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TECHNICAL REPORT

Generic protocol for ECDC studies of influenza vaccine effectiveness against confirmed infection using healthcare worker cohorts

Version 2.0

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Contents

Abbreviations

ARI	Acute respiratory infection
COVID-19	Coronavirus disease 2019
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
GISAID	Global Initiative on Sharing Avian Influenza Data
HCW	Healthcare worker
IPC	Infection prevention and control
ILI	Influenza-like illness
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
RT-PCR	Reverse transcription polymerase chain reaction
PPE	Personal protective equipment
VC	Vaccination coverage
VE	Vaccine effectiveness
RSV	Respiratory syncytial virus
VEBIS	Vaccine Effectiveness, Burden and Impact Studies
WHO	World Health Organization

1 Background

1.1 Context

Influenza is a disease of public health importance due to the substantial seasonal morbidity and mortality and the high pandemic potential of its aetiologic agents, influenza viruses. Diagnosis of influenza is mainly based on laboratory testing (i.e. molecular testing) of nasopharyngeal samples. Although patients generally prefer saliva testing, as it is less invasive, saliva specimens are used for diagnosis less often [1–3] due to lower sensitivity, probably due to lower viral load in this type of specimen. Influenza viruses are able to escape the human immune system through continuous evolution that can be caused by point mutations (antigenic drift) or recombination events (antigenic shift) [4]. For this reason, influenza vaccine components are re-evaluated each year and annual revaccination is recommended. Observed influenza vaccine effectiveness (IVE) varies from year to year, between population subgroups (e.g. age and risk groups) and according to the measured outcome (laboratory-confirmed influenza virus by (sub)type/clade or clinical outcome). IVE may vary between vaccine types and products, by time since vaccination and according to previous influenza infection and influenza vaccination history.

In many countries, healthcare workers (HCWs) are included among the high-risk groups for influenza infection and priority groups for influenza vaccination due to occupational exposure and the need to ensure work continuity during seasonal epidemics. Studies performed before the COVID-19 pandemic suggested that an increase in influenza vaccination coverage in health professionals results in an important decline in nosocomial influenza among patients [5–8]. EU/EEA countries have therefore been encouraged to improve vaccination coverage among HCWs [9,10]. During the COVID-19 pandemic, some studies showed that the co-circulation of influenza and SARS-CoV-2 in winter increased awareness and acceptability of influenza vaccination among HCWs [11–13]. An overview of recommendations for seasonal influenza vaccination, as well as vaccination coverage among EU/EEA countries, can be found in the recently published technical report 'Seasonal influenza vaccination recommendations and coverage rates in EU/EEA Member States'.

1.2 ECDC vaccine effectiveness studies

In 2020, the European Commission stressed the importance of continuously monitoring the safety and effectiveness of vaccines in the EU/EEA in the post-authorisation phase, with particular emphasis on COVID-19 vaccines in the context of the ongoing pandemic [14]. Previously, the 2018 Council Recommendation on Strengthened Cooperation against Vaccine-preventable Diseases asked ECDC and the European Medicines Agency (EMA) to cooperate in ensuring the continued monitoring of the vaccines in use in EU/EEA vaccination programmes [15]. The request was subsequently formalised as part of the extended EMA regulatory mandate [16] and ECDC's newly amended mandate [17], in which the two agencies were requested to develop a structured and independent post-authorisation vaccine monitoring platform, initially prioritising COVID-19 vaccines. ECDC and EMA officially established and launched such a platform in May 2022, with the intention of bringing together public health and regulatory experts to discuss the studies needed to generate real-life evidence on the safety and effectiveness of vaccines in use in EU/EEA vaccination programmes [18].

At the end of 2020, ECDC started building the infrastructure to conduct COVID-19 vaccine effectiveness (CVE) studies in different settings, and to provide information on different outcomes (severe disease, moderate disease, transmission, etc). The studies have been embedded in a project called VEBIS (Vaccine Effectiveness, Burden and Impact Studies). This multi-country study relates to a prospective cohort for this project and is dedicated to studies of CVE and IVE in HCWs from different countries. It is anticipated that more countries will be included in the study over time.

