D2.1 Standard Operating Procedures (SOPs) and Templates: Guidance and Recommendations

777363-DRIVE

Development of Robust and Innovative Vaccines Effectiveness

WP2- Development of study tools

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V0.1	08 Feb 2018	First Draft outline
V0.2	09 Feb 2018	Added report template and draft Chapter 3
V0.3	23 Feb 2018	Draft deliverable for review by work group members
V0.4	16 Mar 2018	Revised deliverable incorporating feedback from WP2
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V 0.8	05 Jun 2018	Further revisions based on feedback received from WP2
V 0.9	27 Jun 2018	Revised version for SC review
V 1.0	23 Jul 2018	Revised version based on SC comments

Contents

Executive Summary

Development of the Standard Operating Procedures (SOPs).

Vaccines are critical in preventing influenza and its complications. DRIVE's objective is the development of a governance model that will facilitate the development of a sustainable study platform of sufficient size to enable vaccine type/ brand-specific vaccine effectiveness (VE) studies. There is a need for a strong focus on the robustness of the data while ensuring compliance with relevant legislation and best practice standards for VE studies.

The primary sources to define the scope of our guidance have been: (1) European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP); and (2) the EU General Data Protection Regulations (GDPR). These documents will also particularly ensure that DRIVE-related VE studies comply with relevant standards. The SOPs will also identify DRIVE consortium responsibility and study site responsibilities. DRIVE-related VE studies comply with relevant standards. The SOPs will also identify DRIVE consortium responsibility and study site responsibilities.

This guidance is also influenced by experience from other programs, such as I-MOVE (Influenza – Monitoring Vaccine Effectiveness), ADVANCE (Accelerated development of vaccine benefit-risk collaboration in Europe) and MOCHA (Models of Child Health Appraised). The secure data and analytics hub for the Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC*)* brings a primary care and clinical informatics perspective to this work.

DRIVE partners involved in task 2.4

SURREY, UCBL, THL, SEQIRUS, GSK, SP, UNIFI, ISS

List of abbreviations

ADVANCE - Accelerated development of vaccine benefit-risk collaboration in Europe
ARI - Acute respiratory infection
CMR - Computer Medical Records
CoC - Code of Conduct of Conduct
CRF - Case report form
DMP - Data management plan
DOI - Declarations of Interests
DRIVE - Development of robust and innovative vaccine effectiveness
EC - Ethics Committee
ECDC - European Centre for Disease Prevention and Control
EFPIA - European Federation of Pharmaceutical Industries and Associations
EHR - Electronic healthcare records
EMA - European Medicines Agency
ENCePP - European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU - European Union
GDPR - General Data Protection Regulation
GP - General Practice
IAF - Informed Assent Form
ICF - Informed Consent Form
ICMJE - International Committee of Medical Journal Editors
I-MOVE- Influenza - Monitoring Vaccine Effectiveness
ILI - Influenza-like illness
IMI - Innovative Medicines Initiative
IRB - Independent Review Board
ISC - Independent Scientific Commitee
ISO - International Organization for Standardization
ISPE - International Society for Pharmacoepidemiology
IVE - Influenza vaccine effectiveness vaccine effectiveness
MOCHA - Models of Child Health Appraised of Child Health Appraised
QA/QC - Quality Assurance/Quality Control
RCGP - Royal College of General Practitioners
RSC - Research and Surveillance Centre
RSV - Respiratory Syncytial Virus
SAP - Statistical Analysis Plan
SARI - Severe acute respiratory infection
SOP - Standard Operating Procedures
STROBE - Strengthening the reporting of observational studies in epidemiology
SWOT - Strengths, Weaknesses, Opportunities, and Threats
TND - Test-negative design
VE - Vaccine effectiveness
VPD - Vaccine preventable disease
WHO - World Health Organization
WP - Work package

Chapter 1 – Introduction and methods

Vaccines are critical in preventing influenza and its complications. Over the last 30 years there have been significant achievements in developing epidemiological vaccine research networks, and estimating vaccine effectiveness based on generic protocols. These have used standard methodologies and specific case definitions involving laboratory confirmation, and have generally been conducted by public health institutes.

The landscape changed when the European Medicine Agency (EMA) issued guidance that there should be: *Continuous monitoring of vaccines' effect via vaccines effectiveness studies*.

