D4.3 Study Report Template

777363 – DRIVE

Development of Robust and Innovative Vaccine Effectiveness

WP4 – Framework for analysis and study reports

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Description of Work	Version	Date
	V1.5	09/03/2018

1.1 Document History

Version	Date	Description
V1.0	28/11/2017	First Draft
V1.1	15/12/2017	Comments from core group incorporated
V1.2	16/01/2018	Comments from all task partners incorporated
V1.3	30/01/2018	Second draft
V1.4	06/03/2018	Second draft with SC comments incorporated
V1.5	09/03/2018	Final version

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1.2 Publishable Summary

In DRIVE, data from several independently operating national or regional study sites will be analysed jointly to obtain a large geographical coverage and sufficient sample size for brand-specific VE estimates. In order to harmonize the study-specific reports, DRIVE WP4 has developed a report template that can also be used for reporting the results of the joint analyses.

The draft report template was prepared by a small working group led by ISS and circulated for feedback within some of DRIVE partners (FISABIO, P95, UNIFI and THL) that have provided expertise in VE report development.

Separate sections have addressed stakeholder specific needs (e.g. EMA, PHIs and the general public). This template will be D4.3 and will be updated annually based on feedback from the DRIVE stakeholders and other Work Packages.

This document outlines the findings and results of the seasonal IVE for both the joint analyses and at each of the study site level, considering the different study design applied and for groups interested in adhering to the same protocol.

Study Report template

DRIVE

Development of Robust and Innovative Vaccine Effectiveness

Date: gg mm yyyy

Influenza season covered: yyyy – yyyy

Study Site: xxxxxxxxxxx (if used at the study site level)

Suggested citation: DRIVE. Report on influenza vaccine brand-specific effectiveness studies

- *to revise relatively to the content*

N.B. All the text in blue should be removed and updated where applicable

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1 List of abbreviations and acronyms

CDC	Centers for Disease Control and Prevention
DRIVE	Development of Robust and Innovative Vaccine Effectiveness
ECDC	European Centre for Disease Prevention and Control
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
EU/EEA	European Union/European Economic Area
GA	Grant Agreement
GP	General Practitioner
ICD	International Classification of Diseases
ILI	Influenza-like illness
ISC	Independent Scientific Committee
DRIVE	Development of Robust and Innovative Vaccine Effectiveness
ECDC	European Centre for Disease Prevention and Control
IVE	Influenza Vaccine Effectiveness
KOM	Kick-off meeting
KPI	Key Performance Indicator
RT- PCR	Real Time Polymerase Chain Reaction
PHI	Public Health Institute
SOP	Standard Operating Procedures
TC	Teleconference
QCAC	Quality Control and Audit Committee
MS	Member States
OR	Odds ratio
SARI	Severe Acute Respiratory Infection
VC	Vaccination coverage
MAH	Marketing Authorization Holders

- *to revise relatively to the content*

2 National institutions/organizations participating in the studies

MOCK TABLE

Country	Site	Type of Study (i.e. TND/cohort studies/Electronic database/Innovative studies/secondary register data)	Participant Institution/s	Contact person/s

- *to revise relatively to the content*

3 Responsible parties

- *to describe names, titles, qualifications, addresses, and affiliations for all responsible parties including: main author(s) of the protocol, principal investigator, a coordinating investigator for each country in which the study is to be performed, and other relevant study sites. A list of all collaborating institutions and investigators should be made available upon request. Role and responsibilities of all included parties should be described.*

4 Executive Summary

- *to summarize the key points of the full report. It should be organized according to the following sections: Background, Methods, Results and Conclusions. The writing should be kept simple and concise.*

  ½, max 1 page in length

5 Lay Summary

- *A brief summary of the studies that serves the general purpose of explaining research to non-experts, both members of the general public and other researchers who are not specialists in this specific field. The text should provide answers to the essential questions: Who, What, Where, When, Why, How?*

  ½, max 1 page in length

6 Amendments and updates:

- *Any substantial amendment and update to the study protocol after the start of the data collection, including a justification for each amendment or update, dates of each change and a reference to the section of the report.*

7 Milestones:

- *Table with meet dates for the following milestones with respect with the protocol:*

  .1. Start of data collection/surveillance period

  .2. End of data collection

  .3. Data cleaning and database available for the analysis

  .4. Final report of study results

  .5. Any other important timelines in the conduct of the study.

