D3.4 Report on the comparison of adapted local protocols and Ethical Committee evaluation in each study site

777363 – DRIVE

DEVELOPMENT OF ROBUST AND INNOVATIVE VACCINE EFFECTIVENESS

WP3 – Evaluation of studies' quality and feasibility

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Publishable Summary

In order to better assess differences on the ethical submission process and the received feedback in participating countries, DRIVE carried out a web-based survey targeting public health institutes, conducting pilot observational studies to address the IVE by vaccine brand/type 2017-2018 influenza season.

The results of the survey can be used to support the evaluation of the quality and feasibility of the pilot studies for determining type/brand-specific seasonal influenza vaccine effectiveness, in order to identify possible obstacles and to share common principles among participating study sites in the following seasons.

List of abbreviations

DRIVE = Development of Robust and Innovative Vaccine Effectiveness
FISABIO = Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana
GDPR = General Data Protection Regulation
GP = General Practitioner
IMI = Innovative Medicines Initiative
ISS = Italian National Institute of Health (Istituto Superiore di Sanità)
IVE = Influenza Vaccine Effectiveness
NPS = NasoPharyngeal Swab
PHI = Public Health Institute
SARI= Severe Acute Respiratory Infection
SP = Sentinel Practitioner
THL = National Institute for Health and Welfare (Terveyden ja hyvinvoinnin laitos)
TND = Test-Negative Design
UNIFI = University of Florence
VAHNSI = Valencia Hospital Network for the Study of Influenza
WP = Work Package

Objectives

DRIVE is currently developing generic protocols for field-based influenza vaccine effectiveness (IVE) studies, based on population-based database and test negative case-control studies to be applied starting from 2018-2019 influenza season. The objective of D3.4 “Report on the comparison of adapted local protocols and Ethical Committee evaluation in each study site” for the 2017-2018 influenza season was to assess local protocols for differences regarding the ethical submission process in the study sites currently participating in DRIVE, namely Finland, Italy and the Valencia Region in Spain, as well as study sites confirming their participation in DRIVE by May 2018.

For the following influenza seasons, the aim of the present deliverable will be to collect information from all PHIs and Associate Partners of DRIVE, in order to assess adapted local protocols for differences and the rationale for those differences.

Methods

Survey

A structured survey was prepared by UNIFI and pilot-tested by the Istituto Superiore di Sanità (ISS), the Public Health Institute of Italy. Following pilot-testing, the survey was amended into an even more structured format to simplify the interviewing process and increase consistency. Topics of interest investigated were: inclusion of the study into the national influenza surveillance system, the need for ethical committee approval to conduct the IVE study, the type of ethical committee (national/regional/institutional; professionals involved), country-specific regulations to be followed, the need to administer the informed consent form to study participants, information regarding data storage, last feedback received from the ethical committee and time required to receive such feedback, info regarding the laboratories performing the specimen analyses, changes foreseen in the ethical submission process after enforcement of the General Data Protection Regulation (GDPR) (Regulation EU 2016/679). The survey can be found in **Annex 1**.

Expert respondents

The targeted experts for this influenza season were consortium experts involved in carrying out pilot studies to address influenza vaccine effectiveness by vaccine type/brand. The countries for which data collection in DRIVE was expected in the initial season were Finland, Italy and the Valencia Region in Spain. The survey was administered online using the SurveyMonkey tool. It is available at the link: https://www.surveymonkey.com/r/GY3GQPR. In addition, experts were also interviewed by teleconference in order to gather a more in-depth representation of how the ethical submission process is structured in each country.

In addition, the National Influenza Centre of Austria (at Medizinische Universität Wien) was invited to participate in the web-based survey in early May, after confirming its participation in DRIVE.

Results

Finland

During the 2017-2018 influenza season, THL, the Public Health Institute of Finland, performed a pilot population- based study which made use of secondary data from existing health care databases. The study was part of the national routine practice for assessing influenza vaccine effectiveness by using data derived from the National Vaccination Register (all vaccinations administered in public primary health care), National Infectious Disease Register (all influenza findings from all laboratories) and Register of Primary Health Care Visits (all public primary health care visits), complemented with data from other routine administrative registers. Since it made use of secondary data from routine databases, an ethical evaluation was not mandatory, according to the relevant regulations. However, the investigators have requested an evaluation from an institutional ethical review group, mainly composed of clinicians and experts in legal and insurance matters or coroners (the composition of the institutional ethical work group varies). THL Ethical Review Group has no public website, as it is for internal use of the institute and only reviews projects conducted by THL that do not need an 'official' Ethical Committee review. The documents submitted to the THL ethical committee were the cover letter by the principal and other investigators, the protocol, including a summary, the principal investigator's judgement on the ethical aspects of the study, including its scientific relevance, risks for the study subjects and other ethical issues associated with the conduction of the study, information on the samples to be collected, the scheme of data management, data protection, retention time, archiving, and the description of the personal data file (According to §10 of the personal Data Act 523/1999).
When consulted, the institutional ethical committee provides clearance within about four weeks. In addition, an approval was needed from all register controllers of the used registers.
The registers cover all citizens of Finland, and the study participants were not contacted. In this kind of pure register based study, collection of informed consent from the study subjects is not required.
The following are the main country-specific regulations that are to be followed to perform register-based IVE studies in THL:
General Data Protection Regulation, 679/2016/EU
Personal Data Act (Henkilötietolaki) 523/1999
Act on the Openness of Government Activities (Laki viranomaisen toiminnan julkisuudesta) 621/1999
Information Society Code (Tietoyhteiskuntakaari), 917/2014
Infectious Diseases Act (Tartuntatautilaki) 1227/2016
Act on the National Institute for Health and Welfare (Laki Terveyden ja hyvinvoinnin laitoksesta) 668/2008
Archives Act (Arkistolaki) 831/1994
Act on National Personal Records Kept under the Health Care System (Laki terveydenhuollon valtakunnallisista henkilörekistereistä) 556/1989
The Statistics Act (Tilastolaki) 280/2004
Act on Determining the Cause of Death (Laki kuolemansyyn selvittämisestä) 459/1973
Act on the Status and Rights of Patients (Laki potilaan asemasta ja oikeuksista) 785/1992
Act on the Status and Rights of Social Welfare Clients (Laki sosiaalihuollon asiakkaan asemasta ja oikeuksista 812/2000
Act on the statistics of the National Research and Development Center for Welfare and Health (Laki sosiaali- ja terveysalan tutkimus ja kehittämiskeskuksen tilastotoimesta) 409/2001
Population information act (Laki väestötietojärjestelmästä ja väestörekisterikeskuksen varmennepalveluista) 661/2009