Influenza vaccine effectiveness data is increasingly being collected from alternative settings and using alternative methods beyond the classical general practitioner (GP) or hospital case ascertainment including computer medical records (CMRs) and other real world datasets. There is a need for a strong focus on the robustness of the data, especially information on vaccine types and brand, uncertainties on past vaccine exposure, and on confounders.

DRIVE's objective is to establish a network that enables brand-specific IVE studies for all influenza vaccines in use in the EU. Further focus is on the development of a governance model that will facilitate a sustainable platform of sufficient size to enable vaccine type/brand-specific vaccine effectiveness (VE) studies.

Work Package 2 within DRIVE aims to develop tools to harmonise the approach to implementation of VE studies and to comply with relevant legislation and best practice/scientific standards.

This deliverable has been developed in order to inform further the implementation of studies (TND, cohort) in light of the operational aspects and the existing guidance/legislation. A series of standard documents related to pharmacoepidemiological study conduct and data protection have been used to prepare the SOPs. DRIVE is expecting to include innovative approaches, therefore this document will be adapted along the project.

The data sources for DRIVE studies based on the Work Package descriptions:

- Primary care data
- Hospital data
- Vaccine registers
- Population-based registers
- Personal vaccine card information
- Participatory surveillance
- Use of laboratory data

Box 1: DRIVE data sources

Chapter outline

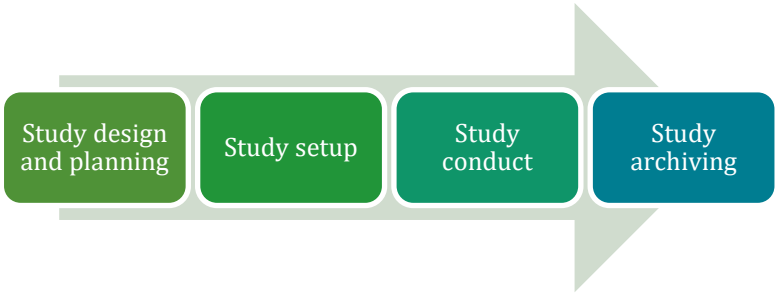
The following chapters set out the guidance and recommendations for SOPs. These are due for an annual update through the life of the project.

Table 1: Chapter outline

Chapter	Topics covered	Type of supporting document
1) Introduction	Outline	
2) Integrity & Transparency	Independence	Code of Conduct (IMI ADVANCE)
	Transparency	Code of Conduct (IMI ADVANCE)
	Data integrity and validity of approaches to using data	TRANFoRm, MOCHA publications, MOCHA publications
3) Data Management in DRIVE including data protection and privacy	SOP for data management	GDPR chapter 5 / ENCePP for secondary data collection DRIVE D4.2 Data management Plan GDPR Privacy Impact Assessment (Article 35) / GDPR Chapter 4 DRIVE Data management Plan
4) Data quality in DRIVE	SOP for data quality assessment	EU General Data Protection Regulation (GDPR) 2016 UK Data Protection Act 1998 International Conference on Harmonisation, Harmonised Tripartite Guideline for Good Clinical Practice (1996)Harmonisation, Harmonised Tripartite Guideline for Good Clinical Practice (1996)

DRIVE Site Study Timeline

DRIVE studies would typically be carried out according to following stages. The various activities that take place during these stages and responsibilities of parties involved are given below and outlined in the framework for observational studies given in DRIVE D7.1 and D7.2. We have mapped the activities in the various stages to relevant guidelines produced within DRIVE and/or external sources. Activities that we have not be able to identify appropriate guidelines at the time of submitting this deliverable will be revisited during subsequent iterations.



