

D1.02 Governance Standard Operating Procedure (SOP)

DRIVE 116134-2 DEVELOPMENT OF ROBUST AND INNOVATIVE VACCINE EFFECTIVENESS

WP1 – Development of a governance model for joint influenza vaccine effectiveness studies in Europe

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Abbreviations

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: European Union

FISABIO: Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana

GA: Grant Agreement

GCP: Good Clinical Practice

GEP: Good Epidemiological Practice

GVP: Good Pharmacovigilance Practice
IMI: Innovative Medicines Initiative
ISC: Independent Scientific Committee
IVE: Influenza Vaccine Effectiveness
KOM: Kick-off meeting
KPI: Key Performance Indicator
PHI: Public Health Institute
SOP: Standard Operating Procedures
TC: Teleconference
QCAC: Quality Control and Audit Committee
WHO: World Health Organization
WP: Work Package

Executive Summary

This Standard Operating Procedure (SOP) presents a set of governance principles and step-by-step instructions to help consortium members and external experts carrying out the following key tasks in the project:

1. the endorsement of the scientific deliverables by an Independent Scientific Committee (ISC);
2. the guarantee of the quality, compliance and auditing of the project by a Quality Control and Audit Committee (QCAC) and;
3. the strategy for engaging researchers in DRIVE.

The SOP aims to achieve operational efficiency and alignment between partners of the consortium throughout the 5-year project duration with regular updates.

1. Construction of the Governance Model

The project governance of DRIVE, established in the Document of Action, balances ECDC requirements and EFPIA accountability to regulatory bodies with the collaborative principles of IMI projects. The governance structure is presented in Figure 1.

