Global: Market Research and Patient Support Program Source Data Quality Check (SDQC) Guidance and Form

1. PURPOSE

This document provides additional guidance on the procedural details for the Source Data Quality Check (SDQC) in Market Research Programs (MRPs) and Patient Support Programs (PSPs) (hereafter referred collectively as "MAP" [**M**arket Research **A**nd **P**atient Support Program]) as described in the corresponding *Global: Market Research and Patient Support Program Pharmacovigilance Compliance (SOP-0102065)*. SDQC is a key monitoring activity to be conducted for MAP in order to assess whether adverse events (AE)/Special Situation Reports (SS) have been adequately identified and further reported by the third party/Roche personnel running the program. This document also describes the type of actions that need to be taken in the event a missed AE/SS is identified.

2. SCOPE

This document applies to:

- All programs and activities defined as Market Research and Patient Support Programs (MAP), in accordance with *Global: Market Research and Patient Support Program Pharmacovigilance Compliance (SOP-0102065)*.
- All Activity and Program Owners, who by default become MAP Owners in accordance with *Global: Market Research and Patient Support Program Pharmacovigilance Compliance (SOP-0102065)*, once the program/activity definition for MAP is met.
- All other Roche personnel who have a role in the conduct and management of MAPs (as per the roles and responsibilities defined in *Global: Market Research and Patient Support Program Pharmacovigilance Compliance (SOP-0102065)*).
- All MAPs whether conducted at the Global, Regional or Affiliate level within the Pharma organization.

3. BASIC PRINCIPLE OF SDQC IN MAPs

The principle of SDQC is to review a sample of source data generated by a MAP to determine whether AE/SSs in the sample have already adequately been identified and reported to Roche. In other words, this is a check that staff working on the MAP understand what an AE/SS is, identify and report them correctly to Roche. If deficiencies in identifying AE/SSs in the sample are identified, corrective action must be taken including 100% review of all source data for the relevant SDQC period.

SDQC must be performed according to the frequencies and timelines in Table 1. More than one SDQC might be required according to the MAP duration. Key aspects for the adequacy of SDQC are:
(i) identifying the correct source data and (ii) reviewing the correct sample of source documents for each separate SDQC (Table 2).

SDQC should not replace additional, existing quality measures/activities that take place at Service Providers or by Roche personnel, as part of the overall MAP process (known as "in-process

quality"). Such quality measures/activities should remain in place to ensure compliance with the MAP process (SOP) and to ensure that all AE/SS are identified and reported to Safety Unit.

4. SOURCE DATA

Source Data is all original (primary) documents, data and records generated in the course of a MAP by all parties involved in the MAP. Any data generated is MAP source data regardless of "document"/record format.

Source data for SDQC is all and any documents, data and/or records that could contain AE/SS either intentionally or unintentionally, i.e., is source data where it is predicted AE/SS could be collected or where there is even a slight possibility that AE/SS could be collected (for example the MAP was not designed to collect AE/SS but the nature of the MAP could collect AE/SS information incidentally). Hence, a full review of all source data that could be generated for a MAP must be undertaken to ensure all source data is identified and in turn the correct source data is included for SDQC (this may be all source data generated by a MAP).

In order to minimize the risk of deficiencies in the SDQC process, it is recommended to work closely with Service Providers and the MAP Owner to identify all potential sources of source data generated as part of MAPs prior to program start (with ongoing assessment during program conduct). The correct source data for inclusion in SDQC should be identified as part of this assessment. Service Providers and the MAP Owners need to notify the PV Approver in case they wish to make any change in regards to sources of source data i.e., to create a copy of source documents or development of any additional type/format of source data. Roche needs to be aware about all potential sources of source data generated as part of a Roche MAP.

Examples of Source Data include but are not limited to:

- Recorded telephone call (voice record or transcript)
- Recorded video
- Database or customer relationship management (CRM) record
- Email communication
- MAP related forms
- Handwritten or electronic notes
- Letters
- Paper documents e.g., adverse event forms, completed questionnaires, Medical records
- Online survey to collect data as part of MAP e.g., to complete an online survey which could collect safety information.

5. DETERMINATION OF SOURCE DATA VOLUME FOR SDQC

Determination of the volume of source data i.e., the number of records, for a SDQC period (refer to Table 1) is a crucial aspect for adequacy of SDQC. The volume of source data is the total number

of records assessed as required for inclusion in SDQC (as described above), for the given SDQC period.