1. Study design and planning

Activity	Comments and applicable document to be followed
Development of site study protocol	D7.1/D7.2 Study protocols http://www.drive-eu.org/wp-content/uploads/2018/05/ANNEX1_DRIVE_D7.1_Core-protocol-for-test-negative-design-studies_0.9.pdf http://www.drive-eu.org/wp-content/uploads/2018/05/ANNEX2_DRIVE_D7.2_Core-protocol-for-population-based-database-cohort-studies_0.9-1.pdf
Review and approval of protocol	ISC will produce a report which will document their review and also address EFPIA comments and related answers (D1.02 Governance Standard Operating Procedure (SOP)) http://www.drive-eu.org/wp-content/uploads/2018/03/D1.2-Governance-Standard-Operating-Procedures-SOP.pdf
Country selection process/site selection process	'Site selection' will be covered by the tendering process of WP2 (Task 2.7/deliverable D2.5). National and regional public health institutes with established IVE studies and organizations with corresponding tasks may also join DRIVE as Associate Partners.
ICF/IAF (Informed Consent Form / Informed Assent Form) preparation if applicable	ICF process is covered in the generic study protocols. We will also liase with WP8 regarding ethics during the future updates.
Statistical analysis plan	D4.4 Generic SAP http://www.drive-eu.org/wp-content/uploads/2018/04/DRIVE_D4.4_genericSAP_FINAL.pdf
Set of the study Database, CRF, Data Management Plan	D4.2 Data management plan http://www.drive-eu.org/wp-content/uploads/2018/03/D4-2_Generic-DMP_FINAL.pdf

DRIVE consortium responsibility

DRIVE will produce and update the aforementioned generic protocols and guidelines and assist study sites in fulfilling them as needed. DRIVE may also provide resources to set up an IVE study for sites that have not assessed IVE before or want to set up a novel approach of assessing IVE

Sites' responsibility

Deliverable D7.1 and 7.2 provides details about responsibilities of study sites. Each study site should specify the target groups for which influenza vaccination is recommended. For TND studies study sites would need to specify if the study is nested in to the influenza surveillance scheme (the ILI sentinel surveillance system) or is organized differently. Furthermore, they would need to specify national policy for influenza surveillance and vaccination and available vaccine brands on the market. For cohort studies, each study site should describe the source population and definition of the study cohort.

Study sites are encouraged to follow DRIVE guidance such as generic protocol and key requirements on disclosing the study period, study population.

Study sites should describe the way to determine the date of occurrence for specific events. They should also define the non-specific outcome(s) and the methods for detecting them in the databases.

2. Study Setup

Activity	Comments and applicable document to be followed
Study material preparation	
EC/IRB submission/Approval	According to local laws and regulations; which is mentioned in the generic study protocols
Study protocol (Summary) Disclosure	D7.1/D7.2 Study protocols
Site Initiation	
Monitoring plan	

DRIVE consortium responsibility

If needed, DRIVE may provide technical assistance to help increase the studies' compatibility with the DRIVE protocols. DRIVE collects copies of the approvals from Ethics Committees and other relevant bodies (or, where ethics committee approval is not needed e.g. because the study is considered a part of a public health institute's statutory responsibilities, a written explanation) and submits them to IMI.

Sites' responsibility

Study sites will specify case finding criteria and any exclusion criteria applied. Furthermore, the study site will describe procedures used to identify study participants.

Study sites will describe the precise method for ascertainment of vaccination status and potential confounding factors included in the study. The specification should also include how the confounders were identified.

Ethical approvals obtained by the study sites should be archived as per local law and relevant approval materials should be provided to DRIVE. These details include procedures to comply with national ethics committee requirements and the type of informed consent obtained. The study sites are expected to provide a copy of the ethical approval, Independent Review Board (IRB) or equivalent. If ethical approval is not needed, the site should obtain from the ethic committee a waiver or an official communication documenting that this is not needed.

Study sites will specify details about any trainings organized.

3. Study conduct

Activity	Comments and applicable document to be followed
Monitoring	
Amendments: • Protocol • ICF/AF • SAP	
Database freeze	D4.2 Data management plan http://www.drive-eu.org/wp-content/uploads/2018/03/D4-2_Generic-DMP_FINAL.pdf
Statistical analysis	D4.4 Generic SAP http://www.drive-eu.org/wp-content/uploads/2018/04/DRIVE_D4.4_genericSAP_FINAL.pdf
Study report	D4.3 Report template http://www.drive-eu.org/wp-content/uploads/2018/03/D4-3_Report-templates_Final-version.pdf D4.6 Points to consider document on the interpretation of VE results
Public disclosure of study results (summary)	Recommended: e.g., http://www.encepp.eu/encepp_studies/indexRegister.shtml https://www.clinicaltrials.gov/
Publication (manuscript/ Presentation at scientific meetings)	ICMJE criteria http://www.icmje.org/icmje-recommendations.pdf ENCePP Code of Conduct http://www.encepp.eu/code_of_conduct/documents/ENCePPCoCAnnex2_ChecklistofCodeofConduct.pdf

DRIVE consortium responsibility

Studies are conducted independently by the participating sites. Apart from answering specific questions by the study sites (e.g. regarding the compatibility of the data with DRIVE pooled analysis), the DRIVE consortium does not participate in study conduct.