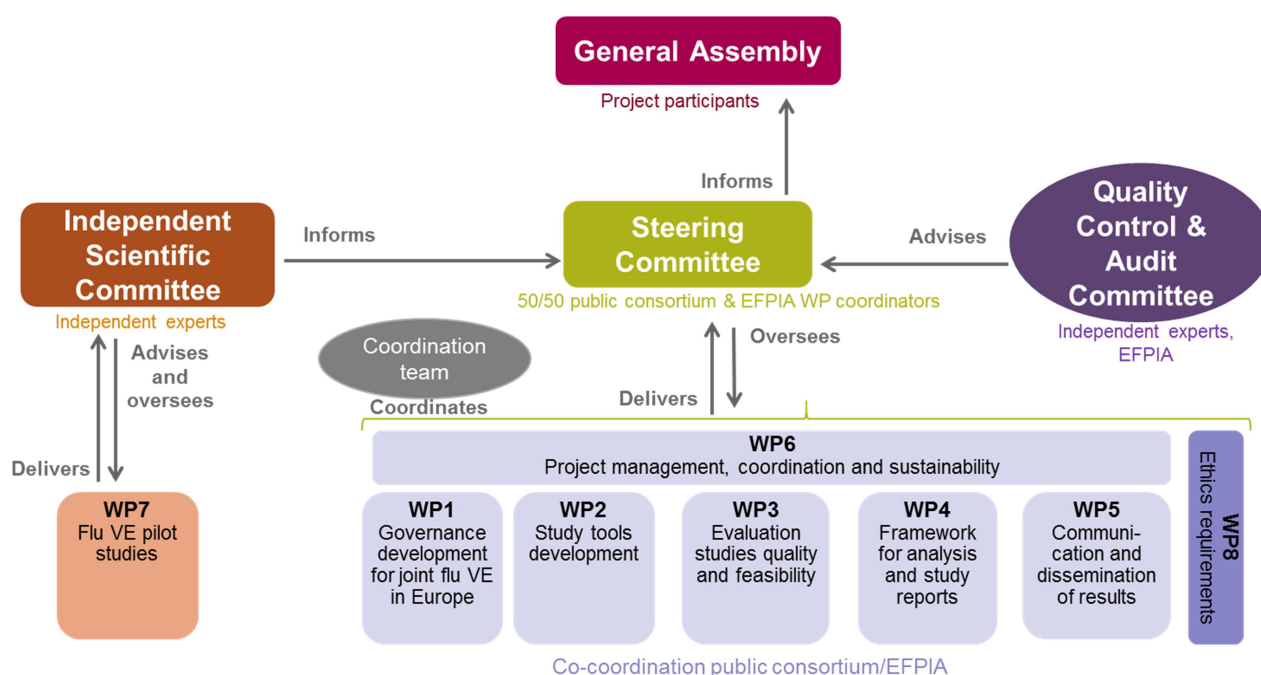


Figure 1: Project Governance

As per IMI project structure, each Work Package (WP from 1 to 6 and WP8) is co-lead by a public consortium member and an EFPIA member. Public and EFPIA beneficiaries jointly contribute to the tasks and deliverables assigned to their WP. The Steering committee is composed of the WP leaders and Co-coordinators with an equal repartition of voting rights for a shared decision making between public consortium and EFPIA members.

To initiate the DRIVE project with the development of a sustainable network for influenza vaccine effectiveness (IVE) studies, the governance has been adapted to be acceptable by all parties. The WP7 who is responsible of conducting the IVE studies will be independent from EFPIA members. In the interest of independence of the scientific results, rigour and transparency, an Independent Scientific Committee (ISC) will evaluate and endorse the WP7 deliverables. A Quality Control and Audit Committee (QCAC) will advise on the compliance and quality of the project.

This governance framework will be developed further along the 5 years project to facilitate transparent and scientifically robust collaboration between public and private partners.

a) Independent Scientific committee (ISC)

The ISC's mandate is to evaluate and endorse the scientific deliverables of the DRIVE project developed by the Work Package 7 (WP7) and to provide advices on their review process and communication components. The contributions of the EFPIA consortium in reviewing scientific deliverables will only be made in writing to maintain independence and ensure transparency and traceability.

i) Roles and responsibilities

- ✓ Review WP7 scientific deliverables
 - Protocols for type- and brand- specific influenza vaccine effectiveness (IVE) (field-based and population-based database studies); updates from ECDC template based on IVE pilot studies
 - Seasonal report of IVE studies conducted
 - Report on feasible novel and innovative approaches for measuring IVE
 - Report on virus characterisation and molecular epidemiology
 - Provide comments and suggested changes to WP7
 - Receive written feedback from EFPIA members and decide on integration of EFPIA comments or organize point by point response with WP7; Produce a document summarizing the review
 - Endorse the final scientific deliverables of WP7
- ✓ Establish a detailed work plan following the project governance recommendations (including designation of a chairperson and members who will review each deliverable based on individual expertise and project needs)
- ✓ Advise on the independence and transparency of the scientific review
- ✓ Review key scientific communications components

Scientific secretariat of the ISC will be ensured by FISABIO, IRD, Synapse (under the Work Package 6 task 6.1.2).

ii) Composition

- From 5 up to 10 independent external experts (experts from organisations who are non-partners in DRIVE)
- The project Coordinator (FISABIO - Javier Díez Domingo or his representative) as an observer

iii) Selection process

The selection of potential members is managed by the DRIVE Steering Committee using a transparent and documented process. The DRIVE Consortium generates a list of potential candidates through a voting system based on the following criteria:

- ✓ Expertise in at least vaccine effectiveness surveillance (influenza specific) or statistics (specific to vaccine effectiveness analysis)
- ✓ Other preferred expertise areas: Influenza strain surveillance and testing, vaccination programs, observational research, secondary database research, influenza clinical expertise
- ✓ No recent affiliation with any of the consortium member institutions (based on date of the IMI call text April 2016)
- ✓ Preferably EU experts (or experts with a good knowledge of EU environment) coming from various stakeholder groups (public health institutes, regulatory authorities, research institutes and organisations)
- ✓ Expected additional representation of international organisations (WHO, CDC, ECDC)

FISABIO is in charge of contacting potential candidates to discuss ISC membership.

The ISC is expected to be active from January 2018, commencing with an induction meeting preferably face-to-face organised by FISABIO/Synapse between ISC members and Steering Committee members (WP leaders).

