NON-INTERVENTIONAL POST-AUTHORIZATION SAFETY STUDY PROTOCOL

Study Title	A Cross-Sectional Post-Authorization Safety Study to Assess Healthcare Provider's Level of Awareness of Risk Minimisation Materials for Truvada® for Pre-Exposure Prophylaxis in the European Union
Protocol ID	GS-EU-276-4027
Protocol Version/Date:	Original: 30 August 2016 Version 1.1 16 February 2017 Version 1.2 13 June 2017
EU PAS Register No	EUPAS19479
Active substance	Emtricitabine / tenofovir disoproxil (as fumarate) 200 mg/245 mg film-coated tablets
Medicinal Product	Truvada®
Marketing Authorization Numbers	EU/1/04/305/001 EU/1/04/305/002
Procedure number	EMEA/H/C/000594
Joint PASS	No
Research Question and Objectives	The objective is to determine healthcare providers' level of awareness of Risk Minimisation Materials and appropriate use and risks associated with Truvada for a PrEP indication
Country (-ies) of study	France, Germany, Ireland, Netherlands, Norway, Spain, United Kingdom
Gilead Study Director / Author/Contact Person:	Name: David Magnuson, PharmD Telephone: +1-650-522-6075
Marketing Authorization Holder	Gilead Sciences International Ltd, Cambridge Granta Park Cambridge CB21 6GT, United Kingdom
Gilead Qualified Person Responsible for Pharmacovigilance:	Name: Anne-Ruth van Troostenburg de Bruyn, tGP MD(Lond) FFPM DipPharmMedRCP Telephone: +44 (0) 1223 824641 Fax: +44 (0) 1223 897290

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1.1. LIST OF IN-TEXT TABLES

GLOSSARY OF ABBREVIATIONS AND DEFINITION OF TERMS

CRO	Contract Research Organization
DSPH	Drug Safety & Public Health
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
FDA	(United States) Food and Drug Administration
GPP	Good Pharmacoepidemiology Practices (guidelines for)
GSI	Gilead Sciences, Inc.
GVP	Good Pharmacovigilance Practices (guidelines for)
HCP	Healthcare Professional (Provider)
HIV-1	Human Immunodeficiency Virus-1
HMA	Heads of Medicines Agencies
IEC	Independent Ethics Committee
IRB	Institutional Review Board
PAS	Post-Authorization Study
PASS	Post-Authorization Safety Study
PrEP	Pre-exposure Prophylaxis
PRAC	Pharmacovigilance Risk Assessment Committee
REMS	Risk Evaluation and Mitigation Strategy
RMMs	Risk Minimisation Materials
RMP	Risk Management Plan
STI	Sexually Transmitted Infection
US, USA	United States, United States of America

2. RESPONSIBLE PARTIES

Table Responsible Parties

Responsibility	Name, Title, Qualifications, Affiliation, Address	Contact Information
Marketing Authorization Holder	Karen Jourdan-Brown Associate Director, Regulatory Affairs Gilead Sciences International Ltd, Cambridge CB21 6GT United Kingdom	Email: Karen.Jourdan-Brown@gilead.com Phone: +44 20 8587 2523
Study Director	David Magnuson, PharmD Director, Epidemiology Gilead Sciences 333 Lakeside Drive Foster City, CA 94404, USA	Email: David.Magnuson@gilead.com Phone: +1 (650) 522-6075
Clinical Operations	Christophe De Belder, MSc Senior Clinical Trials Manager Gilead Sciences Europe Ltd, 2 Roundwood Avenue Stockley Park Uxbridge UB11 1AF, UK	Email: Christophe.DeBelder@gilead.com Phone: +44 2085872552
Pharmacovigilance	Drug Safety Public Health Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA	Phone: +1 (800) 445 3235 Fax: +1 (650) 522 5477 Email: Safety_fc@gilead.com
EU QPPV	Anne-Ruth van Troostenburg de Bruyn Senior Director, DSPH Gilead Sciences International Ltd. Flowers Building, Granta Park Cambridge, Cambridgeshire CB21 6GT United Kingdom	Phone: +44 (0) 1223 824641 Email: Anna.vanTroostenburg@gilead.com

3. PROTOCOL SYNOPSIS/ABSTRACT

Gilead Sciences Europe, Ltd.
2 Roundwood Avenue, Stockley Park, Uxbridge
MIDDLESEX UB11 1AF, UNITED KINGDOM

