PASS information

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<tr><td>Title</td><td>Impact of EU label changes and regulatory communication on SARS-CoV-2 adenovirus vector vaccines in context of thrombosis with thrombocytopenia syndrome (TTS): risk awareness and adherence (RiskAware TTS)</td></tr>
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<tr><th>Product</th><th>INN Active ingredient</th><th>ATC-code</th></tr>
<tr><td>1</td><td>COVID-19 Vaccine (ChAdOx1-S [recombinant])</td><td>J07BX03</td></tr>
<tr><td>2</td><td>COVID-19 vaccine (Ad26.COV2-S [recombinant])</td><td>J07BX03</td></tr>
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<tr><td>1</td><td>Vaxzevria (previously COVID-19 Vaccine AstraZeneca)</td></tr>
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<tr><td>Joint PASS</td><td>No.</td></tr>
<tr><td>Research question and objectives</td><td>This study aims to evaluate the impact of the regulatory actions for Vaxzevria and for COVID-19 Vaccine Janssen following the 2021 safety reviews.
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	1. To determine the extent of how regulatory actions for thrombosis with thrombocytopenia syndrome (TTS) have changed national vaccination policy 2. To determine the level of **healthcare professional awareness and knowledge** of the risk of TTS and their adherence to Summary of Product Characteristics (SmPC) recommendations for SARS-CoV-2 adenovirus vector vaccines 3. To determine the extent of **change in healthcare professionals´ attitudes** towards COVID-19 national vaccination campaigns and recommendations 4. To determine the extent of **change in citizens' attitudes** towards vaccination against SARS-CoV-2
Country(-ies) of study	Denmark (DK) Greece (GR) Latvia (LV) Netherlands (NL) Portugal (PT) Slovenia (SI)
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MAH contact person	Not applicable. This study is initiated and funded by EMA following procurement procedure EMA/2017/09/PE (Lot 3).

1 Table of contents

2 List of abbreviations

COVID	Corona Virus Disease
CT	Coordination Team
D	Deliverable
DHPC	Direct Healthcare Professional Communication
DK	Denmark
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
ER	Emergency Room
EU	European Union
GP	General practitioner
GR	Greece
HCP	Healthcare professional
LV	Latvia
M	Month
NHS	National Health Service
NL	Netherlands; Netherland's research team
NT	National Team
PRAC	Pharmacovigilance Risk Assessment Committee at EMA
PT	Portugal
RIVM	National Institute for Public Health and the Environment, NL
SC	Study Coordinator
SCP	Social and Clinical Pharmacy, University of Copenhagen
SI	Slovenia
SmPC	Summary of Product Characteristics
TTS	Thrombosis with thrombocytopenia syndrome
USA	United States of America
UU	Utrecht University
WP	Work Package

3 Responsible parties

Name	Role	Country
Prof. Olaf Klungel, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, the Netherlands	Consortium Director	The Netherlands
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Prof. Anna Birna Almarsdóttir, Professor, Social and Clinical Pharmacy, Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen	Lead Investigator Denmark Steering Committee Coordinating Team Member	Denmark
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Dr Elita Poplavska, Assistant Professor, Institute of Public Health, Riga Stradins University, Riga, Latvia	Lead Investigator Latvia Steering Committee	Latvia
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Dr Inês Ribeiro Vaz, Unidade de Farmacovigilância do Porto, Faculdade de Medicina da Universidade do Porto, Porto, Portugal	Lead Investigator Portugal Steering Committe	Portugal

Prof. Mitja Kos, MPharm, University of Ljubljana, Faculty of pharmacy, Department of Social Pharmacy, Ljubljana, Slovenia	Lead Investigator Slovenia Steering Committee	Slovenia
Dr E.R. (Rob) Heerdink , Associate professor of Clinical Pharmacoepidemiology at the Division of Pharmacoepidemiology and Clinical Pharmacology of the Department of Pharmaceutical Sciences, Utrecht University, The Netherlands.	Advisor Coordinating Team Member	Netherlands
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Paula Barão Sousa Ferreira, MSc, Lisboa, Setúbal e Santarém Pharmacovigilance Centre (Faculty of Pharmacy	Investigator Portugal	Portugal

University of Lisbon, Portugal	Steering Committee (Alternate)	
Dra. Ana Marta Silva, Unidade de Farmacovigilância do Porto, Faculdade de Medicina da Universidade do Porto, Porto, Portugal	Investigator Portugal Steering Committee (Alternate)	Portugal
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More details about the investigators and the tasks and structure of the various teams (Coordination, National and Steering) are available under Annexes 3 and 4, respectively.

4 Abstract

Summary of the study protocol.

Title

Impact of EU label changes and regulatory communication on SARS-CoV-2 adenovirus vector vaccines in context of thrombosis with thrombocytopenia syndrome (TTS): risk awareness and adherence (RiskAware TTS).

EU PE&PV research network ROC24 EMA/2017/09/PE, Lot 3 Protocol version 2, 7 March 2022, EUPAS 44970.

Author: Teresa Leonardo Alves, Pharm D, MPh, PhD, Researcher, National Institute for Public Health and the Environment (RIVM).

Rationale and background

The European Medicines Agency (EMA) has provided recommendations in 2021 to learned societies and healthcare professionals when assessing people with signs and symptoms of thrombosis with thrombocytopenia syndrome (TTS) after being vaccinated with adenovirus vector vaccines Vaxzevria or COVID-19 Vaccine Janssen.
In addition, the EMA also published safety updates on these vaccines, highlights from expert meetings and news items on its website.

Research objectives

This study aims to evaluate the impact of the regulatory actions for Vaxzevria and for COVID-19 Vaccine Janssen following the 2021 review. The study's objectives are:

1. To determine the extent of how regulatory actions for thrombosis with thrombocytopenia syndrome (TTS) have changed national vaccination policy
2. To determine the level of healthcare professional awareness and knowledge of the risk of TTS and their adherence to Summary of Product Characteristics (SmPC) recommendations for SARS-CoV-2 adenovirus vector vaccines
3. To determine the extent of change in healthcare professionals´ attitudes towards COVID-19 national vaccination campaigns and recommendations
4. To determine the extent of change in citizens' attitudes towards vaccination against SARS-CoV-2

Study design

The study has a qualitative approach and is composed of three work packages involving a literature review, web-based questionnaires, and semi-structured interviews.
Work package 1 will compile an overview and timeline for national COVID-19 vaccination policies and any changes thereof prompted by the TTS risk communication. This includes changes to national vaccination policies, defining risk group(s), age group(s) prioritization, recommendations for second vaccine dose or for other SARS-CoV-2 vaccines. The methodology in Work package 1 comprises a review of available (grey) literature and policy documents to identify the events and changes in vaccination policies in the countries participating in this study.
In Work package 2 we investigate the impact of the regulatory measures and communication and of the changes that occurred on national vaccination policies, on healthcare professionals (HCPs) who have been actively involved either in the vaccination against COVID-19, in the provision of information about its risks, or in the

monitoring and treatment of side-effects thereof. The methodologic approach in Work package 2 includes web-based questionnaires and semi-structured interviews.
In Work package 3, we investigate the impact of the measures and of the changes in vaccination policies on citizens eligible to be vaccinated against COVID-19. The methodologic approach in Work package 3 includes web-based questionnaires.

Population

Work package 1: this study is conducted in 6 EU member states: DK, GR, LV, NL, PT, SI.
In work package 2: to identify the participants in the interviews in Work package 2 an inventory was done per country, to enable identification and recruitment of the most relevant professionals, including those specialties treating TTS in each country, when available.
In Work package 3: each of the six participating countries has selected the most suitable strategy to obtain a sample of their country's adult population. The aim is to recruit diverse responders to include different sociodemographic subgroups of the adult population.

Variables

In the web-based survey to healthcare professionals, variables of interest will cover:

(1) HCP's own working/vaccination duty context (vaccination centres, own medical practice, hospital).
(2) Source of information about the risk for TTS (through media, professional society, direct healthcare communication, SmPC, instructions from authorities).
(3) Knowledge and awareness about the direct healthcare professional communications (DHPCs).
(4) Whether they have witnessed any TTS cases in their vaccination practice.
(5) Knowledge and awareness of the signs and symptoms of TTS and the need to refer to specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat the condition; any instructions from vaccination authorities and/or national competent authorities for medicinal products and/or clinical practice guidelines when coming across TTS[1].
(6) Provision of information to citizens about the TTS warning signs/symptoms and need to seek further health assistance should they occur.
(7) Knowledge and awareness of (updated) clinical guidelines and recommendations from learned societies for treating TTS (e.g., with anticoagulants) when available/applicable.
(8) Knowledge and awareness of the contraindications to use adenovirus vector vaccines in patients who have experienced TTS following vaccination with Vaxzevria.
(9) Change to attitudes towards the COVID-19 vaccination campaign and national vaccination programme after TTS risk communication.
(10) Willingness to receive future (booster) vaccination(s) against COVID-19.

In the interviews, healthcare professionals will be asked about:
- how they perceived the events and the risk communication about the two adenovirus vector vaccines in their country;
- the views and actions of HCPs regarding the Janssen and Vaxzervia vaccines;
- their concerns, ideas, and questions about the risk communication and the impact thereof.

In the web-based survey to citizens, variables of interest will cover:

[1] Depending on country.

(1) Respondent characteristics: age, gender, belonging to a risk group for COVID-19 and/or a professional group with vaccination priority according to the national vaccination policy.
(2) Present status of vaccination against COVID-19 and period of first /second/booster vaccination.
(3) Vaccine(s) received.[2]
(4) Awareness and perceptions about the benefits and risks of the SARS-CoV-2 adenovirus vector vaccines.
(5) Awareness and perceptions about the risk for TTS from adenovirus vector vaccines.
(6) Source of information about the risk for TTS.
(7) Awareness about changes in COVID-19 vaccination policy and their impact on own perceptions and attitudes regarding vaccination against COVID-19.
(8) Changes to own attitudes towards vaccination against COVID-19 and use of COVID-19 vaccines: no vaccination against COVID-19, postponement of vaccination, decision to change vaccine.
(9) Changes to own attitudes towards vaccination programmes in general.
(10) Changes to own attitudes towards potential vaccination of their young adult-teenager children against COVID-19.
(11) Willingness to receive future (booster) vaccination(s) against COVID-19.

Data sources

In this study, no established data sources are used.
In Work package 1 – The data to compile the overview and timeline of COVID-19 vaccination policies in each country will be collected through a grey literature review.
In Work package 2 - Data will be obtained through cross-sectional data collection, including both survey among healthcare professionals and semi-structured interviews with healthcare professionals.
In Work package 3 - Data will be obtained through cross-sectional data collection, through survey among citizens

Study size

Work package 1 will cover policy decisions from 6 EU member states (DK, GR, LV, NL, PT, SI).
Work package 2 aims to survey 500 healthcare professionals in 5 EU member states (GR, LV, NL, PT, SI) and interview 30-50 professionals in 6 EU member states (DK, GR, LV, NL, PT, SI).
Work package 3 will survey 900 citizens in six EU member states (DK, GR, LV, NL, PT, SI).

Data analysis

Each National Team will compile the overview and timeline of their national COVID-19 vaccination policies according to a standardised and agreed format. The impact of the risk communication on national vaccination policy will be categorized. Given the variation in vaccination policies, survey data will be analysed at national level. The surveys will generate descriptive statistics. For both the open-text answers of the surveys and the interviews, the analysis involves a qualitative content analysis.

[2] Our recruitment does not restrict respondents to citizens who have received adenovirus vaccines. We are also interested in finding out whether citizens' choice of vaccine/or their decision not to take vaccine has been affected by the risk communication.

Milestones

Milestone	Planned date
Start of data collection	04 November 2021 (Start of Month 1)
End of data collection	04 July 2022
D1: Deliverable 1 Preliminary study plan	*03 December 2022*
D2: Deliverable 2 Study Protocol	*21 January 2022*
Milestone 1: National overviews of COVID-19 vaccination policy available	*15 April 2022*
Milestone 2: Draft questionnaires in pilot phase	*18 April 2022*
Milestone 3: Questionnaires ready to be implemented	*9 May 2022*
Milestone 4: Recruitment of Respondents completed	*30 June 2022*
Milestone 5: Coordinating team receives all the data from NTs	*08 July 2022*
Milestone 6: Draft report has been written and agreed upon by NTs and CT	*19 August 2022*
Milestone 7: Draft Manuscript has been written and agreed upon by NTs and CT	*05 September 2022*
D3: Deliverable 3 Final report of study results	*19 September 2022*
D4: Deliverable 4 Manuscript	*18 October 2022*

5 Amendments and updates

Revision and reformatting of protocol submitted on 21 January.

6 Milestones

Milestone	Planned date
Start of data collection	04 November 2021 (Start of Month 1)
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D1: Deliverable 1 Preliminary study plan	*03 December 2022*
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Milestone 7: Draft Manuscript has been written and agreed upon by NTs and CT	*05 September 2022*
D3: Deliverable 3 Final report of study results	*19 September 2022*
D4: Deliverable 4 Manuscript	*18 October 2022*

7 Rationale and background

The European Medicines Agency (EMA) has provided recommendations in 2021 to learned societies and healthcare professionals when assessing people with signs and symptoms of thrombosis with thrombocytopenia syndrome (TTS) after being vaccinated with adenovirus vector vaccines Vaxzevria or COVID-19 Vaccine Janssen[1] [2].
In addition, the EMA also published safety updates on these vaccines, highlights from expert meetings and news items on its website[3] [4] [5] [6] [7] [8] [9] [10].

8 Research question and objectives

This study aims to evaluate the impact of the regulatory actions for Vaxzevria and for COVID-19 Vaccine Janssen following the 2021 review. In this context, the impact of regulatory actions means looking into:

- Whether national COVID-19 vaccination policies were altered following the regulatory actions.
- Whether healthcare professionals are aware and know about the risk of thrombosis with thrombocytopenia syndrome when administering these vaccines.
- Whether attitudes of healthcare professionals and public have changed towards national COVID-19 vaccination programmes after the 2021 recommendations.