In case of departure of an ISC member, his/her replacement will follow the same process.

b) Quality Control and Audit Committee (QCAC)

The QCAC will be tasked with the quality control and auditing of the overall project with a specific focus on compliance, quality and regulatory aspects. This committee has an advisory role.

i) Roles and responsibilities

- Establish a detailed work plan following the project tasks and needs, including a defined audit procedure and list of audits to be conducted, as well as a quality control procedure and/or checklist for review of documents and processes. The procedures should follow the appropriate international standard guidelines.
- Audit the project governance in accordance with the procedure defined upfront:
 - Verify adequacy and transparency of funding sources and funding allocation;
 - Verify adequacy and transparency of the review processes and appropriate documentation for WP1-6/8 and for WP7 deliverables
 - Verify adequate declaration of potential conflicts of interest; evaluating potential conflicts of interest
- Ensure that adequate quality control is performed on sites and supervise auditing for the WP7 studies (e.g. onsite visits for protocol implementation per season); advise WP3 on the development of the two deliverables: D3.4 *Report on the comparison of adapted local protocols and Ethical Committee evaluation in each study site*, D3.5 *Report on quality and feasibility evaluation*. A CRO will be selected to provide operational support for the conducting of one site audits.
- Report findings to the Steering Committee and provide advice, recommendations and proposed action plans, when needed. It will be used to update relevant deliverables (e.g. deliverable D1.2 *Governance SOP*).

ii) Composition

- 3 independent external experts (experts from organisations who are non-partners in DRIVE) who act on their own and do not represent their institution or organisation
- 4 qualified EFPIA representatives
- The project Coordinator (FISABIO - Javier Díez Domingo or his representative) as an observer

iii) Selection process

The selection of potential members will be managed by the DRIVE Steering Committee using a transparent and documented process. A list of potential candidates will be proposed by the DRIVE Consortium based on agreed criteria defined below:

- ✓ Expertise in quality processing, compliance, medical governance, study auditing (e.g. qualifications in GCP GVP GEP) and financial auditing
- ✓ No recent affiliation with any of the consortium member institutions (based on date of the IMI call text April 2016)

Preferably EU experts coming from various stakeholder groups (public health institutes, regulatory authorities, research institutes and organisations).

Qualified EFPIA representatives will be proposed by each company.

The QCAC is expected to be active from March 2018, commencing with an induction meeting preferably face to face organised by FISABIO/Synapse between QCAC members and Steering Committee members (WP leaders)

In case of departure of a QCAC member, his/her replacement will follow the same process.

2. Implementation of the Governance Model

a) Decision making flow and review process

There are two distinct decisions-making flow and review processes in DRIVE:

- WP1 to WP6 and WP8 deliverables will be endorsed by the Steering Committee and will follow usual IMI rules (joint review made by public and private Steering Committee members)
- WP7 deliverables will be endorsed by the Independent Scientific Committee and will follow a specific review process (EFPIA comments provided separately to the ISC)

Refer to the DRIVE internal procedure “Deliverables review process” for further details on WP1 to WP6 and WP8 deliverables’ review process.

The aim of this section is to detail interactions between the WP leaders and the 2 governance bodies of ISC and QCAC.

i) WP7 deliverables review and ISC endorsement

The following key steps will be proposed to the ISC for the WP7 deliverables review process:

- WP7 will send the draft deliverables to the members of the ISC
- Designation of ISC members who will review the draft deliverables and will provide comments
- FISABIO/Synapse will facilitate the compilation of ISC comments along with the ISC chairperson
- EFPIA will review in parallel the draft deliverables and will provide written comments to the ISC separately
- ISC will meet to discuss all comments, preferably during a face-to-face meeting (organised by FISABIO/Synapse)
 - ISC will provide a point-by-point response to the EFPIA’s comments and will decide whether to integrate the comments
 - ISC will address its recommendations to WP7
- WP7 will update the deliverables accordingly and will send it to the ISC; WP7 will decide on integration of ISC comments or organize point by point responses; if needed another review may be organised;
- ISC will endorse the final version of the deliverables

All WP7 deliverables will include, as an annex, the minutes of the ISC regarding that particular deliverable.