8 Background

- *To summarize the general background according to the impact/severity of the season/circulating strains*

Influenza is a major Public Health problem. Vaccines are the cornerstone for preventing influenza. However, controversies on real impact and level of protective Influenza Vaccine Effectiveness (IVE) and vaccination programs are present-day.

The new Guideline on Influenza Vaccines (non-clinical and clinical model) guidance of the European Medicines Agency (EMA) requests influenza vaccine effectiveness (IVE) evaluation for all individual vaccine brands used in the EU. Marketing Authorization Holders (MAH) are requested to respond to the regulatory requirements and corresponding overlap with public health mandate.
In this context, a new public-private partnership named DRIVE (Development of Robust and Innovative Vaccine Effectiveness), launched by the Innovative Medicines Initiative (IMI) in 2017, aims to establish a sustainable platform for studies in the European Union.

This draft report template was developed based on STROBE [1,2] checklist for cohort, case-control, and cross-sectional studies.

- *If the template is used at the study site level then each individual/country study site to describe the country background:*
  - *briefly explain influenza and influenza-like illness epidemiology in the season*
  - *briefly describe influenza vaccine policy and campaign at the study site level (duration, target categories, free of charge, etc.)*
  - *Influenza vaccine coverage at the study site level (if data for the current season are not available refers to the previous one)*

9 Study objectives

- *List the study objectives according with the study design used at the study site level (TND case control studies, electronic database studies, cohort studies, innovative studies, ect) according with the study protocols delivered in WP7.*

9.1 Primary objective/s

- *List primary objectives according with the Study protocols delivered in WP7 or with the objectives used at the study site level*

9.2 Secondary objective/s

- *List secondary objectives according with the Study protocols delivered in WP7 or with the objectives used at the study site level*
- *Evaluate also other potential exploratory objectives that could be evaluated*

10 Ethics approval/informed consent

- *Describe ethics approval process and include the Ethics approval and the informed consent used in specific Annexes*

11 Methods

11.1 Study design

- *Describe the study design according with the Study protocols delivered in WP7 or with the study design used at the study site level*

11.2 Study setting and study period

- *Study setting is defined by each study site depending on the available data. The study period for the primary analysis is one influenza season, i.e. the time period when influenza viruses circulate in the population. This period has been approximated to last from around week 40/42 until week 17/20 each year and can be extended by each study site to fully cover the vaccination campaign and the epidemic. It can also be divided into several shorter time periods to take into account differences in influenza activity over time.*

11.3 Study population and data collection

- *Describe the study population (e.g. type of population, selection process, etc.), the data collection method used for:*

  - *Baseline clinical data*
  - *Verification of immunization status*
  - *Assessment of outcomes*
  - *Laboratory assays and time points*
  - *Diagnosis of influenza (+ other resp. viruses)*
  - *Influenza typing/subtyping*

11.4 Data source

- *Describe the data sources used for the study*

11.5 Case definition

- *Describe the case definitions adopted in the study. List, describe and provide a concise case definition for the different outcomes used and how these outcomes are identified in the databases (codes included) if electronic database study or cohort study are used [3,4].*

11.6 Inclusion criteria and Exclusion criteria

- *Brief description of Inclusion criteria and Exclusion criteria applied in the study (see WP7, DLs7.1/7.2)*

11.7 Sample size description

- *Describe the sample size calculations depending on the study design used. This section should describe the sample size for the individual study site level, if this report is use by a site to report on their results, or the sample size for joined analysis if the report is use to present the consortium level results.*

