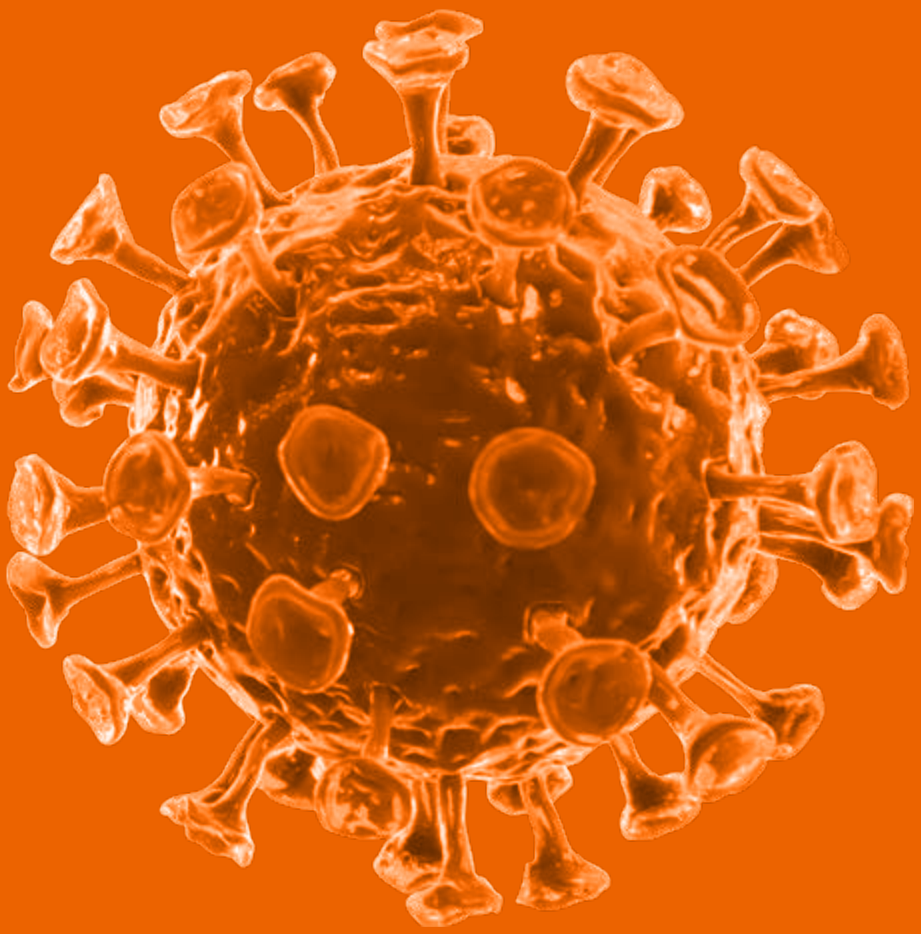
PROTOCOL TEMPLATE

TO BE USED AS A TEMPLATE FOR OBSERVATIONAL STUDY PROTOCOLS

COHORT EVENT MONITORING (CEM) FOR SAFETY SIGNAL DETECTION AFTER VACCINATION WITH COVID-19 VACCINES



ADDENDUM

TO COVID-19 VACCINES: SAFETY SURVEILLANCE MANUAL – MODULE ON MONITORING AND RESPONDING TO ADVERSE EVENTS OF SPECIAL INTEREST (AESI)

World Health Organization

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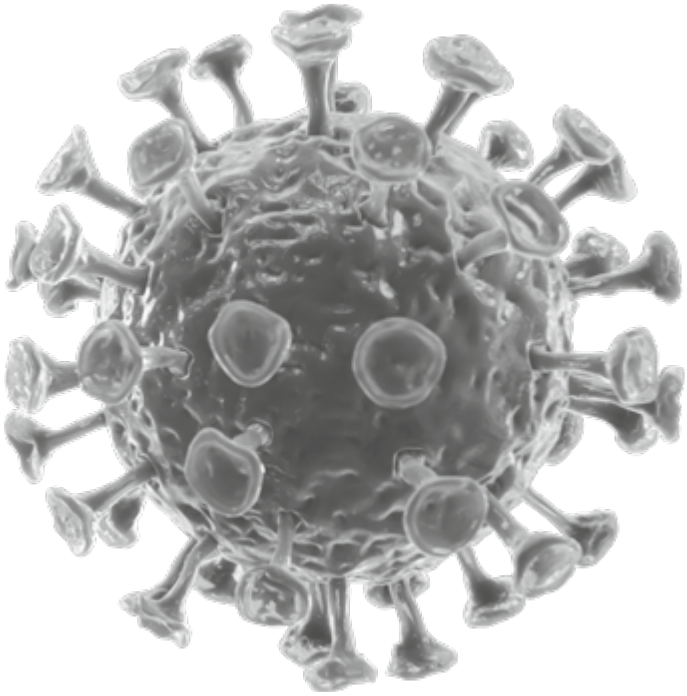