For the purpose of SDQC in a MAP, a record is defined as follows:

- A single record/single piece of source data is generated each time a single interaction or the outcome of an interaction that takes place with a program participant, is recorded. Examples of interactions include (but are not limited to):
    - A direct communication with a health care provider, patient, caregiver or someone else e.g., relative
    - Completion of an online (web-based) survey set-up to collect information
    - Submission of program related information to a mailbox, as determined by MAP design e.g., enrollment forms
- Examples of singular records include (but are not limited to):
    - 1 entry of an individual data set into a database e.g., CRM
    - 1 fully completed survey or questionnaire (regardless of the number of questions, i.e., one question does not equal one piece of source data)
    - 1 recorded video session related to a single participant
    - 1 recorded telephone call (per participant, transcript or voice record)
    - 1 email trail

SDQC should be conducted on original/primary records (see section 4) to ensure any safety information is collected “verbatim” as required by European GVP legislation. However, there may be occasions where the primary data/records are generated in a secondary format in order to retrieve, review and archive it. On these occasions, care should be taken to document the original/primary source of the date and why it is being reviewed in an alternative format, and to take care when counting the source records to be reviewed. Some examples of these scenarios include (but are not limited to):

- Web-based activities that cannot be reviewed online: e.g., 100 web-based surveys that is completed on-line, but requires to be exported from the site in an aggregate export/excel format for review/analysis. Although there may be 1 export/excel sheet, this sheet includes information from 100 surveys (the original/primary records), hence review of the export/excel would be review of 100 separately completed records.
- Phone calls where the calls cannot be recorded but transcripts are created – local legislation may prevent phone calls from being recorded, and as a result a transcript or notes of the call may be documented elsewhere, e.g., in a database. While the phone calls remain the original/primary records, it is not possible to conduct SDQC on these. Hence, SDQC should be conducted on the first documented version of the call. In addition (and if possible), extra steps should be taken in this scenario, to affirm the quality of transcribed data, e.g., an additional party could listen in on a call as it takes place, then review the details documented. This approach can also serve to assure that any safety information is reported.

SDQC for a MAP should be completed as per individual MAP. For example, if multiple MAPs are using the same mailbox or database, the volume of source data for SDQC should be calculated

per MAP and not based on the volume of source data in the whole mailbox or database for the SDQC period.

6. FREQUENCY OF SDQC AND TIMELINES FOR COMPLETION OF SDQC

Depending on the MAP type and duration, more than one SDQC may be required to cover the MAP duration from Actual Start Date to Actual End Date. The below Table 1 shows the minimum frequency of SDQC required. More frequent SDQC may be performed if assessed as required by the PV Approver (see notes for Table 1).

Table 1

		Duration of MAP	
		Less than or equal to 3 months	**Greater than 3 months**
Minimum Frequency of SDQC	**MRP**	Not mandatory- unless program is locally assessed as requiring SDQC for the reasons listed*	Every 90 days (from Actual Start Date)
	PSP	End of program (Actual End Date)	Every 90 days (from Actual Start Date)

Timelines to complete and document outcomes of SDQC in the MAP Tracking System: Within 90 calendar days from the SDQC due date. These are considered Roche internal timelines and should not be communicated to Service Providers.

The last SDQC should cover the entire period from the previous SDQC end date until the MAP Actual End Date.

*Frequency of SDQC can be increased if there are contributing risk factors - examples of which are listed below:

- High number of Participants
- High number of Interactions
- Program designed in a manner which is likely to generate safety data
- Non-compliance of Service Provider
- Repeated late reporting of adverse event reports or missed adverse event reports
- History of Audit/Inspection findings that could impact program conduct

To achieve compliance with these timelines, it is highly recommended that the Service Provider/Roche personnel completing SDQC, sends the completed form to Safety Unit well in advance of the end of the timeline, for timely uploading in MAP tracking system.

7. SELECTION OF SOURCE DATA FOR SDQC

Specific sample sizes must be used based on the volume of source data i.e., number of records generated for the SDQC period (see Table 2†).