The component related to CVE against confirmed SARS-CoV-2 infection in hospital-based HCWs started in late 2021 and is ongoing. It included a total of 19 hospitals during the first two years of implementation. A generic protocol for this study is available: 'Generic protocol for ECDC studies of COVID-19 vaccine effectiveness against confirmed SARS-CoV-2 using healthcare worker cohorts, version 3.0'.

Combining this IVE study with the CVE study against confirmed SARS-CoV-2 infection using HCW cohorts constitutes an example of integrated VE studies for vaccine-preventable acute respiratory infections of public health importance. These studies contribute to similar integration efforts taking place at national and international levels.

1.3 Aim of the protocol

This document presents the second version of the generic protocol for a prospective multi-country cohort study to measure the effectiveness of influenza vaccines in hospital-based HCWs during the 2023–24 winter season. This study is embedded in the CVE study set up under the VEBIS multi-country cohort study investigating CVE in HCWs. Six study sites used the first version of this document during the 2022–23 winter season to determine the feasibility of performing this study in hospital-based HCWs. In three study sites, it was used to validate the use of saliva as an adequate sample for influenza testing in this population (report available by request). The IVE study was considered feasible and was permitted to start at the beginning of influenza circulation (week 40, 2023). Saliva could not be validated as an adequate sample for influenza testing due to the low number of influenza cases detected in symptomatic HCWs; therefore, this study will be repeated during the current 2023–24 season. The protocol for the pilot study is available in the document 'Pilot protocol for influenza vaccine effectiveness against laboratory-confirmed influenza infections using healthcare worker cohorts'.

Countries, hospitals or study sites can use this generic protocol to conduct similar studies that are not included in the ECDC VEBIS project. Additional documentation is available upon request from vpd.vpd@ecdc.europa.eu and/or adminepidemio@epiconcept.fr.

➢ *This arrow symbol with italicised text indicates areas where countries, hospitals or study sites need to adapt the information to their situation when creating a new protocol based on the ECDC protocol.*

2 Objectives

2.1 Primary objective

The primary objective of this study is two-fold:

- To measure IVE against laboratory-confirmed influenza infection among hospital-based HCWs eligible for influenza vaccination.
- To determine the reliability of RT-PCR testing using saliva specimens compared with specimens from nasopharyngeal swabs among symptomatic hospital-based HCWs.

2.2 Secondary objectives

The secondary objectives of this study are to measure influenza VE by:

- Type/subtype and/or clade/subclade of circulating influenza virus;
- Vaccine type/brand;
- Age group;
- Underlying conditions.

➢ *Each study site, hospital or country to specify the particular objectives of their study.*

3 Methods

3.1 Study setting

The study is embedded in the CVE cohort study among hospital-based HCWs or performed in similar settings (see version 3.0 of the CVE protocol).

➢ *Each study site, hospital or country to provide a brief description of existing cohorts.*

3.2 Study design

This is a dynamic prospective cohort study.

3.3 Study population

The study population is composed of HCWs eligible for influenza and COVID-19 vaccination, with no contraindications to receive these vaccines.

3.4 Inclusion criteria

All categories of hospital-based HCWs may be included. HCWs participating in CVE studies will be invited with priority. HCWs that participated in the previous phases of the CVE and IVE studies are welcome to return to the study.

3.5 Exclusion criteria

HCWs who are not eligible for influenza vaccination, for whom vaccination is contraindicated or who have not signed an informed consent form will be excluded from participation in the study.

3.6 Study period

The study should be conducted only after the study protocol is approved by the relevant ethical review committee. The study period will be from week 40, 2023 to week 20, 2024.

➢ *Each study site, hospital or country to define the study period.*

3.7 Exposure

3.7.1 Vaccination status documentation

Influenza vaccination status will be documented. Vaccination status ascertainment will depend on how the vaccination is delivered and registered in each setting. Self-reported vaccination status should be verified and confirmed through occupational health, vaccine registry, vaccination card or any other potential data source available at the study site level. Participants should be informed in the consent form that these additional sources will be accessed, when relevant, to confirm their vaccination status.

Vaccine documentation should include:

- date of vaccination;
- vaccine brand;
- method of ascertainment (e.g. self-reported, documented, vaccine registry, etc).

The following exposure definitions will apply:

Current seasonal influenza vaccine:

- A HCW is considered as vaccinated against influenza if the vaccination occurred 14 or more days before disease onset.
- A HCW is considered as unvaccinated if vaccination did not occur in the current season or was received less than 14 days before disease onset or the sample collection date of the laboratory test.