Study Title:	A Cross-Sectional Post-Authorization Safety Study to Assess Healthcare Provider's Level of Awareness of Risk Minimisation Materials for Truvada® for Pre-Exposure Prophylaxis in the European Union
Rationale and Background:	A CHMP positive Opinion was received on 21 July 2016 and European Commission Decision was received on 18 August 2016 for a Type II Variation for Truvada (emtricitabine/tenofovir disoproxil fumarate) to extend the indication for Pre-exposure Prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults at high risk. Additional risk minimisation measures for the use of Truvada for PrEP are included in the Truvada European Union (EU) Risk Management Plan (RMP) to minimise the risks of HIV-1 acquisition, including infection resulting from non-adherence, and development of resistance in individuals with unrecognized or acute HIV-1 infection.
Research Question and Objectives:	The objective is to determine healthcare providers' level of awareness of Risk Minimisation Materials and appropriate use and risks associated with Truvada for a PrEP indication
Study Design:	This study consists of a cross-sectional survey, which will be conducted in France, Germany, Ireland, Netherlands, Norway, Spain, and the United Kingdom in order to assess prescriber awareness of the Risk Minimisation Materials (RMMs). The survey will be conducted once in each country chosen for this survey at least 6 months after the RMMs have been approved and distributed and, where required, the protocol has been approved by the National Competent Authority and Ethics Committee(s). Healthcare professionals (HCPs) who were mailed the RMMs will be invited to participate on a volunteer/"opt-in" basis. Survey reminders will be sent during the survey recruitment period. Data from all respondents will be included in the analysis and final report. Qualitative (pilot) testing will be done in the United Kingdom and in each of the selected countries for this survey. The questions for the survey may be revised based on the results of the qualitative testing. Translation of the questionnaire and validation of the translation will be done prior to launching the survey in non-English speaking countries.

Population:	The study population will be comprised of HCPs in selected countries where the Truvada for PrEP RMMs have been distributed. Inclusion Criteria: • Prescribers who volunteer to participate in the survey
Variables:	Prescriber's awareness will be evaluated and expressed as proportions or scores. Prescriber's identity will remain confidential and demographic variables will include medical specialty, practice setting and country only. Data on individual PrEP users will not be collected.
Data Sources:	The data source for the survey will be health care providers who volunteer to be surveyed. Responses will be aggregated and summarized overall, as well as by country and by provider specialty.
Study Size:	A minimum of 200 fully completed surveys will be the target for the final analysis. A minimum of 20 completed surveys will be the target for France, Germany, Ireland, the Netherlands, Spain and the United Kingdom and a minimum of 10 completed surveys will be the target for Norway.
Data Analysis:	Responses to questions for all completed surveys will be analyzed using descriptive statistical analysis. Data from partially completed surveys will be evaluated separately. Characteristics for responders and non-responders will be compared based on country and HCPs specialty. Continuous variables will be described by the mean, standard deviation, median and range. Categorical variables will be described by the number and proportion in each category. The amount of missing data for each variable will be reported. Data will be presented by means of summary tables, graphs and listings. No formal hypothesis testing will be conducted. Gilead considers 80% the threshold for acceptable awareness of the RMMs. An enrollment progress report will be issued at the end of November 2017 or 30 days after receipt of 100 completed surveys, whichever occurs sooner. The numbers of invitees and respondents will be recorded, and the response rates will be reported overall and by country.

Milestones:	Start of data collection: The survey will be conducted in each of the selected countries at least 6 months after the RMMs have been approved and distributed and, where required, the protocol has been approved by the National Competent Authority and Ethics Committee(s). End of Data collection: The survey will be closed in all countries on 30 March 2018. Enrollment Progress report: At the end of November 2017 or 30 days after receipt of 100 completed surveys, whichever occurs sooner. Final Study report: Approximately 6 months after final survey data collected. Target date 28 September 2018.

This study will be conducted in accordance with the guidelines of Good Pharmacoepidemiology Practices (GPPs) and Heads of Medicines Agencies (HMA) Good Pharmacovigilance Practices (GVP) including archiving of essential documents.

4. AMENDMENTS AND UPDATES

This is an updated version of the protocol.

Amendment or Update Number	Date	Section of Study Protocol	Amendment or Update	Reason
1.2	13 June 2017	Title Page Synopsis Protocol	Inclusion of 6 months minimum timeline for conduct of survey in each country after RMMs have been approved and distributed.	PRAC final Assessment Report provided on 18 May 2017
1.1	16 February 2017	Title Page Synopsis Protocol Survey Questions	Removal of all text relating to a drug utilization study Inclusion of countries to be included in the survey Revision of protocol based on comments and suggestions from PRAC Removal of survey questions relating to drug utilization and rewording of survey questions based on comments and suggestions from PRAC All survey questions were removed from the protocol and are in a separate document	PRAC Rapporteur PASS protocol preliminary assessment report provided on 12 January 2017

5. MILESTONES

Milestone	Planned Date
Start of data collection	The Survey will be launched in each country at least 6 months after the RMMs have been approved and distributed and, where required, the protocol has been approved by the National Competent Authority and Ethics Committee(s). First survey planned for launch around 31 July 2017.
End of data collection	30 March 2018
Registration in the EU PAS register	2nd quarter 2017
Enrollment Progress report	At the end of Nov 2017 or within 30 days from the collection of 100 complete survey responses, whichever occurs sooner.
Final report of study results	Approximately 6 months after final survey data collected. Target date 28 September 2018

6. RATIONALE AND BACKGROUND

6.1. Rationale for the Current Study

A CHMP positive Opinion was received on 21 July 2016 and European Commission Decision was received on 18 August 2016 for the Type II Variation for Truvada® (emtricitabine/tenofovir disoproxil fumarate) to extend the indication for Pre-exposure Prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults at high risk.

Additional risk minimisation measures for the use of Truvada for PrEP are included in the Truvada European Union (EU) Risk Management Plan (RMP) to minimise the risks of HIV-1 acquisition, including infection resulting from non-adherence, and development of resistance in individuals with unrecognized or acute HIV-1 infection. RMMs will be distributed to potential prescribers of Truvada for PrEP. The survey will be implemented to assess the level of awareness of the RMMs, as well as guidance in the SmPC, in educating HCPs on the appropriate use and risks of Truvada for a PrEP indication.

7. RESEARCH OBJECTIVES

The objective is to determine healthcare providers' level of awareness of Risk Minimisation Materials and appropriate use and risks associated with Truvada for a PrEP indication.

8. RESEARCH METHODS

8.1. Study Design

This study consists of a survey which will be conducted once in each of the chosen countries at least 6 months after the RMMs have been approved and distributed and, where required, the protocol has been approved by the National Competent Authority and Ethics Committee(s). The survey will be conducted in order to assess prescriber's level of awareness of the risk minimisation materials in the following EU countries: France, Germany, Ireland, Netherlands, Norway, Spain, and the United Kingdom. These countries were selected based on the incidence of new HIV cases per year, the national regulatory review and approval process for the RMMs, and where Truvada for PrEP is anticipated to be prescribed. HCPs who were mailed the RMMs will be invited to participate on a volunteer/"opt-in" basis. Survey reminders will be sent during the survey recruitment period. Data from all respondents will be included in the analysis and final report.

8.1.1. Pre-testing of the survey

In order to ensure the questions for the survey can be understood by HCPs, qualitative (pilot) testing will be conducted by approximately 3 HCPs in the United Kingdom followed by a qualitative testing by 2 HCPs in each of the other selected countries. Based on the results of the qualitative testing, the questions for the survey may be revised accordingly. This testing will be done in English and other applicable languages. Prescribers who participate in the qualitative testing will receive an honorarium in line with Fair Market Value and applicable local regulations.

8.1.2. Translation of the survey

Translation of the survey will be done for non-English speaking countries. Qualitative testing will be conducted and the survey will be finalised prior to execution in any non-English speaking country. All translations to the respective languages will be done using forward and backward translations.

8.2. Setting

The survey questions will collect data from HCPs regarding their level of awareness of the RMMs and appropriate use and risks of Truvada for PrEP. The study population will be HCPs who have been mailed the Truvada for PrEP RMMs. The HCPs that will be invited to participate in the survey will represent practice specialties which are considered likely to prescribe Truvada for PrEP (e.g., HIV-1 specialists). Additional practice specialties may be added at a later date.

8.3. Variables

The study questionnaire is designed to collect information on the following variables:

- awareness of the RMMs for Truvada for PrEP
- awareness about the appropriate use and risks associated with Truvada for PrEP
- demographic information of the prescribers (medical specialty, practice setting, country). The identity of participating HCP's will remain confidential and will not be provided to the sponsor.