The scientific secretariat will be in charge of managing ISC interactions between ISC and WP7 leaders for WP7 deliverables review.

The schema of the figure 2 below provides the expected timelines.

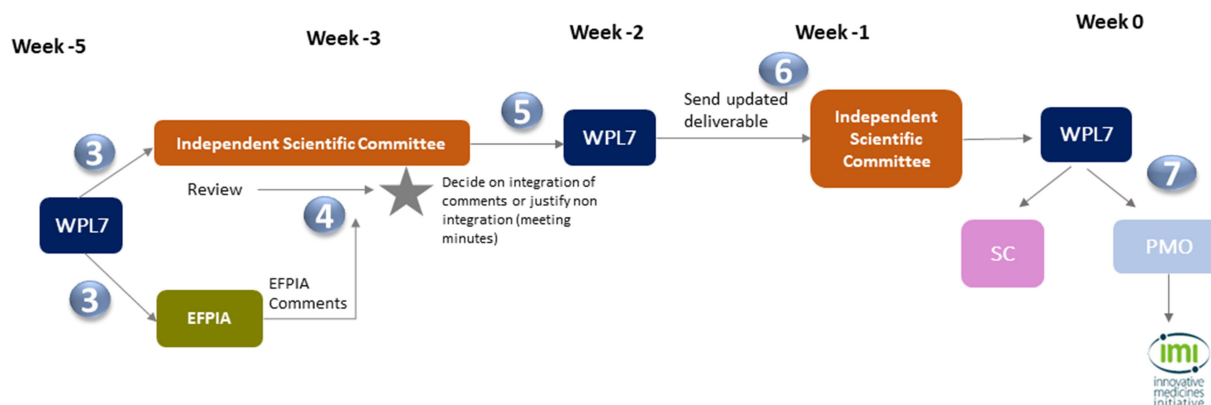


Figure 2: WP7 review process

Annual brainstorming meetings will be organised between WP7 and EFPIA. The objective will be to discuss EFPIA's requirements on WP7 deliverables in order to fulfil the regulatory needs.

ii) QCAC way of working

The QCAC will establish its way of working based on project tasks and needs and will submit its plans to SC for advice and to check consistency with the project Governance. QCAC should plan for at least one face-to-face meeting per year.

b) Legal framework for the independent external experts

This section describes what will be proposed in the Advisory Agreement (Annex 10 of the Consortium Agreement) by the Project Coordinator (on behalf of the Consortium as per the mandate provided via article 11.5.1.4 of Consortium Agreement) to the 5 up to 10 members of the ISC and 3 members of the QCAC. The contract will be established between FISABIO and either the expert's organisation or the expert directly:

- Preferably, the expert will join for the entire duration of the Project, but the contract will be a one (1) year agreement with automatic renewal unless terminated by the expert in writing with two months prior notice before the end of the term.
- DRIVE will propose compensations for experts/organisations based on ECDC standards and rules for meeting attendance (annexed to the Advisory Agreement).
- Payments will be made by FISABIO using the DRIVE budget issued by the European Commission.
- Compensation includes:

- FISABIO will manage directly all expenses related to travel and accommodation for DRIVE meetings attendance;
- In addition, a daily allowance will be paid by FISABIO to the expert/organisation, based on ECDC country rates, to compensate any other expenses incurred for meeting attendance.

Compensation will be declared by the expert to its organisation in full transparency. Compensation may be adapted or reduced to comply with the expert' organisation specific rules.

