional solicited systemic reactions reported by study subjects were malaise (27.0% and 30.3%), headache (11.3% and 14.9%), and fever (4.7% and 5.3%) in the Tdap and DTaP groups, respectively.

Most systemic site reactions were mild or moderate in intensity (Grade 1 or 2). Grade 3 solicited systemic reactions were reported in 1.7% of Tdap subjects and 2.2% of DTaP subjects. Grade 3 fever was reported in 0.2% of subjects in both study groups.

No deaths were reported in the study. A total of 9 subjects (4 Tdap subjects and 5 DTaP subjects) reported 10 SAEs through Day180 post-vaccination. All SAEs resolved, and none were considered by the Investigators to be related to study vaccine.

Td528

“Immunogenicity and Safety of Sanofi Pasteur’s Tdap Combined Vaccine (ADACEL) as a Booster Dose, versus Local DT Vaccine in Healthy Children or versus Local Td Vaccine in Healthy Adolescents and Adults in China”

➤ Description

Phase III, mono-center, randomized, blind-observer, open-label, controlled, 2-armed study conducted in China.

➤ Methods

- Objective(s)
 - To describe diphtheria and tetanus seroprotection rates and pertussis booster response rates induced by each of the study vaccines: Adacel vaccine (in all study age groups), local DT vaccine (in children), and local Td vaccine (in adolescents and adults)
 - To further describe in each group the immunogenicity of the study vaccines at baseline and 1 month after the vaccination
 - To describe the safety of the study vaccines.
- Study design
2 groups in the different age increment receiving either Adacel (group 1) or a local DT/Td vaccine:

	Group 1	Group 2	
	ADACEL	Local DT	Local Td
Children aged 4 through 11 years	360	360	-
4 – 6 years	at least 90	at least 90	-
7 – 11 years	at least 90	at least 90	-
Adolescents and adults aged 12 through 64 years	360	-	360
12 – 17 years	at least 60	-	at least 60
18 – 45 years	at least 60	-	at least 60
46 – 64 years	at least 60	-	at least 60

- Study population /Sample size

Table 4 Number of subjects per age group in the different vaccination groups for Full-analysis-set (=Safety analysis set) and Per-Protocol-Set (source: Table 6.2, study report)

Age	Analysis set	Adacel	DT	Td	All
4-11 y	FAS	359	360	-	719
	PPS	354	354	-	708
12-64 y	FAS	362	-	358	720
	PPS	362	-	357	719

➤ Results

- Immunogenicity results

Seroprotection (≥ 0.1 IU/mL) against Diphtheria and Tetanus was similar in both vaccination groups. Concentrations of ≥ 1.0 IU/mL against Diphtheria were seen in the Adacel group in 94.6% (4-11yoA) and 74.3% (12-64 yoA) of subjects and similarly for DT and Td. Concentrations of ≥ 1.0 IU/mL against Tetanus were seen in the Adacel group in 100% (4-11yoA) and 74.3% (12-64 yoA) of subjects and also similarly for DT and Td.

Statistically significant differences are seen between the age groups for anti-PT and anti-FHA both pre- and post-booster and for anti-PRN and anti-FIM pre-booster, with the older age group showing higher GMCs.

- Safety results

The frequencies and gradings of local and systemic reactions were similar between the vaccine and age groups. Adacel had a slightly higher rate of injection site reactions in children than the DT vaccine.

Unsolicited events were most often classical symptoms of childhood diseases (cough) in children or infections/infestations (nasopharyngitis, gastrointestinal infection, tonsillitis, pelvic inflammatory disease or upper respiratory tract infection). Few unsolicited non-serious AEs were assessed as related to vaccination, and only in children, by the Investigator (cough, diarrhea, dizziness, rash, injection site pruritus). No unsolicited reaction was assessed as Grade 3. No SAE or death was reported during the study.

Td527

“Clinical Safety Study of the Tdap Combined Vaccine (ADACEL®) as a Booster Dose in Healthy Adults and Children in China”

➤ Description

Phase I-like, open-label, mono-center safety study conducted in China. Small scale study in Chinese subjects to fulfil requirements of Chinese health authorities.

➤ Methods

- Objective(s)

Primary objective

To describe the safety in terms of occurrence of serious adverse reactions and Grade 3 adverse reactions after administration of Sanofi Pasteur's Tdap vaccine (ADACEL) given as a single dose in 20 adults and 20 children.

Secondary objectives

To describe the full reactogenicity profile after administration of Sanofi Pasteur's Tdap vaccine (ADACEL) given as a single dose in 20 adults and 20 children.

- Study design

Group 1: 20 adults (18 through 64 years of age) received a single booster dose of Tdap vaccine (ADACEL).

Group 2: 20 children (4 through 8 years of age) received a single booster dose of Tdap vaccine (ADACEL)

- Study population /Sample size
Generally healthy subjects, 40 subjects overall.
In Group 1, the male/female sex ratio was 1 (10 men versus 10 women), the age was on average 44.2 years, ranging from 21.7 to 63.8 years.
In Group 2, the **male/female sex ratio** was **0.43**, with more female than male subjects (6 boys versus 14 girls), the age was on average 5.8 years ranging from 4.1 to 7.9 years.

➤ Results

- Safety results

No Grade 3 solicited injection site reactions were reported in adults. 3 of 20 subjects in the pediatric group showed a grade 3 local reaction (erythema and swelling).

