GLOBAL PHARMACOVIGILANCE & EPIDEMIOLOGY | Bristol-Myers Squibb

BRISTOL-MYERS SQUIBB / SYNEOS HEALTH

SERVICE PROVIDER PARTNERSHIP

AE/SAE Management Plan Template for NIR Studies w/Primary Data Collection

SPECIFIC VERSION DATE	16-December-2019
SPONSOR	Bristol-Myers Squibb Research and Development
PRODUCT	BCR-ABL1 tyrosine kinase inhibitor
PROTOCOL #	CA180-653
PROTOCOL TITLE	Determining Change In Cardiovascular And Metabolic Risks In Patients With Chronic Phase Chronic Myeloid Leukemia Receiving BCR-ABL Tyrosine Kinase Inhibitor First-Line Therapy In The United States.
SYNEOS HEALTH STUDY #	16BMS0059
MODE OF AE/SAE DATA COLLECTION	☒ Paper AE/SAE ☐ EDC AE/SAE

KEY NOTES:

- For each study CA180-653, this document will be updated to reflect study-specific details in Section 1 which are additional to and/or differ from Section 2: Core AE/SAE Management Plan.
- The scope of this document is limited to the receipt and processing of individual case safety reports and pregnancy reports in study CA180-653.

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1.1 STUDY-SPECIFIC AE/SAE MANAGEMENT PLAN APPROVALS

AUTHOR	
Akanksha Bhargava Safety and PV Specialist I, SPVG Syneos Health	Date
SYNEOS HEALTH APPROVALS	
Kevin Dopke Project Director	Date
Mahnaaz Khatib Manager, Safety & Pharmacovigilance	Date
BMS / GPV&E APPROVALS	
Joseph Sewter, MBA Group Director, Adverse Event Processing & Submissions	Date

1.1 STUDY-SPECIFIC AE/SAE MANAGEMENT PLAN APPROVALS

AUTHOR	
Akanksha Bhargava Safety and PV Specialist I, SPVG Syneos Health	17-DEC-2019 Date
SYNEOS HEALTH APPROVALS	
Kevin Dopke Project Director	20Dec2019 Date
Mahnaaz Khatib Manager, Safety & Pharmacovigilance	18-DEC-2019 Date
BMS / GPV&E APPROVALS	
Joseph Sewter, MBA Group Director, Adverse Event Processing & Submissions	16-DEC-2019 Date

1.2 STUDY-SPECIFIC CONTACT INFORMATION

↓ BMS			
CONTACT NAME/TITLE	**PHONE #**	**E-MAIL ADDRESS**	**FAX #**
BMS GPV&E		worldwide.safety@bms.com	1-609-818-3804
BMS AE/SAE Reconciliation Request		aepbusinessprocess@bms.com	
↓ Syneos Health			
CONTACT NAME/TITLE	**PHONE #**	**E-MAIL ADDRESS**	**FAX #**
Syneos Health SPVG – Notification of AE/SAE	1-888-750-8020	SafetyPV@Syneoshealth.com	1-866-880-9343
Study Query Central E-mail Address		SafetyPV@Syneoshealth.com	
Akanksha Bhargava Safety and PV Specialist I	+91 2048529720	Akanksha.bhargava@syneoshealth.com	N/A
Hima Mathews, Safety and PV Specialist II	+91-9970849873	hima.mathews@Syneoshealth.com	N/A
Kevin Dopke Project Director	1 215 944 3897	Kevin.Dopke@Syneoshealth.com	

1.3 REGULATORY REPORTING FOR SUSARS

COUNTRY/REGULATORY AUTHORITY	REGULATORY AUTHORITY SUBMISSION	EC/IRB SUBMISSION*	INVESTIGATOR ALERT LETTERS	INVESTIGATOR SEMI-ANNUAL SUSAR REPORT
United States / FDA	BMS	Not Applicable	Not Applicable	Not Applicable

* Country specific Ethics Committee reporting regulations determine whether BMS or a third party will complete the submission. Country requirements will be supplied by BMS.

1.4 STUDY-SPECIFIC SAE MANAGEMENT CONSIDERATIONS/PROCESSES

Please indicate if there are study specific SAE management considerations/processes for this protocol:

☐ **NO**, processes as described in the attached SAEMP are accurate as recorded.
The remainder of this page will remain blank.

☒ **YES**, specific SAE management considerations/processes are listed below:

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*If **YES** box was checked above, list study-specific considerations/processes here:*

This study is a NIR study: Non-serious and Serious Adverse Events will be managed/handled in adherence to the process flows defined in Section 1.4.

Section 2.2 Databases

Bristol-Myers Squibb (BMS) Global Pharmacovigilance and Epidemiology (GPVE) will maintain the safety database for the study while Syneos Health will maintain the clinical database.

Syneos Health will maintain the SAE/AE/AESI/Pregnancy tracking database. The SAE/AE/AESI/pregnancy reports in the tracking Safety Database will be assigned unique case numbers. Numbering scheme: Protocol-Site ID-Patient ID-AE number. Example: 180653-001-001-01.

Note: BMS will hold the Safety database for this study and Syneos Health Safety Database is used for tracking of the SAE/AE/AESI/pregnancies only.

At set-up of the Syneos Health AE tracking database, MedDRA 19.1 has been installed. This version will not be updated.

Section 2.5 Training of Investigators and Staff on AE/SAE Reporting Procedures

Syneos Health Safety and Pharmacovigilance (SPVG) will track Pharmacovigilance team completion of protocol-specific training and attendance at start-up meetings. Documentation will be maintained on the Syneos Health shared network drive.

Section 2.6 Procedures

Following the, start of first TKI (tyrosine kinase inhibitor) all SAEs/AEs under study, whether or not related to the product(s) under study, must be collected. All AEs will be recorded in the eCRF.

Per revised Protocol of 19-September-2018, for all events related to BMS products (serious and non-serious) events must also be recorded on the Solicited and Non-interventional Research AE/SAE Form and reported to BMS (or designee). Serious AEs related to BMS product must be reported within 24 hours/1 business day to comply with regulatory requirements. A form should be completed for any event where doubt exists regarding its status of seriousness. Non-serious AEs must be reported to BMS (or designee) within 7 business days. Non-serious AEs should be reported as SAEs if they become serious.