Health insurance act (Sairausvakuutuslaki) 1224/2004
National Pensions Act (Kansaneläkelaki) 568/2007
In addition to these laws/acts, there are decrees, which regulate their implementation.
Personal and clinical information are collected through a web-based platform and managed in the THL central database under control of data management professionals in THL.
At the moment of participation in the survey, no change in the institutional ethical submission process was envisioned for when the new reform of EU data protection rules (GDPR, Regulation (EU) 2016/679) would have become enforceable (from 25 May 2018). GDPR may delay the process of getting approvals from the register controllers.

Italy

Study nested into the national surveillance system
In Italy, the IVE study has been conducted since the 2009/2010 season (excluding seasons 2012/13 and 2013/14) in the framework of the I-MOVE network[1] within a sample of sentinel GPs under the national influenza surveillance system (InfluNet) that includes the epidemiological and virological influenza surveillance systems. In Italy, annual influenza vaccination targets persons aged 65 years or above and high-risk subjects.
InfluNet was implemented in Italy in the 1999/2000 influenza season, and is based on voluntary participation of an average of 830 (range 648-902) sentinel practitioners (including general practitioners and paediatricians) per year, covering about 1.5-2% of the general population. The system aims to monitor the incidence of influenza-like illness, define the extent of the seasonal epidemics, and collect information on circulating strains. Sentinel Practitioners (SP) are asked to report weekly influenza like illness cases (according to the EU ILI case definition) occurring during the year, from week 42 to week 17, using standardised forms. Specific information regarding age (0-4, 5-14, 15-64, >64 years) and influenza vaccine status are collected and reported using web-based electronic Case Report Forms (CRF)[2]. Data are kept on a server based at ISS. Analysis is performed weekly and published by the ISS and the Ministry of Health on their respective websites.
For surveillance of circulating virus strains – sampling kits are sent out to regional coordinators for surveillance that randomly select 1 SP per week between week 46 and week 10 to collect throat swabs of the first ILI-patient seen. These specimens are tested at the regional Reference Laboratories distributed in 15 different Italian regions. Results are collected and reported using web-based electronic CFR from the National Influenza Centre. Every year approximately 2,000 sentinel samples and 10,000 hospital samples are collected with a proportion of positive specimens of about 34%.
Since the influenza virological surveillance is under the framework of the Influnet surveillance system, the swabs are taken according to national guidelines that fall into routine activities of the GPs, therefore informed consent is not needed to collect specimens. The ethical committee approval was required only to collect the minimum data set needed to fulfil the I-MOVE protocol requests.

Test-negative design/Hospital-based study
In Italy, since 2014 a network of four hospitals under the project I-MOVE+ (that will end in October 2018) is also in place; it is aimed at measuring effectiveness of the vaccines against hospitalised severe influenza among population aged 65+, that is one of the target for seasonal influenza vaccination. In this study, the study population is represented by the community-dwelling individuals aged ≥ 65 years hospitalised with severe acute respiratory infections (SARI) in one of the participating hospitals, with no contraindication for influenza vaccination. The protocol is submitted each June to

[1] https://sites.google.com/site/epiflu/
[2] https://old.iss.it/site/RMI/imove/default.aspx?ReturnUrl=%2fsite%2frmi%2fimove%2f

the National and local (hospital) Ethical Committee[3]. In addition to the study protocol, the documents that were submitted to the ethics committee comprised the informed consent form, the declaration of sponsorship, the Principal Investigator declaration and the study budget.
The national ethical committee is based at the ISS and composed of the following professional figures: clinicians, pharmacologist, paediatrician, biostatistician, pharmacist, expert in legal and insurance matters/coroner and an expert in bioethics. Approval was received after approximately four weeks after the submission of the documentation to the national ethical committee. Study participants are requested to sign the written informed consent form (**Annex 2**).
Starting from 2018/19 season for the test-negative design (TND) case control study, no ethical committee clearance will be needed, since the data collection (a restricted number of variables have been included: e.g. chronic condition, date of vaccination and vaccine brand) for evaluating the IVE at national level has been nested into the Influnet national surveillance that is listed among surveillance systems and registers of national relevance by the Decree of the President of the Council of Ministers (DPCM) issued on 3 March 2017[4].
The country-specific regulation to be followed to perform IVE studies in Italy is Legislative Decree no. 196 on personal data protection issued on June 30th, 2003.

For both the InfluNet surveillance and TND case-control study personal information are stored in a server through a web reporting *ad hoc* platform for data collection. Warning and blocking procedures are set on this dedicated web-based application, to improve the quality and completeness of data. Data are anonymized and a unique ID is attributed to each ILI case, making possible for the SP to update information on the patient, if needs be. At ISS a weekly check is performed with standardized analysis procedures. In case of missing or inconsistent information, SPs are requested, by telephone and/or email, to complete or check the information[5].
At the moment of participation in the survey, no change in the ethical submission process was envisioned to meet the new EU Regulation on data protection (GDPR, Regulation (EU) 2016/679).