ADDENDUM

TO COVID-19 VACCINES: SAFETY SURVEILLANCE MANUAL – MODULE ON MONITORING AND RESPONDING TO ADVERSE EVENTS OF SPECIAL INTEREST (AESI)

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Protocol template to be used as template for observational study protocols for cohort event monitoring (CEM) for safety signal detection after vaccination with COVID-19 vaccines.

ISBN 978-92-4-002739-8 (electronic version)
ISBN 978-92-4-002740-4 (print version)

Acknowledgements

The preparation of this protocol was commissioned by World Health Organization (WHO), coordinated by Christine Guillard with the support of Noha Iessa, in the Pharmacovigilance (PVG) team, within the Regulation and Prequalification department at WHO Headquarters, Geneva, Switzerland. This document is based on the principles described in the WHO COVID-19 vaccines: safety surveillance manual.[1] It was developed under the guidance of the WHO Global Advisory Committee on Vaccine Safety (GACVS). Active surveillance protocols developed by United States Centers for Disease Control and Prevention (US CDC)[2] and European Medicines Agency vACcine Covid-19 monitoring readinESS (EMA-ACCESS)[3] projects were reviewed. Key aspects of these protocols were adapted to low- and middle-income country (LMIC) settings.

Special acknowledgements to Steven Anderson, Barbara Law and Saad B. Omer, members of the Scientific Committee, who provided expert advice throughout the project. The protocol was written by Kaatje Bollaerts and Anke Stuurman with technical input from Wendy Hartig-Merkel, Omar Okasha, Elodie Sole, Thao Mai Phuong Tran from the P95 Excellence in Pharmacovigilance and Epidemiology team.

The significant contributions of Bartholomew Dicky Akanmori, Don Ananda Chandralal Amarasinghe, Madhav Ram Balakrishnan, Oleg Benes, Jose Luis Castro, Amavi Edinam, Sujeet Jain, Houda Langar, Jayantha Bandula L. Liyanage, Helvert Felipe Molina Leon, Diadié Maiga, Sergio Raul Munoz Navarro, Irma Desiree Pastor, Jinho Shin from WHO regional offices and the pharmacovigilance (PVG) team in WHO headquarters are gratefully acknowledged. Sarah D. Bennett, Laura Conklin, Jane Gidudu and Zunera Gilani from the US CDC provided useful comments and advice.

1 Covid-19 vaccines: safety surveillance manual. (https://www.who.int/publications/i/item/10665338400, accessed 9 March 2021).

2 Centers for Disease Control and Prevention. V-safe active surveillance for COVID-19 vaccine safety 2020 [updated 19 November 2020; cited 2021-01-15], (https://www.cdc.gov/vaccinesafety/pdf/V-safe-Protocol-508.pdf, accessed 9 March 2021).

3 ACCESS (vACCinecovid-19 monitoring readinESS). Cohort event monitoring to assess safety of COVID-19 vaccines using patient reported events, a protocol template from the ACCESS project - EUPAS 38915. 2020 [updated 10 January 2021]. (https://vac4eu.org/wp-content/uploads/2021/02/3a.Cohort-event-monitoring-to-assess-safety-of-COVID-19-vaccines-using-patient-reported-events-a-protocol-template-from-the-ACCESS-project.pdf, accessed 9 March 2021)

Introduction

WHO has published the COVID-19 vaccines: safety surveillance manual to guide the processes for collecting, analysing and sharing safety data and information on COVID-19 vaccines within and across countries.[4] To accompany this manual and facilitate the conduct of active safety surveillance studies using harmonized tools and methods, a protocol template for cohort event monitoring (CEM) studies has been developed. **The present template protocol is for CEM studies of COVID-19 vaccines for the purpose of safety signal detection.** The protocol synopsis was developed under the guidance of a scientific committee including former and current Global Advisory Committee on Vaccine Safety (GACVS) committee members, and reviewed by the GACVS during its meeting held on 1-3 December 2020.[5]