Data on individual PrEP users will not be collected.

8.4. Data Sources

The survey will be sent to HCPs who received the Truvada for PrEP risk minimisation materials. Gilead will provide the list to the survey vendor. The data source for the survey will be prescribers who volunteer to be surveyed. Responses will be aggregated and summarized overall, as well as by country and by provider specialty.

8.5. Study Size

A minimum of 200 completed surveys will be obtained for the final analysis. The target minimum number of responders is 20 for France, Germany, Ireland, the Netherlands, Spain and the United Kingdom and 10 for Norway. Table 1 shows the margins of error for different numbers of responders. With a target of 200 responders and the observed value of prescriber awareness of 80%, the true value is estimated to lie within the margin of 73.8% - 85.3%.

Table 1. Precision of Margin of Error with Different Numbers of Responders

Number of Responders	Margin of Error	
100	70.8%	87.3%
200	73.8%	85.3%
300	75.0%	84.4%

8.6. Data Management

The survey questionnaire will be self-administered online via a secure electronic data entry system. Participants will receive specific access codes to enable them to enter their data. The data entry system will be made available for the study duration, through 30 March 2018. After that time, the system will be closed for data entry and the data extracted and analyzed.

8.7. Data Analysis

Responses to questions for all completed surveys will be analyzed using descriptive statistical analysis (count, ranges, proportions, and /or scores). Responses to questions for partially completed surveys will be analyzed separately. The results of each survey will be described separately, and the results will be presented overall, as well as by country and provider specialty where sample size allows. Characteristics for responders and non-responders will be compared based on country and HCPs specialty. Continuous variables will be described by the mean, standard deviation, median and range. Categorical variables will be described by the number and proportion in each category. Frequency point-estimates with two-sided 95% confidence intervals (CIs) using the binomial distribution (e.g., Wald or Clopper-Pearson method, as appropriate) will be constructed to describe the proportion of prescribers aware of specified risks.
Gilead considers 80% the threshold for acceptable awareness of the risks for the individual questions 1 and 5 in the survey. Each of the statements in question 1 will be assessed independently. This is the threshold used in other risk minimisation programs, such as the Risk Evaluation and Mitigation Strategy (REMS) program in the United States.

The amount of missing data for each variable will be reported. Data will be presented by means of summary tables, graphs and listings. The numbers of invitees and respondents will be recorded, and the response rates will be reported overall and by country.

Analyses will be performed according to a pre-specified statistical analysis plan.

8.8. Quality Control

The electronic data entry system will require that respondents answer certain questions before proceeding in order to ensure that surveys are completed as fully as possible. The data will be stored on a secure network drive or a secure and validated cloud-based data storage system, with access for only authorized personnel from the study team and their delegates.

8.9. Limitations of the Research Methods

This survey may be limited by social desirability bias if prescribers are hesitant to admit their lack of awareness of the specified risk or materials. The survey instruments will be designed with the intention of minimising this possible bias. In addition, random sampling will not be feasible for these surveys and non-response is a common problem in observational studies. However, the study will attempt to obtain as representative a sample as possible. The survey will also be administered online, which may exclude participants who are less comfortable with internet surveys. However, the number of respondents who are uncomfortable with internet surveys is expected to be low, and paper surveys would produce a larger respondent burden which would be expected to deter participation. The survey is unable to assess awareness both before and after the distribution of the RMMs or changes in awareness as a result of the RMMs. Although this survey can only assess knowledge following the distribution of the RMMs, it will still provide an important assessment of the awareness of the prescribing population of the appropriate use and risks of interest.

8.10. Other Aspects

Every effort will be made to ensure that this study is completed. Gilead will only terminate the study if there is sufficient cause following consultation with the PRAC. Should this be necessary, Gilead will arrange discontinuation procedures and notify the appropriate regulatory authorities in accordance with local legislation.

9. PROTECTION OF HUMAN SUBJECTS

9.1. Good Pharmacoepidemiology and Pharmacovigilance Practices

The study will be conducted in accordance with the guidelines of Good Pharmacoepidemiology Practices (GPPs), Heads of Medicines Agencies (HMA) Good Pharmacovigilance Practices (GVP), and European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP), including archiving of essential documents.

9.2. Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Review

This study will not collect patient-level data. All national and EU regulations will be followed regarding the requirement for IRB or IEC review and approval for this study.