Brand-specific seasonal influenza vaccine:

- A HCW is considered as vaccinated against influenza with a brand-specific vaccine if vaccination with the named brand occurred 14 or more days before disease onset.
- A HCW is considered as unvaccinated if vaccination did not occur in the current season or was received less than 14 days before disease onset or the sample collection date of the laboratory test.

➢ *Each study site, hospital or country to describe how vaccination status will be ascertained. Ideally, study sites should ensure that vaccination status is documented.*

3.8 Definitions of outcomes

The **primary outcome** is confirmed influenza infection detected by laboratory RT-PCR in any participant, regardless of symptoms or the type of specimen used for testing (nasopharyngeal swab or saliva sample).

The **secondary outcome** is symptomatic laboratory-confirmed influenza, defined as influenza infection detected by laboratory RT-PCR in a nasopharyngeal swab or saliva specimen in a participant who reported one or more of the following clinical criteria to conform with the acute respiratory infection (ARI) case definition [19]:

- sudden onset of symptoms;

AND

- at least one of the following four respiratory symptoms:
  - cough;
  - sore throat;
  - shortness of breath;
  - coryza.

AND

- a clinician's judgement that the illness is due to an infection.

The ARI case definition is more sensitive than the influenza-like illness (ILI) case definition that is usually used for influenza surveillance at the primary care level [19]. However, the high sensitivity of this case definition is necessary for the second primary objective of this study: to validate saliva sample specimens taken from symptomatic patients.

Data on symptoms will be collected to assess whether cases meet the ARI case definition (see above) or the ILI case definition [19], which requires cases to report one or more of the following clinical criteria:

- sudden onset of symptoms;

AND

- at least one of the following four systemic symptoms:
  - fever and feverishness;
  - malaise;
  - headache;
  - myalgia;

AND

- at least one of the following four respiratory symptoms:
  - cough;
  - sore throat;
  - shortness of breath;
  - coryza.

3.9 Sample size and power calculation

The sample size for cohort studies depends on the vaccination coverage in the population, the assumed IVE (based on estimates from the literature), the estimated incidence of influenza infection over the follow-up time in the unvaccinated study population (or other chosen denominator), and the desired precision.

In the current study, the sample size is limited to the number of participants in in the CVE study. Power calculation will be performed according to the influenza incidence in the community of participating hospitals.

3.10 Study procedures

3.10.1 Study preparation

This study is embedded in the CVE cohort study among hospital-based HCWs. The study procedures are detailed in the respective protocol (version 3.0).

The participating HCWs should be asked to provide informed consent to have their samples tested for different respiratory pathogens (influenza, SARS-CoV-2, respiratory syncytial virus (RSV), etc.) if multiplex PCR testing will be used (Annex).

➢ *Each study site, hospital or country to describe the study procedure.*

3.10.2 Enrolment: questionnaire and respiratory samples

Once informed consent has been obtained, HCWs should be enrolled regardless of their individual influenza or COVID-19 vaccination status and should:

- Provide a nasopharyngeal swab and/or saliva sample for RT-PCR testing;
- Complete the enrolment questionnaire, which collects demographic, clinical and epidemiological information; information about vaccination history; and information about their behaviour at work and in the community.

Note that no specific serology sample will be collected for influenza serology. Residual samples from the CVE study may be used for retrospective serology testing only if the HCWs provide informed consent (see Annex).

➢ *If the study site, hospital or country is also participating in the CVE study, it will use the same updated forms and data for the influenza study.*

3.10.3 Active follow-up

The objective of follow-up is to identify new cases of influenza and changes in vaccination status (e.g. previously unvaccinated people who received the vaccine) among the cohort participants.

Study participants should be regularly and actively followed up through monitoring and molecular testing:

- **Monitoring**: Participants are followed up with a weekly survey to report changes in health or vaccination status, as well as likely professional or personal exposures. The questionnaire can be completed by the HCWs or by a study site monitor as part of regular weekly contact.
- **Molecular (RT-PCR and genomic sequencing) testing**: Samples are to be collected from participants weekly, whether or not symptoms are present, and tested by RT-PCR for influenza. Samples can be either nasopharyngeal swabs or saliva specimens, which can be taken by a trained study monitor or by the HCWs themselves after suitable training.

