ANNEX 4 SPECIFIC ADVERSE DRUG REACTION FOLLOW-UP FORMS

TABLE OF CONTENTS

ANNEX 4.1 SPECIFIC ADVERSE REACTION FOLLOW-UP QUESTIONNAIRE FOR LIVER INJURY (DRUG INDUCED LIVER INJURY FORM)

DILI (Drug Induced Liver Injury) check list Teriflunomide *(HMR1726D)To be attached to the corresponding completed SAE/ER and AE forms, concomitant treatment page and to all necessary reports (lab test, discharge summary)*

Sanofi Case ID- internal use only	Date of report Click here to enter a date.	Study ID *if applicable*	Patient ID *if applicable* Country of origin
Reporter Name: Reporter Type: MD ☐Nurse ☐Pharmacist☐ ☐other, Please specify ___	Reporter telephone	Reporter email	Country of case

PREVIOUS RELEVANT HISTORY AND CONCURRENT DISORDERS	NO	YES	*Specify details – ONSET Date DD/MM/YYYY*
Is the patient pregnant	☐	☐	
Hepato-biliary	☐	☐	
Allergic disease	☐	☐	
Allergy to drug	☐	☐	
Auto-Immune	☐	☐	
Heart/vascular disease	☐	☐	
Respiratory disease	☐	☐	
Cancer	☐	☐	
Surgical/Dental operation	☐	☐	
Alcohol consumption	☐	☐	*Number of drinks per day*
Acupuncture	☐	☐	
Occupational/toxic agent exposure	☐	☐	
Travels to Africa	☐	☐	
Travels to Asia	☐	☐	
Intravenous drug abuse	☐	☐	
Other	☐	☐	

DOCUMENTATION OF THE ADVERSE EVENT		
Main diagnosis:		**Start Date**
Are the following signs and symptoms associated?	*tick box if applicable* ☐	
Asthenia	☐	
Fever	☐	
Pruritus	☐	
Jaundice	☐	
Joint pain	☐	
Abdominal pain	☐	
Vomiting	☐	
Skin eruption	☐	**Type:**
Purpura	☐	

Hepatomegaly	☐	
Splenomegaly	☐	
Lymph nodes	☐	
Ascites	☐	
Asterixis	☐	
Coma	☐	
Malaise (with or without loss of consciousness)	☐	
INR>2 or prothrombin T.<50%	☐	
Dizziness	☐	
Hypotension	☐	
Arrhythmia	☐	

CENTRAL LABORATORY DATA *performed:* **NO** ☐ **YES** ☐ **Date:**

LOCAL LABORATORY DATA *performed:* **NO** ☐ **YES** ☐ **Date:**

ADDITIONAL TEST DATA (to be performed at local level)

	Not tested	Negative result	Positive result	Date of test MM/DD/YYYY	Titration
HBa Ag	☐	☐	☐		
Anti-Hbs Ab	☐	☐	☐		
Anti-Hbc Ab	☐	☐	☐		
Anti-Hbc/IgM Ab	☐	☐	☐		
Anti-HAV/IgM Ab	☐	☐	☐		
Anti-HCV Ab	☐	☐	☐		
PCR-C	☐	☐	☐		
Anti-CMV IgM Ab	☐	☐	☐		
Anti-EBV Ab	☐	☐	☐		
Anti-nuclear Ab	☐	☐	☐		
Antinative DNA Ab	☐	☐	☐		
Anti smooth muscle Ab	☐	☐	☐		
Anti mitochondrial AB	☐	☐	☐		

OTHER INVESTIGATIONS

Date DD/MM/YYYY	NATURE	RESULTS
Click here to enter a date.		
Click here to enter a date.		
Click here to enter a date.		

LIVER BIOPSY NO ☐ YES ☐ *if YES is ticked a report needs to be attached*	DATE DD/MM/YYYY

LIVER IMAGING *if YES is ticked a report needs to be attached*	DATE DD/MM/YYYY	BRIEF RESULTS
ULTRASONOGRAPHY NO ☐ YES ☐		
CT SCAN NO ☐ YES ☐		
MRI NO ☐ YES ☐		

I. CONCOMITANT OR PREVIOUS DRUGS POSSIBLY SUSPECTED OF INDUCING Liver Injury

Name	Indication	Daily Dose	Route	Start Date	End Date
				Click here to enter a date.	Click here to enter a date.
				Click here to enter a date.	Click here to enter a date.