9.3. Informed Consent

Each survey participant will be asked to provide consent to use their responses to the questions for the purposes of the study. Each survey participant's confidentiality will be protected, and only reported to Gilead if the participant reports safety information and provides permission to be contacted for follow-up by Gilead.

9.4. Confidentiality

The identity of the participants will not be provided to the sponsor unless they report safety information and provide permission to be contacted for follow-up by Gilead.

10. MANAGEMENT AND REPORTING OF SAFETY INFORMATION

The objectives of this study include the determination of a HCP's level of awareness of RMMs and the appropriate use and risks associated with the use of Truvada for a PrEP indication. This healthcare provider survey is observational in nature and does not evaluate safety in individual patients. Adverse events will not be solicited in this observational study. In the event that adverse events are incidentally reported through the survey, reporting of these adverse events will be done by the clinical research organization (CRO) and sent to Gilead Drug Safety and Public Health (DSPH) within 24 hours of awareness by Gilead and/or CRO to Gilead DSPH, Safety_FC@gilead.com or fax + 1-650-522-5477. These events will be collected and reported to the regulatory agencies in accordance with standard safety reporting procedures. All study data will be in aggregate form only.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

11.1. Study Report and Publications

A study report will be prepared and provided to the applicable regulatory agencies. Gilead will ensure that the report meets the standards set out in the Guideline on Good Pharmacovigilance Practices (GVP) Module VIII. An enrollment progress report will be submitted at the end of November 2017 or 30 days after collection of 100 complete survey responses, whichever occurs sooner. The final study report will be submitted within 6 months of study completion. The target date is 28 September 2018.

Future publications in the form of abstracts and manuscripts have not been planned to date. Gilead shall communicate to the EMA and the competent authorities of the Member States in which the product is authorized the final manuscript within two weeks after first acceptance for publication.

12. APPENDICES

Appendix 1. ENCePP Checklist for Study Protocols

Study title: A Cross-Sectional Post-Authorization Safety Study to Assess Healthcare Provider's Level of Awareness of Risk Minimisation Materials for Truvada® for Pre Exposure Prophylaxis in the European Union

Study reference number: GS-US-276-4027

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[1]	☒	☐	☐	5
1.1.2 End of data collection[2]	☒	☐	☐	5
1.1.3 Study progress report(s)	☒	☐	☐	5
1.1.4 Interim progress report(s)	☐	☐	☒	
1.1.5 Registration in the EU PAS register	☒	☐	☐	5
1.1.6 Final report of study results.	☒	☐	☐	5

Comments:

The study progress report will provide an enrollment update.

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain:	☐	☐	☐	
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	6
2.1.2 The objective(s) of the study?	☒	☐	☐	7
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	8
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

The objective is to determine healthcare providers' level of awareness of risk minimisation materials and appropriate use and risks associated with Truvada for a PrEP indication.

[1] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[2] Date from which the analytical dataset is completely available.

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, new or alternative design)	☒	☐	☐	8.1
3.2 Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	8.1
3.3 Does the protocol specify measures of occurrence? (e.g. incidence rate, absolute risk)	☐	☐	☒	
3.4 Does the protocol specify measure(s) of association? (e.g. relative risk, odds ratio, excess risk, incidence rate ratio, hazard ratio, number needed to harm (NNH) per year)	☐	☐	☒	
3.5 Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☒	☐	☐	10

Comments:

Data from the survey will be summarized descriptively (counts, proportions, etc.); no measure of association will be estimated.

Section 4: Source and study populations	**Yes**	**No**	**N/A**	**Section Number**
4.1 Is the source population described?	☒	☐	☐	8
4.2 Is the planned study population defined in terms of:				
4.2.1 Study time period?	☐	☒	☐	
4.2.2 Age and sex?	☐	☒	☐	
4.2.3 Country of origin?	☒	☐	☐	8
4.2.4 Disease/indication?	☒	☐	☐	8
4.2.5 Duration of follow-up?	☐	☒	☐	8
4.3 Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	8

Comments:

The study population will be healthcare providers who were mailed the Truvada for PrEP risk minimisation materials.

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.1 Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☐	☐	☒	

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.2 Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☐	☐	☒	
5.3 Is exposure classified according to time windows? (e.g. current user, former user, non-use)	☐	☐	☒	
5.4 Is exposure classified based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	

Comments:

Study is cross-sectional survey of healthcare professionals.