3.11 Data collection and data sources

Data are to be collected using a standardised questionnaire or data collection form.

At enrolment, data could be collected using an online platform and, if available, some data may be extracted from electronic medical records, or through a combination of both approaches. The minimum data that should be collected at enrolment are:

- age;
- sex;
- smoking status;
- body mass index (BMI);
- presence of chronic disease(s) (at least one chronic condition, specific conditions);
- vaccination status for influenza and COVID-19;
- molecular testing results.

The weekly monitoring form can be completed by the participant using an online platform. If a participant receives a confirmed diagnosis of influenza, they should also complete the associated online questionnaire (this can also be done by a study site investigator during weekly contact). The minimum data that should be collected during follow-up of a confirmed influenza case are:

- absence or presence of symptoms, with date of onset of symptoms;
- date of specimen collection and RT-PCR results;
- clinical course of infection (including outpatient and inpatient visits);
- current vaccinations (COVID-19, influenza, RSV or pneumococcal).

In addition to the questionnaires and electronic medical records, data may also be collected through vaccine registries, occupational health registries or other relevant sources, as needed and with informed consent. For each variable, possible and optimal data sources should be identified.

➢ *Each study site, hospital or country to detail data sources to be used for each variable.*

3.12 Data analysis

Data validation, cleaning and verification will be carried out at the study level.

The pooled analysis will be carried out in a similar way to the study site-specific analysis. The study participants will be described according to the baseline characteristics. Confounding and effect modifications will be assessed in stratified analyses.

Participants will be followed from baseline to censoring from the study, either due to detection of infection or disease (i.e. detection of outcome) or study exit. For the (sub)type-specific IVE, we will censor to the date of specimen collection for the specific (sub)type or study exit. Reinfection with a different (sub)type will be allowed in the study.

IVE will be measured by comparing outcomes by person-time at risk among vaccinated and unvaccinated groups. IVE will be calculated using Cox regression (IVE = 1 − hazard ratio (HR) of influenza vaccination). Country or study site may be included as a fixed effect or as a random effect in a multilevel model. Statistical heterogeneity between study sites will be determined, using the Q-test and the I2 index.

Sensitivity analyses will be conducted by:

- excluding those vaccinated 0–13 days before symptom onset or date of sample collection;
- excluding the HCWs tested via saliva specimens.

For the validation study to assess the reliability of saliva samples for influenza detection, we will estimate the degree of agreement between the results of the RT-PCR tests of saliva samples and nasopharyngeal swabs using Cohen's kappa coefficient [20]. If sample size allows, the IVE will be measured by type of specimen collected. If both specimens are collected at the same time from the same person, we will use the nasopharyngeal swab results in the IVE analysis.

4 Laboratory methods

The following two specimen types can be collected as part of this study:

- **Nasopharyngeal swabs**: to be taken by a dedicated medical staff member (i.e. research nurse) or by the study participants if they undergo a brief training;
- **Saliva samples**: to be taken by study participants after they undergo a brief training.

Specimens are collected at enrolment and weekly during the study period. Laboratory confirmation of influenza infection is done by RT-PCR. Samples will undergo subtyping for circulating influenza A viruses (subtypes H3 and H1) and lineages of influenza B.

For the validation study, pairs comprised of one saliva specimen and one nasopharyngeal swab from the same symptomatic HCW that were collected at the same time and transported in the same conditions will be tested by RT-PCR. The results will be compared using Cohen's kappa coefficient (Section 3.12) [20].

All or a random sample of viruses will undergo gene sequencing of at least the influenza virus hemagglutinin segment. The sampling procedure can include sequencing of all viruses, where technically possible, or a random sample thereof. See the supplementary material for data collection of genomic information.

Where possible, samples will also be tested for other respiratory pathogens. This could include SARS-CoV-2 and other coronaviruses, RSV, enteroviruses, human metapneumovirus, bocavirus and adenoviruses, using multiplex PCR.

Note that no specific serology sample will be collected for influenza serology. Residual samples from the CVE study can be used for retrospective serology testing only if the HCW provides informed consent (see Annex).