Spain

Hospital studies (Valencia)

Since 2011, FISABIO has conducted a hospital-based TND study applying an active annual surveillance scheme in the Valencia Hospital Network for the Study of Influenza (VAHNSI) to monitor influenza virus epidemiology and its impact in different age and risk groups. For the 2017-2018 influenza season FISABIO enlarged the time window of the VAHNSI study from 1st of September to 30th of June (4 months longer than currently) to capture, in the period 1st September to 30th June (10 consecutive months) admissions with laboratory confirmed (RT-PCR), respiratory syncytial virus (RSV) and their seasonality with confidence.
The study was approved seven years ago. In order for the study to be performed, the study protocol was accepted by the Ministry of Health and by the National Ethics Committee[6]. In addition to the study

[3] The website of the National Ethical Committee based at ISS is: https://www.iss.it/?p=120
[4] http://www.gazzettaufficiale.it/eli/id/2017/05/12/17A03142/sg
[5] Seasonal influenza vaccines in Italy: assessing effectiveness and safety. Season 2015-2016.
Stefania Spila Alegiani, Valeria Alfonsi, Antonino Bella, Stefania Giannitelli, Paola Ruggeri, Alessia Ranghiasci, Eva Charlotte Appelgren, Enrica Tavella, Caterina Rizzo and the Working group I-MOVE and SVEVA 2017, iii, 80 p. (in Italian)
Available at: http://old.iss.it/binary/publ/cont/17_19_web.pdf

Rizzo C, Bella A, Alfonsi V, Puzelli S, Palmieri AP, Chironna M, Pariani E, Piatti A, Tiberti D, Ghisetti V, Rangoni R, Colucci ME, Affanni P, Germinario C, Castrucci MR. Influenza vaccine effectiveness in Italy: Age, subtype-specific and vaccine type estimates 2014/15 season. Vaccine. 2016 Jun 8;34(27):3102-3108. doi: 10.1016/j.vaccine.2016.04.072. Epub 2016 May 4.
[6] http://grupos.fisabio.san.gva.es/web/rvb/comite-de-etica

protocol, the documents that were submitted to the ethics committee comprised the informed consent form, the declaration of sponsorship, the Principal Investigator declaration and the study budget.
It took approximately six weeks to receive the approval after the submission of the documentation to the ethical committee. The National Ethical Committee is composed by clinicians, lay persons, pharmacologists, general practitioners, paediatricians, pharmacists, lawyer, epidemiologists. Whenever changes in the research protocols were needed, notification of such changes were reported to the ethical committee in due time, preferably by May.

An independent contract research organization monitors and audits the activities of the study and their compliance with Good Epidemiological Practices, as stated in the International Ethical Guidelines for Epidemiological Studies, The Council for International Organizations of Medical Sciences (CIOMS), 2009.
For the 2017/2018 influenza season, written informed consent was gathered before enrolling patients into the test-negative design study. Patients enrolled include non-institutionalized patients, inhabiting continuously in the participating hospitals catchments' area for at least the previous six months, able (or her/his legal tutor) to give informed written consent, and that remain in the hospital for at least 24 hours.
As far as the informed consent form is concerned, two different documents have been prepared, depending on the age of the subjects to be enrolled (**Annex 3**). One is administered to patients >18 years. For patients <12 years, the informed consent form has to be read and accepted by parents or legal tutors. In case study subjects are aged between 12 and 18 years, one informed consent (assent) is to be signed by the patients, another one by their parents/legal tutors.
In the informed consent the objectives of the study are described, as well as the nature of processed data (aggregated), the recipients of possible data transfers (FISABIO research centre), the rights of data subjects (in particular, the possibility to withdraw at any time without the need to provide justification) and the consequences of not participating in the study. It is specified that the study is carried out according to the following ethical regulations: updated Declaration of Helsinki and Standards of Good Epidemiological Practice) and that personal data are treated in accordance to Law 15/99 "Protección de Datos de Carácter Personal".
FISABIO received the approval to share data with the Global Influenza Hospital Surveillance Network (https://www.gihsn.org/), a platform aimed to generate strong epidemiological and medical evidence on the burden of severe influenza and the public health impact of influenza vaccines. The platform is in place since 2011, it gathers several sites throughout the world and is affiliated with national health authorities.
Specimens are transported to FISABIO laboratory[7].
Personal and clinical information are collected through a web-based platform.

Sentinel surveillance (regional public health institutes)

In Spain more generally, annual influenza vaccination is targeted for persons aged 60-65 years or above and for high risk persons.
The regional influenza surveillance networks are based on voluntary participation of physicians (including general practitioners and paediatricians) and generally cover about 1-5% the general population of the region per year. Sentinel practitioners are asked to report weekly influenza like illness cases (according to the EU ILI case definition) occurring during the season, using standardised

[7] Mira-Iglesias Ainara, López-Labrador F Xavier, Guglieri-López Beatriz, Tortajada-Girbés Miguel, Baselga-Moreno Víctor, Cano Laura, Mollar-Maseres Juan, Carballido-Fernández Mario, Schwarz-Chavarri Germán, Díez-Domingo Javier, Puig-Barberà Joan, Valencia Hospital Network for the Study of Influenza and Respiratory Viruses Disease. Influenza vaccine effectiveness in preventing hospitalisation of individuals 60 years of age and over with laboratory-confirmed influenza, Valencia Region, Spain, influenza season 2016/17. Euro Surveill. 2018;23(8):pii=17-00318. Available at: https://doi.org/10.2807/1560-7917.ES.2018.23.8.17-00318

forms. Specific information regarding age and influenza vaccine status are collected and reported to the local PHI. Analysis is done weekly and published by the PHIs, sometimes online.
The networks are considered parts of the regional public health programmes and therefore do not require ethics committee reviews nor written informed consent. Oral informed consent is obtained from patients.