Sites' responsibility

Study sites will define the information source used to collect the variable in the study and the data collection tools used to collect information from the source. They will also describe if and how informed consent is obtained.

Study sites will provide details about laboratory testing. This includes details of specimen collection (including description of the criteria and the procedure for swabbing at the site level), the specimen storage and transport procedures. They will also provide details of the laboratory tests used, the selection of specimens and the procedures for genetic and antigenic characterization. Details of QA/QC (Quality Assurance/Quality Control) schemes participated will also be provided.

4. Study Archiving

Activity	Comments and applicable document to be followed
Study material archiving	Guidance for Document Version Control and Archiving

DRIVE consortium responsibilities

DRIVE D4.2 outlines the responsibilities with regard to data management including data archiving in the DRIVE consortium. DRIVE uses validated statistical software for data management (entry, transfer etc.) and provides annotated programming and back-up(s) of electronic data and records in different locations than the primary database. If needed, DRIVE will provide a data storage index for audit and inspection purposes. The consortium has a list of essential study documents and written procedures for review, approval and versioning of any documents. It provides standard templates of commonly applicable study related documents (at minimum protocol, statistical analysis plan informed consent, study report) and study specific procedural documents (project management plan, document management plan, data management plan). For electronic documents, it ensures that strong passwords are used and encryption is applied when transferring protected health information.

Study site responsibilities

DRIVE D7.1 and D7.2 outline the responsibilities with regards to data management including data archiving for each study site within DRIVE. It specifies that study sites have the responsibility for ensuring that they have adequate processes to collect and validate their data, including any checks in place in the data entry system to avoid mistakes in data entry, and information on whether source data verification was conducted.

Each study site should also provide a codebook that includes the variable names, variable descriptions, and the coding of variable values, if not following the DRIVE procedures / codebooks / tools accessed through the DRIVE website (www.drive-eu.org).

Each study site should have procedures for data management including procedures for data checking and data cleaning.

Chapter 2 – Integrity and Transparency

Areas covered

Code of conduct, scientific independence, integrity, integrity of data systems.

Source documents considered

Source document name & version	Web URL	Parts included/not included
Code of Conduct (IMI ADVANCE)	http://www.advance-vaccines.eu/app/archivos/publicacion/16/ADVANCE_WP1_Deliverable-1.9_Final-Public.pdf	

Adoption of a Code of Conduct

Initially, the authors of this deliverable evaluated several codes of conduct produced by various initiatives involved in vaccine research. Subsequently, during internal meetings it was suggested that it would be appropriate for DRIVE to consider adopting the Code of Conduct of the Accelerated development of vaccine benefit-risk collaboration in Europe (ADVANCE) project due to its relevance to DRIVE. A number of other codes of conduct (including the ENCePP Code of Conduct[1,2,3]) have been considered when developing the ADVANCE Code of Conduct. The ADVANCE CoC groups recommendations across 10 topics into mandatory recommendations that must be applied ("must") and recommendations that are desirable to be applied ("should").

The key topic headings in this code of conduct are:

1. Scientific integrity
2. Scientific independence
3. Transparency
4. Conflict of interest
5. Study protocol
6. Study report
7. Publication
8. Subject privacy
9. Sharing of study data
10. Research contract

Table 1. Summary of the recommendations of the ADVANCE Code of conduct for collaborative vaccine studies

Topic	**Recommendations to be applied in all studies ("must")**	**Other recommendations to be considered for all studies ("should")**
1. Scientific integrity	1. All study team members are qualified to fulfil their role	
	2. All study team members act in accordance with core values of honesty, accuracy and objectivity	
	3. Study team members adhere to IEA Good epidemiological practice and ISPE Good pharmacoepidemiological practices	