All AEs and SAEs related to BMS product must be reported by confirmed facsimile (fax) transmission or reported via electronic mail to:

SAE Email Address at Syneos Health: SafetyPV@Syneoshealth.com
SAE Facsimile Number at Syneos Health: 1-866-880-9343
If only limited information is initially available, follow-up reports may be required.

Section 2.6.6 Pregnancy

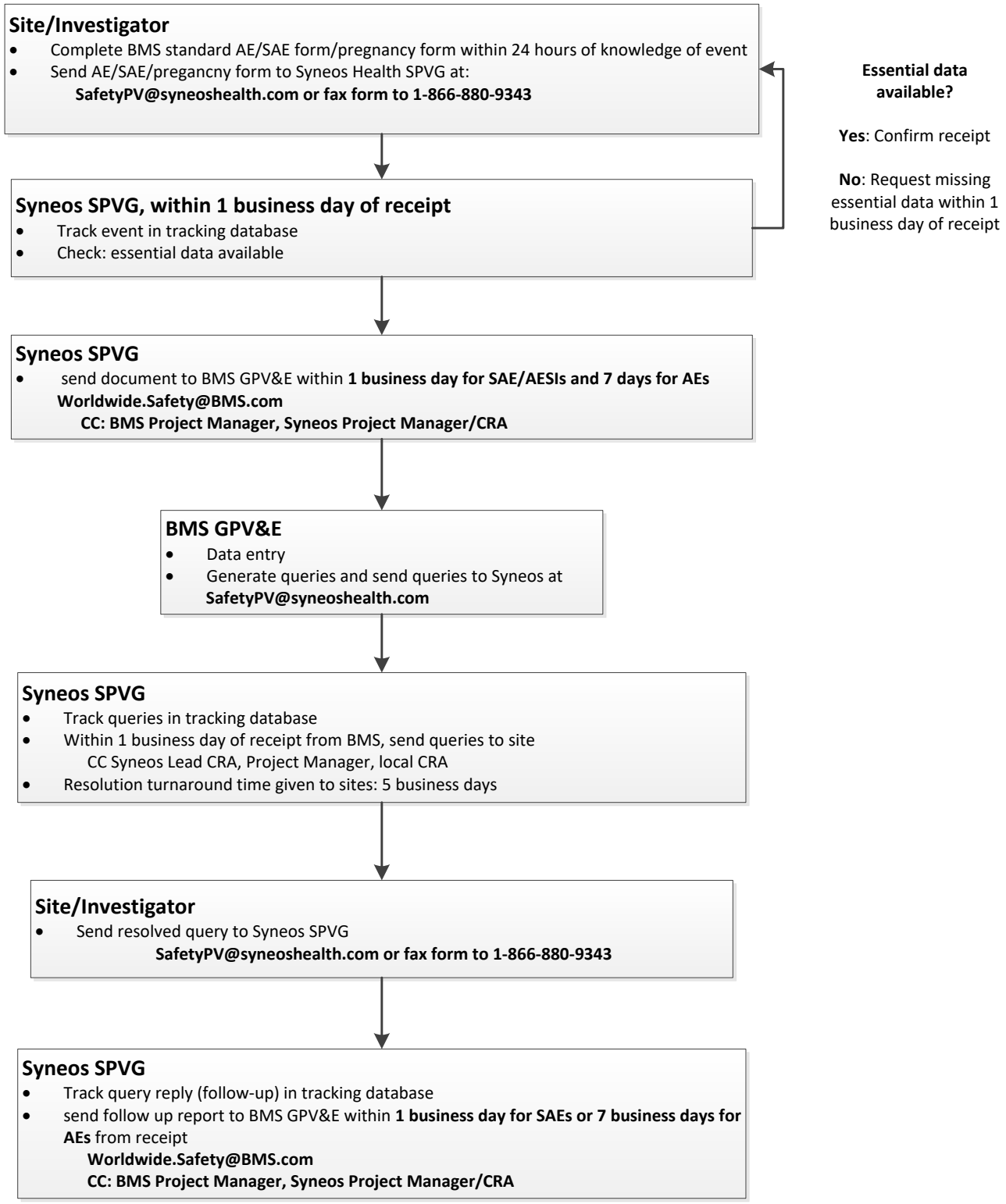
If it is discovered a patient is pregnant or may have been pregnant at the time of exposure to the BMS product under study, the pregnancy, AEs associated with maternal exposure and pregnancy outcomes must be recorded on a Pregnancy Surveillance Form and reported to Syneos SPVG within 24 hours/1 business day of becoming aware of the pregnancy. If only limited information is initially available, follow-up reports may be required. The original BMS forms are to remain on site. Follow-up information should be obtained on pregnancy outcomes for one year following the birth of the offspring. Any pregnancy that occurs in a female partner of a male participant on BMS product also be reported. Information on this pregnancy will be collected on the Pregnancy Surveillance Form.

Section 2.6.10 Reconciliation Between Safety and Clinical Database

Syneos Health data management will reconcile AEs and SAEs between the BMS safety database and the clinical database. The reconciliation will be performed quarterly and prior to database finalization activities. BMS GPVE will E-mail upon request from Syneos Health, the GPVE reconciliation report. Requests for reconciliation should be sent to aepbusinessprocess@bms.com. Data Management will identify any discrepancies between the BMS safety database and clinical database. Data Management will issue queries in the clinical database based on discrepant data. A list of SAEs entered in the clinical database but missing from the BMS safety database will be sent to the Safety Associate by the Data Manager.

Note – AEs and SAEs related to BMS product will be reconciled.
After completion of a scheduled reconciliation, the AE-SAE reconciliation is finalized and all required signatures from Syneos Health and BMS will be obtained. The documentation will be filed in the Electronic Trial Master File (e-TMF) by data manager.