3. Adaptation plan for the Governance Model

Throughout the duration of the 5-year project, the Governance model will be evaluated and updated whenever needed. The action plan proposal includes the following key steps and related timelines:

- Determination of the Key Performance Indicators (KPIs) for Governance evaluation:
 - Definition of the criteria (Dec 2017 –Apr 2018)
- Yearly evaluation of the Governance model:
 - Internal consultations among partners
 - Conduction of a survey to identify lessons learnt (May 2018)
 - External consultations
 - Gathering discussions with external stakeholders (Nov-May 2018)
 - Conduction of a survey to identify critical success factors and barriers could be planned for the second evaluation (Mar 2019)
- Update of the Governance model whenever needed (Jun 2018)
- Iterative process
 - Reiteration of the process above after second (Jun 2019) and third seasons (Jun 2020)
- Preparation of the Final report on governance and principles D1.3 (Sep 2021)

4. Strategy for research stakeholder engagement

This chapter describes the strategy for engaging with research stakeholders in the DRIVE project (including modalities and general processes).

a) Sharing of data collected/generated in Europe

Targeted stakeholders:

DRIVE will enable and facilitate the integration of relevant data already-collected for influenza VE studies from existing systems in place with Public Health Institutes (PHIs) and other research institutes or organizations (e.g. public disease surveillance systems, vaccine and infectious diseases registries linkage, I-MOVE). This will be the most efficient and valuable way to rapidly increase data capacity and develop a sustainable platform. If vaccine brand-specific information or influenza laboratory confirmation is not collected on a routine basis or in specific studies by such existing systems in a particular country, data collection will be considered as DRIVE-led. The rationale and feasibility of collecting such important data has to be discussed in the early stages.

Proposal and added value:

DRIVE will invite institutes and organisations to integrate brand-specific vaccine effectiveness as a secondary objective in their studies; meaning adding value to their data by exploring available information on vaccine brand and adding the brand specific analysis to their routine analysis and providing this additional information to their institutes. DRIVE will provide support where and when needed to support this secondary objective (generic protocols and analysis plans). DRIVE will propose such institutes and organizations to become Associate Partners of DRIVE by agreeing to share relevant data for the purpose of a pooled analysis or meta-analysis and contribute to the related scientific discussions. As such they will be associated members of the WP7 group and will review the WP7 deliverables.

The potential added value to Associate Partners includes:

- Being part of a pan-European platform ultimately generating yearly influenza VE type and brand-specific data; sharing scientific and methodological aspects of the IVE assessment and of the pooled analyses, and being associated with the related scientific publications in accordance with ICJME criteria;
- Increasing the value of their current monitoring system and IVE analysis when accounting for brand specific aspects;
- Access to tools to support and enhance their existing systems (i.e. collection of vaccine brand / type specific data, influenza laboratory confirmation, standardised approach to collect the data and generate the IVE estimates)
- The opportunity to contribute to the discussions on innovative and approaches to IVE

Legal and budget considerations:

- The Associate Partner will sign an Associate Partner Agreement with FISABIO in order to formalize the status as Third Party (under article 11 of the GA) and define the terms and

conditions of their collaboration. The agreement can be made only with a legal entity, not with an individual.

- The Associate Partner will receive money to cover the transfer costs and the effort made to contribute to the project: data sharing, intellectual contribution, collection of specific data for DRIVE (i.e. vaccine brand specific information, influenza laboratory confirmation) and attendance to DRIVE meetings.
- The Associate Partner will remain the owner of the data it generates;
- In consideration of the money provided to him, the Associate Partner will grant to all Beneficiaries access rights to its data in the same conditions as the Beneficiaries as mentioned in the Consortium Agreement, for the implementation of the project:
 - Data generated routinely before or during the project will be accessible only by WP7 for the project implementation and by the Quality Control and Audit Committee for auditing purposes;
- Representative(s) of the Associate Partner will attend relevant project meetings for contribution to the scientific discussions; travel and accommodation will be managed by the Associate Partner as part of the compensation received.
- Preferably the Associate Partner will join the project for the entire duration of the Project but the contract will be a one (1) year agreement with automatic renewal unless terminated by the Associate Partner in writing with two months prior notice before the end of the term.