Topic	Recommendations to be applied in all studies ("must")	Other recommendations to be considered for all studies ("should")
2. Scientific independence	4. Study is conducted without undue influence of any financial, commercial, institutional or personal interest in a particular outcome of the study	5. Autonomy of members of study team for making scientific decisions in their organisation is documented
	6. Scientific independence is safeguarded by clear and transparent roles and responsibilities, peer review process, transparency measures and disclosure of all funding sources	
3. Transparency	7. Study is registered in a publicly accessible database before the start of data collection or extraction	11. Final study report or summary is uploaded in publicly accessible database where study is registered
	8. Sources of funding are made public at the time of registration, in the protocol and in the presentation of results	12. After study completion, study information is made available from outside the study team in a collaborative approach
	9. Declarations of Interests (DoI) are made available at an early stage of the study, regularly updated and disclosed are made available at an early stage of the study, regularly updated and disclosed	13. In case of primary data collection, participants in the study or their representatives may receive main study results and interpretation thereof
	10. All comments received on study protocol and results with impact on the study are documented	
4. Conflict of interest	14. Actual or potential conflicts of interest (and perceptions thereof) are addressed at the planning phase of the study. Research contract includes a description of the management of conflicts of interest. All DoI are made publicly available.	15. A standard form is used to declare all interest that may lead to conflicts
5. Study protocol	16. A study protocol is drafted as one of the first step in any research projects	18. The process for reaching an agreement on the design options of the study is agreed beforehand
	17. Study protocol is developed by persons with relevant expertise	22. Detailed draft protocol undergoes independent scientific review
	19. Protocol includes a section with ethical considerations involved and information on funding, affiliations, potential conflicts of interest, data protection and incentives to subjects. Protocol is approved by relevant research ethics committee	23. Protocol is registered in publicly accessible database before the start of data collection
	20. Protocol includes description of each party to study design, protocol writing and work programme	
	21. Regulatory obligations and recommendations applicable to the study are described	

Topic	Recommendations to be applied in all studies ("must")	Other recommendations to be considered for all studies ("should")
	24. Changes to the protocol that may affect the interpretation of the study are identifiable and reported in the study report	
	25. Key statistical analyses are described	
6. Study report	26. Set of principles are followed for reporting results including documentation of important safety concerns and deviations from protocol or statistical analysis plan, sources affecting data quality, strengths and limitations, and sources of funding	27. STROBE statement and internationally agreed guidelines are consulted when analysing and reporting data
		28. Draft study report undergoes independent scientific review
		29. Study report or summary of the results is included in the publicly accessible database
7. Publication	30. All study results are made publicly available. Authorship of publications follows the rules of ICMJE	32. Preliminary or partial results of discontinued study are reported and identified as such
	31. Research contract allows the principal investigators and relevant study team members to publish study results independently from the funding or data source. The study requester/funder may provide comments	
	33. Procedures are in place to rapidly inform regulatory and public health authorities of study results, independently from submission of a manuscript	
8. Subject privacy	34. Privacy of study subjects in relation to personal data is core principle of any medical research	
	35. In case where personal data are collected, the applicable legislation is followed	
9. Sharing of study data	38. Sharing of study data is based on a written request specifying the ground of the request. The study team verifies the compliance of the request with the data protection legislation	36. There is an open and collaborative approach to sharing study data with persons from outside the study team
	39. Requests for data sharing are justified based on public health interest	37. Data are shared only after the study report is finalised
	41. Analyses performed with shared data follow the provisions of the ADVANCE Code of Conduct	40. Study team or delegated committee takes the decision to share study data
10. Research contract	42. The research contract does not lead investigators, directly or indirectly, to act against the principles of the Helsinki Declaration or applicable legal or regulatory obligations	44. Unique multiparty contract is preferred in cases where several parties interact

Topic	Recommendations to be applied in all studies (“must”)	Other recommendations to be considered for all studies (“should”)
	43. Clarity and transparency are key elements of the research contract	45. The research contracts indicates that the study will follow the ADVANCE Code of Conduct and provides core information

The governance aspect of robustness will be evaluated within WP1 by developing metrics of scientific independence and transparency, both at the study level and at the level of the DRIVE consortium and platform governance model. WP1 will evaluate the codes of conduct further and specify which topics would be considered within DRIVE.

In later iterations of this deliverable, we will incorporate results of work currently being carried out by WP1 on governance principles.

DRIVE consortium responsibility

The DRIVE consortium will consider the Code of Conduct while conducting the research studies.

Sites’ responsibility

The study sites will be informed about the Code of Conduct and advised to adhere to best practices guidelines outlined in the code of conduct.