The study's objectives are:

1. To determine the extent of how regulatory actions for thrombosis with thrombocytopenia syndrome (TTS) have changed **national vaccination policy**, including change in risk and age group prioritization, change in recommendations for the second vaccine dose and recommendations for other SARS-CoV-2 vaccines available at the time, by country, and by vaccine brand.

2. To determine the level of **healthcare professional awareness and knowledge** of the risk of TTS and their adherence to Summary of Product Characteristics (SmPC) recommendations for SARS-CoV-2 adenovirus vector vaccines, with particular focus on the following elements:
    2.1. Receipt and awareness of the direct healthcare professional communications (DHPC).
    2.2. Knowledge and awareness of the signs and symptoms of TTS and the need for healthcare professionals to refer to specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat the condition.
    2.3. Knowledge and awareness of (updated) clinical guidelines and recommendations from learned societies for treating TTS (e.g., with anticoagulants), by learned society, by country, by dissemination method and date.
    2.4. Knowledge and awareness of the contraindication to use a second dose of adenovirus vaccine in patients who have experienced TTS after a 1st dose vaccination with Vaxzevria.

3. To determine the extent of **change in healthcare professionals´ attitudes** towards COVID-19 national vaccination campaigns and recommendations, by country, by age group, and by national vaccination strategy (i.e., through vaccination centre, general practitioner, specialist etc.).

4. To determine the **extent of change in citizens' attitudes** towards vaccination against SARS-CoV-2, by country, by age group, by gender, and if feasible, by type of regulatory action.

9 Research methods

9.1 Study design

9.1.1. Qualitative approach

Our study is of exploratory nature and has a qualitative approach. It is composed of three work packages involving a literature review, web-based questionnaires, and semi-structured interviews.

The study consists of three work packages:

- **WP1** focuses on the national vaccination policies implemented in the EU member states included in this study.
- **WP2** regards the impact of the regulatory measures on healthcare professionals (HCPs), whereas
- **WP3** concerns the impact of the regulatory measures on the citizens/adults eligible to be vaccinated against COVID-19.

Work package 1 will compile an overview and timeline for national COVID-19 vaccination policies and any changes thereof prompted by the TTS risk communication. This includes changes to national vaccination policies, defining risk group(s), age group(s) prioritisation, recommendations for second vaccine dose or for other SARS-CoV-2 vaccines.
The methodology in WP1 comprises a review of available (grey) literature and policy documents to identify the events and changes in vaccination policies in the countries participating in this study. National teams will gather information about vaccination policies (and changes) in their country. The EMA risk communication activities/events and the changes to national vaccination policies over time will be plotted per country and presented visually. The information about risk communication measures at national level will be gathered with support from the EMA, via national competent authorities.

In Work package 2 we investigate the impact of the regulatory measures and communication of the changes to national vaccination policies on healthcare professionals (HCPs) who have been actively involved either in the vaccination against COVID-19, or in the provision of information about its risks, or in the monitoring and treatment of side-effects thereof. The methodologic approach in Work package 2 includes web-based questionnaires and semi-structured interviews.
In Work package 3, we investigate the impact of the measures and of the changes in vaccination policies on citizens eligible to be vaccinated against COVID-19. The methodologic approach in Work package 3 includes web-based questionnaires.

The methodologic approach in WP2 and WP3 includes web-based questionnaires, to be hosted either nationally (DK, SI) or by Utrecht University (GR, LV, NL, PT). In the latter option, Utrecht University provides the digital platform for other countries but each country team remains responsible for the questionnaire implementation in their country and for the analysis of those data.

In the national surveys, we will use the national timelines constructed in WP1 to provide the context of vaccination against COVID-19 at the referred time. This will help respondents better recollect the period we are referring to and will avoid any confusion with current vaccination policies.
Once the responses have been collected, we will quantitatively analyze the respondents' characteristics per country, and descriptively and qualitatively the responses to the questions on COVID-19 vaccination. WP2 focusing on HCPs will also include the implementation of semi-structured telephone or online interviews.

9.1.2. WP 1: Document analysis to reconstruct timeline of events at national level

The country teams (see Annex 3) will conduct an online search for relevant documents on the national COVID-19 vaccination policy of their own country following instructions described in Annex 5 and collecting information into the format provided in Annex 6. They will analyze these documents to produce an overview and timeline for their national COVID-19 vaccination policies and any changes thereof prompted by the TTS risk communication. The implications and timelines of recommendations from the EMA and national advisory boards, will also be included in the overview.

The country teams involved in WP1 are the same as in remaining working packages and are detailed in Annex 3.

The coordination team will gather information about EMA and national drug regulatory activities, such as DHCPs[3], safety updates, and news items to establish a general EMA timeline on regulatory events with respect to Vaxzevria and the Janssen vaccine. The coordination team will also analyse the PRAC meeting highlights on the EMA website to collect details about the review of safety signals by PRAC. EMA provided relevant links to information on both vaccines, including assessment history on updates to the product information, safety updates, DHPCs, PRAC meeting highlights, news items published, and other recommendations related to TTS. Should there be questions regarding the EMA information, the coordination team will contact EMA for further clarification or support. The research team is aware that it will be important to use the correct terminology when describing the various regulatory documents and policy papers.

The country teams will gather information about events and vaccination policies in their own countries. In addition, where available/applicable, country teams are expected to collect any updated clinical guidelines and recommendations from learned societies for treating TTS.
A standard format to prepare the overview and timeline is included in Annex 6, to map and assess developments in national COVID-19 vaccination policies and any changes ensuing from the communication around the TTS risk.

In addition to EMA data, information from national vaccination authorities and national medicines agencies will be used, as well as that from national health authorities. EMA has also provided support in obtaining information by sending a Non-Urgent Information request to National competent authorities of the Member States involved in this study. This information will be used to corroborate data collected during the online search. If any specific questions relating to national vaccination policies exist and no public information is available to solve the issue, the coordination team may contact ECDC for support, as appropriate. EMA has provided the contractor with publicly available information on national vaccination campaigns, from the ECDC website.

Annex 6, provides a format to collect information on the vaccination policies. Given the variation in practices and terminology across countries, in addition to the proposed summary tables of Annex 6, the national teams will also compile, per country, an appendix to the study report, which will list each document/communication included in the summary table and:

- Their name/title
- The type of document (policy/guideline/recommendation/communication/press release)
- The actual wording of the vaccination recommendation in English language (when not available, local language is considered acceptable)
- Link to the source of information.

[3] Please note that the date and method of dissemination of DHPCs is decided in agreement with the national competent authorities and may differ per country.

In order to assess feasibility, a pilot will take place whereby the appendices for two countries will be prepared and further discussed with the EMA team. The study coordination team will communicate when results of the pilot are available for discussion.

The degree and reach of national vaccination policies will be categorized in an attempt to ascertain the impact of the risk communication on the national vaccination policy:

- Highest impact /Long-term decision – Country permanently discontinued the administration of adenovirus vector vaccines.
- Significant impact/Long-term decision – Country made changes to both target groups and prioritisation
- No impact/No visible decision – Country made no alterations to previous established vaccination policies.
- Significant impact/Short-term decision – Country temporarily discontinued vaccination with adenovirus vaccines.

We will also seek to ascertain whether EMA risk communication has been used as a reference/basis for any of the policy decisions, both throughout data collection or through direct feedback during the interviews.

9.1.3. WP2: Health care professionals' awareness and knowledge about the risk of TTS, their adherence to recommendations for SARS-CoV-2 adenovirus vector vaccines and their attitude changes towards national campaigns

9.1.3.1. Healthcare professional questionnaire

A web-based questionnaire will be used to gauge the HCPs' awareness and knowledge of the TTS risk and their perspective on the risk communication provided. A question whether the survey respondent is involved in the treatment of TTS will be added. This survey will also focus on eventual changes to attitudes following the 2021 regulatory recommendations on the risk of TTS after vaccination against COVID-19 with adenovirus vector vaccines.

This web-based questionnaire will be adapted to the various target groups, considering the healthcare professionals who are responsible and/or involved in the vaccination against COVID-19 in the different countries. When possible, we will also include healthcare professionals involved in the treatment of adverse events from COVID-19 vaccination. Given the variation in health systems across Europe, healthcare professionals involved in (mass) vaccination can be general practitioners, physicians working at Public Health Services, national or local health authorities, and when applicable, specialists or other HCPs. The sample is likely to vary per Member State. For instance, in some countries, pharmacists and/or veterinaries can vaccinate the public against COVID-19, whereas in other Member States they are not authorized to do so. An inventory has been conducted per country to identify and recruit the most relevant professionals using professional networks. As the study has a qualitative design, a proportional representation of different HCP categories in the response to the survey is not envisaged. Furthermore, the researchers consider that it is not feasible to obtain a proportional representation of the various HCP categories given the variability and complexity in the implementation of the immunization campaign across the different countries.

For the web-based questionnaire, relevant HCPs will be approached for participation in 5 countries (GR, LV, NL, PT, SI). Since the adenovirus COVID-19-vaccines were halted in Denmark, the health professionals survey will not take place in this country. Respondents will be recruited through professional associations and/or national health service directories in each country. We aim to have at least 500 healthcare professionals' responses in total, with 50-150 completed questionnaires per country, according to the country's population. In a country

with a lower number of inhabitants, the community of physicians is smaller. We expect that in less-populated countries saturation will be more rapid as communication in a smaller community can be more homogeneous.

Member State (million inhabitants)	Minimum target of completed questionnaires by HCPs
Latvia (1.9)	50
Slovenia (2.1)	50
Portugal (10.3)	125
Greece (10.6)	125
Netherlands (17.3)	150
TOTAL	500

This descriptive study does not aim to provide a quantitative measurement. Our proposed methodology assumes that by completing 50 to 150 questionnaires per country saturation will be achieved. In qualitative study design, saturation implies that no new information is obtained when additional respondents are included[11] (Saunders et al). The maximum variation (purposive) sampling is intended to reveal a spectrum of knowledge, awareness about and attitudes towards the TTS risk, thus we expect that data from 500 completed surveys will be sufficient to reach saturation and to display the variety in participating member states. Since we aim to characterize knowledge and behaviour in a specific group (HCPs involved in Covid-19 vaccination), we consider non-probability sampling (convenience sample) to be acceptable.

Web-based questionnaires will be developed using both open and closed questions. The survey will also allow respondents to write free text. This enables additional qualitative content analysis (see 9.7 Data analysis). Potential limitations and sources of bias are further discussed under item 5.

These questionnaires will be first developed in English, then jointly reviewed, then translated into Dutch and pilot tested only in the Netherlands due to the study's tight timeline. The content of the questionnaire will be developed in a manner to ensure content validity at EU level. We do not expect the questionnaire's content to be interpreted differently across different countries/languages, as it will be later adapted to reflect the country's situation. Furthermore, the validity of translations across the 6 countries will be ensured through back-to-back translations conducted by the panel of researchers involved at national level. Bearing these aspects in mind, we consider that a single pilot testing will suffice to uncover any weakness in design. Extending the pilot testing to other countries would imply an extension of the study timeline for other two months, as it would demand back-to-back translations in all participating countries. This would also require additional funding to cover extra resources.
After pilot testing, the questionnaires will subsequently be improved, translated back into English and then into the language(s) of the participating countries, as needed, according to protocol. (See Annex 8).

For each national questionnaire, visual cues for national timelines of activities/events/policy changes will be included in the relevant questions. This will provide respondents with the context for the vaccination campaigns in 2021. An example of such a timeline is available in Annex 7. These visual cues are based on the plotted timelines of national vaccination policies, which result from WP1.

To investigate the impact of the regulatory actions and communications thereof, as well as any subsequent policy changes, we will ask healthcare professionals to reflect on how these have affected their practice. Direct questions will be posed regarding their awareness of risks, attitude towards vaccination (e.g., discontinuation of a specific vaccine) before and after the policy alterations. Questions will be specifically formulated to include phrases such as 'before the changes' and 'after the changes,' and when available/applicable, we will include the specific change date, the national authority/body responsible for issuing the vaccination policy and a link to a description of the policy change.

The Healthcare professional (HCP) surveys will include questions to ascertain:

a. HCP's awareness and knowledge about the benefits and risks of the SARS-CoV-2 adenovirus vector vaccines.
b. HCP's awareness and knowledge about the risk of TTS.
c. HCP's knowledge of and adherence to SmPC recommendations for SARS-CoV-2 adenovirus vector vaccines and/or the recommendations on prevention of TTS included in vaccination instructions (as recommended by national vaccination authorities).
d. HCP's attitudes towards national vaccination campaigns and recommendations, and eventual changes thereof following the 2021 regulatory review.

9.1.3.2.. WP2 - Healthcare professional interviews

Deeper insight in the knowledge, attitude and perceptions of HCPs will be gained by conducting semi-guided (telephone or online) interviews.

The interviews with HCPs will provide additional in-depth information about how HCPs have perceived the timeline of events and the risk communication about the two adenovirus vector vaccines in their country and whether they agree with our proposed classification of the impact or the communication on their national policy. They will also be invited to reflect about their experiences, attitudes, and behaviour. Special attention will be paid to scope professionals' motivations and beliefs towards COVID-19 vaccination. This will provide details about personal views, which cannot be obtained through the survey. Since HCPs play a crucial role in reassuring and advising people about vaccinations, their perceptions about the risk communication will provide the PRAC greater insight into the impact of its recommendations in actual practice, as well as help explain any country differences.

The individual interviews will be conducted in six countries (DK, GR, LV, NL, PT, SI). These interviews will be held with five to eight HCPs per country, professionals who were actively involved in vaccinating citizens against COVID-19 or treating any eventual adverse events arising from COVID-19 vaccination in the period between April and June 2021. For more information about the recruitment for these interviews please consult section 10.2. WP 2 – Healthcare professionals' interviews - Recruitment of professionals.