11.8 Exposure (vaccination)

11.8.1 Vaccinees definition

- *Explain who is considered vaccinated according with study protocols (see WP7, DLs7.1/7.2)*
- *Detail explanation of how the type/brand of vaccine, dose, fully vaccinated status etc. are defined (see WP7, DLs7.1/7.2)*

11.8.2 Ascertainment of vaccination

- *Description of how the vaccination status, vaccine type, brand and the date of vaccination are assessed (e.g. GPs, vaccine registry).*

11.8.3 Target group for vaccination

- *List and describe target group for vaccination at the study site level or for each study site for the consortium level report.*
- *List the available vaccine types/brand at the study site level*

11.9 Risk groups, confounding factors and effect modifiers, other variables

- *List all underlying conditions, confounding factors and effect modifiers and other variables collected for each patient (see WP4, D4.1) and how they are defined*

11.10 Outcome

11.10.1 Swabbing procedures

- *Describe the procedures for the swabbing for each site (i.e. systematic swabbing, at clinician discretion, exhaustive etc).*

11.11 Influenza laboratory confirmation

- *Describe the laboratory methods used (if applicable)*
- *Describe the handling of the samples*

11.12 Data quality, management and verification procedures

- *Describe all the procedures for data cleaning and data transformation used*

11.13 Analysis of safety

- *Adverse event information was not expected to be systematically available from the source data used, and therefore was not routinely collected in this study*

11.14 Statistical methods

- *Describe all statistical methods applied to the study according with the SAP (at study site level or consortium level) (see WP4, DL4.4), including procedures used to control for confounding and, for meta-analyses, methods for combining results of studies. Any methods used to examine subgroups and interactions. How missing data were addressed. Any sensitivity analyses. Including:*

11.14.1 Descriptive
11.14.2 Measure of effect
11.14.3 Stratified analysis and Multivariate analysis
11.14.4 Potential biases
11.14.5 Sensitivity analysis
11.14.6 Meta-analysis (if applicable)

12 Results

- *This section should describe IVE results by each study site, design (e.g. electronic database, cohort, case-control,…) and setting (e.g. primary care, hospital based)*

Mock Figure X: ILI influenza positivity rate and vaccination coverage, by week of onset, included in the study, season xxxx/xxxx

- *Include the figure*

Mock Figure X: ILI influenza cases (n=XXX) by week of onset and (sub)type/lineage, included in the study, season xxxx/xxxx, overall and by site/country/age groups