Chapter 3 – Data management in DRIVE

SOP for data management including collection / transfer of personally identifiable information and storage archiving of data

Scope

Principles for the collection and management of data containing personally identifiable information in influenza vaccine effectiveness studies.

Source documents considered

Source document name & version	Web URL	Parts included/not included
DRIVE D3.2 SWOT analysis plan and list of quality criteria	http://www.drive-eu.org/wp-content/uploads/2018/03/D3-2_SWOT-analysis-plan-and-list-of-quality-criteria_Final.pdf	
DRIVE D4.2 Data management Plan	http://www.drive-eu.org/wp-content/uploads/2018/03/D4-2_Generic-DMP_FINAL.pdf	
DRIVE D7.1 Core protocol for type/brand -specific influenza vaccine effectiveness studies (test-negative design studies)	http://www.drive-eu.org/wp-content/uploads/2018/05/ANNEX1_DRIVE_D7.1_Core-protocol-for-test-negative-design-studies_0.9.pdf	
DRIVE D7.2 Core protocol for type/brand -specific influenza vaccine effectiveness studies (population-based database cohort studies)	http://www.drive-eu.org/wp-content/uploads/2018/05/ANNEX2_DRIVE_D7.2_Core-protocol-for-population-based-database-cohort-studies_0.9-1.pdf	
General Data Protection Regulation (GDPR)	https://gdpr-info.eu/art-42-gdpr/	Included: Chapter 4
Guidelines for Good Database Selection and use in Pharmacoepidemiology Research	https://www.pharmacoepi.org/pub/?id=1c2a306e-2354-d714-5127-9fd12e69fa66	Information from whole document included

Objective

The aim of this SOP is to define the minimum dataset required from study sites and outline best practice for data management, including the collection of data and processing of personally identifiable information, although this SOP is applicable to all study sites, even those that only handle aggregated, pseudonymised data.

Definitions, abbreviations

Aggregate data - Data that was gathered from many subjects, which has been grouped based on specific information and summarised. Also sometimes referred to as pooled data.

Anonymisation - The process of turning data into a form that does not link individuals' data to the subjects.

Data controller - The natural person which alone or in collaboration with others determines the purposes and means of personal data processing.

Data processor/ Data analyst - Anyone who processes personal data for a controller.

Data owner - The institution which (primarily) surveys, stores and uses the data. Data owners possess legal power of control over the data.

EU General Data Protection Regulation (GDPR) - The legislation which replaces the Data Protection Directive 95/46/EC and was designed to harmonise data privacy laws across Europe, to protect and empower all EU citizens' data privacy, and to reshape the way organizations across the region approach data privacy.

Harmonised data - Data that follow a consensus to be formatted in the same way.

Patient-level data - Data that are extracted patient by patient and includes their specific medical information, such as diagnosis and medication.

Personal data - any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.

Privacy by design - An approach that promotes compliance with privacy and data protection from the start of a project. GDPR require us to demonstrate this for: (1) all new IT systems that access or store personal data (pseudonymised data can still be personal); (2) Developing policies or strategies that have privacy implications; (3) Data sharing initiatives; (4) Using data for a new purpose.

Privacy Impact Assessment (PIA) - A tool that can help organisations identify the most effective way to comply with their data protection obligations and meet individuals' expectations of privacy.

Pseudo-anonymisation - The process of replacing one or more identifying fields within a dataset by one or more artificial identifiers, or pseudonyms. A process recognised within GDPR to enhance protection of personal privacy.

Secondary data - Data that was previously collected by someone for purposes different than the DRIVE project at the time of the collection (e.g. electronic healthcare data).

Third party - Anyone who processes data under the 'direct authority' of a controller or processor.

Minimum dataset

See the most recent versions of DRIVE D7.1 and D7.2 which define the data elements to be used for estimating VE in brand-specific studies including a complete list of variables required from test-negative case control and cohort VE study designs.

Data Management

DRIVE D4.2 Data management Plan provides the general framework regarding data management, data protection, data ownership, accessibility and sustainability requirements.

DRIVE consortium responsibilities

See Chapter 4

Study site responsibilities

See Chapter 4

SOP revisions

SOP version no	Date of change	Description of change	Prepared by	Approved by

Chapter 4 – Data quality assessment in DRIVE

SOP for Data Quality Assessment

Scope

The procedure covers databases for vaccine effectiveness (VE) studies within the DRIVE project to:

- verify that appropriate data quality management systems are in place in all participating VE studies within the DRIVE project;
- verify the quality of reported data for key data points at each study site;
- contribute to the strengthening of data management systems and capacity building within the DRIVE project.