Implementation:

YEAR 1 (influenza season 2017-18):

- Starting in November 2017: potential Associate Partners who have already expressed their interest in joining DRIVE will be contacted by FISABIO. This corresponds to those who attended the TC organised after the KOM on July 19th 2017.
A 2 pager with Q&A will be sent along with the DRIVE collaborator survey part 1 (focus ?). Follow up discussions will be led by FISABIO with the support of WP1, WP7 and WP5 leaders; teleconferences and, when possible, face-to-face meetings will be the preferred options for exchange.
Other potential Associate Partners already identified by WP7 will then be contacted following the same process as described above.
- Potential Associate Partners willing to join the DRIVE project will be asked to complete the collaborator survey part 2. (focus ?)
- Surveys completed by potential Associate Partners will be gathered by FISABIO; relevance of data and allocated budget will be decided by the DRIVE Steering Committee.
- Associate Partner Agreements will be managed by FISABIO.
Potential Associate Partners will be able to join DRIVE for the pooled analysis of the first influenza season retrospectively until June 2018

YEAR 2 (influenza season 2018-2019)

- In preparation for the second influenza season, invitations will be extended to other institutes and organisations in Europe who have existing systems in place. These potential Associate Partners will be identified through the WP5 activity on Stakeholder Database.
Availability of the pooled results from the first influenza season should be used to further develop external communication and related documents to encourage interest from additional potential Associate Partners in joining DRIVE; it will be led by WP5

- The process to contact potential Associate Partners will be the same as described above.

b) Building new capacity in Europe

Targeted stakeholders:

DRIVE is also inviting Public Health Institutes (PHIs) who do not yet have a system able to provide relevant IVE data but who are willing to develop such a system in their country or region to become Associate Partners of DRIVE.

Proposal and added value:

DRIVE will propose to provide financial, operational, technical and methodological guidance and support to PHIs willing to develop a system or improve their system in their country or region for the collection of relevant data on brand specific IVE. DRIVE will also support ways to develop and test innovative methods and approaches for IVE. These PHIs will transfer collected data for the pooled analysis and will contribute to the related scientific discussions. As such they will be associate members of the WP7 group and will review the WP7 deliverables.

The potential added value for PHIs may be to:

- Develop a new system with DRIVE support which will include providing budget for implementation and data collection, study related documents (e.g. study protocols) and scientific and operational advice relevant for IVE studies
- Implement potentially cost effective and sustainable innovative approaches to IVE estimation
- Be part of a pan-European platform generating yearly brand specific IVE data; share scientific and methodological aspects on the pooled results and participate in the scientific publications of the results;

Legal and budget considerations:

- DRIVE will propose an Associate Partner Agreement with FISABIO in order to formalize the status of the PHI as Third Party (under article 11 of the GA), with the same legal considerations as described above, only budget and detailed activities will be adapted to fit with the corresponding proposal of building new capacity.
- Preferably the Associate Partner will join the project for the entire duration of the Project but the contract will be a two (2) year agreement with automatic renewal of one year unless terminated by the Associate Partner in writing (2 months prior notice) after the end of the initial 2 years term.

Implementation will be planned for the second year (Influenza season 2018-2019). Further discussions are necessary within the DRIVE Steering Committee to detail that process.

c) Answering gap analysis and innovative approach

Targeted stakeholders:

Based on the existing PHI IVE evaluation systems in place and the willingness of PHIs to join the

project, DRIVE will evaluate on a yearly basis the gaps (brand data & brand coverage, EU representativeness, specific population and innovative methods and approaches) to build a sustainable platform in Europe and will develop a public call for proposals for additional research collaborators, such as academic institutes, GPs or hospital networks, other initiatives or projects. This approach will follow a yearly tender process (starting from the season 2018/19) and the selection of research collaborators will be managed by the Steering committee. Opportunity to test innovative approaches will be considered.

Proposal and added value:

DRIVE will ask potential Research Collaborators to share relevant data with DRIVE (based on the request for proposals) and to contribute to their integration into the pooled analysis.