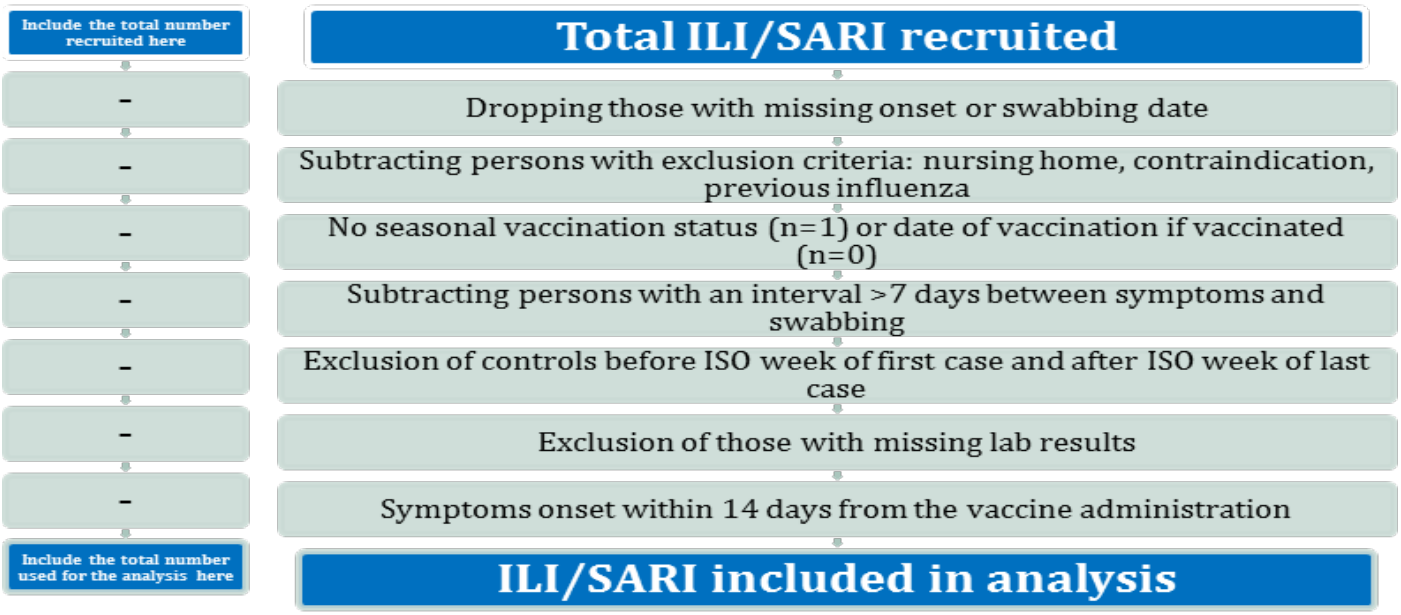
- *Include the figure*

12.1 Case-control study results

12.1.1 Descriptive results

- *Demographic and other baseline characteristics (A text describing the baseline characteristics should be included). Tables and figures showed below are only an example of mock table to be used*

Mock Figure X: Flowchart of data exclusion for analysis, season xxxx/xxxx



Mock Figure X: ILI influenza positivity rate and vaccination coverage, by week of onset, included in the study, season xxxx/xxxx

- *Include the figure*

Mock Figure X: ILI influenza cases (n=XXX) by week of onset and (sub)type/lineage, included in the study, season xxxx/xxxx, overall and by site/country/age groups

- *Include the figure*

Mock Table X: Characteristics of influenza confirmed cases and corresponding test-negative controls included in the study, season xxxx/xxxx

	Cases				Controls	P-value
	(n =)				(n =)	
	Influenza any subtype	Influenza subtype X[a]	Influenza subtype Y[a]	Influenza subtype Z[a]		

	(n =)	(n =)	(n =)	(n =)		
	n (%)	n (%)	n (%)	n (%)	n (%)	
Age group (years)						
Sex						
Female						
Male						
Chronic conditions*						
No						
Yes						
Interval onset to swab (days)						
0-1						
2-4						
5-7						
Target group for vaccination						
No						
Yes						
Pregnant women						
No						
Yes						

[a] *specify influenza virus subtype/lineage circulating during the season*
**if available list all available chronic conditions collected*

12.1.2 Vaccination against seasonal influenza 20xx/xx among cases and controls

- *Describe how many cases and controls received the seasonal influenza vaccine, and the coverage by vaccine type, brand by age, by country*

Table X. Seasonal influenza vaccine coverage by age group, 20xx/xx season.

Age-group (n = xx)	Vaccination status				
	Case		**Controls**		Total
	No (XX; %)	Yes (XX; %)	No (XX; %)	Yes (XX; %)	
Total					

Table X. Seasonal influenza vaccine coverage by vaccine type/brand, by age group, 20xx/xx season.

Vaccine type/brand	**Age group (years)**	Cases No (XX; %)*	Controls No (XX, %)

* If the TND study is used, consider to divide the column in cases and controls

- *Only for joined results provide the vaccine coverage by study site/Country*

Table X. Seasonal influenza vaccine coverage by Study site/Country, by age group, 20xx/xx season.

Country		Cases No (XX; %)*	Controls No (XX, %)
	Age group (years)		

12.1.3 Crude and adjusted vaccine effectiveness in preventing influenza infection

- *A text describing main estimates should be included together with a set of tables and figures (below a set of mock of tables and figures are reported)*

Figure X: Crude and Adjusted VE by influenza (sub)type/lineage, age groups, vaccine type/brand and target categories, week of onset 20XX/XX season

- *Vaccine type/brand: XXXXXXXXXXXX (to be repeated for each vaccine type/brand)*

	Influenza subtype X (n = xxx)				Influenza subtype Y (n =xxxx)				Influenza subtype Z (n = xxx)				Total (n = xxx)			
	Crude VE	*(95 % CI)*	Adjusted* VE	*(95 % CI)*	Crude VE	*(95 % CI)*	Adjusted* VE	*(95 % CI)*	Crude VE	*(95 % CI)*	Adjusted* VE	*(95 % CI)*	Crude VE	*(95 % CI)*	Adjusted* VE	*(95 % CI)*
Age-Group (as per SAP)																
Target categories (as per SAP) No																

Yes				
Week of onset xx-xx xx-xx xx-xx				
Other potential sub-group considered (e.g. pregnant women, chronic condition, HCW) (as per SAP)				

12.1.4 Sensitivity analysis

- *Describe the sensitivity analysis conducted (if applicable)*

12.1.5 Confounders and effect modifiers

- *Describe for which confounder data were adjusted for and the results of the evaluation of the potential effect-modification.*

12.1.6 Limitations

- *Describe the overall limitations of the study conducted*

12.1.7 Missing data

- *Report reasons for dropouts and proportions for each group, if applicable.*

12.2 Results from population based cohort studies based on databases

12.2.1 Descriptive results

- *Demographic and other baseline characteristics (A text describing the baseline characteristics should be included together with a set of mock descriptive tables and figures)*

Selecting relevant cohorts

Name of the cohort	Total source population (N)	Excluded population (N, %)	Cohort population (N)
Exclusion reason 1			
Exclusion reason 2			

Vaccination coverage in cohort

Age (date)	Vaccination coverage (%)
Age group 1	
Age group 2	

Characteristics of individuals followed as not vaccinated and as vaccinated (brand specific vaccination) in the cohort, age group 1

Name of the cohort 1	Population not vaccinated (N)	Follow-up not vaccinated (person years)	Population vaccinated (N)	Follow-up vaccinated (person years)	P-value
Sex					
Female					
Male					
Confounders/effect modifiers					
Condition 1					
Condition 2					
Condition 3					

12.2.2 Vaccination against seasonal influenza 20xx/xx

- *Describe the follow-up time as not vaccinated and vaccinated (brand specific vaccination), and the number of cases right-censored for different reasons (databases for population based cohorts)*

Table X. Seasonal influenza vaccine coverage by age group, 20xx/xx season.

Age-group	Vaccination status		Total
	No (%)	Yes (%)	
Total			

Table X. Seasonal influenza vaccine coverage by vaccine type/brand, 20xx/xx season.

Vaccine type/brand	Age group	No (%)
Total		

12.2.3 Crude and adjusted vaccine effectiveness in preventing influenza infection

- *A text describing main estimates should be included together with a set of tables and figures (below a set of mock of tables and figures are reported)*

VE of brand specific influenza vaccination against specific outcome (laboratory confirmed influenza/influenza type X/influenza subtype (lineage) X)

- *Vaccine type/brand: XXXXXXXXXXXX (to be repeated for each vaccine type/brand)*

Age	Cases not vaccinated (n)	Cases vaccinated (n) (brand specific)	Population not vaccinated (N)	Follow-up not vaccinated (person years)	Population vaccinated (N) (brand specific)	Follow-up vaccinated (person years)	Proportion of positive samples (%)	Crude VE (%) and 95% CI	Adjusted VE (%) and 95% CI
Influenza									
Age group 1 Age group 2									
Influenza subtype X									
Age group 1									
Age group 2									
Influenza subtype Y									
Age group 1									
Age group 2									
Influenza subtype Z									
Age group 1									
Age group 2									

VE against unspecific outcome (e.g. suspected or diagnosed influenza)

Age	Cases not vaccinated (n)	Cases vaccinated (n) (brand	Population not vaccinate	Follow-up not vaccinated (person	Population vaccinated (N)	Follow-up vaccinated	Crude VE (%) and	Adjusted VE (%) and 95% CI

		specific)	d (N)	years)	(brand specific)	(person years) (brand specific)	95% CI	
Influenza								
All age Age group 1 Age group 2								
Influenza subtype X								
Age group 1								
Age group 2								
Influenza subtype Y								
Age group 1								
Age group 2								
Influenza subtype Z								
Age group 1								
Age group 2								

12.2.4 Limitations

- *Describe the overall limitations of the study conducted*

12.2.5 Handling dropouts or missing data

- *Report reasons for dropouts and proportions for each group, if applicable.*

12.3 Results of innovative studies

- *This section should describe IVE results considering the protocols developed in WP7 (Task 7.1.3)*

12.4 Results of aggregated data meta-analysis

- *If applicable and performed describe here aggregated data meta-analysis on seasonal overall and brand-specific IVE (%) pooled across study sites in line with the objective outlined in the general protocols developed in WP7.*

13 Discussion

- *Summary of the results.*

Discuss limitations of the study taking into account circumstances that may have affected the quality or integrity of the data, limitations of the study approach and methods used to address them (e.g. response rates, missing or incomplete data, imputations applied), sources of potential bias and imprecision and validation of the events. The direction and magnitude of potential biases should be discussed.

- *Limitations*
- *Interpretation*
- *Context of over available data*

14 Conclusions

- *Addressing EMA specific needs [If applicable, please describe here the relevance of your results from regulatory point of view - -]*
- *Addressing PHI specific needs*
- *Addressing General public specific needs*

15 References

[1] Sharp SJ, Poulaliou M, Thompson SG, White IR, Wood AM (2014) A Review of Published Analyses of Case-Cohort Studies and Recommendations for Future Reporting. PLoS ONE 9(6): e101176. https://doi.org/10.1371/journal.pone.0101176

[2] STROBE Statement—Checklist of items that should be included in reports of cohort studies https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_cohort.pdf

[3] European Commission (2012/506/EU). Amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council (notified under document C(2012) 5538). Available at https://ecdc.europa.eu/en/infectious-diseases-public-health/surveillance-and-disease-data/eu-case-definitions (Accessed 01/02/2018)

[4] Rondy Marc, Gherasim Alin, Casado Itziar, Launay Odile, Rizzo Caterina, Pitigoi Daniela, Mickiene Aukse, Marbus Sierk D, Machado Ausenda, Syrjänen Ritva K, Pem-Novose Iva, Horváth Judith Krisztina, Larrauri Amparo, Castilla Jesús, Vanhems Philippe, Alfonsi Valeria, Ivanciuc Alina E, Kuliese Monika, van Gageldonk-Lafeber Rianne, Gomez Veronica, Ikonen Niina, Lovric Zvjezdana, Ferenczi Annamária, I-MOVE+ hospital working group, Moren Alain. Low 2016/17 season vaccine effectiveness against hospitalised influenza A(H3N2) among elderly: awareness warranted for 2017/18 season. Euro Surveill. 2017;22(41):pii=17-00645. https://doi.org/10.2807/1560-7917.ES.2017.22.41.17-00645

16 Other information:

16.1 Funding:

- *Describe source of funding and role of funders in the study.*

16.2 Dissemination:

- *Including any plans for submission of final reports.*

17 Appendix list

17.1 Protocol and amendments
17.2 Data collection form
17.3 Ethical committee approval (if applicable)
17.4 Informed consent (if applicable)