Process Flow:



1.5 STUDY-SPECIFIC DOCUMENT HISTORY

VERSION	DATE	AUTHOR	DESCRIPTION
1.0	24-April-2017	BMS GPV&E & Syneos	Initial AE/SAE Management Plan
2.0	16-December-2019	BMS GPV&E & Syneos	Annual revision of AE/SAE Management Plan on updated BMS template. Updates made to process flow, Section 1.4 and Contact List, AE/SAE sections per amended protocol, company name and safety email address

SECTION 2: **CORE AE/SAE MANAGEMENT PLAN**

2.1 CORE AE/SAE MANAGEMENT PLAN APPROVALS

SYNEOS HEALTH APPROVALS	
Mahnaaz Khatib Manager, Safety & Pharmacovigilance	Date
Kevin Dopke, Project Director	Date
BMS / GPV&E APPROVALS	
Joseph Sewter, MBA Group Director, Adverse Event Processing & Submissions	Date

2.1 CORE AE/SAE MANAGEMENT PLAN APPROVALS

SYNEOS HEALTH APPROVALS	
M Chakt	18-DEC-2019
Mahnaaz Khatib Manager, Safety & Pharmacovigilance	Date
	20 Dec 2019
Kevin Dopke, Project Director	Date
BMS / GPV&E APPROVALS	
J C Sewter	16-DEC-2019
Joseph Sewter, MBA Group Director, Adverse Event Processing & Submissions	Date

2.2 DATABASES

Bristol-Myers Squibb (BMS) Global Pharmacovigilance and Epidemiology (GPVE) will maintain the safety database for the study while Syneos Health will maintain the clinical database.

2.3 REFERENCED STANDARD OPERATING PROCEDURES

The following Standard Operating Procedures (SOPS) will be followed for the management of AE/SAEs in this study:

2.3.1 BMS SOPS

- RD-SOP-010514: Safety Data Management in Non-Interventional Research (NIR)

2.3.2 Syneos Health SOPS

- SOP-SAFE-005: Safety Database Creation, Change and Maintenance
- SOP 4400: Receipt of Written ICSR Information (Syneos health harmonized SOP)
- SOP SAFE-015: Developing a Safety Monitoring Plan
- SOP SAFE-016: Case Processing of Serious and Non-Serious Adverse Events and Adverse Reactions for Clinical Trials
- SOP SAFE-017: Setting Up and Archiving Safety Project Files Related to Adverse Event Reports and Project-specific Reference Materials
- SOP SAFE-027: Pregnancy Reporting
- OG-DM-010: Reconciliation of Data between the Clinical and Safety Databases.

***NOTE**: Where the SAE MP differs from the SOP on AE/SAE reporting, the SAE MP takes precedence. Where differences arise between <CRO> SOPs and BMS SOPs, the BMS SOP will take precedence.*

2.4 RESPONSIBILITIES

TASK	BMS	SYNEOS HEALTH
Training of investigators and staff on AE/SAE procedures		X
Maintain clinical database		X
Maintain safety database of AE/SAEs	X	
Receipt of AE/SAEs from investigators		X
Assess AE/SAEs for minimal data elements		X
Generate AE/SAE queries	X	
Send and track AE/SAE queries to investigators		X
Ensure that all query responses and requested additional/supporting documentation on a case-by-case basis are provided to Sponsor		X

TASK	BMS	SYNEOS HEALTH
Generate and submit Detail Query Report *(inclusive of **ALL** GPV&E generated AE/SAE queries)* to Sponsor on a bi-weekly basis		X
Data entry and coding of AE/SAEs in safety database	X	
Medical review safety database single cases	X	
Verify investigator seriousness assessment was provided, obtain if missing		X
Verify investigator causality of SAEs was provided, obtain if missing		X
Assess expectedness of AE/SAEs	X	
Determine reportability of AE/SAEs	X	
Safety database single case narrative writing for AE/SAEs	X	
Generate analysis of similar events	X	
Generate CIOMS/MedWatch for SUSARs	X	
Provide data for AE/SAE reconciliation	X	X
AE/SAE reconciliation with clinical database	X	X
Final review/ approval of AE/SAE reconciliation or key data transfers/database lock	X	X

NOTES

- *Based on the study specific Transfer of Obligations, this table may be revised per study.*

2.5 TRAINING OF INVESTIGATORS AND STAFF ON AE/SAE REPORTING PROCEDURES

Syneos Health will ensure that investigators and staff *(including the principal investigator and primary study coordinator)* are trained in AE/SAE reporting procedures.

2.6 PROCEDURES

2.6.1 Receipt, Logging, and Triage

2.6.1.1 Related and non-related non-serious adverse events (NSAEs) are individually collected *(initial and follow-ups)* and reported to BMS within 7 business days of becoming aware of the events.

2.6.1.2 Related and non-related serious adverse events (SAEs) are individually collected *(initial and follow-ups)* and reported to BMS within 24 hours/1 business day of becoming aware of the events.

2.6.1.3 Pregnancies are individually collected and reported to BMS within 24 hours/1 business day of becoming aware of the events.

2.6.1.4 Investigator sites should report all initial AE/SAEs and follow-up to SAEs, whether related or unrelated to the study drug, to Syneos Health by fax or E-mail within 24 hours of awareness (Refer to Section 1.2 for Syneos Health AE/SAE Notification Fax Number and E-mail Address):

2.6.1.5 Calendar 'Day 0' is defined as the day BMS or <CRO> personnel become aware of an AE/SAE.

2.6.1.6 Syneos Health will document the AE/SAE awareness date and confirm receipt to the sender by E-mail or fax.

2.6.1.7 Upon receipt of the AE/SAE report, Syneos Health will review it to verify that the following minimum essential information has been received:

- Subject identification
- Suspect product
- Reporter identification
- An event or outcome that can be identified as serious

2.6.1.8 If the minimum essential information is not provided, Syneos Health will contact the reporter with a request for the missing essential information.

2.6.1.9 AE/SAE forms must be completed in English. Syneos Health will forward any source documents received in other languages to a translations service to be translated into English. Certificates of translation will be filed in the subject's AE/SAE folder.

2.6.1.10 Occasionally, BMS or Syneos Health personnel may contact the site for further information. In such cases, the BMS employee or Syneos Health Medical Monitor should immediately provide a telephone contact report to BMS GPVE with the new AE/SAE information.

2.6.2 Data Entry/Tracking

2.6.2.1 For all AEs/SAEs, syneos Health tracking of the fields below is completed within 1 business day of receipt.

- Receipt date
- Country
- Project number
- Sponsor name
- Reporter identification*
- Subject identification number*
- Suspect product*
- Event term*
- Seriousness (case level)
- Causality assessment

* Refer to Section 2.7.1.8 regarding minimal essential information.