Table 2

Volume of source data/records	Source data/records sample size to be checked
Less than 45	All
≥ 45 -100	45
≥ 101- 250	101
≥ 251 - 500	210
≥ 501 – 750	300
≥ 751 – 1000	380
≥ 1001	380

†This sample size calculation is powered to detect, with 95% confidence, that the Service Provider/Roche personnel running the program has identified Adverse Events/Special Situation Reports correctly in 95% of cases.

When selecting source data for inclusion in SDQC, the sample must be selected from all and any source data previously assessed as required for inclusion in SDQC (see section 4) for the specific period the SDQC should cover.

Source data for review should be selected randomly. If there are several types of source data i.e., hard copies, phone calls, a representative sample of each type of document should be selected. E.g., if hard copies form a larger parts of the source data volume and phone calls a smaller part, the representation should be balanced accordingly.

8. CONDUCT OF SDQC

SDQC must always be conducted by a different person from the one responsible for initial identification of AEs/SS during the execution of MAP program.

When SDQC is performed, review is completed on the source data generated, for a given MAP, in a relevant SDQC period covered. For certain types of MAP (refer to Table 1), a final SDQC must be performed once the program is completed i.e., after the Actual End Date is reached.

Randomly selected source data should be reviewed and a copy of all reviewed source data must be retained/archived (e.g., by scanning the reviewed samples or tracking the sample reviewed) in accordance with COREMAP. Reviewed source data must be retained/archived in a location to enable access upon request e.g., during audit or inspection.

Global: Market Research and Patient Support Program Source Data Quality Check (SDQC) Guidance and Form

SDQC may be completed internally by Roche, or by a Service Provider under one of the following contractual scenarios:

Depending on the contractual agreement SDQC responsibility could be with:

- Safety Unit conducts the SDQC
- Safety Unit e.g., for Roche managed programs, delegates the SDQC to an independent external Service Provider with PV experience
- Safety Unit delegates the SDQC to the Service Provider running the MAP, if they have demonstrated capability to conduct this (capability must be assessed and documented)

Prior to delegation of SDQC to the Service Provider, Roche should conduct an assessment of the capability of the Service Provider to adequately conduct the SDQC. This assessment should form part of the selection process and Oversight Plan for a MAP Service Provider.

Final accountability for ensuring SDQC is completed and documented, lies with the relevant MAP Owner and PV Approver for the MAP.

A high level overview of the SDQC process can be seen in Diagram 1.

The SDQC process should start as soon as possible after the SDQC due date (as per the MAP tracking tool). Please ensure a process is in place to notify Service Providers or MAP Owners regarding SDQC due dates. The timeline for conducting SDQC from the SDQC due date is 90 calendar days. It is recommended to define with your Service Providers and/or MAP Owners the timelines, within the 90 days, for SDQC to be completed and the SDQC form sent to Roche.

If, as a result of the SDQC process, one missed AE/SS is identified, 100% review of all source data for the relevant MAP, for the SDQC period covered, must be completed and documented in the MAP tracking system. For the 100% review process you will have an additional 90 days from the SDQC deadline date to complete the review. Hence, if SDQC is completed early in the given 90 day timeline, additional time is made available for completion of 100% review should it be required e.g., if SDQC is completed after 30 days and 1 missed AE is identified, the remaining 60 days for SDQC completion is added to the 90 days for 100% Review = 150 days to complete 100% review (see Diagram 2).

Results of SDQC (including final SDQC) should be documented using the SDQC Completion form in Appendix 1.