Laboratory Tests	Date	Baseline Values	Result	Normal High / Low

ANNEX 4.2 SPECIFIC ADVERSE REACTION FOLLOW-UP QUESTIONNAIRE FOR PANCREATIC EFFECTS (PANCREATIC DISORDER FORM)

Pancreatic Disorder
Information to be transmitted to Global Pharmacovigilance & Epidemiology Dpt

*** To be attached to the corresponding completed AE/SAE form**

PROJECT: Protocol N° if clinical trial: |__|__|__| |__|__|__|__|

Date of this report: ……/……../……..…. Patient ID: |__|__|__|__|__|__|__|__|__|
day month year

INVESTIGATOR/REPORTER NAME:

……

Phone number:……

GPE case ID (for Sanofi internal use):

_____

1. PATIENT INFORMATION

Initials	**Age**	**DOB**	**Gender:** ☐ Male ☐ Female
Known allergies			

2. DRUG BEING REPORTED

Name: _____

3. SYMPTOMS

Were any of the following symptoms associated with the event:

Symptoms	**Date of Onset**	**Description**	**Outcome**
Abdominal Pain ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Malaise ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Nausea ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Vomiting ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Jaundice ☐ Yes ☐ No			☐☐ Recovered ☐ Recovering

			☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Fever ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Weight Loss ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal
Abdominal bleeding ☐ Yes ☐ No			☐ Recovered ☐ Recovering ☐ Continuing ☐ Not Recovered ☐ Recovered with Sequelae ☐ Fatal

4. Any known results of genetic tests indicating an increased risk for pancreatitis?

☐ Yes, please provide details below ☐ No

_____

_____

5. Any anatomic anomalies potentially associated with pancreatitis?

☐ Yes, please provide details below ☐ No

_____

_____

6. PAST MEDICAL HISTORY

Please indicate if the patient had or has one or more of the following conditions

Condition		Date diagnosed	Treatment (if available)
Pancreatitis	☐ Yes ☐ No		
Cholelithiasis/ choledocholithiasis	☐ Yes ☐ No		
Hepatitis	☐ Yes		

	☐ No		
Abdominal tumor	☐ Yes ☐ No		
Abdominal surgery	☐ Yes ☐ No		
Abdominal trauma	☐ Yes ☐ No		
Condition		**Date diagnosed**	**Treatment (if available)**
Hypertriglyceridemia	☐ Yes ☐ No		
Hyperparathysoidism	☐ Yes ☐ No		
Hypercalcemia	☐ Yes ☐ No		
Human immunodeficiency virus	☐ Yes ☐ No		
Post-ERCP	☐ Yes ☐ No		
Malignancy Specify:_____	☐ Yes ☐ No		
Other suspected disorders Specify:_____	☐ Yes ☐ No		

7. SOCIAL HISTORY

Alcohol Consumption (Drinks/day) _____
Tobacco user: ☐ Yes ☐ No _____ pack years

8. MEDICATION HISTORY

8.1. Please indicate if the patient has taken one or more of the following medications

Medication		**Start Date**	**End Date**	**Dose**	**Frequency**	**Reason for Discontinuation**	**Investigator Causality**[1]
Leflunomide	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Azathioprine	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Valproic Acid	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Estrogen	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Corticosteroids Specify:_____	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Statins: Specify:_____	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐

[1]Physician's assessment of relatedness to Pancreatitis

9. INVESTIGATIONS

9.1. Laboratory Tests

Investigation		**Date**	**Baseline Values**	**Result**	**Normal High / Low**
Red blood cell count	☐ Yes ☐ No				
WBC count	☐ Yes ☐ No				