A total of 30 – 48 participants from the interviews (5 to 8 participants per country) is considered sufficient to provide in-depth information and reach saturation for the total number of participants. A purposive sampling method to ensure heterogeneity of participants will be used. The researchers will strive to recruit HCPs across different specialties to diversify the responses obtained.

While we can expect HCP's availability to be limited due to the pandemic (as they are usually working overtime), we consider feasible to interview 5 to 8 HCPs per country. Conducting online interviews allows easier recruitment of HCPs as it facilitates efficient scheduling and is less time-consuming for interviewees and researchers. The intention of the interviews in general is to gain a better insight and more detail on the views and actions of HCPs regarding the Janssen and Vaxzervia vaccines and an opportunity for them to present their concerns, ideas, and questions. We expect that the total number of participants will be sufficient to provide rich in-depth information on how HCPs have perceived the events and the risk communication about the two adenovirus vector vaccines in their country and that differences between countries will be uncovered. When available, the preliminary results from the survey will be used to help develop the interview guide for the semi-structured interviews, i.e., the main version in English. The interview guide will be developed and reviewed by researchers. The interview guide will be pilot tested in NL. Once the English version of the final guide is agreed upon, national teams will adapt it to national settings and translate according to protocol (Annex 8). The in-depth interviews will be held locally by national teams. Audio recordings will be transcribed verbatim.

9.1.4. WP3: Mapping citizen awareness and measuring citizen knowledge about TTS - Citizen questionnaire study

A web-based questionnaire will be conducted in a sample of citizens to measure their attitudes towards vaccination against SARS-CoV-2 and more specifically, their attitudes as to vaccination with adenovirus vector vaccines and their risk perception about TTS. The data from these national citizen questionnaires will enable an analysis by age group, gender and COVID-19 risk group. Questions will be formulated to obtain as much information as possible about the influence of the various regulatory actions of adenovirus vector vaccines and their effects on citizens' attitudes. Each of the six participating countries (DK, GR, LV, NL, PT, SI) selected the most suitable strategy to obtain a sample representative of their country's adult population. The various recruitment possibilities were discussed during joint meetings before deciding at national level. The minimum target of citizens to recruit will consider the country's population, but we aim to include at least 100-200 subjects per country, with a minimum of 900 citizens in total. For this descriptive study, we expect that this respondent population will be sufficiently large to display the variety in attitudes towards COVID-19 vaccination.

Member State (x million inhabitants)	Minimum Target of completed citizen questionnaires
Latvia (1.9)	100
Slovenia (2.1)	100
Denmark (5.9)	150
Portugal (10.3)	175
Greece (10.6)	175
Netherlands (17.3)	200
TOTAL	900

Again, direct questions will be posed regarding citizens' awareness of risks, their risk perceptions both about COVID-19 infection and about risks from COVID-19 adenovirus vector vaccines, their attitude towards vaccination (e.g., discontinuation of a specific vaccine) before and after the policy alterations. Questions will be specifically formulated to include phrases such as 'before the changes' and 'after the changes,' and when applicable, we will include a specific change date and a link to a description of the policy change.

These questionnaires will be first developed in English, then jointly reviewed, then translated into Dutch and pilot tested in the Netherlands. They will subsequently be improved, translated back into English and then into the language(s) of the participating countries, as needed, according to protocol (Annex 8). Due to the tight study timeline pilot testing in more than one country is not feasible. However, the pilot testing in the Netherlands will provide information on essential ambiguities in the questions and will improve survey quality. The translation of the survey into the six different national languages will be conducted according to the translation protocol (Annex 8). The protocol foresees an independent review of each translated survey by a native speaker not involved in the study team. In doing so, we aim to identify culture- and language-specific issues to enable adjustment when needed.

10 Setting

This is a multi-country study in six European countries: **Denmark** (DK), **Greece** (GR), **Latvia** (LV), **Netherlands** (NL), **Portugal** (PT) and **Slovenia** (SI)). The countries have a wide geographic spread, contrasting healthcare systems and cultures and a wide variation in vaccination policies following the EMA recommendations, namely:

- Discontinuation of administration of adenovirus vector vaccines in the national vaccination programme (Denmark).
- Changes to target group and prioritisation (Greece, Netherlands, Portugal).
- No alterations to previous established vaccination policies (Latvia).

- Temporary discontinuation of the Janssen vaccine in October 2021, followed by recommendation to use only mRNA vaccines (Slovenia).[4]

10.1 WP 2 – Healthcare professionals' surveys and interviews - Recruitment of professionals

We ran an inventory per country, to enable identification and recruitment of the most relevant professionals, including those specialties treating TTS in each country, when available.

The inventory of relevant HCPs to be included in the survey and/or interviews was built at national level through various strategies:

- In Denmark - it was the result of informal consultation and joint discussion.
- In Greece, it was the result of informal consultation and joint discussion with professionals involved in the vaccination campaign.
- In Latvia, the professionals were identified through informal consultation, joint discussion, and publicly available listings of professionals (1) involved in the vaccination campaign, (2) mentioned as target audience by the NCA for DHPCs and (3) identified in the national TTS diagnosis and treatment guideline.
- In the Netherlands, the professionals were selected after informal consultation and joint discussion with colleagues active in COVID-19 vaccination research, and COVID-19 behavioural research.
- In Portugal, the selected professionals were based on the target-audience of the materials produced. Both the National Competent Authority and Health Authority provided a "list" of professional categories to whom these materials should be addressed (information available on their websites).
- In Slovenia it was the result of informal consultation and joint discussion.

The information contained below provides information on eligibility of healthcare professionals per country.

[4] As of November 30th, 2021, both Vaxzevria and the COVID-19 Vaccine Janssen are only available at patients' request (provided they are well-informed about the potential adverse effects) or in situations where SARS-CoV-2 mRNA vaccines are contraindicated.

Country	Method	Healthcare professionals to be included	Approach to recruitment	Alternative approach for recruitment	Additional information
Denmark	Interviews	1. General practitioners, physicians and nurses from national and private vaccination centres, and emergency rooms (ER) at hospitals 2. Decision makers	General practitioners will be recruited via professional association and health authority newsletters. Physicians and nurses from vaccination centres via contact points in these centres, and at the ERs via contact points of the ERs. Decision makers will be recruited via contact points at the Danish Health Authority.	Not applicable	Not applicable
Greece	Survey	1. General practitioners, internists, and pulmonologists from the vaccination programmes 2. Community pharmacists	1. Contact with healthcare professional groups 2. E-mail lists for healthcare professionals 3. Direct contact with heads of departments in hospitals or primary healthcare centres 4.Healthcare professional groups on social media (Facebook, LinkedIn) 5. Snowballing through already recruited healthcare professionals	Not applicable	Given that nurses were involved in administering the vaccine, but had no official consultation responsibilities, targeting this specific group of professionals in our survey is still open for discussion
	Interviews	In addition to those above, also hematologists and a decision-maker (member of vaccination committee)	Direct Contact	Not applicable	Not applicable

Country	Method	Healthcare professionals to be included	Approach to recruitment	Alternative approach for recruitment	Additional information
Latvia	Survey	1. General practitioners working in outpatient healthcare facilities or clinics with a contract with the Latvian national health service (NHS)	1. We are planning to recruit GPs based on the publicly available NHS list of specialists/clinics providing vaccination	Not applicable	TTS is treated mainly by GPs and haematologists. There are approximately 20 haematologists in Latvia, it is unlikely we will be able to recruit a meaningful number of responders.
	Interviews	In addition to those above, Decision makers	Not applicable	Not applicable	Not applicable
Netherlands	Survey	1. General practitioners, haematologists and pharmacists 2. Physicians and nurses working at regional and municipal public health services involved in vaccination programmes	1. General practitioners, haematologists and pharmacists will be recruited through existing networks and professional organizations via newsletters 2. Physicians and nurses will be recruited through direct contact from the National Institute for Public Health and the Environment (RIVM)		
	Interviews	1. General practitioners, haematologists and pharmacists 2. Physicians and nurses working at regional and municipal public health services involved in vaccination programmes 3.Experts from the national pharmacovigilance centre 4. Decision-makers	Direct contact through informal consultation and publicly available information.	Not applicable	Not applicable

Country	Method	Healthcare professionals to be included	Approach to recruitment	Alternative approach for recruitment	Additional information
Portugal	Survey	1. Nurses who administered vaccines 2. Physicians who performed the diagnosis and treatment of TTS (clinical haematologists, internal medicine, GP, vascular surgery, neurology, among others) 3. Community pharmacists	1. The recruitment strategy for the healthcare professionals' online questionnaire will include professional networks, collaboration with professional associations (Pharmacists, Physicians and Nurses) and social media	Not applicable	Not applicable
	Interviews	1. Healthcare Professionals from different settings (physicians from distinct categories, pharmacists, and nurses) and policy makers	1. Recruitment via professional networks or associations	Not applicable	Not applicable
Slovenia	Survey	1. General practitioners and nurses involved in the vaccination 2. Physicians who performed the diagnosis and treatment of TTS (clinical haematologists, but also internal medicine specialists and general practitioners, among others) 3. Community pharmacists	Recruitment via professional networks or associations	Not applicable	Not applicable
	Interviews	1. Decision makers and public health experts involved in the national COVID-19 vaccination strategy 2. Healthcare Professionals from different settings involved in vaccination or TTS diagnosis/treatment	Direct contact through informal consultation and publicly available information.	Not applicable	Not applicable

10.2 WP 2 – Healthcare professionals' interviews - Recruitment of professionals

The individual interviews will be conducted in six countries (DK, GR, LV, NL, PT, SI). This approach was chosen for practical reasons as it enables easier contract and scheduling, it conveys the possibility for professionals to talk more openly in their own language and to share information that would otherwise not be shared in group setting. Potential limitations of this methodological choice are further discussed under Item 5.
These interviews will be held with five to eight HCPs per country, professionals who were actively involved in vaccinating citizens against COVID-19 or treating any eventual adverse events arising from COVID-19 vaccination in the period between April and June 2021. When possible, we will also aim to interview a healthcare professional who has acted as decision-maker, thus responsible for adopting or adapting the EMA communication into national policies (through dedicated task forces, advisory boards, etc). We will identify the members of national task forces/expert advisory teams in each participating country and will invite the HCPs among them to participate. To identify the relevant national task forces and expert advisory teams, the information in WP1 for reconstructing the timeline and COVID-19 vaccination policies will be used. Each national team will compile a list of relevant national task forces and expert advisory teams. Members of these task forces/teams are identified, for example by consulting public websites, experts and governmental organisations. Depending on the national situation, the national teams will select suitable respondents for the interviews. However, as the COVID-19 pandemic is still ongoing and these task forces/ expert advisory teams are still operational, their participation might be impaired.

10.3 WP 3 – Citizens - Recruitment

Each of the six participating countries (DK, GR, LV, NL, PT, SI) has selected the most suitable strategy to obtain a sample of their country's adult population, as described below. In some countries, snowball sampling is foreseen. Nevertheless, we will aim to recruit diverse responders to include different sociodemographic subgroups of adult population. In the Netherlands, a representative sample of the population will be canvassed. However, this sample will not have the power to establish any causality between risk communication and impact on awareness, knowledge and attitudes. While we strive to obtain data saturation, there is no way in which we can prove it quantitatively and thus formally confirm that it has been achieved[12] .It should be noted that given this is a qualitative study, the goal is that of obtaining a breadth of responses which reflect the diversity in attitudes and behaviours that are to be found in each country. Given the varying sampling methodologies, overall representativeness cannot be guaranteed. Nevertheless, we will strive to have all sociodemographic groups represented in each country through methods described below.

Country	**Method**	**Approach to recruitment**	**Alternative approach for recruitment**	**Additional information including representativeness**
Denmark	Survey	1. Through social media (via snowballing)	Not applicable	The effort will be targeted so that those who first receive the links belong to different ages and educational backgrounds then recruitment will occur through snowballing (asking recipients to forward the link).
Greece	Survey	1.Through social media platforms (Facebook,	3. Direct questionnaire implementation using	In Greece, no service nor specific platform is

		blog forums) 2. Distribution of cards/leaflets with the QR code or link to the online questionnaire will be at venues visited by citizens such as municipalities, community pharmacies, primary health care settings, etc.	portable electronic devices (laptops/tablets) by approaching citizens at public venues (subject to ongoing COVID-19 mitigation measures).	available to collect a representative sample and there is limited time available for recruitment. Social media recruitment yields a good response and targets varied age groups and socioeconomic /educational backgrounds. Distribution of cards will allow outreach to citizens who might not be familiar with social media platforms. Finally, direct collection will facilitate surveying citizens less familiar with technology (elderly groups, people with IT difficulties, etc.) and allow them to complete the questionnaires.
Latvia	Survey	1. Through social media, online groups, and mailing lists (via snowballing)	2. Recruit responders via community pharmacies and primary care practices	Social media recruitment results in a sample that represents diverse sociodemographic subgroups of the general population. We consider that snowball sampling is appropriate to capture a wide range of views from different socioeconomic groups.
Netherlands	Survey	1. A citizen research panel, outsourcing through an independent research company	Not applicable	The independent research company operates an extensive citizen research panel. The characteristics of panel members are

				known to the company which then selects a sample representative of the Dutch population. The company is a designated supplier selected by RIVM and applies validated strategies to reach the target response.
Portugal	Survey	1. Through on social networks (Facebook, LinkedIn),), targeting websites, sending the questionnaire to contact lists (via snowballing)	Not applicable	We are unable to use online panels We do not foresee selection bias when using contact lists as we will not use prespecified lists related to vaccination, but the mailing lists from our home institutions (two Portuguese universities). These contact lists include individuals from different age groups, socioeconomic strata, and education levels (academia, administrative and technical staff, study assistants, housekeeping services, etc.)
Slovenia	Survey	1. Recruit via "online panels," from one of the agencies providing services in market/social/public opinion research	2. use an alternative agency to provide an "online panel" 3. Recruit citizens via social media platforms (Facebook, blog forums)	Such panels are highly responsive. They are also weighted according to the population characteristics (e.g., age, gender).