Diagram 1: High Level Overview of SDQC Process

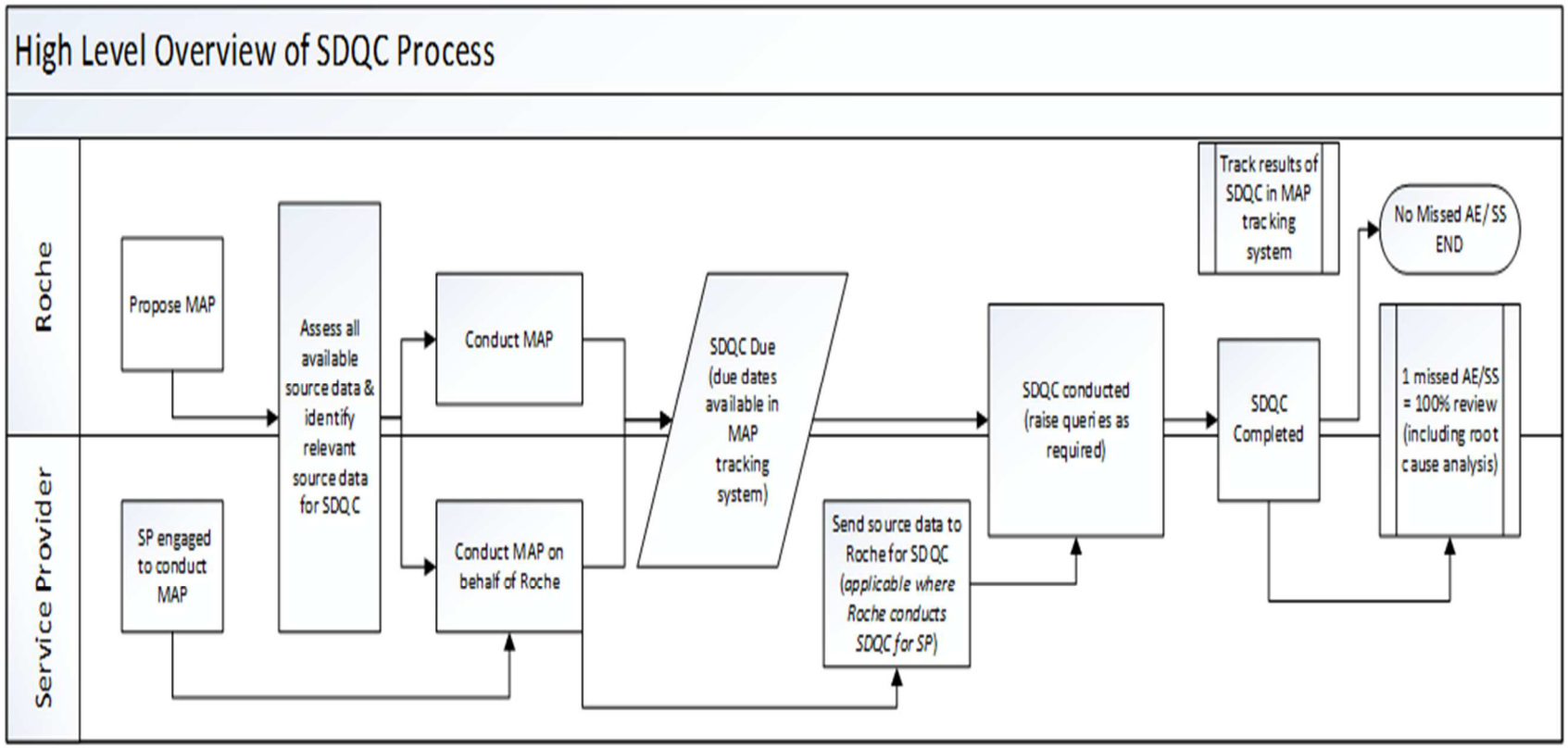
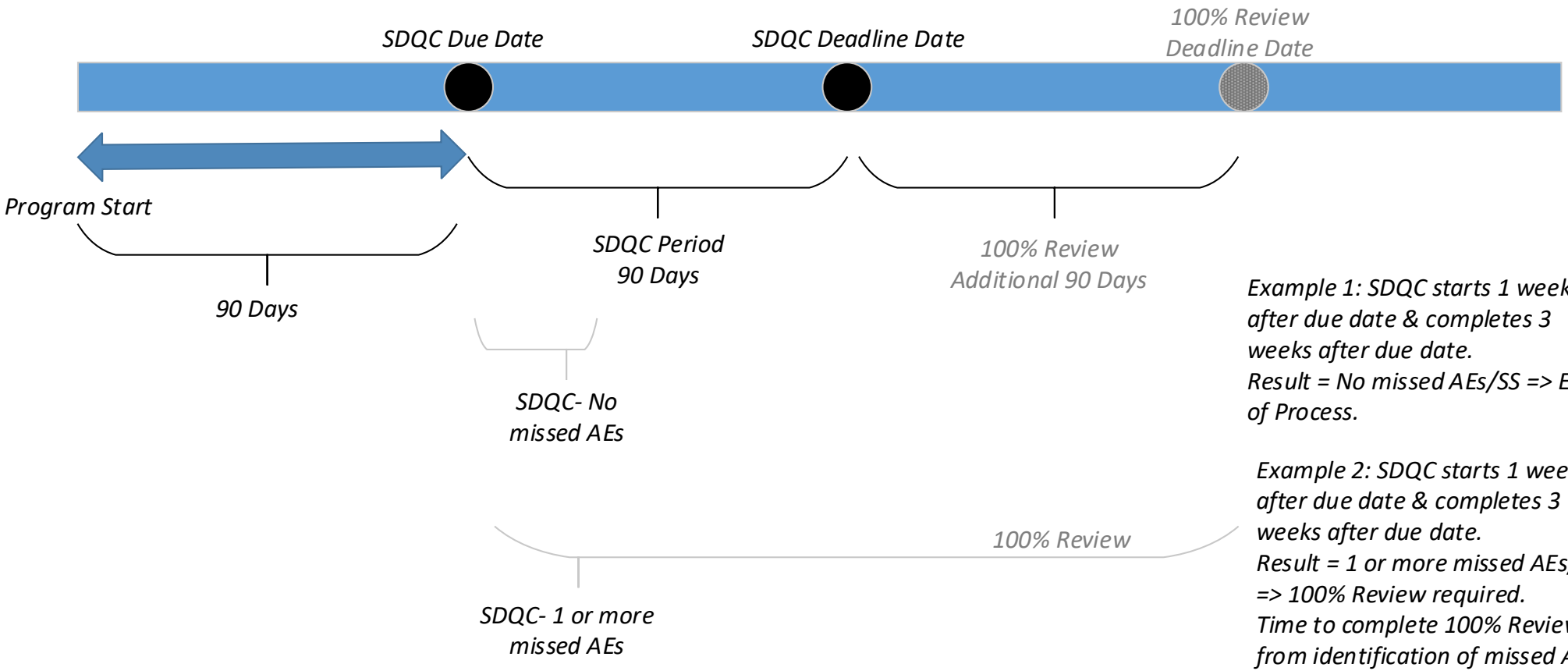