Blood urea nitrogen	☐ Yes ☐ No				
Blood glucose	☐ Yes ☐ No				
Amylase	☐ Yes ☐ No				
Lipase	☐ Yes ☐ No				
Gamma GT	☐ Yes ☐ No				
Investigation		**Date**	**Baseline Values**	**Result**	**Normal High / Low**
Tripsinogen Activation Peptide	☐ Yes ☐ No				
Alanine aminotransferase (ALT)	☐ Yes ☐ No				
Aspartate aminotransferase (AST)	☐ Yes ☐ No				
Alkaline phosphatase	☐ Yes ☐ No				
Bilirubin	☐ Yes ☐ No				
Calcium	☐ Yes ☐ No				
Other Investigation		**Date**	**Baseline Values**	**Result**	**Normal High / Low**

9.2. Imaging studies

Investigation		**Date**	**Results**
Abdominal ultrasound	☐ Yes ☐ No		
Contrast enhanced abdominal CT	☐ Yes ☐ No		
Magnetic resonance imaging (MRI)	☐ Yes ☐ No		

Endoscopic Retrograde Cholangiopancreatogram (ERCP)	□ Yes □ No		
Magnetic Resonance Cholangiopancreatogram (MRCP)	□ Yes □ No		

10. Action taken with Aubagio as result of the adverse events:

Drug Withdrawn ☐ **Dose Reduced ☐** **Dose not changed ☐**

Was Aubagio re-administration? □ Yes □ No

Did the patient experience any adverse event, upon re-administration of Aubagio?

_____

11. MANAGEMENT

11.1. Causal relationship

Is there a reasonable possibility that the pancreatic disorder is associated with the use of the drug being reported?

□ Yes □ No □ Unable to assess

11.2. Has any treatment been given to the patient to treat pancreatitis? □ Yes □ No

Medication	Dose	Frequency	RoA	Start date	End date

12. ABREVIATIONS

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ERCP	Endoscopic retrograde cholangiopancreatogram
MRCP	Magnetic resonance cholangiopancreatogram
RoA	Route of administration

ANNEX 4.3 SPECIFIC ADVERSE REACTION FOLLOW-UP QUESTIONNAIRE FOR TERATOGENICITY (PREGNANCY REPORTING FORM)

PREGNANCY / DRUG EXPOSURE VIA PARENT DATA COLLECTION FORM

Grey fields are for Sanofi use only

1- DATE REPORT RECEIVED		
COMPANY RECEIVED DATE:	☐ Initial ☐ Follow-up	
CASE NUMBER	**PRODUCT RECEIVED / PRODUCT CODE**	**SANOFI / CRO CONTACT**
LOCAL ID: GLOBAL PV ID:		NAME: TELEPHONE:
SOURCE	**STUDY INFORMATION (IF APPLICABLE)**	**WHO RECEIVED MEDICATION?**
SPONTANEOUS/UNSOLICITED ☐ (includes pregnancy registry) STUDY/SOLICITED (includes PSP/MRP ☐	STUDY ID / REGISTRY ID: CENTER ID: PATIENT ID: TREATMENT ID:	☐ MOTHER ☐ FATHER INITIALS _____ INITIALS _____ (FIRST, MIDDLE, LAST) (FIRST, MIDDLE, LAST) Initials not to be collected for case report from clinical studies

2- REPORTER INFORMATION		
NAME (first/last):	STREET:	
OCCUPATION: ☐ CONSUMER ☐ STUDY INVESTIGATOR ☐ LAWYER ☐ MEDICAL DOCTOR ☐ PHARMACIST ☐ OTHER HCP (HEALTHCARE PROFESSIONAL) ☐ OTHER	CITY/STATE/PROVINCE:	
PHONE:	POSTAL CODE:	COUNTRY:
DOES MOTHER AGREE TO PROVIDE INFORMATION? YES ☐ NO ☐ DOES FATHER AGREE TO PROVIDE INFORMATION? YES ☐ NO ☐		