2.6.3 Notification of AE/SAE to BMS

2.6.3.1 Syneos Health will forward the AE/SAE report, any query responses generated by <CRO> and additional/supporting documentation by fax or E-mail within 24 hours/1 business day of receipt for serious events and 7 business days of receipt for non-serious reports to BMS GPVE as follows:

E-mail: worldwide.safety@bms.com

Fax: 609-818-3804

2.6.3.2 Syneos Health will verify BMS GPVE receipt of information confirmation via the transmittal confirmation sheet for fax transmissions and via the return receipt for E-mail transmissions.

2.6.4 eDC Contingency Plan *(when applicable)*

In the event that the electronic data capture system is down, the following steps will occur:

2.6.4.1 Site will complete the paper version of the AE/SAE Report (refer to Section 2.8) and fax it to Syneos Health. Syneos Health will fax the AE/SAE Report within one business day to BMS GPV&E. Syneos Health >will also send an E-mail with a scanned copy of the AE/SAE Report for informational purposes only to Syneos Health Study Team including Medical Monitor(s), BMS Medical Monitor(s) and BMS Clinical Protocol Manager.

2.6.4.2 Once the electronic data capture system comes back on-line, it will be the responsibility of the site to enter the AE/SAE into the electronic data capture system. Syneos Health will not be responsible to follow-up with the sites to ensure this is done. Once the system is available, the electronic version of the AE/SAE will be considered the most up-to-date and accurate version.

2.6.5 Follow Up/Queries

2.6.5.1 Syneos Health will routinely query for any missing information on the AE/SAE Form.

2.6.5.2 BMS GPVE will forward additional queries to Syneos Health at the centralized E-mail address listed in Section 1.2 of this SAE MP. The BMS query E-mail header will include the protocol number, site and subject numbers, and safety database system number.

2.6.5.3 Syneos Health will follow Syneos Health SOP OG-DM-010, to ensure that queries are properly captured and tracked in the clinical database.

2.6.5.4 Queries will be forwarded to the investigator and resolutions pursued as defined below.

2.6.5.5 syneos Health will request that the site provide additional or missing information within 5 business days.

2.6.5.6 Syneos Health will follow-up regularly with the investigator site staff to ensure that queries are resolved within the required timeframe.

2.6.5.7 When new follow-up information is received it will be managed according to the steps outlined in Section 2.7.

2.6.6 Pregnancy

2.6.6.1 All pregnancies in a study subject, or partner of a study subject, during the study period must be reported by fax or E-mail using the BMS Pregnancy Surveillance Form Part I (Antepartum Information) within 24 hours of awareness to Syneos Health. Following delivery or termination of a pregnancy, the BMS Pregnancy Surveillance Form Part II (Pregnancy Outcome) should be faxed or E-mailed to Syneos Health. Spontaneous abortions and congenital anomalies should be reported on an AE/SAE form. In those cases where a subject or a subject's partner delivers a child, the BMS

Pregnancy Surveillance Form Part III (Infant Follow-up) should be faxed or E-mailed to Syneos Health.

2.6.7 Unexpected Benefit

2.6.7.1 All cases of Unexpected Benefit occurring in France need to be reported within 24 hours of awareness to Syneos Health.

2.6.8 Case Completion

2.6.8.1 In general, AEs/SAEs are followed until the event resolves or stabilizes and follow-up queries are resolved.

2.6.8.2 Once an AE/SAE has resolved/stabilized, and there are no outstanding follow-up queries, the SAE report can be considered complete.

2.6.8.3 AE/SAE reports may be considered complete before resolution/stabilization, or before outstanding queries are resolved, if follow-up information is determined to not be forthcoming.

2.6.9 Case Filing and Retention

2.6.9.1 Documentation related to the AE/SAE report is stored securely within Syneos Health until the project is completed.

2.6.10 Reconciliation between Safety/Clinical Database

2.6.10.1 Syneos Health will reconcile AE/SAEs between the BMS safety database and the clinical database. Frequency of reconciliation will be determined prior to study commencement and documented in the study specific section. BMS GPVE will E-mail upon request from Syneos Health, the GPVE reconciliation report. Requests for reconciliation should be sent to **aepbusinessprocess@bms.com.**

2.6.10.2 Reconciliation will be performed at the case level. Individual data elements do not require reconciliation.

2.6.10.3 After completion of a scheduled AE/SAE reconciliation, both Syneos Health and BMS GPV&E personnel will sign-off on completion of the reconciliation process. All records associated with each scheduled reconciliation process will be stored by the Syneos Health in their document management system in association with the protocol.

2.7 ATTACHMENTS

2.7.1 AE/SAE Forms – NIR Studies

AE/SAE REPORT

Non-Interventional Research AE/SAE Form

Bristol-Myers Squibb Company

DATE SUBMITTED TO BMS: Click here to enter a date.

PROTOCOL / PROGRAM NUMBER:	PROGRAM NAME: (IF APPLICABLE)	SITE NUMBER:	PATIENT ID:	COUNTRY:

☐ INITIAL REPORT ☐ FOLLOW-UP REPORT

PATIENT INFORMATION INITIALS: | DOB OR YOB: Click here to enter a date. | ☐ MALE ☐ FEMALE | RACE:

EVENT: | ☐ SERIOUS AE* OR ☐ NON-SERIOUS AE | IF AIDS DEFINING, CODE:

*SERIOUS CRITERIA:
☐ LIFE THREATENING ☐ RESULTED IN DEATH
☐ HOSPITALIZATION/ PROLONGATION DATE OF DEATH: Click here to enter a date.
☐ CONGENITAL ANOMALY/ BIRTH DEFECT CAUSE OF DEATH:
☐ PERSISTENT/ SIGNIFICANT DISABILITY ☐ IMPORTANT MEDICAL EVENT

EVENT ONSET DATE: Click here to enter a date.
RESOLUTION DATE: Click here to enter a date.

EVENT INTENSITY / GRADE OR CTC CODE / GRADE:
☐ MILD / GRADE I ☐ VERY SEVERE / GRADE IV
☐ MODERATE / GRADE II CTC CODE
☐ SEVERE / GRADE III CTC GRADE

EVENT OUTCOME:
☐ RESOLVED ☐ RESOLVED W/ SEQUELA
☐ RESOLVING ☐ DEATH
☐ DID NOT RESOLVE ☐ UNKNOWN

REPORTER CAUSALITY ASSESSMENT: ☐ NOT RELATED TO BMS PRODUCT ☐ RELATED TO BMS PRODUCT

EVENT DESCRIPTION:

RELEVANT LAB DATA: ☐ UNK ☐ NONE
MEDICAL HISTORY: ☐ UNK ☐ NONE
CONCOMITANT MEDS: ☐ UNK ☐ NONE

BMS PRODUCT:	INDICATION:	BATCH NUMBER:	EXPIRATION DATE:
			Click here to enter a date.