Austria

Influenza virus activity in Austria is monitored, within the frame of the Austrian Influenza Sentinel Network, by the Diagnostic Influenza Network Austria (DINÖ), a group of sentinel physicians throughout Austria, which collect clinical nasopharyngeal swab (NPS) samples, as well as epidemiological information. It allows not only to detect the beginning, the peak and the end of the epidemic influenza virus activity in Austria, but also to estimate the annual impact of the influenza virus epidemic activity on the Austrian population. Within this sentinel network, nasopharyngeal swabs are collected from selected patients with acute influenza infections in Austria from calendar week 40 of one year to week 16 of the following year. Specimens are sent to the Centre of Virology at the Medical University of Vienna (National Reference Laboratory) and investigated for the presence of influenza viruses and influenza virus positive NPS-samples are further analysed to identify the type, subtype and strain. These surveillance results allow evaluate the similarity of circulating strains vs vaccine strains. Furthermore, these surveillance data provide the background for the calculation of vaccine effectiveness estimates. Every year a retrospective statistical analysis of fully anonymized viral and epidemiological data is performed. NPS-samples of patients for which vaccination status is missing are excluded from IVE estimates.
Ethics committee approval to perform IVE studies is required for the duration of one year (each season an amendment is needed). The feedback received from the ethics committees on the protocol used in the last influenza season was positive. The ethical committee[8] is based at the Medical University of Vienna and composed of clinicians, psychologists, lay persons, pharmacologists, general practitioners, paediatricians, microbiologists, biostatisticians, pharmacists, experts in legal and insurance matters or a coroner, experts in bioethics, representatives of patient associations. The documents that are to be submitted to the ethics committee comprise basic parameter of the study, description of study participants, a summary of the study protocol including hypotheses, risk evaluation, number of participants, methodology, criteria for inclusion/exclusion, the detailed study protocol, information on sponsorship, information on the submitter who claims study approval, information on statistics, information on insurance, information on centres participating in the study, the CV of the project leader and declarations on conflict of interest.
Usually, about two months are required to receive the approval by the ethical committee. The investigators need to submit the documentation to the ethical committee by May. Informed consent is not required, as data are fully anonymized. The study is performed according to the Declaration of Helsinki and its Amendments and the research protocol is approved by the ethics committee of the Medical University of Vienna. Data are kept on paper and also digitally stored using Microsoft Access.

The main characteristics of the ethical submission process in countries that have conducted IVE studies in the 2017-2018 influenza season and that participate in DRIVE are summarized in **Table 1**.

[8] http://ethikkommission.meduniwien.ac.at/

Conclusions

In Italy and Austria observational studies conducted have been nested into the respective national influenza surveillance system; in Finland the IVE study performed used only data collected from the pre-existing national routine administrative registers without contacting the study subjects. In Italy and Finland, no ethical committee clearance appears to be mandatory for yearly IVE assessment. In Italy, activities performed as part of the DRIVE Project become part of the routine activities performed by physicians involved in the surveillance, and consequently, patients and study subjects are not requested to sign an informed consent. In Finland, the register-based studies are not in the scope of the ethics committee evaluation.

In Austria, although the IVE study was nested into the national influenza surveillance system, ethics committee approval was nonetheless required; informed consent was not collected from patients, on account of anonymization and aggregation of data.

In the case of the hospital-based active and prospective epidemiologic surveillance of hospitalizations related to influenza and respiratory syncytial viruses that is being carried out in the Valencia Region, and of the hospital-based TND case control studies conducted in Italy, approval by the reference Public Health Research Ethics Committee was obtained. An informed written consent/assent/ Legally Authorized Representative form is requested, according to patient characteristics.

When clearance from an Ethical Committee is required, documents to be submitted to the Ethical Committee generally comprise the study protocol, the informed consent form (when applicable), the declaration of sponsorship, the Principal Investigator declaration and the study budget.

The confidentiality legislations and requirements in personal data handling are being followed in all study sites. Personal information are anonymized or pseudo-anonymized and security of all data are guaranteed by normalized procedures.

In all the study sites, the International Ethical Guidelines for Epidemiological Studies are followed and Good Epidemiological Practice guidelines are implemented.

Table 1 Characteristics of the ethical submission process in countries that have conducted IVE studies in the 2017-2018 influenza season and that participate in DRIVE

	Finland	**Italy**		**Spain**		**Austria**
		Study nested into national surveillance system	TND/Hospital-based study	Valencia (hospital)	Spain (regional surveillance)	
Study nested into national surveillance system (yes/no)	Yes (Routine databases)	Yes	No	No	Yes	Yes
The study made use of secondary data from routine databases (yes/no)	Yes	Yes	No	No	No	No
Ethics committee approval required for performing IVE studies each season (yes/no)	No	No	Yes	No, only the first season (7 years ago)	No	Yes
Informed consent needed (yes/no)	No	No	Yes	Yes	No	No
Dates in which the investigators need to submit the documentation to the ethics committee	N.A.	N.A.	June/July	May	N.A.	May
Ethical committee used (national/regional/local/institutional)	Institutional	N.A.	National/local (hospital)	Regional	N.A.	Institutional
Feedback received from the ethics committees on the protocol used in the last influenza season (approved/ not approved/ approved after revision of the protocol)	Approved	N.A.	Approved	Approved	N.A.	Approved
Time needed to receive approval by the ethical committee (in weeks)	4	N.A.	4	6	N.A.	8