SANOFI

3 - PARENT INFORMATION AT THE TIME OF THE PREGNANCY

	AGE/ BIRTH DATE For clinical study, Year of birth to be collected only	RH (RHESUS) FACTOR	HT / UNIT	WT / UNIT	SIGNIFICANT MEDICAL CONDITIONS*
MOTHER					SMOKING HISTORY:_____CIGARETTES PER DAY** ALCOHOL:_____DRINKS PER DAY SUBSTANCE ABUSE: (specify)_____ HYPERTENSION: ☐ NO ☐ YES ☐ UNK DIABETES: ☐ NO ☐ YES ☐ UNK EPILEPSY: ☐ NO ☐ YES ☐ UNK IF YES, SPECIFY THE TYPE: …. PSYCHIATRIC ILLNESS: ☐ NO ☐ YES IF YES, SPECIFY: …
					SEROLOGY: HIV: ☐ NO ☐ YES ☐ UNK HEPATITIS: ☐ NO ☐ YES ☐ UNK
					OTHER HISTORY (including thyroid disorders, asthma, allergic disease, heart disease, sexual transmitted disorder, education level, learning difficulties, congenital malformations, environmental exposures):
FATHER					SMOKING HISTORY:_____CIGARETTES PER DAY ALCOHOL:_____DRINKS PER DAY SUBSTANCE ABUSE: (specify):_____ HYPERTENSION: ☐ NO ☐ YES☐ UNK DIABETES: ☐ NO ☐ YES☐ UNK EPILEPSY: ☐ NO ☐ YES ☐ UNK PSYCHIATRIC ILLNESS: ☐ N☐ YES ☐ UNK
					SEROLOGY: HIV: ☐ NO ☐ YES ☐ UNK HEPATITIS: ☐ NO ☐ YES ☐ UNK

3 - PARENT INFORMATION AT THE TIME OF THE PREGNANCY

	OTHER HISTORY (including thyroid disorders, asthma, allergic disease, heart disease, sexual transmitted disorder, education level, learning difficulties, congenital malformations, environmental exposures):

*Include information on race, ethnicity, consanguinity or occupation if you consider it would contribute significantly to the investigation and evaluation of certain adverse findings in the pregnancy or its outcome or on the health of the fetus/child; per local privacy law.

**Mention if mother quit smoking or materially reduced her usage before or during pregnancy and when.

4 – SPECIFIC TO THE PREGNANCY PREVENTION PROGRAMME, IF APPLICABLE (e.g. valproate…)

WAS THERE A NEGATIVE PREGNANCY TEST AT TREATMENT INITIATION? ☐ NO ☐ YES ☐ UNK. ☐ NA*

WAS THE PATIENT GUIDE RECEIVED? ☐ NO ☐ YES ☐ UNK. ☐ NA*

WAS THE PATIENT CARD RECEIVED? ☐ NO ☐ YES ☐ UNK. ☐ NA*

WAS AN ANNUAL REVIEW COMPLETED BY A SPECIALIST? ☐ NO ☐ YES ☐ UNK ☐ NA*

WAS THE ANNUAL RISK ACKNOWLEDGMENT FORM SIGNED? ☐ NO ☐ YES ☐ UNK. ☐ NA*

*Not applicable

5- IMMUNIZATION / GYNECOLOGY

MATERNAL IMMUNIZATION				GYNECOLOGICAL DETAILS			
RUBELLA:	☐ NO	☐ YES	☐ UNK	WERE CONTRACEPTIVE METHODS USED:	☐ NO	☐ YES	☐ UNK
TOXOPLASMOSIS:	☐ NO	☐ YES	☐ UNK	IF YES, SPECIFY: CONTRACEPTION TYPE:	☐ ORAL	☐ LOCAL	☐ IUCD
CMV:	☐ NO	☐ YES	☐ UNK	:			
				CONTRACEPTION NAME:_____			
				CONTRACEPTION DOSE:_____			
				CONTRACEPTION START AND STOP DATES:_____			
				DETAILS OF POSSIBLE CAUSE TO CONTRACEPTION FAILURE:			

5- IMMUNIZATION / GYNECOLOGY

	NON COMPLIANCE WITH PRIMARY METHOD (E.G HORMONAL/IUD ☐ NO ☐ YES ☐ UNK NON COMPLIANCE WITH BARRIER METHOD ☐ NO ☐ YES ☐ UNK OTHER (EG., DRUG DRUG INTERACTION, EPISODE OF GI DISORDER, …) ☐ NO ☐ YES ☐ UNK NORMAL MENSTRUAL CYCLES ☐ NO ☐ YES ☐ UNK INFERTILITY ☐ NO ☐ YES ☐ UNK IF TREATMENT SPECIFY:

6- PREGNANCY INFORMATION

DATE OF LAST MENSTRUAL PERIOD (LMP) LMP:_____ - _____ - _____ (DD-MMM-YY) ESTIMATED DATE OF DELIVERY (EDD) EDD:_____ - _____ - _____ (DD-MMM-YY)	DATE OF POSITIVE PREGNANCY TEST (IF ANY) _____ - _____ - _____ (DD-MMM-YY) DATE OF PREVIOUS NEGATIVE PREGNANCY TEST (IF ANY) _____ - _____ - _____ (DD-MMM-YY)
MEDICAL ASSISTANCE / HOSPITALIZATION DURING PREGNANCY? ☐ NO ☐ YES DETAILS: _____	MULTIPLE FETUSES/CHILDREN? ☐ NO ☐ YES

IS THE OUTCOME OF CURRENT PREGNANCY KNOWN AT THE TIME OF THIS REPORT? ☐ NO ☐ YES

OBSTETRICAL HISTORY	NUMBER/ YEAR/COMMENTS
PREVIOUS PREGNANCIES (if ectopic or molar pregnancy or other complication, please specify):	
LIVE BIRTHS, WITHOUT CONGENITAL ANOMALIES/ MALFORMATIONS/NEURODEVELOPMENTAL DISORDERS/AUTISM SPECTRUM DISORDERS (ASD)	
LIVE BIRTHS, WITH CONGENITAL ANOMALIES/ MALFORMATIONS/NEURODEVELOPMENTAL DISORDERS/AUTISM SPECTRUM DISORDERS (specify type of congenital anomalies/developmental disorders/ASD):	

6- PREGNANCY INFORMATION

SPONTANEOUS ABORTIONS PRIOR TO 20 WEEKS GESTATION (specify gestational age):	
ELECTIVE TERMINATION (FETAL DEFECTS) (specify gestational age):	
ELECTIVE TERMINATION (NO FETAL DEFECTS OR UNKNOWN) (specify gestational age):	
FETAL DEATHS (>20 WEEKS GESTATION) (specify gestational age, cause(s)/Post Mortem findings):	

MATERNAL/PATERNAL/RELATIVES (including grand-parents) **HISTORY**:

CONGENITAL MALFORMATION	☐ NO	☐ YES, SPECIFY RELATION/DETAILS: _____
CHILDREN DYING YOUNG	☐ NO	☐ YES, SPECIFY RELATION/DETAILS: _____
CHROMOSOMAL ABNORMALITY	☐ NO	☐ YES, SPECIFY RELATION/DETAILS: _____
DEVELOPMENTAL DELAY	☐ NO	☐ YES, SPECIFY RELATION/DETAILS: _____
HEREDITARY DISEASE	☐ NO	☐ YES, SPECIFY RELATION/DETAILS: _____
PERTINENT GYNECOLOGIC INFORMATION	☐ NO	☐ YES, SPECIFY RELATION / DETAILS: _____
CONSANGUINITY BETWEEN PARENTS	☐ NO	☐ YES, SPECIFY RELATION / DETAILS: _____
OTHER	☐ NO	☐ YES, SPECIFY: _____

7- ADVERSE EVENT (OTHER THAN ABNORMAL PREGNANCY OUTCOMES) INVOLVED DURING THE PREGNANCY ?

☐ NO ☐ YES (please complete corresponding AE form(s))

THE AE OCCURRED IN THE ☐ MOTHER ☐ CHILD	GLOBAL PV DATABASE NUMBER FOR CHILD REPORT # _____

DESCRIBE ADVERSE EVENT(S):

SANOFI

8- MEDICATIONS: (include prescription & OTC medicines and pregnancy/food supplements e.g. folic acid and other vitamins, iron)

PRODUCTS* (LIST SANOFI-DRUG(S) FIRST)	CAUSAL RELATION-SHIP (YES/NO)	FETAL / NEONATAL EXPOSURE **	INDICATION	DOSE/ SCHEDULE/DOSE NUMBER	ROUTE	START DATE+ (DD-MMM-YY)	STOP DATE+ (DD-MMM-YY)	DURATION (DAYS)	BATCH NUMBER (MANDATORY. IF NOT AVAILABLE, ENTER NA/ IF NOT OBTAINABLE AT ALL ENTER NO)	SITE OF ADMIN	SIDE OF ADMIN

*If any medications were possibly involved in the occurrence of the reported disorder; specify action taken & outcome **Fetal Exposure: Select All the Numbers (below) that apply for Fetal Exposure

+Stop And Start Dates: If exact dates are unavailable, provide gestation weeks of exposure or trimesters of exposure.

1. PRIOR TO OR AT TIME OF CONCEPTION
2. DURING PREGNANCY
3. LABOR AND DELIVERY
4. BREAST FEEDING

9- ADDITIONAL MEDICAL DATA

COMMENTS REGARDING MATERNAL HEALTH OR COMPLICATIONS DURING PREGNANCY,

10- PRENATAL TESTING

Specify below or check if none ☐

EXAMINATION	DATE (DD-MMM-YY)	NORMAL ✓	ABNORMAL ✓	SPECIFY ABNORMALITIES
AMNIOCENTESIS				
ALPHA FETAL PROTEIN (AND OTHER SERUM MARKERS)				
CHORIONIC VILLI SAMPLING				
FETAL STRESS TEST				
UTERINE ULTRASOUND (please describe)				
GENETIC SCREENING (specify:_____)				
OTHER (specify:_____)				

11- PREGNANCY OUTCOME

CHILDREN/FETUSES: ☐ SINGLE ☐ MULTI (#_____)

CHILD/ FETUS/	SEX	DATE OF DELIVERY, ABORTION, TERMINATION OR FETAL DEATH (DD-MMM-YY)	APGAR SCORE		DELIVERY MODE (✓)		WEEK OF GESTATION	BIRTH WEIGHT & LENGTH	HEAD CIRCUM (CMS)	*OUTCOME	CONGENITAL ANOMALY		NEONATE DEATH (age at death, specify cause)
			1 MIN	5 MIN	VAG	C-SECT					YES**	NO	
								g cm					
								g cm					
								g cm					

11- PREGNANCY OUTCOME	
1.	* OUTCOME: ENTER THE NUMBER APPROPRIATE TO THE PREGNANCY OUTCOME (ENTER ALL THAT APPLY) 2. LIVE BIRTH (NORMAL) 3. LIVE BIRTH (ABNORMAL)** 4. SPONTANEOUS ABORTION (<20 WEEKS GESTATION) 5. EARLY FETAL DEATH (20-27 WEEKS GESTATION) 6. LATE FETAL DEATH (AT LEAST 28 WEEKS GESTATION) 7. ELECTIVE TERMINATION 8. STILLBIRTH 9. MATERNAL DEATH (IF RESULTING IN FETAL DEATH, ADD APPROPRIATE NUMBER) 10. ECTOPIC PREGNANCY 11. LIVE BIRTH (NORMAL) – DEVELOPMENTAL DISORDERS**
	OF NOTE, CONGENITAL ANOMALIES INCLUDE MALFORMATIONS AND ABNORMAL FUNCTIONS EITHER BEING OBSERVABLE AT BIRTH OR LATER DURING THE CHILD DEVELOPMENT. IF PREGNANCY OUTCOME INVOLVES CONGENITAL ANOMALY **AT BIRTH OR DEVELOPMENTAL DISORDERS, SPECIFY (SEE SECTION 12 FOR NEURO DEVELOPMENT DISORDERS):
	IN CASE OF ABORTION, STILLBIRTHS, FETAL DEATH OR MATERNAL DEATH, WAS AN AUTOPSY PERFORMED? ☐ NO ☐ YES ☐ UNK IF YES, PROVIDE RESULTS FOR EACH WHERE APPLICABLE:
	LABOR/DELIVERY: MODE OF DELIVERY: ANY COMPLICATIONS OF LABOR AND/OR DELIVERY ☐ NO ☐ YES, SPECIFY:
	MEDICATION DURING LABOR ☐ NO ☐ YES, SPECIFY:
	CLEAR AMNIOTIC FLUID ☐ NO ☐ YES NORMAL PLACENTA ☐ NO ☐ YES

11- PREGNANCY OUTCOME

ADDITIONAL INFORMATION ABOUT THE NEWBORN CONDITION:

BREAST FEEDING ☐ NO ☐ YES

NEONATAL ILLNESS ☐ NO ☐ YES, SPECIFY: _____

NEED FOR RESUSCITATION ☐ NO ☐ YES INTRAUTERINE GROWTH RESTRICTION OR IMMATURITY ☐ NO ☐ YES, SPECIFY:

CORRECTIVE TREATMENT RECEIVED BY NEWBORN ☐ NO ☐ YES, SPECIFY: _____

INTENSIVE CARE ☐ NO ☐ YES

TRANSFERRED TO INTENSIVE CARE UNIT OR PEDIATRIC DEPARTMENT ☐ NO ☐ YES DURATION: ___

ADDRESS OF DEPARTMENT _____

INFANT TO BE FOLLOWED UP BY (DOCTOR'S NAME AND ADDRESS)

12- PEDIATRIC ASSESSMENT

CHILD #	CHILD AGE AT THE TIME OF ASSESSMENT	MOTOR DEVELOPMENT		NEUROLOGICAL AND BEHAVIOURAL DEVELOPMENT		GROWTH WEIGHT & LENGTH*	OTHER TYPE OF CONGENITAL ANOMALY*		IF * SPECIFY .
		NORMAL	DELAYED*	NORMAL	DELAYED*		YES*	NO	
						g cm			
						g cm			
						g cm			

*SPECIFY **MEDICAL EVENTS THAT LED TO MEDICAL OFFICE/ER VISIT OR HOSPITALIZATION** OR CONGENITAL ANOMALY **NOT IDENTIFIED AT BIRTH** OR DEVELOPMENTAL DISORDERS/AUTISM SPECTRUM DISORDERS,

PRINTED NAME:_____

SIGNATURE: _____ **DATE:**_____

ANNEX 4.4 SPECIFIC ADVERSE REACTION FOLLOW-UP QUESTIONNAIRE FOR SERIOUS OPPORTUNISTIC INFECTIONS, INCLUDING PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) (PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY FORM)

Progressive Multifocal Leukoencephalopathy (PML) check list*
Information to be transmitted to Global Pharmacovigilance & Epidemiology Dept.

*** To be attached to the corresponding completed AE/SAE Form**

PROJECT:

Protocol N° if clinical trial: |_|_|_| |_|_|_|_|

Date of this report: ……/……../……..…
Day month year

Patient ID: |_|_|_|_|_|_|_|_|_|

INVESTIGATOR/REPORTER NAME:

……

Phone number:……

GPE case ID (for Sanofi internal use):

|_|_|_|_| |_|_| |_|_|_|

1. PATIENT INFORMATION

Initials	**Age**	**DOB**	**Gender:** ☐ Male ☐ Female

2. DRUG BEING REPORTED

Name: _____

3. PML-RELATED QUESTIONS

3.1. PML Diagnosis

3.1.1. Please indicate whether the diagnosis of PML is
☐ Suspected ☐ Confirmed ☐ Indeterminate

If indeterminate, what is the differential diagnosis?

_____

_____

3.1.2. Please indicate basis for diagnosis (check all that apply)
☐ Brain biopsy ☐ CSF PCR ☐ MRI

3.2. Causal relationship

Is there a reasonable possibility that PML diagnosis is associated with the use of the drug being reported?
☐ Yes ☐ No ☐ Unable to assess

3.3. Clinical symptoms

Symptoms		**Date of onset**
Recent changes in personality or mood	☐ Yes ☐ No	
Recent or sudden change in cognitive behaviour Example: confusion, disorientation	☐ Yes ☐ No	
Language or speech disturbances Example: aphasia or dysarthria	☐ Yes ☐ No	
Visual disturbances	☐ Yes ☐ No	
Ataxia/loss of motor coordination/progressive weakness	☐ Yes ☐ No	
New onset of seizures	☐ Yes ☐ No	
Other– if yes, please specify	☐ Yes ☐ No	

3.4. EDSS score

	Date	**Score**
Prior to the onset of symptoms		
After the onset of symptoms		

3.5. Laboratory and JCV information

Test*		Date	Results
JCV DNA Detection by PCR ☐ Yes ☐ No	☐ CSF		
Laboratory used for detection (please provide name and location)	☐ Plasma		
Brain biopsy ☐ Yes ☐ No Hospital facility (please provide name and location)			
CD4 count ☐ Yes ☐ No			
CD8 count ☐ Yes ☐ No			

*Please provide copies of test results

3.6. Other Investigation

Other Investigation	Date	Baseline Values	Result	Normal High / Low

3.7. Imaging information

	Date	Results
Was Brain MRI performed prior to the start of symptoms? ☐ Yes ☐ No		
Was Brain MRI performed for PML diagnosis? ☐ Yes ☐ No		
Was Brain CT performed prior to the start of symptoms? ☐ Yes ☐ No		
Was Brain CT performed for PML diagnosis? ☐ Yes ☐ No		

3.8. PML treatment

Has any treatment been given to the patient to treat PML? ☐ Yes ☐ No

Medication	Dose	Frequency	Route	Start date	End date

4. MEDICAL HISTORY

4.1. Please indicate if the patient had or has one or more of the following conditions

Relevant medical information		Date	Treatment (if available)
HIV or AIDS	☐ Yes ☐ No		
Leukemia/Lymphoma Other Malignancies Please specify:_____	☐ Yes ☐ No ☐ Yes ☐ No		
Opportunistic infection(s) (e.g CMV)	☐ Yes ☐ No		

Specify:_____			
Tuberculosis	☐ Yes ☐ No		
Organ transplant Please specify:_____	☐ Yes ☐ No		
Other autoimmune disease (e.g. SLE, Sjogren's, Behcet's, RA, psoriasis….) Please specify: _____	☐ Yes ☐ No		

4.2. Please indicate if the patient had prior JCV testing

Relevant investigations			**Date**	**Results**
JCV DNA testing before current illness (please provide the name of laboratory where the test was performed)	☐ Yes ☐ No	☐ CSF		
		☐ Plasma		
JCV Serology	☐ Yes ☐ No			

5. DRUG HISTORY

5.1. Please indicate any treatment the patient received/receiving for multiple sclerosis

Medication	**Date of 1st Course**	**Date of Last Course**	**No. of Courses**	**Dose/ Route**	**Reason for Discontinuation**	**Reporter Causality**[1]
Lemtrada™ (alemtuzumab) ☐ Yes ☐ No (if not the drug being reported)						Related ☐ Unrelated ☐ Unknown ☐

Medication	**Start Date**	**End Date**	**Dose/ Route**	**Frequency**	**Reason for Discontinuation**	**Reporter Causality**[1]
Aubagio® (teriflunomide) ☐ Yes ☐ No (if not the drug being reported)						Related ☐ Unrelated ☐ Unknown ☐
Tysabri® (natalizumab) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Gilenya® (fingolimod) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Tecfidera® (dimethyl fumarate) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Interferon beta (any product) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Copaxone® (glatiramer acetate) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Novantrone®, Elsep® (mitoxantrone) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Corticosteroids (most recent course) ☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Other MS Therapies ☐ Yes ☐ No Specify: _____						Related ☐ Unrelated ☐ Unknown ☐
Other MS Therapies ☐ Yes						Related ☐

Specify: _____	☐ No						Unrelated ☐ Unknown ☐
Other MS Therapies Specify: _____	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Other MS Therapies Specify: _____	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐

[1]Physician's assessment of relatedness to PML

5.2. Please indicate if the patient has taken one or more of the following medications

Medication		**Start Date**	**End Date**	**Dose**	**Frequency**	**Reason for Discontinuation**	**Reporter Causality**[1]
Rituxan®, Mabthera® (rituximab)	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Raptiva® (efalizumab)	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Arava® (leflunomide)	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Methotrexate	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐
Other immunosuppressive or chemotherapeutic agents (e.g., cyclophosphamide, tacrolimus, azathioprine, mycophenolate, cyclosporine) Please specify:	☐ Yes ☐ No						Related ☐ Unrelated ☐ Unknown ☐

[1]Physician's assessment of relatedness to PML

Abbreviations

AIDS	Acquired immunodeficiency syndrome
CMV	Cytomegalovirus
CT	Computed tomography
DNA	Deoxyribonucleic acid
EDSS	Expanded disability status scale
HIV	Human immunodeficiency virus
JCV	John Cunningham Virus
MRI	Magnetic resonance imaging
PCR	Polymerase chain reaction