Diagram 2: Overview of SDQC Frequency and Timelines



Example 1: SDQC starts 1 week after due date & completes 3 weeks after due date.
Result = No missed AEs/SS => End of Process.

Example 2: SDQC starts 1 week after due date & completes 3 weeks after due date.
Result = 1 or more missed AEs/SS => 100% Review required.
Time to complete 100% Review from identification of missed AEs to 100% Review Deadline Date, i.e. ~150 days.

9. MAP PROGRAM COMPLETED

Once a MAP has reached its Actual End Date, a final SDQC may be required depending on the program type and duration (see Table 1). A MAP cannot be closed in the MAP tracking system until all SDQCs due for the MAP are conducted and the MAP tracking system updated accordingly.

10. ADDITIONAL INFORMATION

SDQC is a quality assurance step to ensure that the process for identifying and reporting AEs/SSs to Roche drug safety, during conduct of a MAP, is working adequately. If a missed AE/SS should be identified as part of SDQC, an investigation (root cause analysis) should take place to identify the cause of the failure. In some instances, and in addition to 100% review, further actions may be required to address the root cause of the failure. These could include but are not limited to:

- Perform a new capability assessment of the Service Provider in collaboration with the MAP Owner, e.g., evaluate the Service Provider AE/SS reporting process, experience and training status of the staff involved.
- Work closely with the Service Provider to ensure the implementation of an adequate corrective action plan.
    - Consider re-training, if applicable.
- If the program is run by a Service Provider, evaluate the impact of the failure on other programs the Service Provider runs.
- In case of repeated non-compliance without resolution, initiate the discussion with MAP Owner to decide if the contract termination should occur.
- Escalation to Quality Assurance/Quality Responsible/General Manager.

All actions should be documented and could be requested during audits or inspections.