11 Variables

11.1 Work Package 2

In the web-based survey to healthcare professionals, variables of interest will cover:

(11) HCP's own working/vaccination duty context (vaccination centres, own medical practice, hospital).
(12) Source of information about the risk for TTS (through media, professional society, direct healthcare communication, SmPC, instructions from authorities).
(13) Knowledge and awareness about direct healthcare professional communications (DHPCs).
(14) Whether they have witnessed any TTS cases in their vaccination practice.
(15) Knowledge and awareness of the signs and symptoms of TTS and the need to refer to specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat the condition; any instructions from vaccination authorities and/or national competent authorities for medicinal products and/or clinical practice guidelines when coming across TTS [5];
(16) Provision of information to citizens about the TTS warning signs/symptoms and need to seek further health assistance should they occur.
(17) Knowledge and awareness of (updated) clinical guidelines and recommendations from learned societies for treating TTS (e.g., with anticoagulants) when available/applicable.
(18) Knowledge and awareness of the contraindications to use adenovirus vector vaccines in patients who have experienced TTS following vaccination with Vaxzevria.
(19) Change to attitudes towards the COVID-19 vaccination campaign and national vaccination programme after TTS risk communication.
(20) Willingness to receive future (booster) vaccination(s) against COVID-19.

In the interviews, healthcare professionals will be asked about:
- how they perceived the events and the risk communication about the two adenovirus vector vaccines in their country
- the views and actions of HCPs regarding the Janssen and Vaxzervia vaccines,
- their concerns, ideas, and questions about the risk communication and the impact thereof.

11.2 Work Package 3

In the web-based survey to citizens, variables of interest will cover:

(12) Respondent characteristics: age, gender, belonging to a risk group for COVID-19 and/or a professional group with vaccination priority according to the national vaccination policy.
(13) Present status of vaccination against COVID-19 and period of first /second/booster vaccination.
(14) Vaccine(s) received.[6]
(15) Awareness and perceptions about the benefits and risks of the SARS-CoV-2 adenovirus vector vaccines.
(16) Awareness and perceptions about the risk for TTS from adenovirus vector vaccines.
(17) Source of information about the risk for TTS.
(18) Awareness about changes in COVID-19 vaccination policy and their impact on own perceptions and attitudes regarding vaccination against COVID-19.
(19) Changes to own attitudes towards vaccination against COVID-19 and use of COVID-19 vaccines: no vaccination against COVID-19, postponement of vaccination, decision to change vaccine.
(20) Changes to own attitudes towards vaccination programmes in general.
(21) Changes to own attitudes towards potential vaccination of their young adult-teenager children against COVID-19.
(22) Willingness to receive future (booster) vaccination(s) against COVID-19.

[5] Depending on country.
[6] Our recruitment does not restrict respondents to citizens who have received adenovirus vaccines. We are also interested in finding out whether citizens' choice of vaccine/or their decision not to take vaccine has been affected by the risk communication.

11.3 Exposure of interest

The exposure of interest will concern regulatory actions, comprising risk communication activities and materials, among which:

- Updates to Summary of Product Characteristics
- Updates to Package Leaflet/Patient Information Leaflet
- Direct to Healthcare Professional Communication Letter Safety Signal
- Updates to Guidelines/Guidelines from Health Authorities
- Recommendations from professional bodies
- Safety updates on the website of the European Medicines Agency
- Updates to the Risk Management Plan

In addition, other factors might also have affected awareness and knowledge about TTS.

For healthcare professionals:

- Government communications
- Mainstream Media (TV, radio, newspapers)
- Professional or scientific journals
- Manufacturers (e.g., printed, or electronic materials)
- Internet (social media, Facebook, LinkedIn, news portals)
- Symposia or conferences
- Academic studies
- Continuing education
- Informal contacts

For citizens:

- Government communications
- Mainstream Media (TV, radio, newspapers)
- Internet (social media, Facebook, LinkedIn, news portals)
- Informal contacts

12 Data sources

In this study, no established data sources are used.

In WP 1 – The data to compile the overview and timeline of COVID-19 vaccination policies in each country will be collected through a grey literature review.

In WP 2 - Data will be obtained through cross-sectional data collection, including both survey among healthcare professionals and semi-structured interviews with healthcare professionals.

In WP 3 - Data will be obtained through cross-sectional data collection, through survey among citizens.

13 Study size

Work package 1 will cover policy decisions from 6 EU member states (DK, GR, LT, NL, PT, SI). Work package 2 aims to survey 500 healthcare professionals in 5 EU member states (GR, LT, NL, PT, SI) . And interview 30-50 professionals in 6 EU member states (DK, GR, LT, NL, PT, SI).
Work package 3 will survey 900 citizens in six EU member states (DK, GR, LT, NL, PT, SI).

14 Data management

Processing of personal data will comply with the EU data protection legislation and in particular Regulation EU 679/2016 on General Data Protection Regulation (GDPR). Citizens and HCPs will participate anonymously in the questionnaires. All data will be either collected anonymously or anonymised by the national teams. This means that no data that can identify individual citizens or HCPs is to be collected (e.g., name, address, social security number). For HCPs who accept to be contacted for the in-depth interviews, their identification will be kept encrypted to comply with the GDPR. Only fully anonymised data will be shared with the coordinating team. National teams will also be responsible for ensuring (obtaining, compiling, and archiving) ethical approval and participants' informed consent. The coordinating team will provide a template for an informed consent form in English for both groups of respondents, HCPs and citizens, respectively.

15 Data analysis

In WP 1, each national team will provide the overview and timeline of COVID-19 vaccination policies to the study coordination team for compilation according to a standardised and agreed format. These will consist of data collection and grey literature review. These overviews will be scheduled for the start of the project to provide input to the drafting of the surveys and the interview guides. The EMA risk communication activities/ events and the changes to national vaccination policies over time will be plotted per country and presented visually.

The surveys in **WP2** and **WP3** will generate descriptive statistics. For categorical variables, frequencies and percentages will be reported, and for continuous variables, mean, standard deviation (SD), or median and interquartile range (IQR) will be reported. We will conduct univariate and bivariate analyses according to the stratifying variable, where applicable. The difference in risk awareness, knowledge and adherence with regulatory communication on SARS-Cov-2 adenovirus vector vaccines (based on responses received from relevant questions in the surveys) between various groups of HCPs or patients will be assessed by Chi-square test for categorical variables, student t-test for continuous variables with a normal distribution, and Mann-Whitney U test for continuous variables without a normal distribution. Statistical significance will be considered as a p value <0.05. The information received as free text (from open questions in the questionnaires) will be extracted at each national team and enable additional qualitative content analysis (please see below). Moreover, participation rates for each survey (HCP and citizens) will be calculated per each centre. Given the variation in vaccination policies and the need to tailor questionnaires to participating countries, survey data will be analysed at national level. Data will be analysed using IBM SPSS Statistics Version 27 (IBM Corp., Armonk, N.Y., USA).

For the qualitative data, the analysis involves a deductive content analysis based on a close line-by-line reading of the responses and developing a conceptual coding scheme based on the major themes in the interview guides. Transcripts will be coded individually by two researchers in each country in their native languages. Coders from all countries will meet prior to the analysis to predefine categories and codes to be used. They meet again to evaluate the categories identified and to write up the results using illustrative quotes.

16 Quality control

16.1 Tailored quality control

The coordinating team will rely on a peer review model of consultation to inform and direct the study deliverables using the timeline above to monitor and benchmark progress by which outcomes are assessed. To establish a quality control system specific to this study, we have identified key milestones which will attest to the efficient roll-out and continuity of the service.

These are, respectively:

- M1: Milestone 1: Citizens' and HCPs' Questionnaires available
- M2: Milestone 2: Recruitment of Respondents completed
- M3: Milestone 3: Coordinating team receives all the results from national analyses from NTs
- M4: Milestone 4: Draft Report
- M5: Milestone 5: Draft Manuscript

In addition, we also provide below a list of verifiable indicators along the timeline:

Specific Task	Standard Verifiable Indicators
Kick-off meeting	Agenda Meeting Minutes Action Points Agreed Timeline
Development of questionnaire	Draft questionnaire
Pilot testing of questionnaire	Pilot questionnaire and final version of questionnaire
Recruitment of respondents	Number of healthcare professionals and citizens recruited per country
Implementation questionnaire	Response rates (monthly)
Interviews in key countries	Interview/ guides
Drafting preliminary report	Preliminary Report
Review of draft report	Responses received
Drafting manuscript	First draft manuscript
Manuscript review	Responses received

16.2 Overarching quality control

Several quality assurance measures are in place that will be maintained in the proposed consortium. We will take into consideration existing guidelines for qualitative research (such as QOREC) and apply them as appropriate. Additionally, we will share approaches to data collection and analysis. Deliverables are peer-reviewed by an advisor (at least one member of the consortium that is not leading nor actively participating in the study). A declaration of competing interests will be required from all those acting as principal investigators or co-investigators. These will be further presented to the Steering Committee who will then assess and act upon any potential conflict of interest. In addition, we aim to comply with ENCePP standards. We have registered our study on the European Union electronic Register of Post-Authorisation Studies (EU PAS 44970)[13] and have successfully obtained the ENCePP Study Seal (See Annex 2).

16.3 Quality management system for the Coordinator of the consortium (Utrecht University)

The Division of Pharmacoepidemiology & Clinical Pharmacology works according to a quality management system based on ISO 9001 principles. The quality management system is system and process oriented and based on continuous improvement. All primary and secondary processes within the division are included in the quality system, from creating research proposals, through managing PhD projects to data management, reporting and archival. The system is based upon standard operating procedures implemented throughout the division with regular internal audits as well as external audits that lead to certification. The quality management system is based on national and international external quality requirements where available and pertinent, as well national, and international guidelines and legislation concerning data-handling and privacy issues.

16.4 Research Quality Assessment (Utrecht University)

In 2017 (evaluation period 2010-2015), the research quality of the Utrecht Institute for Pharmaceutical Sciences (UIPS) which includes the division of Pharmacoepidemiology & Clinical Pharmacology was assessed by an independent international peer review committee according to the Standard Evaluation Protocol 2015-2021 (SEP) for Research Assessment in the Netherlands. The overall conclusion of the committee was that the division was one of the top ten if not the top five worldwide and that excellent scientific work was being done, grounded in real-world problems and with a notable impact on the regulatory world, particularly in Europe. The scores received were all excellent for the Quality, Relevance to Society and Viability criteria. This report is available upon request.

16.5 Strategies to prevent or counter any events that could hamper or delay the research

Foreseen external delays, methodological or technical problems and their proposed counter measures:

- **Specific requirements for ethical approval for research and data protection** regulations are to be addressed at protocol stage, considering national and European settings.
- To avoid **delays in ethical approval**, the questionnaires will be submitted in English, when possible.
- Given the tight study timeline, **pilot testing in more than one country is not feasible**. The translation of the survey into the six different national languages will be conducted according to the translation protocol (Annex 8). The protocol foresees an independent review of each translated survey by a native speaker not involved in the study team. In this manner, we aim to identify culture- and language-specific issues to enable adjustment as needed.
- To avoid **delays in the questionnaire implementation**, recruitment will be initiated as early as possible.
- **Recruitment of specialists** involved in the provision of guidance or treatment of adverse events arising from COVID-19 vaccination might prove difficult to recruit in less populated countries, where the number of specialists is reduced. The solution will then include an oversampling of other healthcare professionals meeting our inclusion criteria.
- To avoid **delays in data analysis**, specific instructions will be delivered to the country researchers. In exceptional circumstances, the coordination team can resort to directly analyse the data which is stored in the centralized survey database.

17 Limitations of the research methods

Study limitations	Definition	Applicable to	Mitigation strategy

Recall bias	Recall bias occurs when there are systematic differences in the way subjects remember or report exposures or outcomes.	Web-based questionnaires and interviews. Although the current study will use a semi-qualitative descriptive design, recall bias might still occur. Any baseline attitudes of healthcare professionals and patients towards Covid-19 vaccination might now be recalled differently due to the later occurrence of thrombosis events after Vaxzevria or COVID-19 Janssen vaccination and due to their vast media coverage. Communications, safety updates and product information changes by the EMA conducted during late 2021 and 2022[14] [15] [16] [17] might also impact on how participants respond to the questionnaires and interviews.	Recall bias can be an issue, when there is no baseline measurement and when all parameters are to be ascertained retrospectively. However, we will consider this limitation when interpreting our results by considering the direction of the bias on our findings. In the national questionnaires for both citizens and HCPs, each NT will include a visual cue of the national timelines (of activities/events/policy changes) in order to provide the respondents the context of 2021 when the vaccination campaigns were implemented (see example in Annex 7). Another possibility is the use of text, for an example see the Citizen's questionnaire, Q12 and Q13.
Information bias - Hawthorne effect	There is a change in behaviour of research participants in an experimental or observational study, due to the interest, attention, and care that they receive from the researcher	Interviews. Participants' opinion about our outcome of interest might be influenced by the mere fact of being questioned about it by a researcher.	This is a general obstacle in every qualitative study using interviews, but we do not expect a significant effect from this bias on our results if we coordinate efforts to train interviewers.
Selection bias – Country differences	National differences in the healthcare systems of the countries included in this study might also imply differences in information dissemination to healthcare professionals and the public at large.	Web-based questionnaires and interviews.	Consider this limitation when interpreting our results by considering how the variation in health systems might affect our findings.
Study limitations	**Definition**	**Applicable to**	**Mitigation strategy**
Non-responder bias	It implies that non-responders to the survey can have other	Web-based questionnaires and interviews.	At RIVM in the Netherlands, a special research unit studied the Dutch population's behaviour

	characteristics than the responders.	For instance, it could prove challenging to include older people into the web-based survey since many elderlies are not familiar with computer use. Furthermore, it might be difficult to include respondents from vulnerable population groups which are also more vulnerable to COVID-19, such as people suffering from mental disorders, or people with low health literacy.	during the COVID-19 pandemic. This offers us useful information to assess biases in our study results. We will also investigate data available from other national surveys focusing on population behaviour in other Member States, when available. As TTS is a side effect occurring in younger groups, we do not expect that a lower participation of elder population will impact on our results.
Response bias – Acquiescence or agreement bias	Respondents tend to select a positive response option or indicate a positive connotation disproportionately more frequently.	Web-based questionnaires and interviews.	Introducing carefully crafted, open-ended questions and carefully working closed-ended questions and response categories to increase the probability of nuanced and varied responses.
Response bias - Extreme responders	It drives respondents to only select the most extreme options or answers available.	Web-based questionnaires and interviews. We may obtain an overrepresentation of persons who are very engaged or opinionated one way or another about these vaccines.	This may be culturally driven; the team will look at whether this is a phenomenon varying by countries.
Response bias - Question order	A respondent may react differently to questions based on the order in which questions appear in a survey or interview.	Web-based questionnaires and interviews.	The research team will be vigilant about not skewing views we order the questions.
Response bias - Social desirability	Tendency of survey respondents to answer questions in a manner that will be viewed favourably by others.	Web-based questionnaires and interviews	The wording of question needs to be extremely balanced, non-judgmental so that vaccine hesitant persons can respond.