➢ *Each study site to describe all the laboratory procedures:*

- *samples taken, storage, transport;*
- *laboratory platforms and assays used, and performance;*
- *participation in quality assurance or quality control schemes, accreditation (ISO/national standards);*
- *genetic and antigenic testing performed, including the selection of specimens for sequencing.*

5 Limitations

Selection bias is a possible limitation of this study, in the following ways:

- **Previous infections**: HCWs are a population at high risk of exposure to influenza and other respiratory infections. The role of previous influenza infections is difficult to determine, although post-infection immunity is considered broader and longer-lived than the antibody response induced by influenza vaccines (e.g. for influenza A [21]; however, previous infection does not provide sterilising immunity [22]).
- **Indication bias**: there may be a different likelihood of vaccination according to types of professional exposure (i.e. activities) to the virus or due to a participant's underlying conditions. This potential bias will be adjusted for in the analysis using information collected on potential exposures and underlying conditions.
- **Healthy vaccinee effect**: individuals in better health are more likely to get vaccinated and less likely to be infected, which could potentially lead to an underestimation of IVE. In addition, there can be great variation in how likely vaccinated HCWs are to use PPE or to be exposed to the virus.

Misclassification of the outcome can occur due to the different types of samples used in the study. Although indicated for influenza testing for some PCR platforms, saliva samples have to be validated by each laboratory. IVE will be stratified by the type of sample used if the sample size allows.

Reporting bias is possible, as vaccinated cases may be more or less likely to report symptoms and IVE may be overestimated or underestimated accordingly.

Inadequate sample size may limit the power of some stratified analyses.

Unmeasured or residual confounding between vaccinated and unvaccinated participants may be present, such as high-risk behaviour, beliefs affecting exposure and vaccine acceptancy. In addition, pre- or post-exposure prophylaxis is less used in the EU/EEA [23] and can influence the IVE results if unvaccinated individuals are more likely to use chemoprophylaxis.

The quality of self-reporting information may be different between vaccinated and unvaccinated individuals.

Risk of exposure to the influenza virus and the vaccination coverage will be different between hospitals, regions and countries over time. Multilevel analysis and adjustment by time will be used to minimise the effect of these differences.

6 Ethical considerations

The influenza component of the VEBIS study should be approved by the relevant local ethics review committee.

All HCWs approached for enrolment should be informed that participation is voluntary and that they will be able to withdraw from the study, without justification, at any time during the study without consequences. It should be clearly stated that participation in this study will not impact the offer of vaccination.

The informed consent form should include a description of the methods and frequency of respiratory samples, as well as the clinical and epidemiological data that will be collected for the purposes of this investigation (Annex 1). Informed consent should also mention that samples may be shipped outside of the country for additional testing (if applicable) and that samples may be used for future research purposes (if applicable).

6.1 Personal data protection

Each hospital, study site or country conducting the study shall comply with any requirements stemming from data protection legislation or national ethics committee requirements, including obtaining informed consent, where necessary. They shall put in place technical and organisational measures (including for the security of their IT systems) that are adequate to protect the personal data that they process.

ECDC acts as data controller for the purpose of conducting the studies covered by this protocol where they are carried out on behalf of ECDC. Each hospital, study site or country shall ensure that data subjects have received information about any processing operation that is carried out on behalf of ECDC. The privacy statement on VE studies can be used for such purposes.

If a hospital, study site or country carries out additional processing operations on its own initiative, the hospital, study site or country shall be the controller for that specific processing operation and take all the necessary measures accordingly.

7 Data governance

Biological materials and related data should only be collected and stored in collaboration with local health authorities and in compliance with any applicable laws. The governance structure of such collection should conform to all relevant regulations that apply to the study site. All governance systems should follow the principle of accountability and should maintain good stewardship of stored biological materials and related data. None of the regulations concerning the storage, use and final fate of biological samples should contradict or overrule the conditions that were originally stated in (broad) informed consent documents and agreed to by research participants.

Site-specific protocols, along with informed consent forms, should address governance issues surrounding biological materials and data. Data governance statements should address how long data will be stored, when data will be destroyed, access to data during and after the study, and how participants can withdraw permission for use of their data.

All points relative to governance of biological samples and data should be addressed in the informed consent form. For more information, please see the 'International Ethical Guidelines for Health-related Research Involving Humans'.

8 Risks and benefits for subjects

This study poses minimal risk to participants during the collection of respiratory specimens. Results of RT-PCR tests will be shared with participants as soon as they are available. The direct benefit to participants is the detection of potential respiratory infections, which would then allow for appropriate monitoring and treatment.