To where are specimens transported (National/Regional reference lab/other)	Other (Local laboratories)	Regional reference lab	Regional reference lab/hospital lab	Coordinating centre	National or regional reference lab	National reference laboratory
Collection of personal information (kept on paper/stored in local computer memory/ collected through web-based platform)	Web-based platform	Web-based platform	Web-based platform	Electronic case report	Electronic or paper	Kept on paper and stored in a local computer memory
Personal information are anonymized or pseudoanonimized and security of all data is guaranteed by normalized procedures (yes/no)	Yes	Yes	Yes	Yes	Yes	Yes
Compliance to the International Ethical Guidelines for Epidemiological Studies recommendations (yes/no)	Yes (When applicable for register studies)	Yes	Yes	Yes	Not explicitly stated	Yes
Implementation of Good Epidemiological Practice procedures (yes/no)	Yes (When applicable for register studies)	Yes	Yes	Yes	Not explicitly stated	Yes

N.A. Not Applicable

Annexes

Annex 1: Survey to assess ethical submission processes and differences in adapted protocols

DRIVE (Development of Robust and Innovative Vaccine Effectiveness) is a European project under the framework of the Innovative Medicines Initiative (IMI). The goal of DRIVE is to establish a sustainable platform aiming at assessing brand-specific influenza vaccine effectiveness studies in Europe.

This survey targets associate partners, public health institutes and other organizations that performed pilot studies in the current influenza season. The aim of the survey is to assess differences in the adapted local protocols and the rationale for such differences.

Please provide your contact details
Name
Organization
Country
Position
Address
Email
Telephone

Is the IVE study conducted by your unit nested into the national influenza surveillance system?

o Yes

o No

Is ethics committee approval required for performing influenza vaccine effectiveness (IVE) studies?
Yes (please describe the process briefly) _____
No (please elaborate if needed) _____

What are the country-specific regulations that are to be followed to perform IVE studies?_____

Is informed consent needed?
Yes, written consent
Yes, oral consent
No

How were personal information collected? (please select all that apply)
kept on paper
stored in a local computer memory

collected through a web-based platform

If data are digitally collected, please specify the program used
Access
EpiData
Epi Info
Other (Please specify)_____

Which ethical committee is used?
national
regional
local
institutional

Which of these professionals compose the ethical committee?
Clinicians
Psychologists
Lay persons
Pharmacologists
General practitioners
Paediatricians
Microbiologists
Biostatisticians
Pharmacists
Experts in legal and insurance matters or a coroner
Experts in bioethics
Representatives of patient associations
Other (please specify)_____

What was the feedback received from the ethics committees on the protocol used in the last influenza season?
Approved
Not approved
A revision of the protocol was required (Please specify)_____

How long did it take to receive the approval by the ethical committee? Please indicate the time needed for the approval after the submission to the ethical committee
Weeks (please specify how many)_____
Months (please specify how many)_____

To where are specimens transported?
National reference laboratory
Regional reference laboratory
Other (Please specify)____

Do you know if there will be any change in the ethical submission process when the new reform of EU data protection rules (GDPR, Regulation (EU) 2016/679) will become enforceable from 25 May 2018.

Yes (detail if possible)_____

No

Please provide us with the documentation required by the ethical committee for approval of IVE study, including the informed consent form. Documents can be uploaded using the "Choose file" buttons below or sent by email to Miriam Levi (Email: miriam.levi@unifi.it)

Please upload here the informed consent

Only PDF, DOC, DOCX, PNG, JPG, JPEG, GIF files are supported (max 16 MB)
Choose File

Please upload here the patient information sheet

Only PDF, DOC, DOCX, PNG, JPG, JPEG, GIF files are supported (max 16 MB)
Choose File

Please upload here the research protocol

Only PDF, DOC, DOCX, PNG, JPG, JPEG, GIF files are supported (max 16 MB)
Choose File

Please write in the box below any additional comments you might have

Annex 2: Informed consent documentation provided to individuals enrolled in the hospital-based TND case control study conducted in Italy

Studio per la stima dell'efficacia vaccinale sul campo del vaccino antinfluenzale nel prevenire le Sindromi respiratorie acute gravi da influenza confermata in soggetti ultra-sessantacinquenni ospedalizzati

Codice Identificativo | | | |__| |

Consenso informato

Gentile Signora/e,
Il nostro Ospedale, insieme ad altri ospedali italiani, sta partecipando ad uno studio, coordinato dall'Istituto Superiore di Sanità, che ha l'obiettivo di stimare l'efficacia vaccinale sul campo (EV) del vaccino antinfluenzale nel prevenire le Sindromi respiratorie acute gravi da influenza confermata in soggetti ultra-sessantacinquenni ospedalizzati.
A questo scopo desideriamo chiedere il Suo consenso ad effettuare un tampone faringeo o naso-faringeo da parte del personale sanitario coinvolto nello studio, per la diagnosi virologica di influenza e, inoltre, a raccogliere una serie di informazioni personali, sulle sue condizioni di salute, su malattie croniche di base e vaccinazioni effettuate.
I dati che La riguardano saranno raccolti dal nostro ospedale e identificati da un codice. Soltanto il personale dell'ospedale e i ricercatori autorizzati potranno, se necessario, collegare il codice al Suo nominativo. Questi dati, ad eccezione del Suo nominativo, saranno trasmessi all'Istituto Superiore di Sanità, il quale li tratterà esclusivamente in relazione all'obiettivo dello studio.
Le informazioni raccolte saranno utilizzate in modo aggregato e rigorosamente anonimo (sotto forma di percentuali e grandi numeri, senza riferimenti a nomi o persone) in conformità alle Linee guida del Garante per la Privacy per i trattamenti di dati personali (Decreto Legislativo 30 giugno 2003, n. 196).
Potrà esercitare i diritti di cui all'art. 7 del Codice (es. accedere ai Suoi dati personali, integrarli, aggiornarli, rettificarli, opporsi al loro trattamento per motivi legittimi, ecc.) rivolgendosi direttamente all'ospedale (*indicare il nome di una persona fisica o di un ufficio responsabile e un recapito*) o, per il suo tramite, all'Istituto Superiore di Sanità.
La ringraziamo per la collaborazione.