CEM is a flexible active safety surveillance study design that can be used for signal detection and evaluation. CEM has been successfully used in the context of the H1N1 influenza pandemic in 2009, both in high income countries (HICs) and low- and middle-income countries (LMICs).[6] CEM is a prospective, observational, single-arm cohort study design for the early launch of a new medicine or vaccine. CEM studies are designed to capture all adverse events that occur in a defined group of individuals who are exposed to the new medicine or vaccine during routine clinical practice, in a defined period of time.[7,8] Vaccinees are enrolled in the cohort at the moment they are vaccinated for the first time with the monitored vaccine. Demographic and medical information are recorded at this initial encounter. Vaccinees are then followed up at defined intervals. Any adverse events (AEs), of either any severity or of a defined severity, occurring after vaccination are recorded, regardless of whether they are suspected to be caused by the vaccine or not. By capturing these events, regardless of suspicion of causality, the CEM study has the potential to identify previously unrecognised and unsuspected adverse reactions to the vaccine.[9]

How to use this template to develop a CEM study protocol

The protocol template should be completed by adapting it to the specific country(ies) and study population(s). The sections of the protocol template to be adapted have been marked with orange square brackets.

4 World Health Organization. Covid-19 vaccines: safety surveillance manual. Geneva2020. Last accessed 11 March 2021; Available from: https://www.who.int/publications/i/item/10665338400.

5 GACVS. Report of the meeting of the WHO Global Advisory Committee on Vaccine Safety (GACVS), 1–3 December 2020. WER. 2021;96:13-20.

6 Torre CM, Cary M, Borges FC, Ferreira PS, Alarcão J, Leufkens HG, et al. Intensive monitoring studies for assessing medicines: a systematic review. Front Med. 2019;6:147.

7 World Health Organization. A practical handbook on the pharmacovigilance of antimalarial medicines: World Health Organization; 2008.

8 Pal SN, Duncombe C, Falzon D, Olsson S. WHO strategy for collecting safety data in public health programmes: complementing spontaneous reporting systems. Drug Saf. 2013;36(2):75-81. doi: 10.1007/s40264-012-0014-6.

9 Suku CK, Hill G, Sabblah G, Darko M, Muthuri G, Abwao E, et al. Experiences and lessons from implementing cohort event monitoring programmes for antimalarials in four African countries: results of a questionnaire-based survey. Drug Saf. 2015;38:1115-26.

It is important also to note that the adult informed consent form (ICF) template, provided in this template, and the informed consent process must be adapted to local situations, local languages and special populations (e.g., minors, pregnant women, elderly individuals lacking full capacity, migrants, prisoners) that require a tailored approach to consent. This includes possible surrogate decision-makers, such as parents or guardians for young children, or study advocates for inclusion of prisoners, or orphans and additional forms, such as assent forms, as well as tailoring to correspond to the study information provided to participants during the consent process.

All protocols developed using this template should be reviewed by a scientific committee and by relevant ethics committees and institutional review boards, at a national level, or at the level of the study sites, or at the institution of the sponsor, as required by applicable laws and regulation.

Suggested process

- Step 1: Constitute a study coordination team consisting of representatives from the immunization programme, national regulatory authority, pharmacovigilance centre, chair of the national adverse events following immunisation (AEFI) committee, and academia.
- Step 2: Identify the role and responsibilities of the different institutions, and nominate a person to lead and coordinate the process of protocol development and obtain the consensus of the study coordination team. Complete section 6 of the template with this information.
- Step 3: Define the target population, identify study sites, review list of adverse events of special interest (AESI) for the COVID-19 vaccine(s) in use,[10] and complete the protocol (including informed consent forms and data collection tools). If technical assistance from WHO is required at this stage, send an e mail request to gvsi@who.int and the WHO country office focal person.
- Step 4: Discuss the draft protocol with the study coordination team and study site representatives to obtain their input and endorsement and then finalise the protocol.
- Step 5: The final protocol should be reviewed by an independent scientific committee to ensure that it is scientifically sound, and should then be reviewed by the national ethics committee or the independent ethics committee (IEC) or institutional review board (IRB) of participating institution(s).
- Step 6: Develop the study procedures, data management plan and statistical analysis plan.

Disclaimer: WHO cannot accept any responsibility or liability for the conduct of studies by third parties that follow this protocol template. Studies conducted by third parties using this protocol template cannot be considered 'WHO studies' and the WHO logo cannot be used in studies that are not WHO studies.

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10 Law B. SO2-D2.1.2 Priority List of COVID-19 Adverse events of special interest: Quarterly update December 2020. Safety Platform for Emergency vACcines (SPEAC); 2021. Last accessed 11 March 2021; Available from: https://brightoncollaboration.us/wp-content/uploads/2021/01/SO2_D2.1.2_V1.2_COVID-19_AESI-update_V1.3.pdf

Start of CEM study protocol template

Cohort event monitoring (CEM) study for safety signal detection after vaccination with COVID-19 vaccines