11. ROLES AND RESPONSIBILITIES

Role	Responsibilities
MAP Owner	• Collaborate with PV Approver to identify all source data for a MAP, and in particular the source data required for inclusion in SDQC. • Engage with PV Approver and ensure adequate resources have been allocated for the MAP, to confirm PV compliance requirements are met. • Ensure source data is provided by Service Provider as per timelines in the contract to enable the Safety Unit to conduct SDQC (Only applicable for scenario where MAP is run by Service Provider but Roche conducts SDQC). • Ensure Service Provider informs Roche in case of any change in regards to source data for a MAP i.e., creation of additional type or change in the format. • Facilitate resolution of SDQC-related queries. • Collaborate with PV Approver to agree whether all Service Provider SDQC-related deliverables, as per the contract are

Role	Responsibilities
MAP Owner	fulfilled. • (For Service Provider SDQC*)* Notify SDQC responsible of SDQC due dates and deadline date. • In case of issues facilitate resolution with SP and agree on timelines.
PV Approver and/or responsible for SDQC	SDQC must be conducted by a different person to that responsible for initial identification of AEs/SS during the execution of MAP **PV Approver** • Determine the number of records for SDQC period. • Select the sample size for SDQC. • Randomly select source data for SDQC. • Conduct SDQC. • Upload completed SDQC form in MAP tracking system. • If missed AE/SS are identified, ensure the missed AE/SS are reported immediately to Safety Unit. • Conduct 100% review as required i.e., in event of 1 missed AE/SS, within timelines (see Diagram 2). • Complete a CTV form to reconcile that all missed AE/SS have been received by Safety Unit. • Conduct a root cause analysis to determine why safety data was missed and propose preventive actions including relevant stakeholders. • Address and document any actions identified as part of the root cause analysis following the identification of missed AE/SS. *The following responsibilities in regards to the SDQC process may be delegated to a Service Provider. • *Determine the number of records for SDQC period • *Select the sample size for SDQC • *Randomly select source data for SDQC • *Conduct SDQC • *If missed AE/SS are identified, send the missed AE/SS immediately to Safety Unit • *Conduct 100% review as required i.e., in event of 1 missed AE/SS, within timelines (see Diagram 2) • *Complete a CTV form to reconcile that all missed AE/SS have been received by Safety Unit. • *Conduct a root cause analysis to determine why safety data was missed and propose preventive actions including relevant stakeholders to Roche.

Global: Market Research and Patient Support Program Source Data Quality Check (SDQC) Guidance and Form

APPENDIX 1: SDQC COMPLETION FORM

Roche's MAP Identification Number: *(e.g., MAP-GB-1234)*		
Country *(For use where a MAP, is running in more than one country)*		
Program Name:		
Applicable period of time for Source Data Quality Check(SDQC):	**From:** **To:**	
	☐ **Periodic SQDC**(every 90 days) ☐ **Final SDQC** ☐ **Additional SDQC**	
Reason for additional SDQC		
Actual Program Start Date:		
Actual Program End Date *(if this is a final SDQC):*		
Total Number of Source Records in the Review Period:		
Number of records to be checked:		

SDQC Results:	
Date(s) SDQC was performed:	
Service Provider Name (if applicable):	
Name(s) of Person(s)Performing the SDQC:	
Signature of Person Performing the SDQC:	

Global: Market Research and Patient Support Program Source Data Quality Check (SDQC) Guidance and Form

Section A	
Have AEs and/or Special Situation Reports been identified in the sample ☐ Yes ☐ No *Note:* *If "yes", complete* ***Section B*** *If "No" complete MAP tracking system accordingly, and complete the signature section below.*	
Section B Have the AEs and/or Special Situation Reports identified during SDQC already been reported to the Safety Unit during the program? ☐ Yes ☐ No *Note:* *If "Yes", update MAP tracking system accordingly, and complete the signature section below* *If "No" complete <u>all</u> below fields*	
Number of AEs and Special Situation Reports identified in the sample that have not been reported to the Safety Unit	
Date of completion of CTV to confirm missed AE/SS identified in the sample were received by Safety Unit	
<u>To be completed by Roche</u> Print Name: …… Signature of the reviewer: …… Date: ……	
Section C **100% Review details:**	
Date(s) 100% review was performed:	
Number of missed AEs/SS identified during 100% review	
Date of completion of CTV to confirm missed AE/SS identified in the 100% review were received by Safety Unit	

MANDATORY

Details of root cause analysis leading to missed AE/SS and action plan implemented (in addition to the 100% review).

To be completed by Roche

Print Name: ……

Signature of the reviewer: ……

Date: ……

Note: Following signature of 100% review, upload to the MAP tracking system. This will be in addition to SDQC form that was uploaded to the MAP tracking system in section B