Io sottoscritto/a_____nato/a_____il
_____

Dichiaro

di accettare l'esecuzione di un tampone nasale o naso-faringeo da parte il personale sanitario coinvolto nello studio, per la diagnosi virologica di influenza
di autorizzare la comunicazione a terzi (quali parenti o il medico di famiglia), i risultati relativi ai test di laboratorio effettuati;
di rispondere alle domande relative allo studio per la stima dell'efficacia vaccinale sul campo del vaccino antinfluenzale;
di essere stato/a adeguatamente informato/a circa gli scopi dello studio e le metodiche dello stesso;
che il mio consenso è espressione di una libera decisione, non influenzata da promesse di denaro o di altri benefici, né da obblighi di gratitudine o di amicizia e/o di parentela nei confronti del medico responsabile;
di acconsentire al trattamento dei dati necessari allo svolgimento dello studio;
di autorizzare sin d'ora l'utilizzo e la divulgazione, in forma anonima e per sole finalità scientifiche e amministrative e nell'osservanza delle vigenti norme sulla tutela della riservatezza, dei risultati

Il sanitario intervistatore Il paziente

_____ _____

Luogo e data _____

Annex 3: Informed consent documentation provided to individuals enrolled in the hospital-based active and prospective epidemiologic surveillance of hospitalizations related to Influenza and Respiratory Syncytial viruses conducted in the Valencia Region in Spain.

Estudio de casos y controles basado en hospitales sobre la efectividad de la vacuna de la gripe estacional para evitar ingresos asociados a la infección por el virus de la gripe en sujetos de 18 o más años de edad durante las estaciones gripales 2011-2020 y observacional de vigilancia epidemiológica activa de la carga de enfermedad debida a virus respiratorios en los pacientes de cualquier edad ingresados en los hospitales incluidos en el estudio

Se solicita autorización para su participación en este estudio cuyos objetivos son conocer la carga de enfermedad debida a virus respiratorios y la protección que pueda conferir la vacuna de la gripe para evitar ingresos asociados a la infección por gripe en adultos, de 18 o más años de edad.

Se trata de un estudio internacional en el que participan hospitales de la Comunidad Valenciana y hospitales de otros países, China, Brasil, Méjico, Turquía y Rusia y en el que compartimos nuestros resultados con los objetivos descritos.

Si decide participar se le realizará una encuesta sobre las características clínicas de la enfermedad y también socio-sanitarias, y se buscarán datos suyos en bases de datos sanitarias, cuyos resultados se utilizarán, exclusivamente para obtener conclusiones científicas en este estudio. Tardaremos unos 15 minutos en realizar la encuesta.

Si cumple con los criterios de inclusión del estudio, le tomaremos también dos muestras de la pared posterior de la faringe, una por vía oral y otra por vía nasal, que se utilizarán para investigar la presencia del virus de la gripe y otros virus asociados a cuadros respiratorios agudos en el adulto tales como el virus respiratorio sincitial, virus parainfluenza, metaneumovirus, rinovirus, adenovirus, coronavirus y bocavirus. Aunque la toma puede ser molesta no supone ningún tipo de riesgo y las molestias pueden considerarse como muy leves. Si usted así nos lo indica, los resultados de esta prueba les serán comunicados a usted y al hospital.

La participación en el estudio no supone ningún riesgo para Vd., y el beneficio obtenido será para el mejor conocimiento del efecto de las medidas preventivas, no siéndolo para su proceso actual. El resultado obtenido de las pruebas realizadas es útil para los objetivos del estudio pero no es más informativo que las pruebas que le realizan en el hospital. En cualquier caso siga siempre las indicaciones de su médica/médico en el hospital o de su médica/médico de cabecera.

Su participación en el estudio es voluntaria, si decide no participar tenga certeza que no se va a modificar su relación con el personal del hospital. Los datos de la encuesta serán revisados exclusivamente por el equipo investigador y serán utilizados exclusivamente para obtener conclusiones científicas. Los datos obtenidos en cada unos de los centros participantes, incluidos los internacionales, son enviados al centro coordinador (en la actualidad FISABIO, en Valencia) los datos generados en el estudio serán agregados, en las condiciones de confidencialidad exigidas por la legislación española, a los obtenidos en otros países para obtener conclusiones científicas de ámbito global, además de las propias del estudio.

Todos los datos personales están protegidos y serán tratados de acuerdo con lo dispuesto la Ley 15/99 de Protección de Datos de Carácter Personal. El estudio se llevará a cabo según la normativa ética (Declaración de Helsinki actualizada y Normas de Buena Práctica Clínica).

El estudio ha sido sometido a revisión por el Comité Ético de la Dirección General de Salud Pública-Centro Superior de Investigación en Salud Pública (CEIC DGSP/CSISP) y también por el de este hospital, que ha dado su aprobación para que el estudio se pueda llevar a cabo. A excepción de los investigadores de campo y del laboratorio centralizado que analiza las pruebas, ninguno de los investigadores ni de los participantes recibe ninguna compensación económica por participar en el estudio.