18 Other aspects

Plan of operations

Project Stage (% overall study)	Coordinating Team % of specific task	National Teams % of specific task	Coordinating Team % of overall study	National Teams % of overall study
Project Inception (30)	80	20	24	6
Data Collection and Analysis (55)	20	80	11	44
Reporting (15)	80	20	12	3
TOTAL:100%			47	53

19 Protection of human subjects

Processing of personal data will comply with the EU data protection legislation and in particular Regulation EU 679/2016 on General Data Protection. All data will be either collected anonymously or for those citizens who accept to be contacted for the interviews, their identification will be kept encrypted to comply with the General Data Protection Regulation. The research team will also be responsible for ensuring (obtaining, compiling, and archiving) ethical approval or waivers and participants' informed consent.

20 Management and reporting of adverse events/adverse reactions

Not applicable to this study.

21 Plans for disseminating and communicating study results

The coordination team proposes to provide progress updates should there be any delays/deviations from the expected timelines.

Two study deliverables are relevant for dissemination of results (see chapter 6):

- The study report will be submitted to EMA. This report will only be available to the EMA, and is not to be shared publicly, unless otherwise decided by the Agency.
- A manuscript which is to be submitted to a peer-reviewed open access scientific journal so that the study findings can be shared publicly.

In addition, in accordance with the ENCEPP requirements, a summary of the study results will also be uploaded to EU PAS once the study is completed.

Annex 1. List of stand-alone documents

The questionnaires for WP2 and WP3 are added as stand-alone documents.

Number	Document reference number	Date	Title
1	Q_HCP_ EN 3.0	8 April 2022	Questionnaire for healthcare professionals
2	Q_C_EN_3.0	8 April 2022	Questionnaire for citizens

Annex 2. ENCePP study seal - letter confirmation

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

Dr. Olaf Klungel
Utrecht University Pharmacoepidemiology Center
Utrecht, 3508 TB
Netherlands
o.h.klungel@uu.nl

23 February 2022
EMA/119060/2022
ENCePP Secretariat

RE: EUPAS44970 - Impact of EU label changes and regulatory communication on SARS-CoV-2 adenovirus vector vaccines in context of thrombosis with thrombocytopenia syndrome (TTS): risk awareness and adherence

Dear Dr. Olaf Klungel,

On behalf of the ENCePP Steering Group I am writing to you to acknowledge fulfilment of the conditions for your study to qualify for the ENCePP Seal. We have received all required documentation[1] and the study has been included in the EU PAS Register prior to its start.

I am, therefore, pleased to confirm that your study has been awarded *a priori* the ENCePP Seal which will be displayed with the study entry in the EU PAS Register.

I would like to remind you of the additional obligations the ENCePP Seal places on the conduct of your study, namely to adhere to the entirety of the provisions of the ENCePP Code of Conduct throughout the research process. In particular, you are obliged to:

- Update the entry of the study in the EU PAS Register, as milestones are reached or in case of changes to the protocol that may affect the interpretation of the study;
- Update the Checklist for Study Protocols and re-submit it via the EU PAS Register in case of changes to the protocol that may affect the interpretation of the study;
- After finalisation of the study report, provide the final version of the protocol through the EU PAS Register. Both the original and the final versions of the protocol will be made publicly available at that stage.
- Make publicly available a clear summary of the main results of the study, whether positive or negative and including results from prematurely terminated studies according to the timetable agreed in the research contract. In addition, an abstract (in English) of the study results shall be provided, via the EU PAS Register, for publication within 3 months following the final study report.

I also remind you that it is your obligation to inform the ENCePP Secretariat without delay if the study deviates from and/or no longer follows the rules of the ENCePP Code of Conduct. In this event the

[1] Signed copy of Checklist of the ENCePP Code of Conduct, Declaration on compliance with the ENCePP Code of Conduct, ENCePP Checklist for Study Protocols and Declaration of Interests.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

concerned study shall not be entitled to the ENCePP Seal and this information will be made public on the ENCePP website.

We take this opportunity to thank you for your contribution to ENCePP.

Kurz Xavier Digitally signed by Kurz Xavier Date: 2022.02.23 10:40:08 +01'00'

Dr Xavier Kurz
On behalf of the ENCePP Steering Group

Annex 3. Further information about the investigators

Overview of teams

This Annex provides an overview of all the teams involved, both in the coordination and per country, including their background and expertise, as well as contact details.

Country: Denmark

Description of the institution (including location): Social and Clinical Pharmacy (SCP) is a research group under the Department of Pharmacy, Faculty of Health and Medical Sciences, at the University of Copenhagen. SCP's research is within three broad topic areas of Medicines Use, Clinical Pharmacy, and Pharmaceutical Policy. Research within each focus area can be situated on one or more of the levels of the user, organization, and society.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team DK): Anna Birna Almarsdóttir is Professor of Social and Clinical Pharmacy. She has more than 25 years of experience with social and clinical pharmacy research, which have included areas such as health services research, pharmacoepidemiology, and drug utilization research. Her focus is currently on developing clinical pharmacy services (in the primary, secondary and tertiary health care sectors), and pharmaceutical policy analysis using both qualitative and quantitative research methods. Her methods interests are questionnaire construction, scale development, and triangulation of qualitative and quantitative research methods. She graduated as PharmD from the University of Iceland in 1988 and received a PhD degree in Health Policy Analysis in 1994 from the University of North Carolina at Chapel Hill, USA. Her work experience includes Assistant and Associate Professorships in Social Pharmacy, at the Royal Danish School of Pharmacy and the University of Iceland, and Professorships at the University of Iceland and the University of Southern Denmark. In addition, she held a position as Senior Pharmacoepidemiologist at DeCode Genetics Inc and consulted with the pharmaceutical industry in Iceland. Ramune Jacobsen is an Assistant Professor in Clinical pharmacy; she has more than 15 years of experience with social pharmacy and public health research, including implementation and evaluation research in health services for chronic disease management, epidemiological research in disease prevention, and survey-based research for health promotion. She graduated as a Master in Medical Biology in Moscow (Russia) in 1994, and as a Master of Public Health in Kuopio (Finland) in 2003 and earned her PhD in Social Pharmacy in 2010 in Copenhagen (Denmark). Caroline Buhl is a research assistant at the Social and Clinical Pharmacy group. She has a year of experience working in a community pharmacy. Moreover, she has experience in development and analysis of surveys from her master thesis. She received her Master in Pharmaceutical Science from the University of Copenhagen in 2022.

Contact person: Prof. Anna Birna Almarsdóttir

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Country: Greece

Description of the institution (including location): Our Laboratory of Hygiene and Environmental Protection belongs to the Faculty of Medicine, School of Health Sciences, Democritus University of Thrace, Alexandroupolis, Greece. It presents an extraordinarily strong background on epidemiological studies and preliminary experience on pharmacoepidemiologic analysis and data analysis.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team GR): Christos Kontogiorgis, Assistant Professor has experience in pharmacoepidemiologic studies. Theodoros Constantinides, Professor is an expert in epidemiological studies and statistical analysis. Evangelia Nena, Associate Professor, expert on epidemiological studies and statistical analysis. Elena Deligianni, Pharmacologist, MSc, PhD student has expertise in pharmacoepidemiologic analysis and drug utilization studies. Chara Oikonomou, PharmD with expertise in pharmacoepidemiologic analysis and drug utilization studies. Foteini Dermiki-Gkana, PharmD, presents expertise in epidemiological analysis and drug utilization studies.

Contact person: Christos Kontogiorgis, Assistant Professor
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Tel: 2551030601, 6974659919,
Fax: 2551030546

Country: Latvia

Description of the institution (including location): The Institute of Public Health of Riga Stradins University is in Riga, the capital of Latvia. The objective of the RSU Institute of Public Health is to carry out research, undertake academic training and promote the acquisition and improvement of scientific qualifications in public health and healthcare organization. The institute has research expertise in areas such as sexual and reproductive health, HIV, diabetes, nutrition, pharmaceutical policy, health systems, economics, and many others.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team LV): Elita Poplavska, PhD is an assistant professor at the Faculty of Pharmacy and senior researcher at the Institute of Public Health. She holds a PharmD from Riga Stradins University and a PhD in Social and Administrative Pharmacy, University of Minnesota. Her research activities are related to pharmaceutical policy, medicines use research and pharmaceutical promotion involving qualitative and quantitative research methods. Mirdza Kursite, MD, MS is a lecturer at the Faculty of Public Health and Social Welfare. She holds an MD and Master's degree of Health Sciences in Health care from Riga Stradins University. Her research activities are related to patient - physician communication, adherence to therapy and health beliefs involving qualitative and quantitative research methods.

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Country: Portugal

Description of the institution (including location): Porto Pharmacovigilance Centre (PPC) is a Portuguese regional pharmacovigilance centre, part of the National Pharmacovigilance System which coordinated by Infarmed (National Authority of Medicines and Health Products, I.P.). PPC is based on the Department of Community Medicine, Information and Health Decision Sciences of the Faculty of Medicine of the University of Porto since its creation in 2000. The PPC covers a region with 1.8 million inhabitants and 24000 healthcare professionals and works closely with healthcare institutions, namely hospitals, primary health care units and community pharmacies.

Description of the research team/researcher(s) involved as to their background, competences and interests (Country Team PT): Inês Ribeiro Vaz has a Doctorate degree in Clinical Research and Health Services, awarded by the Faculty of Medicine, University of Porto in 2016 with the thesis: "Using Information Systems in Pharmacovigilance. She has a Master on Public Health awarded by the Faculty of Medicine, University of Porto in 2009. Has a degree in Pharmaceutical Sciences awarded by the Faculty of Pharmacy, University of Porto in 1999. Performs duties as technical and scientific coordination of the Porto Pharmacovigilance Centre since 2003 and, over the last 15 years, has published several papers, both as author and as co-author, in pharmacoepidemiology, pharmacovigilance and drug safety.
Ana Marta Silva is also a pharmacist working at Porto Pharmacovigilance Centre since 2013. During this year, she has been working extensively on the pharmacovigilance of vaccines against COVID-19. She is a PhD student with an ongoing thesis about the impact of COVID-19 in pregnant women.
Paula Barão has a Master in Pharmaceutical Care awarded by the Faculty of Pharmacy, University of Lisbon in 2013 and a degree in Pharmaceutical Sciences awarded by the Faculty of Pharmacy, University of Lisbon in 1995. She works as a pharmacovigilance expert at the Lisboa, Setúbal and Santarém Pharmacovigilance Centre since 2011 and is a PhD Student with an ongoing thesis about risk minimization measures on pregnancy.

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Country: Slovenia

Description of institution (including location): Faculty of Pharmacy (FFA), University of Ljubljana (UL) is the only university organization in the Republic of Slovenia for the study of pharmacy and laboratory biomedicine. The Faculty of Pharmacy follows the concept of scientific pharmacy and clinical biochemistry and considers research and study as two inseparable parts. By European standards FFA is a medium-sized faculty. Yearly it admits 150 students of Uniform master's study program Pharmacy, 40 students at University study program Laboratory Biomedicine, 40 students at University study program Cosmetology, 40 students of Master's study program Laboratory Biomedicine, 25 students of Master's study program Industrial Pharmacy, and about 30 students of 3rd cycle of Bologna study program Biomedicine. Established in 1997 the Chair of social pharmacy focuses on the development of academic and experimental grounds for education and research in the broader area of social pharmacy. The area of interest are the influences of drugs as material, biomedical, ethical, and proprietary category on the modern individual and society. Research includes pharmacoepidemiology, pharmacoeconomic and outcomes research. The Chair is devoted to the study of properties and development of information technology in acquisition and transfer of knowledge about medicines. It studies the role of pharmaceutical profession in the modern societies, and the methods of communications between pharmacists and other health professionals, and with lay public. Central concepts of interest are also patient counselling and pharmaceutical care.