No Grade 3 solicited systemic reactions and no unsolicited non serious adverse reactions were reported in both groups.

No SAE and no death occurred throughout the trial.

Rapporteur's comment:

Very small study size. No new information regarding safety.

Td512

Td512 was a descriptive, epidemiological surveillance study. Surveillance using a healthcare organization with large comprehensive medical encounter databases was used in this study to identify any risks or uncommon events associated with use of the recently licensed Tdap5 vaccine that may occur in routine clinical usage in a large population.

The investigational group consisted of all persons who received Tdap5 vaccine during the study period, subgrouped as follows:

- 1) Persons pregnant at the time of vaccination with Tdap5 or who became pregnant within 28 days after vaccination.
- 2) All other Tdap5 recipients (classified by age at vaccination: Subgroup 1, younger than 11 years; Subgroup 2, 11 to 17 years; Subgroup 3, 18 to 39 years; Subgroup 4, 40 to 64 years; and Subgroup 5, older than 64 years).

For all analytical groups, surveillance for SAEs encompassed review of all inpatient and outpatient databases previously enumerated, plus any active surveillance, such as spontaneous reporting, or state mortality reports. SAEs identified from inpatient and outpatient databases were reported via line listings.

Surveillance for Pregnancy

KP study site databases were reviewed to identify Tdap5 recipients who were pregnant at the time of vaccination or within 28 days thereafter. Pregnancies were identified by positive pregnancy tests or prenatal visits within 9 months prior to vaccination with no record of pre-vaccination delivery or abortion, or by prenatal visits, therapeutic abortions, or deliveries within 10 months after vaccination.

Surveillance for All Other Tdap5 Recipients

- For all other Tdap5 recipients, passive surveillance was conducted as described below:

Short-term surveillance: Each individual receiving Tdap5 vaccine served as her/his own control for evaluation of acute events. Rates of events occurring during Days 0 to X (where X=7, 14, 30, and 60) following vaccination were compared to rates of events occurring during Days 61 to 120 following vaccination.

- 6-month surveillance: For each age subgroup, event rates during the 6 months following vaccination among persons receiving Tdap5 vaccine were compared to event rates during the 6 months following vaccination among persons in the same age subgroup who received Tetanus Toxoid and Reduced Diphtheria Toxoid Vaccine Adsorbed (Td vaccine), but no live virus vaccine, during the year prior to initiation of this study.

During the course of the study, KPVSC encouraged all participating clinics and clinicians to promptly report post-vaccination adverse events (AEs) through VAERS and to the manufacturer.

Surveillance included all ER visits and hospitalizations. From the outpatient database, surveillance was limited to the following health outcomes of interest:

- Specified neurological conditions (Bell's palsy, seizure, neuritis [including optic neuritis], neuralgia, neuropathy, Guillain-Barré Syndrome [GBS], encephalopathy, encephalitis, epilepsy, transverse myelitis, and multiple sclerosis)
- Hypersensitivity reactions (including urticaria, angioedema, and anaphylaxis)
- New-onset autoimmune disease (including idiopathic thrombocytopenic purpura [ITP], diabetes, rheumatoid arthritis, hemolytic anemia, lupus, scleroderma, and mixed connective tissue disease). Evaluation of new onset autoimmune disease was restricted to persons who had been continuously enrolled as plan members for at least 2 years.
- Non-traumatic joint disease (arthritis, arthralgia, or arthropathy)
- Visits for management of pregnancy, childbirth, spontaneous or therapeutic abortion, fetal demise or complications thereof among persons given Tdap5 vaccine while pregnant
- Febrile illnesses and severe local reactions within 14 days of Tdap5 receipt for which medical attention was sought

➤ Results:

A total of 124,139 subjects received Tdap5 vaccine. Of these, 57,072 (46.0%) were male and 67,067 (54.0%) were female and 43.0% were White. The mean age was 32.1 years and the number of Tdap5 subjects by age group was: younger than 11 years (n=1049); 11 to 17 years (n=49,165); 18 to 39 years (n=25,566); 40 to 64 years (n=45,295); older than 64 years (n=3064). A total of 203,154 control subjects received Td vaccine in the prior year. The demographic profile of the control population was generally similar to that of the population of Tdap5 vaccine recipients.

In the instances where one of the predefined health outcomes of interest were seen to be statistically significantly more frequent (elevated incidence ration) the conditions were either known prior to vaccination or of indistinct nature (e.g. headache/migraine in the "encephalopathy" nomenclature).

No safety signals were seen in the ER and in the Hospital databases.

There were 65 deaths reported in this study, none of which were considered related to Tdap5 vaccination. None of the SAEs can be considered related to Tdap5 vaccination

Pregnancies

A total of 225 subjects received Tdap5 vaccine during pregnancy or up to 28 days prior to last menstrual period; these subjects were matched to 675 pregnant control subjects who did not receive Tdap5 vaccine. The demographic profile of the pregnant control population was similar to that of the population of pregnant Tdap5 vaccine recipients. The comparison of outcomes in Tdap5-exposed pregnancies and non-Tdap5-exposed pregnancies did not identify any significant safety issues.

V. MEMBER STATES OVERALL CONCLUSION AND RECOMMENDATION

➤ Overall conclusion

The information presented in the studies supplied here is well within the known safety and immunogenicity profile of the product.

➤ Recommendation

No further action required.

VI. REQUEST FOR SUPPLEMENTARY INFORMATION

Not applicable.