Se entregará copia de esta información (página 1 y 2) y del consentimiento (página 3) firmado y fechado.

CONSENTIMIENTO INFORMADO DEL PACIENTE

Estudio de casos y controles basado en hospitales sobre la efectividad de la vacuna de la gripe estacional para evitar ingresos asociados a la infección por el virus de la gripe en sujetos de 18 o más años de edad durante las estaciones gripales 2011-2020 y observacional de vigilancia epidemiológica activa de la carga de enfermedad debida a virus respiratorios en los pacientes de cualquier edad ingresados en los hospitales incluidos en el estudio

Yo, ...

He leído la hoja de información que se me ha entregado.

He podido hacer preguntas sobre el estudio.

He recibido suficiente información sobre el estudio.

He hablado con .....

Comprendo que mi participación es voluntaria.

Comprendo que puedo retirarme del estudio:

1º Cuando quiera.
2º Sin tener que dar explicaciones.
3º Sin que esto repercuta en mis cuidados médicos.

Presto libremente mi conformidad para participar en el estudio.

Y SI ( ) NO ( ) autorizo a que el resultado de la prueba que me han realizado se incluya en mi historia clínica electrónica por el personal de FISABIO y lo podré consultar con mi médico de cabecera.

_____ _____

Fecha Firma del paciente

_____ _____

Fecha Firma del investigador de Campo

Si usted desea cualquier información adicional además de la que se le ha facilitado en el momento de firmar este consentimiento puede obtenerla tanto del Investigador de campo, móvil
como del Investigador Principal del Estudio Dr. Javier Díez Domingo, móvil 654479113.

Estudio de casos y controles basado en hospitales sobre la efectividad de la vacuna de la gripe estacional para evitar ingresos asociados a la infección por el virus de la gripe en sujetos de 18 o más años de edad durante las estaciones gripales 2011-2020 y observacional de vigilancia epidemiológica activa de la carga de enfermedad debida a virus respiratorios en los pacientes de cualquier edad ingresados en los hospitales incluidos en el estudio

Se solicita autorización para la participación de su hijo o hija en este estudio cuyo objetivo es conocer los virus que provocan enfermedades, como la que padece su hija o hijo.

Se trata de un estudio internacional en el que participan hospitales de la Comunidad Valenciana y hospitales de otros países, China, Brasil, Méjico, Turquía y Rusia y en el que compartimos nuestros resultados con los objetivos descritos.

La participación en este estudio es totalmente voluntaria. Si acepta participar se le realizará a Vd. una encuesta sobre las características clínicas de la enfermedad y socio-sanitarias, y se buscarán datos de su hija o hijo en bases de datos sanitarias, cuyos resultados se utilizarán, exclusivamente para obtener conclusiones científicas. Tardaremos unos 15 minutos en realizar la encuesta.

Si su hija-hijo cumple con los criterios de inclusión del estudio, se procederá a la toma de muestras. Si la edad de su hija-hijo es de 14 o más años le tomaremos, con un algodón puesto en un palito (torunda) dos muestras de la pared posterior de la faringe que se utilizarán para investigar la presencia de los virus tales como el de la gripe, el virus respiratorio sincitial, virus parainfluenza, metaneumovirus, rinovirus, adenovirus, coronavirus y bocavirus. Si su hija-hijo tiene menos de 14 años le tomaremos una muestra de la parte anterior de la nariz y otra de la parte posterior. Aunque la toma puede ser molesta no supone ningún tipo de riesgo para el niño o niña y las molestias pueden considerarse como muy leves. Si usted así nos lo indica, el resultado de esta prueba le será comunicado a usted y al hospital, aunque puede tardar más de una semana en conocerse.

El beneficio obtenido será para el mejor conocimiento de las enfermedades y los virus que las producen en la Comunidad Valenciana, y no tendrá ninguna

repercusión en el manejo por el hospital del proceso actual de su hijo o hija. El resultado obtenido de las pruebas realizadas a su hijo o hija es útil para los objetivos del estudio pero no es más informativo que las pruebas que le realizan en el hospital. En cualquier caso siga siempre las indicaciones del médica/médico de su hijo/hija en el hospital o del médica/médico de cabecera de su hijo/hija.

Como su participación es voluntaria, si decide que su hijo o hija no participe tenga certeza que no se va a modificar su relación con el personal del hospital.

Los datos de la encuesta serán revisados exclusivamente por el equipo investigador y serán utilizados exclusivamente para obtener conclusiones científicas. Los datos obtenidos en cada unos de los centros participantes, incluidos los internacionales, son enviados al centro coordinador (en la actualidad FISABIO, en Valencia) los datos generados en el estudio serán agregados, en las condiciones de confidencialidad exigidas por la legislación española, a los obtenidos en otros países para obtener conclusiones científicas de ámbito global, además de las propias del estudio.

Todos los datos personales están protegidos y serán tratados de acuerdo con lo dispuesto por la Ley 15/99 de Protección de Datos de Carácter Personal.

El estudio se llevará a cabo según la normativa ética (Declaración de Helsinki actualizada y Normas de Buena Práctica Clínica).

El estudio ha sido sometido a revisión por los Comité Éticos de Investigación Clínica, CEIC Dirección General de Salud Pública/Centro Superior de Investigación en Salud Pública y el del hospital donde está ingresado su hijo o hija, y han dado su aprobación para que el mismo se pueda llevar a cabo.

A excepción de los investigadores de campo y del laboratorio centralizado que analiza las pruebas, ninguno de los investigadores ni de los participantes recibe ninguna compensación económica por participar en el estudio.

Se entregará copia de esta información (páginas 1 y 2) y del consentimiento (página 3) firmado y fechado.