Description of the research team/researcher(s) involved as to their background, competences, and interests
Established in 1997 the Department of social pharmacy focuses on the development of academic and experimental grounds for education and research in the broader area of social pharmacy. The area of interest are the influences of drugs as material, biomedical, ethical, and proprietary category on the modern individual and society. Research includes pharmacoepidemiology, pharmacoeconomic and outcomes research. The Department is devoted to the study of properties and development of information technology in acquisition and transfer of knowledge about medicines. It studies the role of pharmaceutical profession in the modern societies, and the methods of communications between pharmacists and other health professionals, and with lay public. Central concepts of interest are also patient counselling and pharmaceutical care.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country team SI): Prof. Mitja Kos, M Pharm: Mitja Kos is the Head of the Department of Social Pharmacy and a professor for social pharmacy at the University of Ljubljana, Faculty of Pharmacy, Slovenia. He graduated as a pharmacist in 1999 and defended his doctoral thesis on the topic of off label prescribing in 2005. He has developed expertise in several different fields including pharmacoeconomic and outcomes research, pharmacoepidemiology, medicine pricing and regulation and pharmaceutical care practice. The focus of his scientific and professional activities are health technology assessment, comparative effectiveness, and optimization of drug use. At the Faculty of pharmacy, University of Ljubljana he has built a nationally recognized reference centre for pharmacoeconomic and evidence-based pharmacy practice. Recently, he has served as a member of the Health Council at the Ministry of Health of the Republic Slovenia and as a member of two expert commissions at the Agency for Medicinal Products and Medical Devices of the Republic Slovenia: one focusing on the evaluation of clinical trials and the other on drug prices.
Assoc. Prof. Igor Locatelli, M Pharm: Igor Locatelli graduated in 2002 at the Faculty of Pharmacy, University of Ljubljana, where he has been employed since 2003. He concluded the postgraduate study of Biomedicine at University of Ljubljana in 2008, when he defended his doctoral thesis in clinical pharmacokinetics. Between 2002 and 2010 he worked as a researcher within the Department of Biopharmaceutics and Pharmacokinetics, where he was involved in evaluation of pharmacokinetic and statistical models for analysing the data from preclinical studies and clinical trials. In 2010, he joined the Department of Social Pharmacy, since then his research work embraces studies in pharmacoepidemiology and Pharmacoeconomics with an emphasis on meta-analysis of clinical trials.
Assist. Dr. Nanča Čebron Lipovec, M Pharm: Nanča Čebron Lipovec graduated in 2010 at the Faculty of Pharmacy, University of Ljubljana and started her career as a hospital and clinical pharmacist at the University

Clinic of Respiratory and Allergic Diseases Golnik. In 2012, she became a research fellow at the same institution and started her doctoral studies in the field of Social medicine. In 2016 she defended her doctoral thesis on the topic of the effect of nonpharmacological treatment on metabolic profiles in patients with COPD. In 2017 she joined the Department of Social Pharmacy and is now teaching assistant and researcher in the field of pharmacotherapy and pharmacoepidemiology.
Assist. Prof. Nejc Horvat, M Pharm: Nejc Horvat graduated in 2007 under the supervision of Prof. Dr. Aleš Mrhar and Assist. dr. Mitja Kos. The theme title was Development of a questionnaire measuring patient satisfaction with pharmacy services. In 2014 he defended his doctoral thesis titled: Evaluation of pharmacy services from the patient and expert perspective. Currently, he is a member of different research teams within the Department of Social Pharmacy. His research focus is primarily the outcomes research, particularly evaluation of pharmacy services, health literacy and drug related problems.
Other department members: Assist. Prof. Dr. Lea Knez, M. Pharm., spec.; Assist. Dr. Ana Kodrič, M Pharm, Assist. Dr. Urška Nabergoj Makovec, M. Pharm.; Assist. Dr. Janja Jazbar, M Pharm, Assist. Sara Prelesnik, M. Pharm.

Contact person: Prof. Mitja Kos, M Pharm

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Country: Netherlands

National Institute for Public Health and the Environment of the Netherlands (RIVM)

Description of the institution (including location): The RIVM is the National Institute for Public Health and the Environment of the Netherlands and has been promoting public health and safeguarding environmental quality for over 100 years. The RIVM has expanded to become a knowledge institute at the centre of Dutch society, advising on health and environment. In our role as trusted advisor, we provide the government with impartial advice on infectious diseases, vaccination, population screening, lifestyle, nutrition, pharmaceuticals, environment, sustainability, and safety. We carry out studies, provide advice and recommendations, and direct and implement prevention and control responses. Our work is primarily commissioned by Dutch ministries and inspectorates and projects are also undertaken within international frameworks, such as the European Union and United Nations. We have many national and international partners and are continuing to build new networks in multidisciplinary cooperation. We are committed to supporting government and society in improving health and the environment.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team NL): Teresa Leonardo Alves is currently working as a Researcher for the Health Protection Unit of the National Institute for Public Health and the Environment (RIVM) in Bilthoven, the Netherlands. She holds a Pharm D in Pharmaceutical Sciences from Porto University in Portugal, a Master in Public Health from the Netherlands Institute of Health Sciences (Erasmus University, Rotterdam) and a PhD in Pharmaceutical Policy, Utrecht University, Netherlands. She has more than fifteen years' experience in the coordination and public relations of not-for-profit organizations in the field of pharmaceutical policy, having worked for the *International Pharmaceutical Federation, Health Action International* and the independent bulletin *Prescrire* in a variety of positions covering project management, communications, and policy advocacy. She has developed invaluable knowledge of key stakeholders in European pharmaceutical policy as well as evidence-based advocacy skills. This has required expertise in identifying and maintaining contacts with NGO networks, policymakers, academia, and health authorities. She has also gained extensive experience as a fundraiser, public speaker, event organizer, editor, and coordinator of international studies. From March 2020 to June 2021, she was seconded as Senior Policy Officer at the Ministry of Health, Welfare and Sport in the Netherlands, working on international pharmaceutical policy. At the RIVM, her research has focused on pharmaceutical products and medical devices, covering a wide range of aspects including rational use, shortages, as well as safety and risk minimisation.
Ingrid Hegger has worked at the National Institute for Public Health and the Environment since 1988. In doing so, she became an expert on the regulation of medicinal products, with special interest in biologicals. From 1990 to 1999 she was the Project Manager for the Control Authority Batch Release of immunological medicinal products and plasma derived products. She also acted as Scientific Assessor of biologicals and was member of the Biological Working Part of the European Medicines Agency from 1995 to 1999. She was also a member of the group of experts Sera and Vaccines of the European Pharmacopoeia, Council of Europe, from 1999 to 2007. Between 2001 and 2006, she was a Project leader for the batch release of investigational medicinal products for clinical trials. From 1999 onwards, her focus shifted towards "close-to-policy" projects in the field of health products, pharmaceutical care, and health policy. Between 2003 and 2006, she was a member of the National working party for the implementation of EU directive 2001/20 on clinical trials. She has been involved in many projects covering a wide variety of topics, among which: existing barriers in the regulation of medicinal products, pharmaco-economics, orphan diseases, advanced medicinal products, clinical trials, eHealth, pharmacogenomics, pharmaceutical crime, and risk-based supervision. In addition, her Ph.D. focused on the utilization of knowledge within public health policy and healthcare supervision.

Contact person from your institution for this project: Teresa Leonardo Alves
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Utrecht University

Description of the institution (including location): The division of Pharmacoepidemiology and Clinical Pharmacology of the Utrecht Institute for Pharmaceutical Sciences contributes to a better understanding of the variability in medicines' use and patient outcomes, both from a clinical, policy and methodological perspective. Despite extensive testing before marketing approval, variability in drug response (both efficacy and safety) is more the rule than the exception when medicines are used in daily clinical practice, i.e., in real life. The research program is inspired by societal needs to ensure that medicines deliver their full therapeutic potential. The program has a systems therapeutics focus, integrating various disciplines, dimensions, and phases of a product life cycle to learn about (rather than confirm) drug effects and their determinants both before and after initial marketing approval of the product. The primary conceptual anchors in the research strategy of the program are Epidemiological Methods, Clinical Pharmacology and Systems Therapeutics. Research is organized into three centers with a strong conceptual research strategy: the Centre for Pharmacoepidemiology, Centre for Clinical Therapeutics, and the Centre for Pharmaceutical Policy and Regulation.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team NL):
Dr E.R. (Rob) Heerdink PhD is an associate professor of Clinical Pharmacoepidemiology at the Utrecht Institute for Pharmaceutical Sciences, Utrecht University, and professor of Innovation of Pharmaceutical Care at the University of Applied Sciences Utrecht. He is principal investigator and managing director of the Centre for Clinical Therapeutics. His research is driven by questions from clinical practice and spans from traditional pharmaco-epidemiological methods to systems pharmacy research into context related aspects of pharmacotherapy. He has published over 200 peer-reviewed articles on topics including (psychiatric) pharmacotherapy, drug exposure patterns, adherence and the relation between pharmaceutical care and clinical outcomes and has served as co-promotor for over 25 PhD students. Dr Rob Heerdink is a founding and honorary member of the European Society for Patient Compliance and Persistence (Espacomp).
Dr Shahab Abtahi, MD MSc PhD, is a Postdoctoral Research Fellow at the Division of Pharmacoepidemiology and Clinical Pharmacology at the Utrecht Institute for Pharmaceutical Sciences, Utrecht University. He graduated in 'General Medicine' from Tehran University of Medical Sciences in 2011, obtained a MSc in 'Vitality and Ageing' from Leiden University in 2016 and read his PhD in 'Pharmacoepidemiology' at Maastricht University in 2021. His research is mostly focused on pharmacoepidemiologic studies assessing drugs' effectiveness and safety using electronic healthcare databases, such as the UK Clinical Practice Research Datalink (CPRD), nationwide Danish registries, or Dutch PHARMO Database Network.

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Annex 4. Organisation of work

Teams in the RiskAware TTS project

The Coordinating Team (CT) is composed by:

- Dr Teresa Leonardo Alves and Dr. Ingrid Hegger, Researchers at the Centre for Health Protection, National Institute for Public Health and the Environment, The Netherlands.

- Prof. Anna Birna Almarsdóttir, Research leader at the Social and Clinical Pharmacy research group, Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark.

- Dr E.R. (Rob) Heerdink , Associate professor of Clinical Pharmacoepidemiology at the Division of Pharmacoepidemiology and Clinical Pharmacology of the Department of Pharmaceutical Sciences, Utrecht University, The Netherlands.

The National Teams (NTs) are represented in the Steering Committee by:

- Denmark: Prof. Anna Birna Almarsdóttir, Research leader, Dr. Ramune Jacobsen, Assistant Professor, Caroline Buhl, research assistant, Department of Pharmacy, University of Copenhagen
- Greece: Dr Christos Kontogiorgis, Assistant Professor, Democritus University of Thrace, Department of Medicine, Laboratory of Hygiene and Environmental Protection.
- Latvia: Dr Elita Poplavska, Assistant Professor, The Institute of Public Health of Riga Stradins University.
- Portugal: Dr Inês Ribeiro Vaz, Coordinator, Unidade de Farmacovigilância do Porto, Faculdade de Medicina da Universidade do Porto.
- The Netherlands: Dr Ingrid Hegger, Expert Researcher, the Centre for Health Protection, National Institute for Public Health, and the Environment.
- Slovenia: Prof. Mitja Kos, Head of Department of Social Pharmacy, and Assist. Dr Nanča Čebron Lipovec, both: University of Ljubljana, Faculty of pharmacy, Ljubljana.

The Study Coordinator (SC) is:

- Dr Teresa Leonardo Alves, Researcher at the Centre for Health Protection, National Institute for Public Health and the Environment, The Netherlands.

The Steering Committee is composed by:

- one representative per country and one alternate per country (back-up).
- chair / vice-chair: SC and alternate.

The coordinator of the consortium is:

- Prof. Olaf Klungel, Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht University, The Netherlands.

Timelines and tasks

The study started in **November** with an online kick-off meeting organised by the Study Coordinator (SC), during which all those involved in the project became familiar with their counterparts in other countries and the study coordinator. The Coordinating Team (CT) is responsible for hosting and preparing the content discussions, which will cover communication aspects, data management, and compliance with timelines and feedback procedures. An email-distribution list has been established to share information among all those involved, and telephone and online meetings are scheduled on a regular basis to oversee project implementation and progress.

During November, the development of the study plan has been initiated by the Coordinating Team, but National Teams (NT) were invited to review and provide input. A similar procedure will be implemented for the study protocol in **December and January**.

In December, a standard format to prepare the overview and timeline has been drafted by the SC and agreed upon by the CT and NTs. During M2, the NTs will be responsible for providing the overview and timelines of the COVID-19 policies in their own country. These overviews will provide important background information to the surveys and the interview guide. These national overviews will be compiled later in M3 into an overall overview by the Study Coordinator and will be subsequently reviewed by the Coordinating Team and the National Teams.

In December, the Dutch national team based in Bilthoven (RIVM) is responsible for developing the first draft of the healthcare and patient questionnaires in English. These will be subsequently reviewed by the Coordinating Team and the National Teams.

In March/April, The Dutch team will translate them into Dutch and pilot test them in the Netherlands in a small sample of healthcare professionals and citizens. The questionnaires will subsequently be improved, translated back into English and then into the language(s) of the participating countries, as needed, according to protocol.

Between April and June, National Teams will include seeking Ethical Approval providing the translated final questionnaires.

All National Teams are also invited to start recruiting respondents **from April onwards**, as this is the most limiting factor for a successful implementation. Recruitment of participants and survey implementation are likely to overlap between May and June. Throughout the questionnaire implementation and data analysis, the Coordinating Team will schedule online meetings to receive feedback on project progress.

Between May and June, National Teams will recruit HCPs for interviews and conduct the interviews.

Between June and July, each National Teams is expected to analyse their local data. The coordinating team will compile those and compare results across countries, when applicable.
All the analyses are expected to have been delivered to the Coordinating Team.

Between July and August, the Coordinating team will take the lead on the reporting, drafting both the preliminary report and the preliminary manuscript. Both documents will also be reviewed by the national teams.

The timeline described below provides an overview of the study chronology together with main tasks, including responsible teams, identifying also the main milestones (indicating project progress) and deliverables. It can be subject to adjustments, as necessary.

Timing:
November 2021 to- October 2022 = 12 months

TIMELINE	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct
Project inception												
Organization kick-off meeting	CT											
Kick-off meeting Installation Steering Committee	CT NT											
Development of preliminary study plan	CT NT	CT NT										
Study plan delivery		**D1**										
Development of standard format overview COVID-19 vaccination policy		CT										
Development of instructions for recruitment forms and of harmonized consent forms		CT										
Developing overview and timeline COVID-19 vaccination policy	NT	NT	NT	NT	NT							
Development of questionnaire health care professionals	NL	NL CT	NL CT	NL CT	NL CT	NL CT						
Development of questionnaire citizens	NL	NL CT	NL CT	NL CT	NL CT	NL CT						
Writing and reviewing protocol		CT NT	CT NT	CT NT	CT NT	NL CT						
Protocol delivery						**D2**						
Registration of study and protocol in EU PAS Register, obtaining ENCePP Seal	CT	CT	CT	CT	CT							
Monitoring progress	CT	CT	CT	CT	CT	CT						
Data collection and analysis												
Pilot testing of questionnaire healthcare professionals			NL		NL	NL M1						
Pilot testing of questionnaire citizens			NL		NL	NL M1						
Tailoring questionnaires to national setting and translating							NT					
Seeking Local Ethical Committee Approval						NT	NT	NT				
Hosting web-based questionnaires					CT	CT	CT	CT	CT			

TIMELINE	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**October**
Recruitment of respondents - healthcare professionals							NT	NT				
Recruitment of respondents - citizens							NT	NT				
Implementation questionnaire healthcare professionals							NT	NT				
Implementation questionnaire citizens							NT	NT				
Data analysis questionnaires and delivery							NT	NT M3				
Compiling overviews and timelines COVID-19 vaccination policies				CT	CT	CT	CT					
Development of interview guide			CT				CT	CT				
Recruitment of HCPs for interviews in 6 countries							NT	NT	NT			
Interviews HCPs in 6 countries								NT	NT			
Data analysis interview and delivery								NT	NT			
Monitoring progress	CT	CT	CT	CT	CT	CT	CT	CT	CT			
Reporting												
Drafting preliminary report						CT	CT	CT	CT	CT M4		
Review of draft report										CT NT	CT NT	
Delivery of final report											CT **D3**	
Drafting manuscript									CT	CT	CT M5	
Manuscript review											CT NT	CT NT
Manuscript delivery												CT **D4**

Project management & communication

The coordinating team has installed a steering committee in which all countries involved are represented by 1 person and an alternate person (back-up). This committee is chaired by the **coordinator** of the study (RIVM) who is responsible for organization of meetings (Face-to-Face, tele- and/or web-conferencing) including detailing of agendas, distributing of meeting minutes. An alternate coordinator (back-up) has also been nominated among the committee to ensure continuity.

Liaison with the European Medicines Agency is ensured by the coordinator of the consortium, Prof. Olaf Klungel, since he is the principal contact with regards to the Framework service contract. Meetings between the Agency to discuss the study will be organized at critical moments during the contract (start of contract, final study protocol, results of analysis, study report). These will be attended by the members of the Coordinating team and Committee, as deemed necessary. More frequent meetings can be organized at the request of the Agency or the consortium.

Annex 5. Instructions for document search to reconstruct timeline of events at national level

The organization of vaccination campaigns for COVID-19 varies per EU member state. To reconstruct the timeline of events at national level, each national team will conduct an online search for information on their national COVID-19 vaccination campaign.

The procedure to reconstruct the timeline of events consists of five steps, which will be followed by each national team:

Step 1: Compile a list of all relevant actors involved in the COVID-19 vaccination policies in the country. This list, may include:

- Ministry of Health
- National Health Authorities
- Public Health authorities/bodies responsible for pandemic response and vaccination
- Drug regulatory authorities
- Regional government organisations/authorities/bodies responsible for implementation of vaccination
- Municipal authorities/bodies responsible for implementation of vaccination
- Professional organisations (learned societies) involved in provision of vaccines, information thereof, monitoring and/or treatment of side-effects resulting from COVID-19 vaccine administration

As each country has its own public health system, healthcare structure and governmental organization, the list provided above is not exhaustive and is likely to be adapted. National teams should follow a snowball approach when searching for all relevant organisations.

Step 2: Search for online information and grey literature from the organisations meeting the description above. Many government bodies or authorities provide overviews of COVID-19 vaccination policies.

To gather the unindexed information, a snowball strategy will be applied.

For each member state involved, the search depends on the national situation and may include (this is not an exhaustive list):

- Governmental communications on the COVID-19 vaccination campaign, including press releases and public information on governmental websites.
- Communications from national public health directorates, including press releases and public information on their websites.
- Information from national vaccination authorities, including relevant information on their websites, press releases and any vaccination guidelines.
- Official communications from the national competent authority for medicinal products, including press releases
- Communications from relevant professional organizations (e.g., learned societies for hematologists and GPs)

The timeline will be plotted for the period November 2020 – September 2021. The events regarding the booster campaign for COVID-19 starting in September 2021 will be excluded from this study.

The information collected through snowball approach will be compared with that obtained via the Non-

Urgent Information request issued by the EMA to National competent authorities of the Member States involved in this study.

Step 3: Compile a national timeline with important decisions based on the information gathered.

Step 4: Conduct an expert review of the national timeline compiled.

Step 5: Finalize the national timeline taking into account the expert review

The collated data will provide input to the drafting of the national surveys and to the development of the interview guides.

Documents that contain official announcements about the national vaccination policies, will be included in an appendix for the study report (see also Annex 6).

5.1. Example: How the search strategy was applied in Denmark

Health authorities have regularly disseminated information about decisions regarding public vaccination plans and the availability of vaccines from the outset of the pandemic through national media.

Press conferences were held in Denmark by government officials when important developments in the vaccination programme occurred which needed to be disseminated to the public.

These press conferences were broadcasted in all media and always included the Head of the Danish Health Authority, the Minister of Health, and the Head of Statens Serum Institut; as well as other representatives as needed.

The meetings where the TTS warnings were discussed, officials from the Danish Medicines Agency were represented to give updates.

Press releases, publications or documents from the Danish authorities about the covid-19 vaccination policies in Denmark were then posted on a publicly available site hosted by the Danish Health Authority (sst.dk). All documents relating to the vaccines Vaxzevria and Johnson and Johnson were retrieved from this official homepage sst.dk. The homepage has a search function where additional relevant documents were found by searching the names of the vaccines as included in official documents. Documents retrieved in this manner, were reviewed to confirm their relevance to the study and to check whether additional documents were being referred to. Whenever the later applied, and the referred documents, publications or news releases were not available on sst.dk, then these were retrieved from the homepages of other official bodies, such as Statens Serum Institut (ssi.dk) and Retsinformation (retsinformation.dk).

Relevant government institutions/bodies which were identified:

- **Ministry of Health (DK: Sundhedsministeriet, SUM):** Develops policy, enforces executive orders and legal guidelines regarding health in Denmark.
- **Danish Health Authority (DK: Sundhedsstyrelsen, SST):** Professional health authority in Denmark, makes recommendations regarding health in Denmark and advices the Ministry of Health.
- **Statens Serum Institut (SSI):** Under the auspices of the Danish Ministry of Health. Main duty is to ensure preparedness against infectious diseases and biological threats and control of congenital disorders.

- **Retsinformation.dk** is the Danish state's online open access information system (website) about all legislation in Denmark. Updated at least once daily.

Relevant documents/communications which were identified:

Documents/communication:

- Decisions made by the Ministry of Health (available on the website sum.dk and the website Retsinformation.dk). Terms used:
    - Executive order
    - Legal guideline
    - Press releases
- Publications by the Danish Health Authority (on the website sst.dk). Terms used:
    - Memo/note
    - Vaccination programme
    - Vaccination calendar
    - Press releases
- Statens Serum Institut (SSI, on the website ssi.dk). Terms used:
    - News

Annex 6. Standard format for collecting information on vaccination policies

Given the variation in practices and terminology across countries, in addition to the proposed summary tables below, the national teams will also compile, per country, an appendix to the study report, which will list each document/communication included in the summary table and:

- Their name/title
- The type of document (policy/guideline/recommendation/communication/press release)
- The actual wording of the vaccination recommendation in English language (when not available, local language is considered acceptable)
- Link to the source of information.

A. Vaxzevria: Initial vaccination policy, prior to EMA communication d.d. 29 March 2021

Country	Initial vaccination policy, prior to EMA communication d.d. **29 March 2021**			
	Vaccines used	Target groups	Order of vaccination	Source of information (organization, link to document)
Denmark				
Greece				
Latvia				
Netherlands				
Portugal				
Slovenia				

B. Vaxzevria: Changes in vaccination policy, after EMA communication d.d. 29 March-2021

Country	Initial vaccination policy, after EMA communication d.d. **29 March-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

C. Vaxzevria: Changes in vaccination policy, after EMA communication d.d. 14 April-2021

Country	Initial vaccination policy, after EMA communication d.d. **14 April-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					

Slovenia					

Vaxzevria: Changes in vaccination policy, after EMA communication d.d. 11 May-2021

Country	Initial vaccination policy, after EMA communication d.d. **11 May-2021**			
	Vaccines used	Target groups	Prioritisation	Source information
Denmark				
Greece				
Latvia				
Netherlands				
Portugal				

COVID-19 Vaccine Janssen

A. COVID-19 vaccine Janssen: Initial vaccination policy, prior to EMA communication d.d. 16 April 2021

Country	Initial vaccination policy, prior to EMA communication d.d. **16 April 2021**			
	Vaccines used	Target groups	Order of vaccination	Source information
Denmark				
Greece				
Latvia				
Netherlands				
Portugal				
Slovenia				

B. COVID-19 Vaccine Janssen: Changes in vaccination policy, after EMA communication d.d. 16 April-2021

Country	Initial vaccination policy, after EMA communication d.d. **16 April-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	**Source information**
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

C. COVID-19 vaccine Janssen: Changes in vaccination policy, after EMA communication 22 April 2021

Country	Changes in vaccination policy, after EMA communication d.d. **22 April 2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					

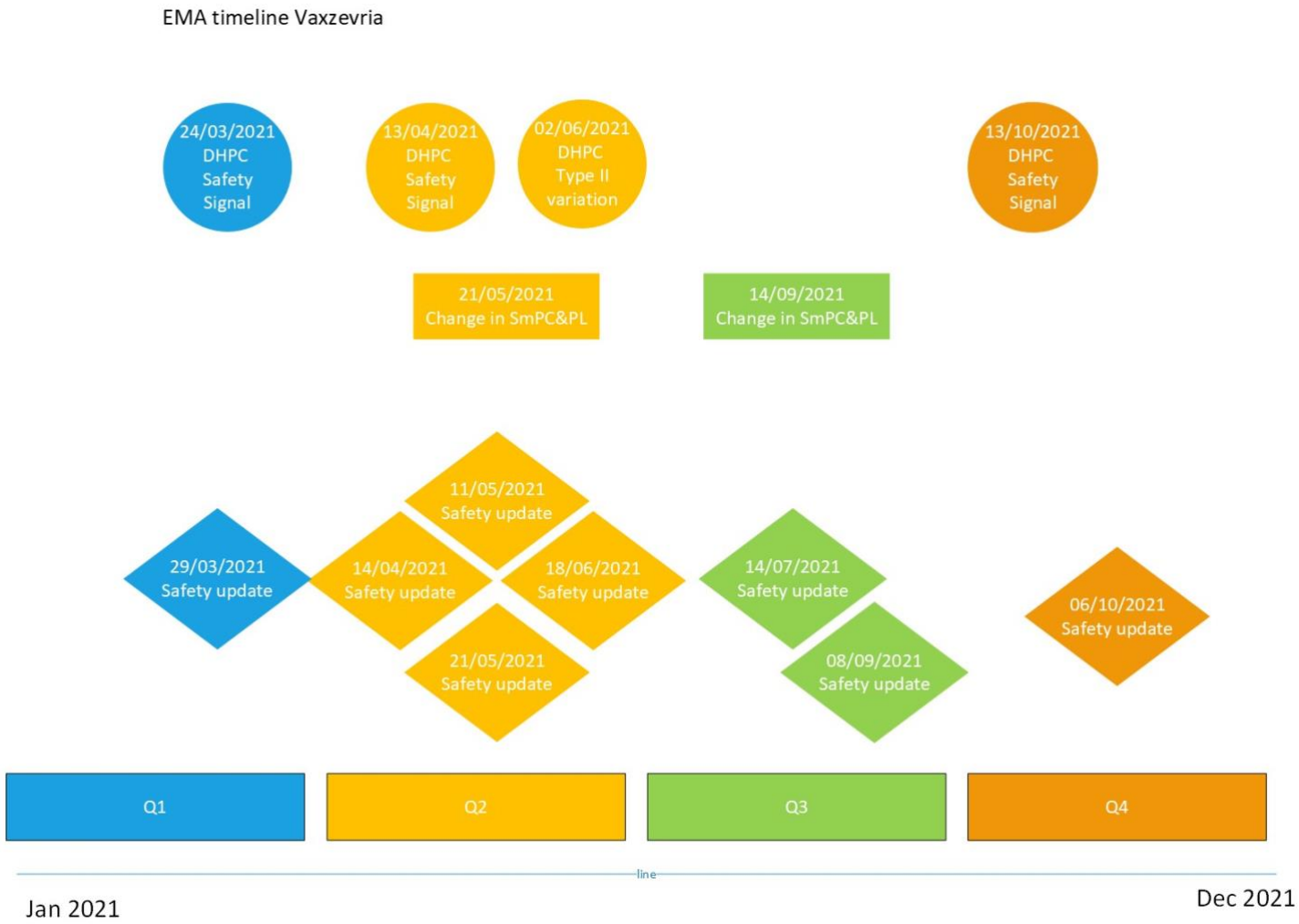
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

D. COVID-19 vaccine Janssen: Changes in vaccination policy, after EMA communication d.d. 11 May 2021

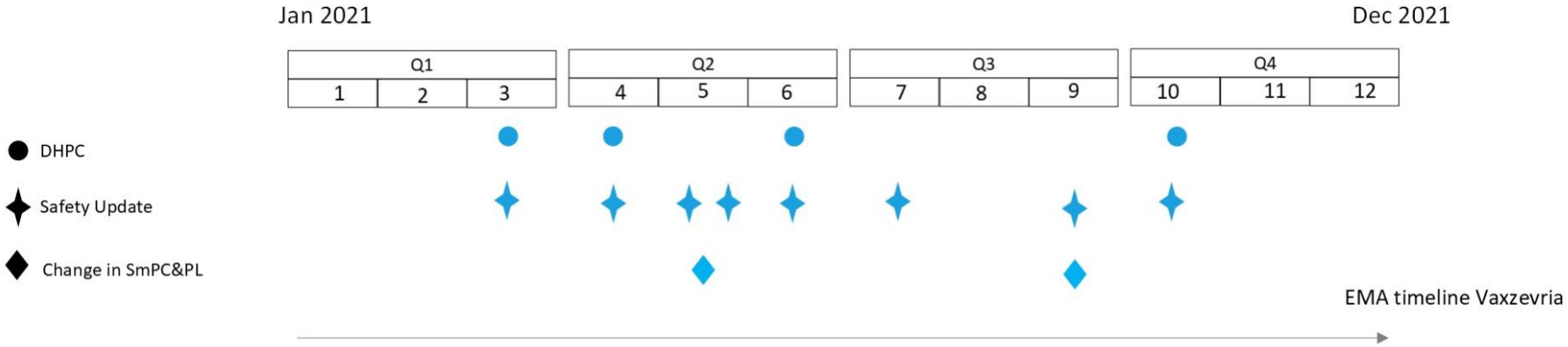
Country	Initial vaccination policy, after EMA communication d.d. **11 May-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

Annex 7. Timeline examples

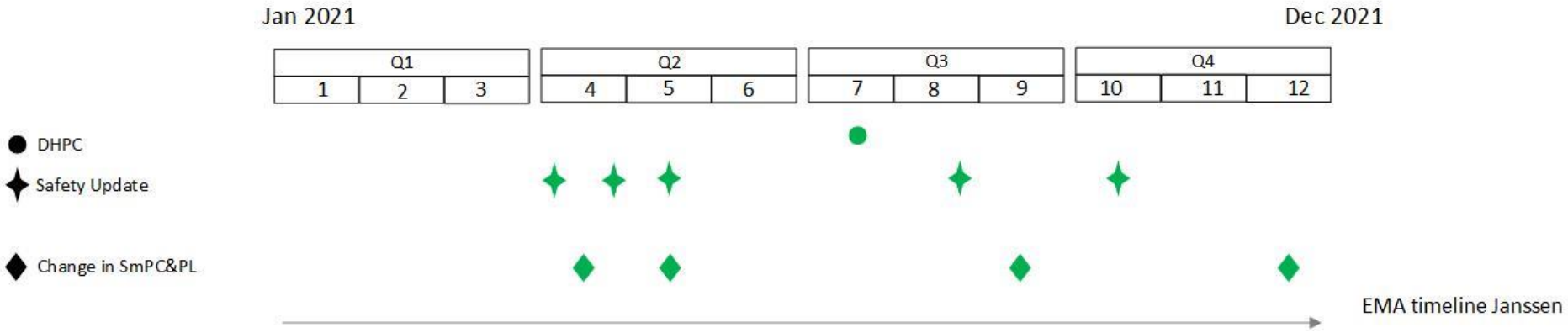
7.1 Example of timeline for EMA regulatory actions – Vaxzevria



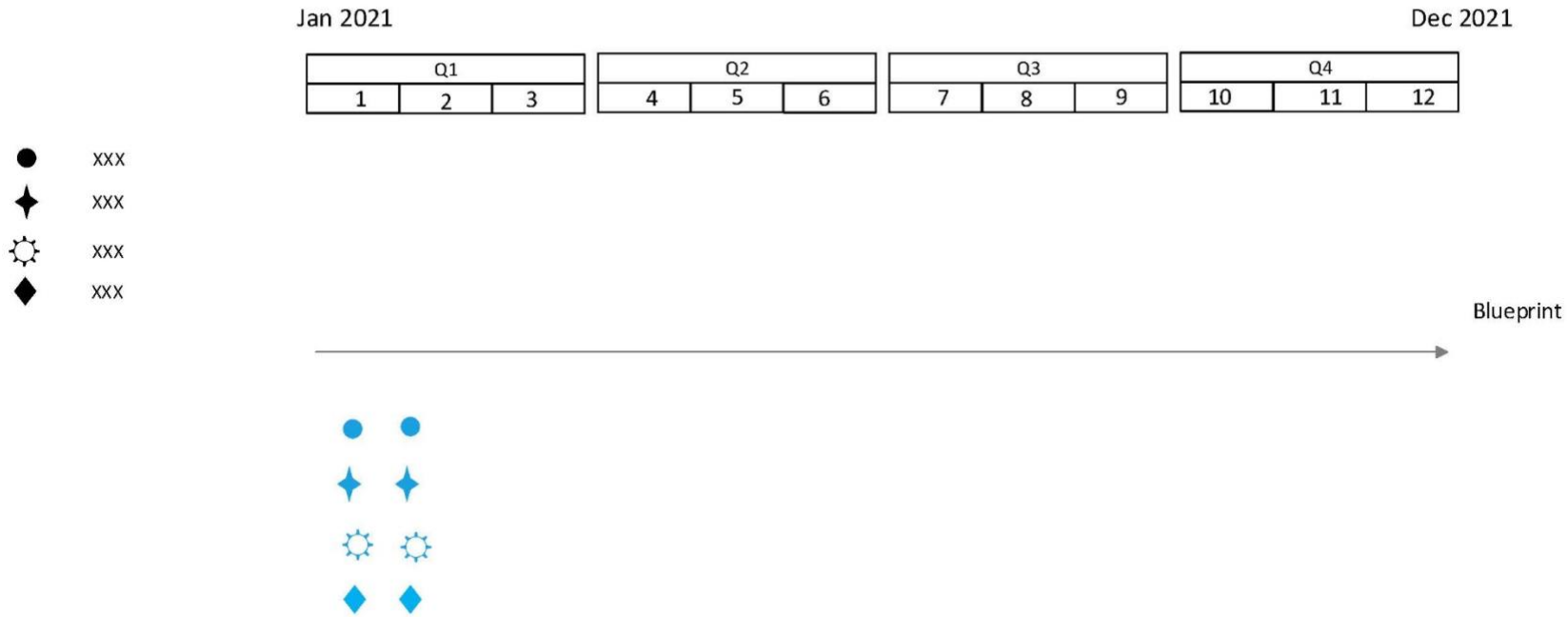
7.2 Example of EMA timeline of regulatory actions - Vaxzevria



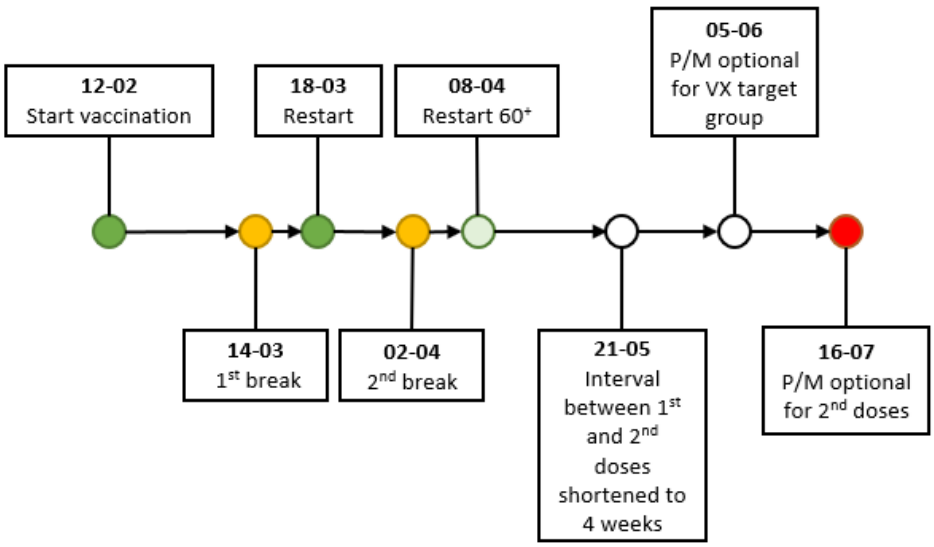
7.3 Example of EMA timeline of regulatory actions – COVID-19 Vaccine Janssen



7.4 Example of empty timeline to be adapted at national level

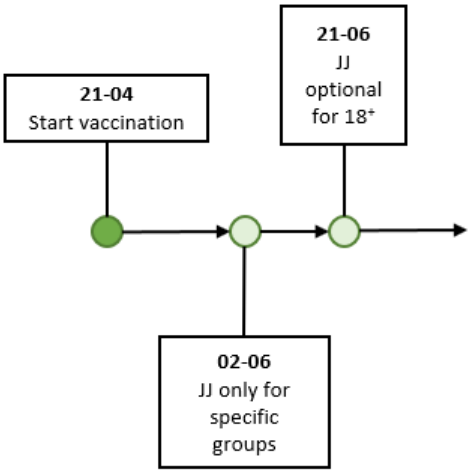


7.2 Timeline of policy changes– Dutch perspective - Vaxzevria



National vaccination with the two-dose Vaxzevria vaccine started on the 2nd of February 2021. At the 14th of March a temporary suspension was put in place due to a possible connection between Vaxzevria and cases of thrombosis with thrombocytopenia. At the 18th of March the national vaccination was restarted. The second temporary suspension was initiated on the 2nd of April after more cases of TTS. From the 8th of April Vaxzevria was only given to those aged between 60-64. On the 21st of May the interval between the first and the second doses was shortened to 4 weeks instead of 12 since there's no longer a shortage of vaccines. From the 5th of June on both Pfizer and Moderna became optional for those aged 60-64 instead of Vaxzevria. Those who have received a first doses of Vaxzevria were recommended to get a second dose of Vaxzevria as well. On the 16th of July both Pfizer and Moderna became optional as a second doses for those who had received a first dosis of Vaxzevria.

7.3. Timeline of policy changes– Dutch perspective - Janssen



National vaccination with the single-dose Janssen vaccine started on the 21st of April 2021. Due to the risk of TTS, Janssen became available only for specific groups on the 2nd of June. These groups include those who are seafaring, homeless, deployed or incarcerated. On the 21st of June, Janssen became optional for anyone aged

above 18 who specifically wanted a single-dose vaccine. They have to make a special appointment if they wish to be vaccinated with Janssen.

Annex 8. Translation protocol

Step 1:

Two native speaking researchers (or translators) translate the documents separately i.e., they translate the citizen's questionnaire, the healthcare professional's questionnaire, or the interview guide in tandem. This process results in individually translated versions of the 2 questionnaires and one interview guide from the two translators.

Step 2:

The two translators then meet, compare, and discuss the wording of each question in their individual versions for each of the questionnaires or the interview guide.

During this process they focus on:

- The target group for the questionnaires and their use of words and specific terms
- How citizens as lay persons use words and terms about medicines and health
- Consistency of wording throughout all questionnaires, although citizen's questionnaire will differ in wording from questionnaires for professionals
- Keeping the wording as simple as possible

This process results in the one consensus version for each of the 2 translated questionnaires or for the interview guide.

Step 3:

Then a third native speaking researcher (or validator), who is also a healthcare professional and has not seen the questionnaires before and is not familiar with the study, reads the agreed-upon version of the translated questionnaires or the interview guide, raising questions and noting any lack of clarity, which are then to be clarified during a meeting with the two translators.

This process results in the validated versions of the 2 translated questionnaires or in the validated interview guide.

Step 4:

The validated versions of the 2 translated questionnaires or the interview guide are then compared to their corresponding English versions and any remaining inconsistencies are resolved by consensus between the two translators and the validator.

This process results in the final versions of the 2 translated questionnaires or in the final interview guide.

Annex 9. Pointers for Interview guide with Healthcare Professionals

According to the study protocol:

"Deeper insight into the knowledge, attitude and perceptions of HCPs will be gained by conducting semi-guided (telephone or online) interviews.

The interviews with healthcare professionals will provide other in-depth information about how HCPs have perceived the timeline of events and the risk communication about the two adenovirus vector vaccines in their country. (Principle #1)

They will also be invited to reflect about their experiences, attitudes, and behaviour. (Principle #2)

Special attention will be paid to scope professionals' motivations and beliefs towards COVID-19 vaccination. (Principle #3)

The interviews will provide details about personal views, which cannot be obtained through the survey. Since HCPs play a crucial role in reassuring and informing people about vaccinations, their perceptions about the risk communication will provide the Pharmacovigilance Risk Assessment Committee with greater insight into the impact of its recommendations in actual practice, as well as help explain any country differences."

			Principle
Information provided on TTS risk associated with adenovirus COVID-19 vaccines	**Information FORMAT**	**Adequate language/format?**	**#1**
		Suggestions?	
	Information CONTENT	**Adequate/Clear/Complete?**	**#1**
		Suggestions?	
	Information CHANNEL	**Adequate/Accessible?**	**#1**
		Suggestions?	
	Information SENDER	**Adequate/Credible/Reliable?**	**#1**
		Importance of National Competent Authorities/health and regulatory authorities?	**#1**
		Suggestions?	
	Information IMPACT	**Understanding the risk**	**#1**
		Understanding who is at risk	**#1**
		Understanding which signs/symptoms should be monitored	**#1**
		Understanding which measures should be taken by HCPs	**#2**
		Affecting confidence/fear in vaccines	**#3**
		Attitudes/Behaviour changes **Brand switching advice** **Vaccination refusal advice**	**#2**
		Comments	

Annex 10. References

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