DOSE, UNITS AND ROUTE OF ADMINISTRATION:	FREQUENCY:	PRODUCT START DATE:	STOP DATE:
		Click here to enter a date.	Click here to enter a date.

ACTION TAKEN REGARDING THE BMS PRODUCT: ☐ NONE ☐ INTERRUPTED ☐ DISCONTINUED ☐ DOSE INCREASED ☐ DOSE REDUCED ☐ IV RATE REDUCED ☐ UNKNOWN

REPORTER INFORMATION:
HCP QUALIFICATION:

TREATING PHYSICIAN INFORMATION:

REPORT PREPARED BY: | DATE REPORT RECEIVED: Click here to enter a date.

NAME OF PROGRAM VENDOR (IF APPLICABLE): | PROGRAM VENDOR E-MAIL:

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2.7.2 AE/SAE Form Instructions – NIR Studies

Non-Interventional Research AE/SAE Form
INSTRUCTIONS

Date Submitted to BMS: Record the date the Form was e-mailed or faxed to Bristol-Myers Squibb.

Initial Report or Follow-up Report: Choose 'Initial Report' for the first time the event is being recorded. When new or changed information is obtained after the initial report has been submitted to BMS, complete a new form, choose Follow-up Report, indicate the event and only the new or changed information. If the event term has changed, it is critical to indicate the changes to the term in the Event Description.

Adverse Event: An adverse event is any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product (ICH E2D).

Event: Signs and symptoms known to be associated should be grouped together as syndromes or diagnosis (e.g. "influenza" instead of "fever, chills and aches"). If recording multiple events include event terms, causalities, onset and resolution dates in Event Description. DEATH is not an acceptable event term. "Sudden death" or the diagnosis leading to death must be reported as the adverse event term.

If event is pregnancy, complete a pregnancy surveillance form. If event is medical device related, also complete a medical device supplemental form.

Serious Adverse Event or Non-serious: Please refer to the protocol for complete definitions of non-serious and Serious Adverse Events (SAEs) as well as any protocol specific requirements.

AIDS-Defining Code: If the event qualifies as an AIDS-Defining Diagnosis, as indicated in the list of AIDS-Defining Diagnoses provided by BMS, record the appropriate code.

Serious Criteria: If event is Serious, choose the appropriate criterion for classification by referring to the protocol. If criterion is Death, the Date of Death and Cause of Death must be reported.

Event Onset date: Record the onset date at which the event was identified as an AE. If subject was hospitalized, the onset date may not correspond to the hospitalization date. **Resolution date: -** Record the resolution date as the date the event resolved entirely or stabilized. If the event is ongoing at the time of reporting, enter "Continuing". If an event(s) was unresolved at the time the patient died, the resolution date(s) should be reported as continuing. - Ensure consistency between the resolution date and the outcome (e.g. - if the outcome is resolved, the resolution date must be specified).

Event Intensity: Mild / Grade I- awareness of event but easily tolerated
Moderate / Grade II- discomfort enough to cause some interference with usual activity
Severe / Grade III - inability to carry out usual activity
Very Severe / Grade IV - debilitating, significantly incapacitates subject despite symptomatic therapy
CTC Code/Grade: Record the CTC code and /or select the appropriate CTC grade according to the version of the "Guide to Grading and Coding Adverse Events" that was provided by Bristol-Myers Squibb for this study or the CTC Grading Scale version specified per protocol.

Outcome: Ensure consistency between the resolution date and the outcome (e.g. if the outcome is resolved, the resolution date must be specified). <Events with a CTC grade 5 must have an outcome of DEATH>.

Relationship to study drug: Check the physician's/investigator's opinion regarding the association of the BMS product to the AE. **The expression "reasonable causal relationship" is meant to convey in general that there are facts (evidence such as de-challenge/re-challenge) or other arguments to suggest a positive causal relationship.**

Related: There is a reasonable causal relationship to BMS product administration and the AE.
Not related: There is not a reasonable causal relationship to BMS product administration and the AE.

Event Description: Describe the event and its treatment e.g., dates and products. Provide any history or intercurrent illness and list concomitant medications [whether or not relevant to the event] and relevant lab/procedure data. If the event is not related to the program product, specify cause if known e.g., underlying illness, concomitant medication, etc.
Dates of hospitalization should be recorded in this section. See "Event" instructions for including multiple events.

BMS Product Information: Record the product name, indication, start/stop dates, total daily dose, route of administration and frequency. If the product was not stopped, enter "Continuing" in the Stop Date.

Action taken regarding BMS Product - Interrupted: product has temporarily ceased or product infusion was started and was prematurely stopped and is expected to be re-introduced. Discontinued: product will not be re-introduced or product infusion has started and cannot be re-introduced.

Reporter Information: Include full name, address, phone/fax number and e-mail address. If reporter is a healthcare professional (HCP) specify qualification.

Note: Since these forms are being transmitted to a central processing center in the United States, the reporter details should only be provided if local country data privacy laws allow transfer of this data out of the country. If reporter details cannot be provided for this reason but the reporter has consented to be contacted for follow-up, the vendor must retain their contact details should the case require follow-up by the local market.

Treating Physician Information: (Complete only if the reporter was a patient/consumer and if reporter provided informed consent to contact the treating physician). Include full name, institution, address, phone number and e-mail address.

IF YOU NEED EXTRA SPACE, USE DUPLICATE PAGES OF THE FORM. PLEASE ENSURE ALL EXTRA PAGES HAVE THE SAME HEADER INFORMATION.
ENTER "NA" IN ANY BOX IF NOT APPLICABLE OR IF INFORMATION IS NOT AVAILABLE.
Please send completed form preferably in English to Worldwide.safety@bms.com
Please report any follow up information within One business day

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2.7.3 Pregnancy Forms

Bristol-Myers Squibb Company

Pregnancy Surveillance Form Part I
(Antepartum Information)

PATIENT IDENTIFIER: (FOR STUDIES, MUST INCLUDE PROTOCOL, SITE & SUBJECT NUMBERS)	CASE # (BMS ONLY)	LOCAL COUNTRY NUMBER: (BMS ONLY)

BMS RECEIPT DATE (BMS USE ONLY)	Click here to enter a date.	GPV&E RECEIPT DATE (BMS USE ONLY)	Click here to enter a date.