Source documents considered

Source document name & version	Web URL	Parts included/not included
D1.2 Governance Standard Operating Procedures (SOP)	http://www.drive-eu.org/wp-content/uploads/2018/03/D1.2-Governance-Standard-Operating-Procedures-SOP.pdf	
DRIVE D3.2 SWOT analysis plan and list of quality criteria	http://www.drive-eu.org/wp-content/uploads/2018/03/D3-2_SWOT-analysis-plan-and-list-of-quality-criteria_Final.pdf	
DRIVE D4.2 Data management Plan	http://www.drive-eu.org/wp-content/uploads/2018/03/D4-2_Generic-DMP_FINAL.pdf	

Objective

The aim of this SOP is to outline a step-by-step approach for undertaking a data quality assurance self-assessment

Data Quality Assessment

DRIVE D3.2 – SWOT analysis plan and list of quality criteria, provides a general framework assessing operational quality and feasibility of VE studies at the site level including data quality. However, it is not a standalone auditing instrument, in particular in the field of health where audits typically also require a review of existing documents and an assessment of the alignment of current practice to existing protocols. It is therefore not to be considered in itself an audit of data quality

DRIVE consortium responsibilities

DRIVE D3.2 and DRIVE D1.2 outlines the responsibilities of the DRIVE consortium including the DRIVE Quality Control and Audit Committee (QCAC) with regards to data management and data quality. It specifies that the DRIVE consortium should use of validated statistical software for data management (entry, transfer etc.). It should provide a data storage index for audit and inspection purposes. It should provide annotated programming and back-up(s) of electronic data and records in

different locations than the primary database. It should provide a list of essential study documents and have written procedures for review, approval and versioning of any documents. It should provide standard templates of commonly applicable study related documents (at minimum protocol, statistical analysis plan informed consent, study report) and study specific procedural documents (project management plan, document management plan, data management plan, safety data management plan). For electronic documents, it should ensure that strong passwords are applied and encryption is applied when transferring protected health information.

Study site responsibilities

DRIVE D7.1 and D7.2 outline the responsibilities with regards to data management for each study site within DRIVE. It specifies that study sites have the responsibility for ensuring that they have adapted DRIVE study SOPs and guidelines including those relating to data management and data quality to be used by the site study teams and provide a summary of systematic or other major deviations from them to WP7. DRIVE D3.2 suggests that each study site should specify these procedures in a study site Data Management Plan.

SOP revisions

SOP version no	Date of change	Description of change	Prepared by	Approved by

Chapter 5 - Summary and next steps

DRIVE's objective is to establish a network that enables brand-specific IVE studies for all influenza vaccines in use in the EU. It is expected that DRIVE will contribute to optimized and targeted data collection for influenza VE studies, build novel data sources and methods for vaccine effectiveness evaluation and address concerns on transparency and scientific independence about study conduct and results.

In this deliverable, we present Standard Operating Procedures as guidelines; recommendations in order to support these DRIVE aims, to facilitate the compliance with relevant legislation and to keep consistency with best practice standards during the conduct of VE studies which are part of DRIVE. We will develop this SOP over the next three years to reflect the analysis which will/could be performed each year based on the collected data. This is crucial in the changed research landscape characterized by the need to collect data on vaccine effectiveness studies and demonstrate clinical efficacy in the context of the EU General Data Protection Regulations (GDPR) and a burgeoning, diverse range of data sources.

"Privacy-by-design" in the new GDPR places an additional burden on how we approach the creation of any system that might include personal data; penalties for the breach of these regulations have become much stricter. The GDPR recognised in law for the first time the process of pseudonymisation to protect personal data, and the need for personal data to be used for the management of health and care systems.

Our development of Standard Operating Procedures for the DRIVE project has benefited from previous initiatives such as ENCePP and ADVANCE (Accelerated development of vaccine benefit-risk collaboration in Europe) which have provided many of the source documents, upon which we can build. The lead authors were part of the ENCePP and ADVANCE projects as well other European consortia I-MOVE and MOCHA (Models of Child Health Appraised), and they have used this experience to ensure that maximum benefit is gained from their learning.

References

Key reference documents are given within the substance of the text.

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