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Annex: sample informed consent form

Cohort study to measure COVID-19 and influenza vaccine effectiveness among hospital-based healthcare workers

[Name of Principle Investigator]

[Name of Organisation]

[Name of Sponsor]

[Name of Project and Version]

This informed consent form has two parts:

I. Information sheet (to share information about the study with you)
II. Certificate of consent (for signatures if you agree to participate)

You will be given a copy of the full informed consent form.

Part I: Information sheet

Introduction
Briefly state who you are and explain that you are inviting the potential study participant to participate in the investigation being conducted. Inform them that they may talk to anyone that they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate or not. Assure the potential participant that if they do not understand some of the words or concepts, you will take time to explain to them as you go along and that they may ask questions now or later.

Purpose
Explain in familiar language why the research is being done and what is expected from the results.

Type of research
Briefly state the methods involved in the study, including the length of the study period and the frequency of blood draws (if any), respiratory swabs, saliva sampling and questionnaires. This will be expanded upon in the procedures section.

Selection of participants
State clearly why they have been selected to participate in this study.

Voluntary participation
Indicate clearly that they can choose to participate or not and reassure there will be no work or health impact should they choose not to participate. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

Study procedure
Describe the type of questions that the participants are likely to be asked and the kinds of samples that will be collected over the course of the study.

Duration
Include a statement about the time commitments required to participate in the study, including the duration of the study period and the amount of follow-up during the study, if relevant.

Risks and discomforts
Explain any risks or discomforts, including the collection of blood or respiratory samples, and any limits to confidentiality.

Benefits
Describe any benefits to the participant, such as getting frequent information about potential SARS-CoV-2 and influenza infections.

Reimbursements

State clearly what reimbursements you will provide the participants with as a result of their participation. We do not encourage incentives beyond reimbursements for expenses incurred as a result of participation in the investigation. The expenses may include, for example, travel expenses and reimbursement for time lost. The amount should be determined in accordance with national regulations.

Confidentiality

Explain how the investigation team will maintain the confidentiality of data, especially with respect to the information about the participant. Outline any limits there are to confidentiality.

Sharing of research findings

Include a statement indicating that the individual findings will be shared with the participant and the overall findings of the investigation will be shared in a timely fashion with the hospital. In the latter, all confidential information will remain confidential. If you have a plan and timeline for the sharing of information, include the details. Also inform the participant that the overall findings of the investigation will be shared more broadly, for example, through publications and conferences, again on the condition that personal identifiable information will remain confidential.

Storage of tissue samples

Explain that you are seeking permission to store their unused respiratory and serology samples for possible future use in either your own research or someone else's research. State that they need to make some decisions about storage and future use of their respiratory and blood samples because they gave you permission only to use it for the current research.

Inform participants that their sample will not be sold for profit and that any research that uses their sample will have been approved by the local ethics review committee.

Right to refuse or withdraw

Explain again the voluntary nature of consent: a participant can refuse to participate or withdraw from the investigation, without justification, at any time by informing one of the members of the investigation team.

If a participant decides to drop out, participants need to inform the investigation team as soon as possible. Any of the previously collected remaining samples and data will be discarded except if the participant informs the investigation team that they can be kept for the purpose of this specific investigation.

PART II: Certificate of consent

Certificate of consent

This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one below. A researcher or the person going over the informed consent form must sign each form. Because the certificate is an integral part of the information sheet and not a stand-alone document, the layout or design of the form should reflect this.

I confirm that I have read the information sheet dated [**dd/mm/yyyy** (version **XX**)] for the study of influenza vaccine effectiveness and validation of the saliva sample for influenza testing. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the sponsor, regulatory authorities and [**any others**], where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

I agree for my anonymised samples to be used in future research, here or abroad, that has ethical approval and will not be undertaken for profit.

Print Name of Participant _____

Signature of Participant _____

Date _____ (day/month/year)

Statement by the researcher/person taking consent

I confirm that the participant was given an opportunity to ask questions about the study, and that all of the questions they have asked have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and that the consent has been given freely and voluntarily.

A copy of this informed consent form has been provided to the participant _____

Print Name of Researcher/person taking the consent _____

Signature of Researcher/person taking the consent _____

Date _____ (day/month/year)

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