The benefits of this collaboration for the Research Collaborators may be to:

- Generate robust brand specific IVE for their target populations
- Participate in the scientific publications process
- Receive funding for their data collection
- Receive funding for building their capacity
- Participate in the DRIVE forum and General Assembly

Legal and budget considerations:

Once the tender process is resolved, DRIVE will propose a Research Agreement with FISABIO to the selected Research Collaborator in order to formalize its status of Third Party (under article 11 of the GA), and define the terms and conditions of the collaboration:

- The Research Collaborator will receive money for the data collection and contribution to the pooled analysis, and for its participation in specific meetings as agreed beforehand; the allocated budget will be appropriately sized to the related work;
- The data collected for the project specific needs/objectives will be provided to FISABIO in open access or, alternatively, the Research Collaborator could remain the owner of the data and grant all relevant Access Rights to Beneficiaries. The access rights will be the same as for all other data collected by other Beneficiaries as per the consortium terms and conditions:
 - Data generated during the project will be accessible only by WP7 for scientific review and by the Quality Control and Audit Committee for auditing purposes;
- The Research Collaborator will join the project for one influenza season as defined in the tender

Implementation:

The tender process will be managed by FISABIO. This will be implemented in time for the second influenza season. The selection of the Research Collaborators will be made by the Steering Committee and the contract will be managed by FISABIO. Further discussions are necessary within the DRIVE Steering Committee to detail the process.

The figure 3 below provides the expected timelines for the tender process.

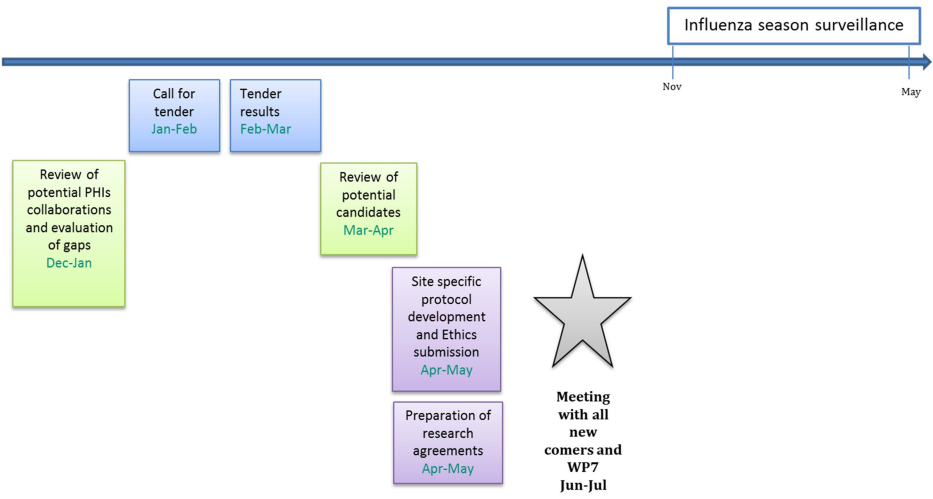


Figure 3: Tender process timelines

5. Appendices

List of WP7 deliverables and expected timelines

WP7 Deliverables	Timelines
D7.1 Protocols for type- and brand- specific IVEs (field-based studies)	
✓ One draft deliverable	Jan 2018
✓ Updates integrating changes needed for the next seasons	respectively May 2019 and May 2020
D7.2 Protocols for type- and brand- specific IVEs (population database studies)	
✓ One draft deliverable	Jan 2018
✓ Updates integrating changes needed for the next seasons	respectively May 2019 and May 2020
D7.3. Report on feasible novel and innovative approaches for measuring IVE	
✓ One draft deliverable	June 2018
✓ Periodic updates	
D7.4. First Seasonal report of conducted IVE studies	
✓ One draft deliverable	June 2018
D7.5 Report on virus characterisation and molecular epidemiology	
✓ One draft deliverable	April 2019
✓ Updates if needed	
D7.6. Second Seasonal report of conducted studies	
✓ One draft deliverable	April 2019
D7.7. Third Seasonal report of conducted studies	
✓ One draft deliverable	April 2020
D7.8. Fourth Seasonal report of conducted studies	
✓ One draft deliverable	April 2021
D7.9 Fifth Seasonal report of conducted studies	
✓ One draft deliverable	April 2022