CONSENTIMIENTO INFORMADO DE LOS PADRES O TUTORES

Estudio de casos y controles basado en hospitales sobre la efectividad de la vacuna de la gripe estacional para evitar ingresos asociados a la infección por el virus de la gripe en sujetos de 18 o más años de edad durante las estaciones gripales 2011-2020 y observacional de vigilancia epidemiológica activa de la carga de enfermedad debida a virus respiratorios en los pacientes de cualquier edad ingresados en los hospitales incluidos en el estudio

Yo, ...
en relación de ….....de ….....

He leído la hoja de información que se me ha entregado.

He podido hacer preguntas sobre el estudio.

He recibido suficiente información sobre el estudio.

He hablado con .....

Comprendo que la participación es voluntaria.

Comprendo que puedo retirarme del estudio:

1º Cuando quiera.
2º Sin tener que dar explicaciones.
3º Sin que esto repercuta en mis cuidados médicos.

Presto libremente mi conformidad para la participación en el estudio.

Y **SI ( ) NO ( )** solicito que se nos informe a mí y al hospital del resultado de las pruebas.

_____ _____
Fecha Firma del padre/madre o tutor

_____ _____
Fecha Firma del investigador de Campo

Si usted desea cualquier información adicional además de la que se le ha facilitado en el momento de firmar este consentimiento puede obtenerla tanto del Investigador de campo, móvil como del Investigador Principal del Estudio Dr. Javier Díez Domingo, móvil 654479113.

Estudio de casos y controles basado en hospitales sobre la efectividad de la vacuna de la gripe estacional para evitar ingresos asociados a la infección por el virus de la gripe en sujetos de 18 o más años de edad durante las estaciones gripales 2011-2020 y observacional de vigilancia epidemiológica activa de la carga de enfermedad debida a virus respiratorios en los pacientes de cualquier edad ingresados en los hospitales incluidos en el estudio

Se te está pidiendo (a tus padres y a ti) que participes en un estudio porque queremos conocer qué virus provocan enfermedades, como la que padeces tú.

Se trata de un estudio en el que participan hospitales de la Comunidad Valenciana y hospitales de otros países, China, Brasil, Méjico, Turquía y Rusia y en el que compartimos nuestros resultados.

Tu participación en este estudio es totalmente voluntaria y si quieres hacerlo deberás firmar este papel de consentimiento. Si participas os preguntaremos sobre la enfermedad y, si cumples con los puntos necesarios, además te tomaremos un poco de moco de la nariz y la garganta para analizar los virus. Para ello te tocaremos la parte de dentro de la nariz o de la garganta con un algodón puesto en un palito (que llamamos torunda). Los virus que vamos a investigar, entre otros, se llaman virus de la gripe, virus respiratorio sincitial, virus parainfluenza, metaneumovirus, rinovirus, adenovirus, coronavirus y bocavirus. Aunque la toma puede ser molesta, no supone ningún tipo de riesgo y las molestias se pasan inmediatamente.

El tratamiento que recibas en el hospital no se modificará por el resultado del análisis. El resultado que te daremos es útil para el estudio pero para temas relacionados con tu salud siempre debes seguir la información que te den tus médicos. Tu participación en el estudio servirá sólo para que los médicos conozcan mejor las enfermedades y los virus que las producen en la Comunidad Valenciana.

Como te dijimos tu participación es voluntaria, si decides no participar no pasará nada malo.

Los datos de cada uno de los hospitales de todos los países que participan se enviarán a un centro de investigación llamado FISABIO, en Valencia, donde se juntarán para obtener conclusiones científicas.

La ley nos pide que seamos muy cuidadosos con tus datos personales por lo que sólo el equipo investigador tendrá acceso a tu encuesta y a los datos de salud que la Conselleria tiene tuyos. Por ello cumpliremos con las obligaciones que vienen recogidas en la Ley 15/99 de Protección de Datos de Carácter Personal. Además el estudio se llevará a cabo según la normativa ética (Declaración de Helsinki actualizada y Normas de Buena Práctica Clínica)

El estudio lo han revisado dos Comités independientes (llamados Comité Ético de Investigación Clínica de la Dirección General de Salud Pública/Centro Superior de Investigación en Salud Pública y el otro comité es el CEIC del hospital donde estás ingresado).

Se te entregará copia de esta información (páginas 1 y 2) y del consentimiento (página 3) firmado y fechado.

CONSENTIMIENTO INFORMADO DEL PACIENTE

Estudio de casos y controles basado en hospitales sobre la efectividad de la vacuna de la gripe estacional para evitar ingresos asociados a la infección por el virus de la gripe en sujetos de 18 o más años de edad durante las estaciones gripales 2011-2020 y observacional de vigilancia epidemiológica activa de la carga de enfermedad debida a virus respiratorios en los pacientes de cualquier edad ingresados en los hospitales incluidos en el estudio

Yo, ...

He leído el consentimiento que se me ha entregado. He podido

hacer preguntas sobre el estudio.

He recibido suficiente información sobre el estudio.

He hablado con .....

Comprendo que mi participación es voluntaria.

Comprendo que puedo retirarme del estudio: 1º Cuando

quiera.
2º Sin tener que dar explicaciones.
3º Sin que esto repercuta en mis cuidados médicos.

Presto libremente mi conformidad para participar en el estudio.

Y **SI ( ) NO ( )** solicito que se me informe a mí y al hospital del resultado de las pruebas.

_____ _____
Fecha Firma del paciente

_____ _____
Fecha Firma del investigador de Campo

Si usted desea cualquier información adicional además de la que se le ha facilitado en el momento de firmar este consentimiento puede obtenerla tanto del Investigador de campo, móvil
como del Investigador Principal del Estudio Dr. Javier Díez Domingo, móvil 654479113.

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