RISK MANAGEMENT PLAN - PART VI

SUMMARY OF THE RISK MANAGEMENT PLAN

Active substance(s) (INN or common name)	Influenza virus (inactivated, split) of the following strains: - A/<Official strain> (H1N1) - like strain (<actual strain>) - A/<Official strain> (H3N2) - like strain (<actual strain>) - B/<Official strain> - like strain (<actual strain>) (Victoria lineage) - B/<Official strain> like strain (<actual strain>) (Yamagata lineage)
Product's concerned (Brand name(s))	Quadrivalent Influenza Vaccine Thiomersal-free (syringe presentation): VaxigripTetra®, Vaxigrip Tetra® or other local tradename Quadrivalent Influenza Vaccine with Thiomersal (multidose vial presentation): VaxigripTetra® or Vaxigrip Tetra®
Name of Marketing Authorization Holder or Applicant	Sanofi group of companies
Data lock point (DLP) for this module	**15-Mar-2019**
Version number of Risk Management Plan (RMP) when this module was last updated	**Version 7.0**

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ABBREVIATIONS

ATM:	Acute Transverse Myelitis
DLP:	Data Lock Point
EEA:	European Economic Area
EPAR:	European Public Assessment Report
EU:	European Union
DART:	Developmental and Reproductive Toxicology
DRIVE:	Development of Robust and Innovative Vaccine Effectiveness
EFPIA:	European Federation of Pharmaceutical Industries and Associations
GBS:	Guillain-Barré Syndrome
HIV:	Human Immunodeficiency Virus
IMI:	Innovative Medicines Initiative
INN:	International Non-proprietary Name
ITP:	Idiopathic Thrombocytopenic Purpura
MDV:	Multidose Vial
NH:	Northern Hemisphere
PBRER:	Periodic Benefit-Risk Evaluation Report
QIV:	Quadrivalent Influenza Vaccine
RMP:	Risk Management Plan
SLE:	Systemic Lupus Erythematosus
SmPC:	Summary of Product Characteristics
TIV:	Trivalent Influenza Vaccine
WHO:	World Health Organization

SUMMARY OF RISK MANAGEMENT PLAN FOR VAXIGRIPTETRA (QUADRIVALENT INFLUENZA VACCINE)

This is a summary of the risk management plan (RMP) for VaxigripTetra® syringe and multidose (MDV) presentations. The RMP details important risks of VaxigripTetra®, how these risks can be minimized, and how more information will be obtained about VaxigripTetra®'s risks and uncertainties (missing information).

VaxigripTetra's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how VaxigripTetra should be used.

Important new concerns or changes to the current ones will be included in updates of VaxigripTetra®'s RMP.

VI.1 THE MEDICINE AND WHAT IT IS USED FOR

VaxigripTetra® is authorised for active immunization of adults and children from 6 months of age and older for the prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine (see SmPC for the full indication). It contains two influenza A virus subtypes and the two influenza B virus types as the active substance and it is given by intramuscular or subcutaneous injection. VaxigripTetra is available under two presentations: syringe (thiomersal-free) and MDV (thiomersal-containing).

In addition, QIV syringe (thiomersal-free) presentation has the following updated indication:

Prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine for:

- active immunisation of adults, including pregnant women, and children from 6 months of age and older,

- passive protection of infant(s) from birth to less than 6 months of age following vaccination of pregnant women.

V1.2 RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of VaxigripTetra®, together with measures to minimise such risks and the proposed studies for learning more about VaxigripTetra®'s risks, are outlined in the next sections.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;

• The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

• The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Information about adverse reactions is collected continuously and regularly analysed, including PBRER (Periodic Benefit-Risk Evaluation Report) assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

VI.2.1 List of important risks and missing information

Important risks of VaxigripTetra® are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered taken. Important risks can be regarded as identified or potential.

Identified risks are concerns for which there is sufficient proof of a link with the use of VaxigripTetra®.

Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation.

Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 1 - List of important risks and missing information

	QIV thiomersal-free	**QIV thiomersal-containing**
Important identified risks	None	None
Important potential risks	None	None
Missing information	None	Use in pregnant or lactating women

VI.2.2 Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

QIV syringe (thiomersal-free) presentation

No risk has been considered important for inclusion in the list of safety concerns of EU RMP.

QIV MDV (thiomersal-containing) presentation

No risk has been considered important for inclusion in the list of safety concerns of EU RMP.

Table 2 – Important risks and missing information with corresponding risk minimisation activities and additional pharmacovigilance activities, if any/ Missing information: Pregnant or lactating women

Missing information – Pregnant or lactating women	
Evidence for linking the risk to the medicine	**QIV MDV presentation**: Based on safety from post-marketing experience with Sanofi Pasteur TIV thiomersal containing, on international recommendations (1)(2)(3)(4)(5) in pregnant women, and satisfactory results of the Developmental And Reproductive Toxicology (DART) Study, Quadrivalent Influenza thiomersal containing vaccine may be administered in pregnant women if necessary (following Health care Professional Benefit Risk assessment). **<u>Supportive data from QIV and TIV Syringe presentations:</u>** Data from four clinical studies conducted with the trivalent influenza vaccine thiomersal free, “Trade Name of IM TIV thiomersal free Sanofi Pasteur, France,” administered to pregnant women during the second and third trimesters (more than 5,000 exposed pregnancies and more than 5,000 live births, followed up to approximately 6 months postpartum) did not indicate any adverse fetal, newborn, infant, or maternal outcomes attributable to the vaccine (6)(7)(8) Data from worldwide use of inactivated influenza vaccines, including experience with use of VaxigripTetra and Vaxigrip in countries where inactivated influenza vaccines are recommended in all stages of pregnancy and data from clinical study conducted in Finland (GQM14 Clinical study) with VaxigripTetra administered in pregnant women during the second and third trimesters (230 exposed pregnancies and 231 live births) did not indicate any adverse fetal or maternal outcomes attributable to the vaccine (9) The lack of harmful effects of inactivated influenza vaccination on maternal health during pregnancy has also been demonstrated in several studies published in the literature (10)(11)(12)(13)(14)(15)(16)(17)(18)(19)(20)(7)(21). No safety concern has been observed from post marketing safety data regarding administration of Vaxigrip®/VaxigripTetra® to pregnant/lactating women up to March 2019.
Risk factors and risk groups	QIV MDV presentation (thiomersal-containing vaccine): No anticipated risk/consequence is identified.
Risk minimization measures	SmPC: Sections 4.6 (Fertility, Pregnancy and Lactation)

VI.2.3 Post-authorisation development plan

VI.2.3.1. Studies which are conditions of the marketing authorisation

The following studies are conditions of the marketing authorization of QIV Syringe presentation:

Table 3 - Studies which are conditions of the marketing authorisation

GQM10 Safety of a Quadrivalent Influenza Vaccine (VaxigripTetra™) in Subjects Aged 6 Months and Older in Vietnam
Purpose of the study: GQM10 is a safety assessment, open-label, uncontrolled, mono-center study describing the safety of a quadrivalent influenza vaccine, VaxigripTetraTM, in subjects aged 6 months and older in Vietnam. The QIV contained the influenza strains recommended by the World Health Organization (WHO) and European Union (EU) for the 2018-2019 northern hemisphere (NH) influenza season.

The following studies are conditions of the marketing authorization of QIV Multidose presentation:

GQM00016 Immunogenicity and Safety of a Multi-Dose Quadrivalent Influenza Vaccine in Children Aged 6 Months to 17 Years
Purpose of the study: GQM00016 is a Phase III, randomized, open-label, active-controlled, multi-center study in 360 children aged 6 months to 17 years to assess the immunogenicity and safety of the quadrivalent influenza vaccine (QIV) in a multi-dose vial (MDV) presentation (thiomersal-containing) compared to the QIV in a syringe presentation (thiomersal-free). Both QIVs contained the influenza strains recommended by the World Health Organization (WHO) and European Union (EU) for the 2017-2018 northern hemisphere (NH) influenza season.

VI.2.3.2. Other studies in post-authorisation development plan

Not applicable.