REPORT TYPE:	☐ SPONTANEOUS OR ☐ STUDY ☐ INITIAL REPORT OR ☐ FOLLOW-UP REPORT	COUNTRY

EVENT: PREGNANCY

EXPOSURE TYPE: ☐ MATERNAL DRUG EXPOSURE OR ☐ PATERNAL DRUG EXPOSURE

FOR PATERNAL DRUG EXPOSURE ONLY: WAS PREGNANT PARTNER INFORMED CONSENT FORM SIGNED? ☐ NO ☐ YES

IF NO, DID THE MALE SUBJECT PROVIDE ALL OF THE PREGNANCY SURVEILLANCE INFORMATION BELOW? ☐ NO ☐ YES

REPORT TYPE: ☐ PROSPECTIVE REPORT OR ☐ RETROSPECTIVE REPORT

WERE THERE ANY ADDITIONAL MATERNAL/PATERNAL ADVERSE EVENTS? ☐ NO ☐ YES

IF YES, REPORT THE ADVERSE EVENTS APPROPRIATELY (FOR STUDIES, REFER TO STUDY-SPECIFIC INSTRUCTIONS)

MATERNAL INFORMATION DATE OF BIRTH:	AGE AT CONCEPTION:	HEIGHT:	WEIGHT:	RACE:
Click here to enter a date.		☐ inches ☐ cm	☐ lb ☐ kg	☐ WHITE ☐ BLACK ☐ ASIAN ☐ AMERICAN INDIAN OR ALASKAN NATIVE ☐ NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER ☐ OTHER RACE:

NUMBER OF PREGNANCIES INCLUDING THIS ONE		NUMBER OF BIRTHS		NUMBER OF LIVING CHILDREN	

ONSET DATE LAST MENSTRUAL PERIOD (LMP):	Click here to enter a date.	APPROXIMATE DATE OF CONCEPTION:	Click here to enter a date.	DATE PREGNANCY WAS CONFIRMED:	Click here to enter a date.
		ESTIMATED DATE OF DELIVERY:	Click here to enter a date.	TEST METHOD:	☐ SERUM ☐ URINE

ESTIMATED GESTATIONAL AGE WHEN PREGNANCY DIAGNOSED: ____ WEEKS DETERMINED BY: ☐ FETAL ULTRASOUND ☐ DATE FROM LMP

CONTRACEPTION AT TIME OF CONCEPTION: ☐ NO ☐ YES ☐ UNKNOWN (IF YES, SPECIFY)

RELEVANT MATERNAL MEDICAL HISTORY/RISK FACTORS	DATE OF ONSET	IF APPLICABLE SPECIFY PERTINENT DETAILS
	Click here to enter a 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.	

PATERNAL INFORMATION: AGE ____ YEARS DATE OF BIRTH: Click here to enter a date.

RELEVANT PATERNAL MEDICAL HISTORY/RISK FACTORS	DATE OF ONSET	IF APPLICABLE SPECIFY PERTINENT DETAILS
	Click here to enter a 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.	

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Bristol-Myers Squibb Company

Pregnancy Surveillance Form Part I
(Antepartum Information)

PATIENT IDENTIFIER: (FOR STUDIES, MUST INCLUDE PROTOCOL, SITE & SUBJECT NUMBERS)	CASE # (BMS ONLY)	LOCAL COUNTRY NUMBER: (BMS ONLY)

MEDICATION NAME AND INDICATION	PREGNANCY RELATED TO MEDICATION?*	DOSE AND UNITS	FREQ	ROUTE **	PERIOD(S) OF DRUG EXPOSURE ***	ONCOLOGY DRUGS ONLY	START AND STOP DATES
1. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING
2. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING
3. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING
4. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING
5. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING
6. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING
7. INDICATION ☐ MATERNAL OR ☐ PATERNAL ☐ NON-STUDY OR ☐ STUDY	☐ NOT RELATED ☐ RELATED					CYCLE #: CUMULATIVE DOSE WITH UNITS	Click here to enter a date. Click here to enter a date. OR ☐ ONGOING

* MANDATORY FOR ALL STUDIES

**ROUTE:
1 = ORAL 2 = INTRAVENOUS 3 = SUBCUTANEOUS 4 = OTHER

***PERIOD(S) OF DRUG EXPOSURE: (INCLUDE ALL THAT APPLY)
0 = PRIOR TO CONCEPTION 1 = 1ST TRIMESTER 2 = 2ND TRIMESTER
3 = 3RD TRIMESTER 4 = LABOR & DELIVERY 5 = UNKNOWN

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Bristol-Myers Squibb Company

Pregnancy Surveillance Form Part I (Antepartum Information)

PATIENT IDENTIFIER: (FOR STUDIES, MUST INCLUDE PROTOCOL, SITE & SUBJECT NUMBERS)	CASE # (BMS ONLY)	LOCAL COUNTRY NUMBER: (BMS ONLY)

PRENATAL DIAGNOSTIC TESTING	BASE-LINE	DATE	TEST RESULTS UNITS	NORMAL RANGE	
				LOW	HIGH
	☐	Click here to enter a 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.			
	☐	Click here to enter a date.			
	☐	Click here to enter a date.			

DESCRIBE RESULTS IN DETAIL, IF APPLICABLE:

REPORTER INFORMATION: ☐ BMS STUDY INVESTIGATOR ☐ NON-BMS STUDY SPONSOR ☐ OTHER*

*QUALIFICATION: (COMPLETE ONLY IF "OTHER" IS CHECKED)

☐ PHYSICIAN ☐ PHARMACIST ☐ NURSE/NURSE PRACTITIONER ☐ OTHER HEALTH PROFESSIONAL
☐ CONSUMER ☐ ATTORNEY ☐ OTHER NON-HEALTH PROFESSIONAL

PERSON COMPLETING THE FORM (IF DIFFERENT FROM INVESTIGATOR/SPONSOR) :

PRINTED NAME

SIGNATURE

DATE: Click here to enter a date.