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	7
6.2 Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	8
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, prospective or retrospective ascertainment, use of validation sub-study)	☐	☐	☒	
6.4 Does the protocol describe specific endpoints relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease, disease management)	☐	☐	☒	

Comments:

Study is cross-sectional survey of healthcare professionals.

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol describe how confounding will be addressed in the study?	☐	☐	☒	
7.1.1. Does the protocol address confounding by indication if applicable?	☐	☐	☒	
7.2 Does the protocol address:	☐	☐	☐	
7.2.1. Selection biases (e.g. healthy user bias)	☒	☐	☐	8
7.2.2. Information biases (e.g. misclassification of exposure and endpoints, time-related bias)	☐	☒	☐	
7.3 Does the protocol address the validity of the study covariates?	☐	☐	☒	

Comments:

Study is cross-sectional survey of healthcare professionals.

Section 8: Effect modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☐	☐	☒	

Comments:

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	8
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☒	☐	☐	8
9.1.3 Covariates?	☐	☐	☒	
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☒	☐	☐	8
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☐	☐	☒	
9.2.3 Covariates? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☐	☐	☒	
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☐	☐	☒	
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD)-10, Medical Dictionary for Regulatory Activities (MedDRA))	☐	☐	☒	
9.3.3 Covariates?	☐	☐	☒	
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☐	☐	☒	

Comments:

The data source is questionnaire responses from healthcare professionals.

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Is the choice of statistical techniques described?	☒	☐	☐	8
10.2 Are descriptive analyses included?	☒	☐	☐	8
10.3 Are stratified analyses included?	☐	☒	☐	
10.4 Does the plan describe methods for adjusting for confounding?	☐	☐	☒	
10.5 Does the plan describe methods for handling missing data?	☒	☐	☐	8
10.6 Is sample size and/or statistical power estimated?	☒	☐	☐	8

Comments:

Data from the survey will be summarized descriptively (counts, proportions, etc.); no measure of association will be estimated.

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	8
11.2 Are methods of quality assurance described?	☐	☐	☒	
11.3 Is there a system in place for independent review of study results?	☐	☐	☒	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☒	☐	☐	8
12.1.2 Information bias?	☒	☐	☐	8
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods)	☐	☐	☒	
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure, duration of follow-up in a cohort study, patient recruitment)	☐	☒	☐	

Comments:

Section 13: Ethical issues	Yes	No	N/A	Section Number
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	☒	☐	☐	9
13.2 Has any outcome of an ethical review procedure been addressed?	☐	☐	☒	
13.3 Have data protection requirements been described?	☒	☐	☐	8

Comments:

Section 14: Amendments and deviations	Yes	No	N/A	Section Number
14.1 Does the protocol include a section to document amendments and deviations?	☒	☐	☐	4

Comments:

Section 15: Plans for communication of study results	Yes	No	N/A	Section Number
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	11
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	11

Comments:

Name of the main author of the protocol: David Magnuson, Pharm.D.

Date: 21 June 2017

Signature: 

Appendix 2. Investigator Signature Page

GILEAD SCIENCES EUROPE, LTD.
2 ROUNDWOOD AVENUE, STOCKLEY PARK, UXBRIDGE
MIDDLESEX UB11 1AF, UNITED KINGDOM

A CROSS-SECTIONAL POST-AUTHORIZATION SAFETY STUDY TO ASSESS HEALTHCARE PROVIDER'S LEVEL OF AWARENESS OF RISK MINIMISATION MATERIALS FOR TRUVADA® FOR PRE-EXPOSURE PROPHYLAXIS IN THE EUROPEAN UNION

Original: 30 August 2016
Version 1.1: 16 February 2017
Version 1.2: 13 June 2017

This protocol has been approved by Gilead Sciences Europe, Ltd. The following signatures document this approval.

David Magnuson

David Magnuson, PharmD
Gilead Study Director (Printed)
Author

Signature

21 June 2017

Date

Anne-Ruth van Troostenburg de Bruyn,
tGP MD(Lond) FFPM DipPharmMedRCP
Gilead EU QPPV (Printed)

Signature

Date

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David Magnuson, PharmD Gilead Study Director (Printed) Author	Signature
Date	
Anna van Troostenburg Anne-Ruth van Troostenburg de Bruyn, tGP MD(Lond) FFPM DipPharmMedRCP Gilead EU QPPV (Printed)	Signature
22 June 2017 Date	