INSTITUTION/ORGANIZATION:

STREET ADDRESS:

CITY:

STATE/PROVINCE:

POST CODE: COUNTRY: PHONE NUMBER:

INVESTIGATOR/SPONSOR/OTHER:

LAST NAME

FIRST NAME MIDDLE INITIAL

SIGNATURE: DATE: Click here to enter a date.

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Bristol-Myers Squibb Company

Pregnancy Surveillance Form Part II (Pregnancy Outcome)

PATIENT IDENTIFIER: (FOR STUDIES, MUST INCLUDE PROTOCOL, SITE & SUBJECT NUMBERS)	CASE # (BMS ONLY)	LOCAL COUNTRY NUMBER: (BMS ONLY)

PREGNANCY OUTCOME:

MODE OF DELIVERY: LABOR/DELIVERY COMPLICATIONS ☐ NO ☐ YES*

IF YES, SPECIFY

☐ SINGLE GESTATION ☐ MULTIPLE GESTATION (# of)

COMPLETE AN OUTCOME FORM FOR EACH FETUS/INFANT

DATE PREGNANCY ENDED: GESTATIONAL AGE AT OUTCOME WEEKS ☐ UNKNOWN

Click here to enter a date. ASSESSED BY: ☐ OBSTETRICAL DATES ☐ FETUS/INFANT PHYSICAL EXAM

DID OBSTETRICAL COMPLICATIONS OR MATERNAL/PATERNAL MEDICAL CONDITIONS OCCUR DURING THIS PREGNANCY?

☐ NO ☐ YES*

☐ UNKNOWN IF YES, SPECIFY:

*FOR ANY COMPLICATIONS NOTED ABOVE, REPORT THE ADVERSE EVENT APPROPRIATELY (FOR STUDIES, REFER TO STUDY-SPECIFIC INSTRUCTIONS)

GENDER:	BIRTH WEIGHT:	BIRTH LENGTH:	HEAD CIRCUMFERENCE:	APGAR SCORE:
☐ MALE ☐ FEMALE ☐ UNKNOWN	/ lbs/oz grams	☐ inches ☐ cm	☐ inches ☐ cm	1 MIN. 5 MIN.

☐ LIVE BIRTH NORMAL (PROCEED TO PART III)

☐ LIVE BIRTH ABNORMAL ☐ FETAL DEATH ☐ NEONATAL DEATH (IF ANY ARE CHECKED, COMPLETE SECTIONS BELOW)

☐ PRE-TERM ☐ TERM ☐ POST TERM

☐ SMALL FOR GESTATIONAL AGE

☐ INTRAUTERINE GROWTH RETARDATION

☐ DRUG WITHDRAWAL SYNDROME IN THE NEONATE

☐ MALFORMATION (SPECIFY BELOW)

☐ POST-NATAL/NEONATAL COMPLICATIONS (E.G. PERINATAL ASPHYXIA, INFECTION, RESPIRATORY DISTRESS) (SPECIFY):

FETAL DEATH

☐ ECTOPIC ☐ MISCARRIAGE/SPONTANEOUS ABORTION ☐ STILLBIRTH

☐ INDUCED ABORTION/ELECTIVE TERMINATION

AUTOPSY/PATHOLOGY REPORT ☐ NO ☐ YES ☐ UNKNOWN

NEONATAL DEATH:

CAUSE: DATE: Click here to enter a date.

PLACENTAL ABNORMALITIES ☐ NO ☐ YES ☐ UNKNOWN

IF YES, SPECIFY:

PATHOLOGY REPORT AVAILABLE ☐ NO ☐ YES ☐ UNKNOWN

FAMILY HISTORY OF CONGENITAL ABNORMALITIES/BIRTH DEFECTS:

☐ NO ☐ YES ☐ UNKNOWN

IF YES, SPECIFY:

PRIOR PREGNANCIES WITH CONGENITAL ABNORMALITIES/BIRTH DEFECTS: ☐ NO ☐ YES

IF YES, SPECIFY #/TYPE :

PRIOR STILLBIRTHS: ☐ NO ☐ YES

IF YES, SPECIFY # :

PRIOR SPONTANEOUS ABORTIONS: ☐ NO ☐ YES

IF YES, SPECIFY #:

SPECIFY ANY PRIOR PREGNANCY COMPLICATIONS:

HISTORY OF FERTILITY TREATMENTS (E.G. IVF):

☐ NO ☐ YES IF YES, SPECIFY:

DESCRIBE ANY CONGENITAL MALFORMATIONS/ABNORMALITIES, STRUCTURAL DEFECTS AND OTHER FETAL/NEONATAL COMPLICATIONS:

CAUSALITY (MANDATORY FOR STUDIES)

IN THE INVESTIGATOR'S OPINION, WAS THE DEFECT/MEDICAL PROBLEM RELATED TO MEDICATION UNDER STUDY? : ☐ NOT RELATED ☐ RELATED

IF RELATED, PLEASE COMMENT ON SPECIFIC EVENT(S) AND MEDICATION(S) BELOW:

IF NOT RELATED, INDICATE WHAT THE DEFECT/MEDICAL PROBLEM WAS ATTRIBUTED TO:

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Bristol-Myers Squibb Company

Pregnancy Surveillance Form Part III (Infant Follow-up)

PATIENT IDENTIFIER: *(FOR STUDIES, MUST INCLUDE PROTOCOL, SITE & SUBJECT NUMBERS)*	CASE # (BMS ONLY)	LOCAL COUNTRY NUMBER: (BMS ONLY)

CURRENT INFANT AGE: AGE UNITS: ☐ DAYS ☐ WEEKS ☐ MONTHS

☐ NO PROBLEMS ☐ MEDICAL PROBLEMS NOTED (SPECIFY AND DESCRIBE FINDINGS AND/OR PLANNED EVALUATIONS; E.G. DIAGNOSTIC TESTING, CONSULTATIONS, ETC)

CAUSALITY (MANDATORY FOR ALL STUDIES): IN THE INVESTIGATOR'S OPINION WERE ANY PROBLEMS NOTED ABOVE RELATED TO THE MEDICATION UNDER STUDY? ☐ NOT RELATED ☐ RELATED (PLEASE SPECIFY):

MATERNAL BREASTFEEDING: ☐ NO ☐ YES HOW LONG:

MATERNAL DRUGS TAKEN WHILE BREASTFEEDING: ☐ NO ☐ YES (IF YES, SPECIFY)

REPORTER INFORMATION: ☐ BMS STUDY INVESTIGATOR ☐ NON-BMS STUDY SPONSOR ☐ OTHER*

*QUALIFICATION: (COMPLETE ONLY IF "OTHER" IS CHECKED)

☐ PHYSICIAN ☐ PHARMACIST ☐ NURSE/NURSE PRACTITIONER ☐ OTHER HEALTH PROFESSIONAL

☐ CONSUMER ☐ ATTORNEY ☐ OTHER NON-HEALTH PROFESSIONAL

PERSON COMPLETING THE FORM (IF DIFFERENT FROM INVESTIGATOR/SPONSOR) :	DATE:
PRINTED NAME	Click here to enter a date.
SIGNATURE	

INSTITUTION/ORGANIZATION:

STREET ADDRESS:	CITY:	STATE/PROVINCE:

POST CODE:	COUNTRY:	PHONE NUMBER:

INVESTIGATOR/SPONSOR/OTHER:

LAST NAME

FIRST NAME MIDDLE INITIAL

SIGNATURE:	DATE:
	Click here to enter a date.

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Pregnancy Surveillance Form - Quick Reference Guide

The Pregnancy Surveillance Form will be completed for all prospective (confirmed pregnancy, prior to delivery or confirmation of congenital anomaly) and retrospective (when congenital anomaly/malformation is confirmed or after delivery has occurred) reports of pregnancy and pregnancy outcomes (live births: normal or abnormal, fetal death, neonatal death etc.) It functions as a data collection and query tool to report pregnancies and related pregnancy information. AE/SAEs for all subjects/patients reported in association with the pregnancy (obstetric complications, maternal medical complications, etc.) are to be reported separately on the clinical or non-interventional SAE form or spontaneous AE/SAE form.

Pregnancy Surveillance Form Part I	Pregnancy Surveillance Form Part II	Pregnancy Surveillance Form Part III
When a pregnancy is confirmed	When the pregnancy outcome is known	When the infant outcome is known.

Site Monitor: When a pregnancy is confirmed, collaborate with the site manager or clinical scientist to ensure that the Investigator has notified the IRB/IEC or Health Authority (if required by local law).

- Ensure that documentation of pregnancy notifications sent by the Investigator to the IRB/IEC are filed in the On-site Investigator File (OSIF) and R&D Study File.
- In countries where notification of the IRB/IEC is handled by the sponsor, the site manager is responsible for ensuring that the documentation of all pregnancy notifications sent to the IRB/IEC are filed within the R&D Study File.
- **Note**: for Paternal Drug Exposure in Interventional Study Reports: If pregnant partner informed consent is not signed, Part I, Part II and Part III information needs to come from the male subject, and not from the female partner herself.

All Pages Header Information

- For studies the "Patient Identifier" is the same as that used throughout the CRF, and populated with the protocol, site and subject numbers i.e. CV131-345-234-1134
- For spontaneous reports, enter local country number (if applicable) at the top left and/or enter a patient identifier (i.e. initials) if available or leave blank
- Parts I, II and III will be completed with all appropriate identifying header information on each page

  Part I - Page 1

  Complete all questions for "PREGNANCY" as the only adverse event; other SAEs reported in association with the pregnancy (obstetric complications, maternal medical complications etc.) are reported separately either on the clinical / non-interventional study SAE form or the Spontaneous AE/SAE forms.

  Part I - Page 2: Medication:
- Include each medication reported as a separate entry.
- Indicate if the drug was associated with maternal or paternal exposure.
- Indicate if the drug was identified as a non - study medication or study medication by the investigator or reporter. Study medications include the medications under study (for non-interventional studies), the Investigational Medicinal Product (IMP), comparator medications and background therapy identified in the protocol.

  "Pregnancy Related to Medication" Column: Check whether or not the pregnancy was related to the medication.

  Dosing Information: For route and period(s) of drug exposure, use the codes indicated at the bottom of the page. For period(s) of drug exposure, include all that apply.

  Part I - Page 3: Prenatal Diagnostic Testing: Indicate if the results are baseline by checking under "baseline"; otherwise leave this box blank when providing the relevant details. Specify the test results (including any relevant units or other data), use the space below this section to describe results in more detail if needed.

  Part II - Pregnancy Outcome: Complete delivery and outcome data as requested at the top of the page. If the outcome involved multiple gestations, please complete a separate outcome form for each fetus/infant. If the pregnancy/outcome involved labor or delivery complications, obstetric complications, or maternal medical conditions, briefly specify them.

  NOTE: If any complications reported above meet the definition of an SAE (or an AE for non-study patients) they should be reported separately on either the clinical or non-interventional SAE form or the spontaneous AE/SAE form. If the outcome is "live birth- normal" check this box, and proceed to the next page or any adverse outcome (live birth abnormal, fetal or neonatal death) complete all requested information to the fullest extent

  For any adverse outcome (live birth abnormal, fetal or neonatal death) complete all requested information to the fullest extent possible. A detailed causality assessment by the investigator is required for any reports from trials and must be provided as noted at the bottom of this page.

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SECTION 3: MASTER TEMPLATE DOCUMENT HISTORY

VERSION	DATE	AUTHOR	DESCRIPTION
1.0	27-June-2013	BMS GPV&E	V1 Master Template
2.0	01-Feb-2017	BMS GPV&E	V2 Master Template
3.0	30-Sept-2018	BMS GPV&E	V3 Master Template: Removal of Adverse event definitions. Process change to reconciliation process.
4.0	12-August-2019	BMS GPV&E	V4 Master Template: BMS SOPs updated (Section 2.3.1). Process change to reconciliation procedure (Section 2.6.9.2).
5.0	12-December-2019	BMS GP&E	V5 Master Template: Collection requirement of Unexpected Benefit for cases occurring in France added. (Section 2.6.7)

SECTION 4: LIST OF ABBREVIATIONS

AE	Adverse Event
BMS	Bristol-Myers Squibb
BMS GPV&E	Bristol-Myers Squibb Global Pharmacovigilance and Epidemiology
EC	Ethics Committee
IMP	Investigational Medicinal Product
IRB	Institutional Review Board
SAE	Serious Adverse Event
SAE MP	Serious Adverse Event Management Plan
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction