Generic protocol
A prospective cohort study investigating maternal, pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2
Reference:
The emergence of a new virus means that understanding transmission patterns, severity, clinical features and risk factors for infection will be limited at the start of an outbreak. To address these unknowns, WHO has provided protocols for special investigations in different settings.

Data collected using these investigation protocols will be critical to refine recommendations for case definitions and surveillance; characterize key epidemiological features of COVID-19; help understand the spread, severity and spectrum of disease and impact on the community; and inform guidance for application of countermeasures such as case isolation and contact tracing. These protocols are designed to enable the rapid and systematic collection of data in a format that facilitates comparison across different settings globally.

They are available on WHO website here: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

COVID-19 investigations and study protocols available include:

1. The First Few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19)


5. Surface sampling of coronavirus (COVID-19) virus: a practical “how to” protocol for health-care and public health professionals

6. Schools and other educational institutions transmission investigation protocol for coronavirus disease 2019 (COVID-19)

7. Longitudinal cohort study on pregnancy & COVID-19: maternal and neonatal transmission protocol

Please contact hrp_covid19pregnancycohort@who.int for questions related to the maternal and neonatal transmission protocol and earlyinvestigations-2019-nCoV@who.int for questions related to other early investigation protocols.

All WHO protocols for COVID-19 are available on the WHO website together with the technical guidance documents.
This protocol may be subject to revisions, pending research governance processes¹.

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For questions related to implementation or other aspects of pregnancy related SARS-CoV-2 research, please send an email to hrp_covid19pregnancycohort@who.int

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¹ Version 2.2 of this protocol and its accompanying appendix dated 14 August 2020 have been approved by the WHO Ethical Review Committee. This updated version (v.2.6 dated 2 December 2020) will undergo an amendment review by the WHO Ethical Review Committee based on revised sample size calculations, including information on the pooled analysis (pp. 10–13, Appendix B), revision of the case report forms (CRFs) (Appendix B), inclusion of draft guidelines on mother-to-child transmission (MTCT) (Apndices I–L) and general revisions to improve coherence and content alignment.
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Protocol summary

To better understand how severe acute respiratory coronavirus-2 (SARS-CoV-2) infection impacts outcomes in women and their neonates during pregnancy and the postpartum period, the World Health Organization (WHO) has developed a standardized research protocol for the investigation of coronavirus disease 2019 (COVID-19) in pregnant women. The protocol addresses key research questions, facilitates systematic and harmonized collection of data and biological specimens, and allows for data comparison and aggregation across different locations while minimizing potential biases. The protocol is designed to be adapted as needed in each study site based on resource availability and local circumstances.

This protocol outlines a prospective cohort study investigating the outcomes of pregnant or recently pregnant women infected with SARS-CoV-2 (exposed) compared to pregnant or recently pregnant women not infected with SARS-CoV-2 during pregnancy (unexposed). The purpose of this study is to determine if SARS-CoV-2 infection during pregnancy increases the risk of adverse pregnancy, postpartum or neonatal outcomes. Additionally, the study characterizes the clinical spectrum of COVID-19 in pregnant women, quantify (if any) the rate of in utero/intrapartum/postnatal transmission, determine the incidence of detectable SARS-CoV-2 RNA in pregnancy-related fluids (i.e. amniotic fluid), breast milk and tissues, and follow clinical outcomes of women and their newborns up to 6 weeks after childbirth.

It is expected that findings from studies implementing this protocol will be published, widely disseminated and used to develop recommendations on the surveillance, management and counselling of women during and after pregnancy, as well as their babies, in the context of the COVID-19 pandemic. Findings related to the implementation of this study protocol will help to inform public health measures, infectious disease and prevention measures, and future research protocols.
List of abbreviations

ARDS  acute respiratory distress syndrome
CIOMS  Council for International Organizations of Medical Sciences
COVID-19  coronavirus disease 2019
CRF  case report form
FGR  fetal growth restriction
GCP  good clinical practice
GDRP  general data protection regulation
IDMC  Independent Data Monitoring Committee
IPC  infection prevention and control
IRB  institutional review board
IUT  intrauterine transmission
LFU  loss to follow-up
LMICs  Low- and middle-income countries
MERS  Middle East respiratory syndrome
MTA  material transfer agreement
MTCT  mother-to-child transmission
NICU  neonatal intensive care unit
RDT  rapid diagnostic test
RT-PCR  reverse transcriptase polymerase chain reaction
SARS-CoV-2  severe acute respiratory syndrome coronavirus 2
TORCH  toxoplasmosis, rubella, cytomegalovirus, herpes simplex
WHO  World Health Organization
WG  working group
Preamble

This protocol is one of the WHO protocols for COVID-19 designed to enable the rapid and systematic collection of data in a format that facilitates comparison across different settings. All WHO investigation protocols for COVID-19 are available on the WHO website.

Any partner who wishes to use this protocol can do so freely and without charge or obligations. We ask implementing study sites to kindly inform the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)/World Health Organization (WHO) about their implementation of this protocol and to provide a contact point. Please share your information with hrp_covid19pregnancycohort@who.int

Implementing partners can opt to manage data onsite or through the central HRP repository subject to local circumstances. A pooled analysis bringing together all consenting and contributing sites will be discussed with sites implementing the study. Sites that agree to pool data under the coordination of WHO/HRP will have the option to independently publish their own data. The analysis of the pooled data will be made available and widely disseminated in collaboration with all contributing sites. All partners will retain control of their site data, regardless of whether or not this data is included in pooled or aggregated analyses.

All sites wishing to participate are invited to do so; however, WHO/HRP provides no guaranteed support for study implementation. Technical, financial or capacity limitations may be present. However, since this protocol proposes a study design that can be adapted to allow for smaller studies (see Appendix D for proposed methodologies), studies that follow the proposed study design may be pooled/aggregated in order to achieve an overall pooled sample size with sufficient statistical power to answer the primary research questions.

It is important to note that this protocol is designed to describe the core data variables in order to answer the key research questions and primary objectives outlined in the protocol. As such, the implementation of this study may include additional objectives or study components, as determined by each implementing site.

Comments for the user’s consideration are provided in purple text throughout the document, as the user may need to modify methods slightly because of the local context in which this investigation will be carried out.
1 Introduction

The World Health Organization (WHO) has established an overarching working group for research institutions implementing research on coronavirus disease 2019 (COVID-19) and pregnancy known as the Pregnancy and COVID-19 Research Working Group. The working group is designed to provide a collaborative forum for scientific discussion of research on this topic, with all implementing partners being invited to join the group. In addition, WHO has established a sub-working group (SWG) that is focused on the implementation of the generic protocol. This SWG allows provision of support to sites implementing the generic protocol, and it has also been used to discuss, explain and agree on the core components of the study. We have established core criteria for study design and core variables that should be included in any local adaptation. Local adaptation of the protocol per site are discussed in relation to what is outlined in the protocol.

In addition, UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)/WHO holds regular individual meetings with all implementing partners that wish to be part of pooled analyses. Specifically, a small number of selected partner sites in low- and middle-income countries (LMICs) receive tailored support plans in their efforts to implement the protocol. These overarching working groups and SWGs have been in place since April/May 2020 and meet regularly to ensure continuous dialogues with implementing and collaborating partners. Further, WHO monitors any studies adaptations to design or implementation that are planned within sites. This work will be used to guide and ensure quality of implementation as well as to provide an overview of sites and their respective timelines and, additionally, ensure any protocol adaptations are within the scope of what is outlined in the generic protocol. We recognize that sites will be implementing the protocol with varied resource availabilities, and parallel initiatives of research capacity strengthening will be tailored as needed for individual sites. Through close work with WHO colleagues outside HRP, in regional and country offices, we will also ensure regular contact points.

2 Research plan

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been identified as the cause of a febrile respiratory disease officially named COVID-19 (1) that, since its appearance, has spread across the globe. COVID-19 was declared a Public Health Emergency of International Concern by the WHO Director-General on 30 January 2020. At the current rate of transmission, a majority of people worldwide, including pregnant women, will be at risk of infection and acquiring the disease. Given a paucity of knowledge regarding SARS-CoV-2 in the context of pregnancy, there is an urgent need to better understand the disease in pregnancy to improve management and outcomes in this population.

The physiological, immunomodulatory and mechanical changes that occur during pregnancy can increase both a woman’s susceptibility to disease and severity for certain infections. At baseline, pregnant women are more vulnerable to respiratory distress from decreased residual lung capacity, increased oxygen consumption and higher circulating blood volume (2). It is currently unknown if pregnant women are more susceptible to infection and severe disease from SARS-CoV-2. Limited data from other coronaviruses, such as severe respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS), suggest mortality rates in pregnant women range between 25-30% (3,4).
It is unknown if SARS-CoV-2 can be transmitted from the mother to the fetus in utero or at childbirth. Although four recent systematic reviews failed to report any evidence for intrauterine infection (5–8), a recent media report and evidence of neonatal IgM antibodies for SARS-CoV-2 suggest otherwise (9–11). Additionally, because nearly all reports are on women who delivered via caesarean, it is unclear if transmission can also occur during vaginal delivery. In other coronavirus outbreaks, such as SARS and MERS, there were no documented reports of in utero transmission from mother to fetus (3).

The impact of SARS-CoV-2 infection on pregnancy is unclear. As the virus so recently emerged, data is lacking on outcomes associated with first or second trimester infection and risk of teratogenicity (12). One study of 8000 pregnant women with SARS-CoV-2 in the United States found that infection was associated with hospitalization, increased risk for intensive care unit admission and of receiving mechanical ventilation, but not death (13). Recent estimates indicate a COVID-19 infection fatality rate of 0.68% in the general population (14), while a large study of symptomatic women of reproductive age (15–44 years) in the United States has reported up to a 70% increased risk of death in pregnant women (15). Additionally, although data is not yet peer reviewed, case studies have reported that SARS-CoV-2 infection during pregnancy may increase risk of perinatal complications, including fetal distress, preterm birth and perinatal death (12,16–18).

This standardized protocol describes a prospective cohort study investigating the longitudinal course of women with exposure, exposure risk or documented infection with SARS-CoV-2 during their pregnancy. The overarching goal of this study is to gain critical knowledge on how infection with SARS-CoV-2 impacts pregnancy and neonatal outcomes, with the additional aims to understand mother-to-child transmission (MTCT) (if any), viral presence in pregnancy-related body fluids (i.e. amniotic fluid), breast milk and tissues, and the clinical presentation of the disease in pregnant women. Additionally, this protocol includes an option for a case control component to investigate disease severity in pregnancy compared to non-pregnant women with COVID-19.

Pooled analyses will be done at global level, and at national or subnational level, subject to priorities of individual partners implementing the protocol. Participation in global analyses is not a prerequisite to implement the protocol.

COMMENT: The introduction should be updated with country-specific data on COVID-19 epidemiology and current research findings prior to submission to local/national institutional review boards (IRBs).

3 Problem statement, aims and objectives

To better understand how SARS-CoV-2 infection during pregnancy impacts outcomes, the WHO has developed a standardized research protocol for the investigation of COVID-19 in pregnant women. The protocol will address key research questions, facilitate systematic and harmonized collection of data and biological specimens, and allow for data comparison and aggregation across different locations while minimizing potential biases. The protocol is designed to be adapted as needed in each study site, based on resource availability and local circumstances.

This protocol is for a prospective cohort study investigating maternal and neonatal outcomes in pregnant women infected with SARS-CoV-2 compared to pregnant women not infected with SARS-CoV-2. The purpose
of this study is to determine if SARS-CoV-2 infection during pregnancy increases the risk of adverse pregnancy or neonatal outcomes. Additionally, this study will characterize the clinical spectrum of COVID-19 in pregnant women, quantify (if any) the rate of in utero/intrapartum/postnatal transmission, determine the incidence of detectable SARS-CoV-2 RNA in amniotic fluid, breast milk, other bodily fluids and tissues, and follow clinical outcomes of women and their newborns up to 6 weeks after childbirth.

It is expected that findings from studies implementing this protocol will be published, widely disseminated and used to develop recommendations on the surveillance, management and counselling of women during and after pregnancy, as well as their babies, in the context of the COVID-19 pandemic. Findings related to the implementation of this study protocol will help to inform public health measures, infection disease and prevention measures, and future research protocols. The overall objective is to assess whether SARS-CoV-2 infection during pregnancy increases the risk of adverse clinical, pregnancy, perinatal or neonatal outcomes.

3.1 Definitions

**Pregnant women:** This protocol uses the term “pregnant women” to describe women who are pregnant or in the immediate postpartum period (up to 48 hours following delivery).

**Perinatal period** denotes the time between 22 weeks gestations and 7 days after birth.

**Neonatal period** denotes the first 4 weeks of a newborn’s life.

**Postpartum period** denotes the 42 days following delivery/pregnancy termination.

3.2 Outcomes and objectives

**Adverse outcomes** of interest:

1. **Maternal and pregnancy outcomes:** (e.g. induced abortion, ectopic pregnancy, miscarriage, delivery mode, preterm birth, fetal growth restriction, haemorrhage, maternal morbidity and mortality);
2. **Perinatal outcomes:** related to the fetus/neonate that occurs after 22 weeks gestation and within 7 days after birth (e.g. stillbirth, admission to the neonatal Intensive care unit (NICU), neonatal mortality within 7 days of life);
3. **Neonatal outcomes:** following birth up to 4 weeks of life (e.g. neonatal morbidity, infection, mortality);
4. **Postpartum outcomes:** maternal outcomes (e.g. infection, bleeding, transmission of SARS-CoV-2) up to 6 weeks after delivery;
5. **COVID-19 outcomes:** (e.g. hospitalization, acute respiratory distress syndrome (ARDS), severity, mortality, viral persistence).

The **primary objectives** of the study are:

1. to analyse if SARS-CoV-2 infection in pregnant women increases the risk of adverse outcomes (as per outcomes 1–4 above) as compared to pregnant women who are not infected with SARS-CoV-2;
2. to estimate the risk of MTCT of SARS-CoV-2 virus during pregnancy, intrapartum, postpartum (including during breastfeeding) among mother–neonate pairs with confirmed SARS-CoV-2 infection in pregnancy;
3. to describe viral presence and persistence in amniotic fluid, placenta, cord blood, fetus, neonate as well as in breast milk and other bodily fluids (urine, faeces, vaginal fluids);
4. to characterize the clinical course and disease spectrum of COVID-19 during pregnancy.
Secondary objectives include, but are not limited, to:

1. estimate the cumulative incidence of asymptomatic, subclinical and clinically apparent SARS-CoV-2 infection during pregnancy, as assessed by seroconversion or a positive reverse transcriptase polymerase chain reaction (RT-PCR) test during and following pregnancy;
2. measure the frequency of detectable RNA for SARS-CoV-2 by RT-PCR and IgG/IgM antibodies in neonates born to women infected with SARS-CoV-2 during pregnancy;
3. characterize the signs, symptoms and disease course of neonates who have SARS-CoV-2 infection following childbirth from a pregnant woman infected with SARS-CoV-2.

Optional secondary objective:
To determine if the disease severity and disease characteristics of COVID-19 are different in pregnant women compared with non-pregnant women of reproductive age. Please see Appendix D for details regarding this optional secondary objective.

COMMENT: Additional secondary objectives can be included in the protocol and will be informed by the outbreak characteristics and by the local context.

4 Required elements of protocol

This generic protocol is designed to be adapted to the local context of the implementing research institutions and sites. The components of this study that should be applied across all study sites include the inclusion/exclusion criteria of study participants and assignment of participants to study groups (see Fig. 1). In addition, it is expected that institutions adopting the generic protocol will utilize the generic case report forms (CRFs) provided in the appendix. These CRFs represent the suggested core of variables that sites should collect data on; however, the CRF is intended to be flexible with online data entry platforms including skip logic to allow sites to omit variables that cannot be collected. In addition, sites are welcome to add additional sections and/or variables to the CRF, if relevant for their context.

5 Methods

5.1 Study design

5.1.1 Objectives 1, 3, 4 and secondary objectives

This is a prospective longitudinal open cohort study of pregnant women exposed to SARS-CoV-2 or not exposed that will be recruited consecutively over time until the desired study sample size is achieved.

It will compare clinical, pregnancy, perinatal and neonatal outcomes for women with confirmed SARS-CoV-2 infection during pregnancy and the postpartum period of 6 weeks following the end of pregnancy (exposed) with pregnant women not diagnosed with SARS-CoV-2 infection during this period (unexposed).

Where possible, assignment of participants into exposed, unexposed and unknown groups will be based on the results of RT-PCR testing. In some settings, analysis of SARS-CoV-2 RT-PCR may not be available due to
limited laboratory capacity. In these situations, the study design may be adapted to use serology testing for IgG/IgM antibodies for group assignment (as described below and in Fig. 2).

Pregnant women will be enrolled into the exposed group of the cohort if they have tested positive for acute SARS-CoV-2 infection by RT-PCR before or until 14 days after pregnancy termination. Diagnostic testing should be available for review to confirm positive RT-PCR testing. Pregnant women will be enrolled into the (SARS-CoV-2 negative) unexposed group after negative RT-PCR and negative antibody testing. Pregnant women with negative RT-PCR (SARS-CoV-2 negative) in settings that do not have access to antibody test will be enrolled in the unknown group. Serology samples may be drawn from this group and saved for future analysis, in case antibody tests become available at a later date.

To conserve the limited number of diagnostic tests for SARS-CoV-2 RNA by RT-PCR, the entry point of the cohort is SARS-CoV-2 testing or screening of suspected cases or asymptomatic pregnant women, irrespective of hospitalization due to COVID-19.

Crossover between groups will be allowed. Women enrolled into the SARS-CoV-2 negative (unexposed) group who seroconvert during the pregnancy will crossover into the SARS-CoV-2 positive (exposed) group. Infants born to mothers enrolled in the cohort, as well as the mothers themselves, will be followed for 6 weeks after childbirth. Women who are SARS-CoV-2 negative with unknown serology (unknown) may crossover into the SARS-CoV-2 negative and serology negative (unexposed) group if/when antibody testing becomes available and they test antibody negative (see Fig. 1).
Figure 1. Study overview, setting with RT-PCR testing available

Presentation of pregnant woman at COVID-19 testing centre, health facility or antenatal care

RT-PCR test

RT-PCR negative

IgG/IgM test

IgG/IgM positive

Exclusion

RT-PCR positive

Enrolment in Exposed group

PCR or seroconversion during pregnancy

RT-PCR negative

No IgG/IgM test available

Save serology samples for future analysis

IgG/IgM negative

Enrolment in Unexposed group

IgG/IgM unknown

Enrolment in Unknown group*

Monthly follow-up during pregnancy

Outcomes of interest:

- Pregnancy outcomes
- Fetal outcomes
- Perinatal outcomes
- Neonatal outcomes (6 weeks postpartum)
- COVID-19 clinical spectrum
- Disease severity
- Viral persistence

In settings that have limited laboratory capacity for analysing RT-PCR specimens, assignment of pregnant women to study groups may be done using IgG/IgM serology testing (see Fig. 2). With this design, women with a positive IgG/IgM serology test would be enrolled in the exposed group. Women with a negative IgG/IgM serology test would be enrolled in the unexposed group. Crossover from the unexposed to the exposed group may occur when a woman seroconverts during the course of the pregnancy, after her initial enrolment in the study.
Figure 2. Study overview, setting with no capacity for RT-PCR testing

Presentation of pregnant woman at COVID-19 testing centre, health facility or antenatal care

IgG/IgM test

IgG/IgM positive
Enrolment in Exposed group

Seroconversion during pregnancy

IgG/IgM negative
Enrolment in Unexposed group

IgG/IgM unknown
Enrolment in Unknown group*

No IgG/IgM test available
Save serology samples for future analysis

Outcomes of interest:
- Pregnancy outcomes
- Fetal outcomes
- Perinatal outcomes
- Neonatal outcomes (6 weeks postpartum)
- COVID-19 clinical spectrum
- Disease severity
- Viral persistence

COMMENT: The WHO Emergency Use Listing dated 2 October 2020 and interim guidance on diagnostic testing for SARS-CoV-2 published 11 September 2020 (19) encourage the use of antigen-based rapid diagnostic tests (RDTs) especially in contexts with limited laboratory capacity. Investigators can opt to assign study participants into groups based on RDT results. While evidence of the performance of these tests is still emerging, kindly refer to the WHO guidance on considerations for the use of RDTs. Note that point-of-care immunodiagnostic tests are only recommended for research purposes and not as a basis for clinical decision-making (20).

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5.1.2 Specific study design for Objective 2

Postpartum and breastfeeding risk of transmission will be assessed in comparison to SARS-CoV-2 non-infected/unexposed mother–neonate pairs.

Optional secondary objective

Additionally, this study protocol provides the option of a nested case-control design, to be considered if the study sites have limited ability to perform antibody testing for all women (unknown exposure group). Please see Appendix D regarding this optional design.

Study setting/s

This study is designed to be conducted in areas with an ongoing COVID-19 outbreak. COVID-19 outbreak areas are defined as areas where disease surveillance detects community transmission of SARS-CoV-2 virus based on WHO epidemiologic studies or local surveillance data. The implementation protocol should clearly define the catchment area of included health facilities and describe the study base of the study sample.

5.2 Study participants and sampling

5.2.1 Study population

- **Inclusion criteria:** pregnant women (up to 2 days postpartum at time of enrolment) (Pregnant women with co-morbidities are eligible)
- **Exclusion criteria:** non-pregnant women. Evidence of immunity to SARS-CoV-2 prior to pregnancy start (+ IgG/IgM SARS-CoV-2 serology and no evidence of ongoing infection as in RT-PCR positivity at the time of enrolment).

NOTE: serology may need adaptation in relation to resources and availability. In some sites, only clinical history, negative PCR and the end point serology may be used.

5.2.2 Exposure status

1. **Exposed** status will consist of pregnant women who have tested positive by RT-PCR for SARS-CoV-2 during their current pregnancy or immediate postpartum period. Alternatively, in settings where RT-PCR is not available and/or RT-PCR samples cannot be analysed, women may be enrolled in the exposed group if they have detectable IgG/IgM antibodies during their current pregnancy or immediate postpartum period and no RT-PCR result. Participants enrolled as unexposed will crossover to the exposed group if there is evidence of seroconversion or positive RT-PCR for SARS-CoV-2 after study enrolment. Women who have detectable IgG/IgM antibodies at the onset of the study will be placed in the exposed group only if they have RT-PCR confirmed SARS-CoV-2 infection documented at enrolment.

2. **Unexposed** status will consist of pregnant women who have had negative testing for SARS-CoV-2 IgG/IgM at time of study entry and at end points: end of pregnancy and/or postpartum period. If women develop acute COVID-19 (as evidenced by positive RT-PCR testing) or demonstrate seroconversion after enrolment, they will crossover to the exposed group. Women with detectable IgG/IgM antibodies at the onset of the study will be excluded if they are RT-PCR negative.
3. **Unknown** status will consist of women who have tested negative or had no testing by RT-PCR for SARS-CoV-2 at time of study entry and at end points: end of pregnancy and/or postpartum period and who have not had IgG/IgM testing. It is recommended that serology samples for this group be drawn and stored for future analysis, if/when antibody testing becomes available at a later date.

5.3 **Recruitment**

Consecutive prospective recruitment will occur in a health-care setting where either screening and/or symptomatic testing of SARS-CoV-2 among pregnant women is ongoing; typically, this can be a clinic catering for individuals seeking care with COVID-19 suspect symptoms. Pregnancy testing may need to be offered to women of reproductive age seeking COVID-19 care, pending local circumstances. Pregnant minors are suggested to be offered inclusion in the study.

If screening for SARS-CoV-2 is applied to pregnant women attending maternal and child health care or antenatal care, this can also be used to recruit consecutive SARS-CoV-2 positive and negative pregnant women.

All pregnant women irrespective of SARS-CoV-2 testing or screening results will be offered to participate until sample size of exposed and unexposed groups are fulfilled.

Recruitment timing in relation to pregnancy assessment and test/screening results may be implemented differentially depending on the facility and staffing resources at each study site.

1. **SARS-CoV-2 positive pregnant women:** Confirmed by RT-PCR testing. The areas of recruitment may differ based on local resources and SARS-CoV-2 testing protocols but should be done in a manner that limits exposure to research staff as well pregnant women. Examples of possible recruitment strategies that can be used include: by telephone consent after obtaining status of SARS-CoV-2 testing of pregnant women, at antenatal care appointments/telemedicine visits (routine screening of all pregnant women for COVID-19 can help to facilitate the identification of those who have tested positive), during hospital admission (including labour and childbirth, triage, NICU) or emergency department visit, or in collaboration with COVID-19 testing sites.

2. **SARS-CoV-2 negative pregnant women:** Recruitment may differ based on local resources and SARS-CoV-2 testing protocols. Examples of possible recruitment strategies for this cohort can include by telephone consent after obtaining a negative SARS-CoV-2 RT-PCR test.

5.4 **Sample size calculation**

The site-specific sample size calculations for this study are informed by estimates of composite adverse pregnancy/neonatal outcome (miscarriage, preterm birth, perinatal death or NICU admission) in women with SARS-CoV-2 infection compared to women without SARS-CoV-2 infection in pregnancy. All sample size estimates provided in this section are based on 80% statistical power and type I error at 5% level. Furthermore, this section provides examples of initial sample size estimates on the basis of the proportion expected to have the outcome of interest among the SARS-CoV-2-unexposed (p₀) and also the effect size (ES). Additional information on sample size calculations can be found in Appendix B.
The final number of pregnant women to be enrolled in each group (SARS-CoV-2 exposed versus unexposed) will need to be further inflated to account for one or more of the following factors as relevant:

1. Anticipated crossover of pregnant women from the unexposed to exposed group, assumed to be 10% (based on the current estimated prevalence of 10%);
2. Loss to follow-up (LFU) during pregnancy for the primary outcomes involving adverse pregnancy outcomes, assumed to be at 5%;
3. LFU throughout pregnancy until 6 weeks postpartum, for primary outcomes assessable from post-childbirth and by the end of 6 weeks postpartum, assumed to be at 10%;
4. For the assessment of MTCT of SARS-CoV-2 via breast milk, the expected proportion of deliveries resulting in a livebirth AND neonate who is also uninfected with SARS-nCOV-2 at birth, assumed to be at XX%.  

The primary outcome is a composite outcome of any of the following: (i) miscarriage, (ii) preterm birth <37 weeks, (iii) perinatal death and (iv) NICU admission. The assumption, based on preliminary SARS-CoV-2 data in pregnant women, estimates that the exposed group will have between 11% to 22.5% risk for the composite outcome and the unexposed group will have a 10% to 15% risk for the composite outcome. That is, a relative risk of 1.1 to 1.5. Table 1 shows examples of sample size estimations for site-specific considerations. The calculations assume equal allocation of 1:1 ratio in terms of group sizes for SARS-CoV-2 exposed to unexposed.

<table>
<thead>
<tr>
<th>Risk ratio</th>
<th>1.1</th>
<th>1.1</th>
<th>1.5</th>
<th>1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>group 1 unexposed</td>
<td>0.10</td>
<td>0.15</td>
<td>0.10</td>
<td>0.15</td>
</tr>
<tr>
<td>group 2 exposed</td>
<td>0.11</td>
<td>0.165</td>
<td>0.15</td>
<td>0.225</td>
</tr>
<tr>
<td>Unadjusted sample size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>14 747</td>
<td>9255</td>
<td>683</td>
<td>423</td>
</tr>
<tr>
<td>N2</td>
<td>14 747</td>
<td>9255</td>
<td>683</td>
<td>423</td>
</tr>
<tr>
<td>Adjusting for LFU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>16 385</td>
<td>10 283</td>
<td>758</td>
<td>470</td>
</tr>
<tr>
<td>N2</td>
<td>16 385</td>
<td>10 283</td>
<td>758</td>
<td>470</td>
</tr>
<tr>
<td>Adjusting for seroconversion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>18 205</td>
<td>11 425</td>
<td>842</td>
<td>522</td>
</tr>
<tr>
<td>N2</td>
<td>14 565</td>
<td>9141</td>
<td>674</td>
<td>418</td>
</tr>
</tbody>
</table>

Sample size calculation for the pooled data will be based on different cohorts and outcomes to allow for outcome-specific and cohort specific analysis, and the single site-specific sample size will vary with national epidemic contexts and national estimates of adverse composite outcomes (see Appendix B for details).

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4 This is currently not included in the sample size calculation assumptions and input parameters presented.
5 These numbers are for illustration purposes and could be adjusted as necessary.
5.5 Methods of data collection

5.5.1 Schedule of the cohort

**Recruitment and enrolment/baseline visit:** Recruitment of pregnant women, study participants, should happen consecutively at the suitable facility. Study participation can be offered before SARS-CoV-2 testing results are available. Enrolment visit will be done at the site facility allowing recruitment of exposed and unexposed pregnant women over time. As per the study inclusion criteria, women may be recruited if they are pregnant or up to 2 days postpartum. Informed consent form will be signed at enrolment, following which baseline data will be collected.

**COMMENT:** Individuals who are approached for participation in the study and have not reached the age of majority, as determined by local laws, will be included in the study if they provide assent, supported by consent of parent or legal guardian. Consent of parent or guardian may be waived if allowed by the local ethical review committee (e.g. in case of emancipated minors).

**Follow-up during pregnancy:** Follow-up visits should occur, at a minimum, once per month from enrolment to the time of pregnancy outcome. The local standard of care for antenatal care and ultrasounds should be followed after enrolment. Care should be taken that pregnant women deemed potentially infectious for SARS-CoV-2 are not present for care simply to fulfil research purposes; instead, they should be clinically evaluated as appropriate by their medical provider. Visits via telemedicine or phone, if deemed appropriate by the health-care provider, are acceptable.

**At birth:** Neonatal and pregnancy outcomes, as well as the clinical status and management of pregnant/postpartum women will be studied. Specimens will be collected for testing.

**Follow up after childbirth:** Mother–newborn pairs will be followed for up to 6 weeks following childbirth. In the event of maternal death, prior to study recruitment, the family of the woman may be approached to ask for the possibility of retrieving clinical data from medical records, as well as information from a family member.

**COMMENT:** Guidance on the option of including a comparison with non-pregnant reproductive aged women infected with SARS-CoV-2 to determine disease severity in pregnant compared to non-pregnant individuals can be found in Appendix D.

5.6 Data collection and management

5.6.1 Questionnaire/CRF and biological specimen

After informed consent is obtained from study participants, a standardized study questionnaire will be administered to participants by research personnel (see Appendix B). If the woman cannot complete the standardized study questionnaire at the time of enrolment, attempts will be made to complete the questionnaire at the soonest opportunity it is reasonable to do so. However, it may not be feasible for the woman to complete the questionnaire at the time of enrolment if she is seriously ill, has an ongoing obstetric emergency or is in labour. If so, the questionnaire should be deferred until a more appropriate time.
At enrolment: Information from this questionnaire, ideally, to be collected at time of enrolment from the pregnant woman if circumstances allow, will include:

- demographic information
  - socioeconomic history (as indicated by wealth index)
- pregnancy characteristics
  - dating of pregnancy
  - ultrasound details
  - gestational age
  - complications
- medical and obstetric history
  - pregnancy history and outcomes (including adverse outcomes in prior pregnancies)
  - medical history
  - medication use
  - immunization history (in particular, seasonal influenza and bacille Calmette–Guérin (BCG) vaccines)
- social history (substance use/abuse)
- family history of congenital anomalies
- signs and/or symptoms of COVID-19 infection (including details and timing in relation to pregnancy and gestational age, as well as presence or absence of laboratory confirmation)
- laboratory evaluation (blood and nasopharyngeal samples)
  - specifically, confirmation of prior SARS-CoV-2 infection by serology
  - TORCH infections (toxoplasmosis, rubella virus, cytomegalovirus, HIV)
  - varicella zoster virus, Zika virus, herpes virus, syphilis, HIV.

At subsequent antenatal care visits, changes that have occurred since time of enrolment (for example, health status, pregnancy complications, ultrasound data, laboratory findings) should be updated.

COMMENT: Ultrasound surveillance during the pregnancy enables the study group to measure the association between timing (trimester) of SARS-CoV-2 infection in the mother and resulting abnormalities detected in the fetus. Thus far, there is no evidence that would suggest that SARS-CoV-2 infection in pregnancy increases the risk for congenital anomalies.

At the end of the pregnancy/study exit, the following information will be collected:

- Pregnancy outcome (e.g. live birth, miscarriage, stillbirth, induced abortion, etc.)
- Maternal and pregnancy outcomes (e.g. severe maternal morbidity, near miss events, early warning signs, preeclampsia, etc.)
- Neonatal outcomes (e.g. preterm birth, small-for-gestational age, SARS-CoV-2 infection, respiratory distress, low 5-minute Apgar score, etc.)
- Ultrasound data (in accordance with standard procedures and following national guidelines)
- Signs, symptoms and diagnostic evaluation of COVID-19 or other infections such as influenza, other viral infections, TORCH infections
- Laboratory evaluation of body fluids including pregnancy related fluids and tissues and breast milk
- Laboratory evaluation of the neonate (including testing for SARS-CoV-2 antibodies, influenza or other viral infections as relevant per epidemic context, arboviruses and TORCH infections).
Six weeks after the end of the pregnancy, the following information will be collected about the outcome of the woman and newborn pair:

- Laboratory evaluation of SARS-CoV-2 antibodies and/or RT-PCR testing for acute infection as relevant, PCR in breast milk and other testing as needed related to symptoms
- Health status and symptomatology of woman and newborn, specifically related to COVID-19, and other postpartum infections.

COMMENT: A standardized questionnaire, specific to this protocol, can be found in Appendix B. This questionnaire contains the core data variables that should be collected from study participants to address the objectives of this study. Further questions may be added at the discretion of the research group. The questionnaire is designed to be administered by trained study personnel, without advanced or specialized medical degrees.

5.6.2 Specimen collection and laboratory investigation

Table 2 outlines the specimen collection schedule for the study.

<table>
<thead>
<tr>
<th>Visits</th>
<th>Exposed cohort</th>
<th>Unexposed cohort</th>
<th>Unknown cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SARS-CoV-2 PCR</td>
<td>SARS-CoV-2 IgG/IgM</td>
<td>TORCH</td>
</tr>
<tr>
<td>At enrolment</td>
<td>a</td>
<td>X^b</td>
<td>X^b</td>
</tr>
<tr>
<td>V1</td>
<td></td>
<td></td>
<td>X^b</td>
</tr>
<tr>
<td>V2</td>
<td></td>
<td>X^b</td>
<td>X^b</td>
</tr>
<tr>
<td>V3</td>
<td></td>
<td></td>
<td>X^b</td>
</tr>
<tr>
<td>Delivery/end of pregnancy</td>
<td>X^c</td>
<td>X^c</td>
<td>X^b</td>
</tr>
<tr>
<td>Neonate^d</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

X Required specimens.

^a Required to show proof of positive test for SARS-CoV-2 RNA by RT-PCR prior to enrolment.

^b Optional, based on local resources and testing availability.

^c Includes umbilical cord blood, placenta, amniotic fluid, products of conception or fetal tissue (if miscarriage, stillbirth or induced abortion), and breast milk (as applicable).

^d Neonatal specimens will include neonatal throat swab and anal swab.

Specimen collection for exposed cohort:
- At enrolment: In settings where RT-PCR analysis is available, positive SARS-CoV-2 testing is required to enrol, therefore is not included as a study diagnostic test. TORCH laboratory studies are considered optional.
- At delivery/end of pregnancy:
  1. RT-PCR testing for umbilical cord blood, placenta, amniotic fluid, products of conception and/or fetal tissue (if miscarriage, stillbirth or induced abortion), breast milk and umbilical cord blood
  2. RT-PCR testing of neonate using throat swab and anal swab
  3. Antibody testing (SARS-CoV-2 IgM/IgG) of cord blood (optional).
Specimen collection for unexposed and unknown cohorts:
- At enrolment: In settings where serology analysis is available, SARS-CoV-2 IgG/IgM is required for enrolment, and SARS-CoV-2 RT-PCR via nasopharyngeal swab and TORCH laboratory studies are considered optional.
- During pregnancy (ideally every trimester): SARS-CoV-2 IgG/IgM is optional.
- At delivery/end of pregnancy: SARS-CoV-2 IgG/IgM is required, and SARS-CoV-2 PCR via nasopharyngeal swab and TORCH laboratory studies are considered optional.

All biological sampling for SARS-CoV-2 RNA (umbilical cord blood, placenta, breast milk, amniotic fluid, neonatal throat swab and anal swab) will follow WHO COVID-19 technical guidance documents on the proper handling and processing of potentially infectious specimens (Laboratory biosafety guidance related to coronavirus disease (COVID-19), published 19 March 2020,\(^6\) and Laboratory testing for coronavirus disease (COVID-19) in suspected human cases, also published 19 March 2020\(^7\)) as well as WHO general laboratory guidance (updated in 2004).\(^8\)

COMMENT: Given the rapidly developing guidance related to SARS-CoV-2, it is recommended that investigators check for updates to these documents prior to study initiation to ensure that current recommendations are being followed.

Specimen collection: All collection tubes will be labelled with a coded identification number that will also be recorded on the interview questionnaire. Time of collection, location and name of the person collecting the specimen should be noted.

COMMENT: In case of a miscarriage, induced abortion or stillbirth, or neonatal death, a post-mortem physical exam is recommended, if consent is obtained from the women to do so. In the event this is performed, fetal and placental tissue samples should be collected and stored at an appropriate facility for further analysis.

Specimen storage, preservation and shipment: Adapted from the interim guidance Laboratory testing for coronavirus disease (COVID-19) in suspected human cases, published 19 March 2020\(^9\) (see Appendix F).

Specimen transportation: Transportation of specimens within national borders should comply with applicable national regulations, international transport should comply with applicable international regulations, and shipping should be performed in accordance with the protocols outlined in WHO’s interim guidance document,\(^10\) published 31 March 2020. Where feasible, WHO reference laboratories should be

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\(^7\) WHO. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases (https://apps.who.int/iris/handle/10665/331501).

\(^8\) WHO. Laboratory biosafety manual, 3rd edition (www.who.int/publications/i/item/9241546506).

\(^9\) WHO. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases (https://apps.who.int/iris/handle/10665/331501).

\(^10\) WHO. Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus (https://apps.who.int/iris/handle/10665/331639).
used.\textsuperscript{11} The original samples will be packed, labelled and marked (if dry ice is used), and documented as Category B. Where possible, biological specimens will be analysed locally and in the study country. Due to limitations in laboratory capacity, transportation of biological specimens to neighbouring countries may be necessary for the purpose of analysis. In these cases, specimens should be destroyed after they are analysed. If this is the case, this will be clearly indicated in the implementation protocol, and detailed material transfer agreements (MTAs) will be needed.

\textbf{COMMENT 1}: Given the rapidly developing guidance related to SARS-CoV-2, it is recommended that investigators check for updates to these documents prior to study initiation to ensure that current recommendations are being followed.

\textbf{COMMENT 2}: If local and/or national laboratory capacity is limited, then samples may need to be sent to neighbouring countries for analysis. In these cases, the details of sample storage and transportation will be detailed in the implementation protocol and a detailed MTA will be needed.

5.6.3 \textit{Laboratory procedures}

Specimens will be processed either in the country in which the research institution is based or in collaboration with an external laboratory partner.

\textbf{COMMENT}: For sample storage, it is important that a governance structure is in place as per the \textit{Council for International Organizations of Medical Sciences} (CIOMS) guidelines.\textsuperscript{12} An additional section on leftover samples/storage may be added after considering the following matters in accordance with the guidelines.

\textbf{Remaining samples}: Samples will be destroyed at the end of the study and analysis period, unless otherwise specified in the site protocol. In these cases, a bio-repository or biobank may be created for possible use in future investigations, and participants need to consent. Storage of remaining samples is NOT a mandatory component to this protocol. The decision is left to the research team to determine if they have the capacity to pursue this endeavour. In some cases, analysis of samples at the clinical site may not be possible and storage of biological specimens may be recommended to ensure timely analysis of the samples, as per the stated aims of the study. In the event that remaining samples can be stored, a proper governance structure has to be put in place. Please see the subsection Ethical considerations, which includes the CIOMS guidelines on storage of biological specimens.

5.7 \textit{Data analysis}

The following primary outcomes correspond to the primary objectives of the study. Sample tables for each study outcome can be found in Appendix B.

\textsuperscript{11} WHO. WHO reference laboratories providing confirmatory testing for COVID-19 (www.who.int/publications/m/item/who-reference-laboratories-providing-confirmatory-testing-for-covid-19).

Primary outcome 1: Determine if COVID-19 infection in pregnancy increases the risk of adverse pregnancy or neonatal outcomes.

Primary outcome 2: To estimate the risk of MTCT of SARS-CoV-2 during pregnancy, intrapartum, postpartum or during breastfeeding among mother–neonate pairs with confirmed SARS-CoV-2 infection in pregnancy.\(^\text{13}\)

Primary outcome 3: To describe viral presence and persistence in the placenta as well as breast milk and other bodily fluids (5).

Primary outcome 4: To characterize the clinical course and disease spectrum of COVID-19 infection during pregnancy.

Secondary outcome 1: To estimate the cumulative incidence of asymptomatic, subclinical and clinically apparent COVID-19 infection during pregnancy, as assessed by seroconversion or an RT-PCR positive test during and following pregnancy.

Secondary outcome 2: Measure the frequency of detectable RNA for SARS-CoV-2 by RT-PCR and IgG/IgM antibodies in neonates born to women infected with SARS-CoV-2 during pregnancy.

Secondary outcome 3: To characterize the signs, symptoms and disease course of neonates who develop SARS-CoV-2 infection following childbirth from a pregnant woman infected with SARS-CoV-2.

COMMENT 1: A study option is available that allows for comparison between pregnant women with COVID-19 to non-pregnant women with COVID-19 infection to determine differences in disease severity (please see Appendix D for details on this study option).

COMMENT 2: Because the benefits outweigh potential risks for transmission, study participants with suspected or confirmed COVID-19 should be encouraged to breastfeed according to WHO guidelines (21).

5.8 Data management and data access
5.8.1 Procedures for ensuring confidentiality

Each participant will be allocated a unique study ID number at enrolment that all documents will subsequently use as identifier. No individual will be identifiable. Security of all study related documents with participant information at the local research site will be ensured by utilizing locked study cabinets for paper study folders and access-controlled with single sign-on features for computer files. The study will remove all identifiers from any data collected for this study at the individual and study site levels. No names or other directly identifying information (such as addresses and dates) will be entered in the regional or global databases including medical data. Subject numbers will be linked to investigator records stored separately and securely making it possible to identify the case in order to correct missing or erroneous data. Identifying information will be maintained by the responsible person in each hospital in accordance with regulatory agencies requirements.

Only anonymized data will be transferred via a web-based electronic data capture system that is general data protection regulation (GDPR) compliant and meets good clinical practice (GCP) and 21 CFR Part 11 regulations. WHO study database will be hosted utilizing AWS Frankfurt data centres in Europe using 256-bit encryption for all data in transit, which is the industry standard AES-256 encryption. Access to the data

\(^\text{13}\) See Appendices I–L for draft guidelines on definition and samples to be collected for testing.
platform will be controlled with logon name, password and user permission levels, and data privacy will be controlled at site level (i.e. users entering data into same site can see data from that site only).

5.8.2 Data management

WHO will offer support to data management and access to an online data entry platform. The WHO team, within the capacity of research strengthening, will support the development of local data platforms. Implementing partners can opt to manage data on site or through the central WHO repository subject to local circumstances. Further, the WHO/HRP will identify an external Independent Data Monitoring Committee (IDMC) to advise on study conduct and interim analyses of global pooled data.

Each site will be invited to share their data for pooled analysis and will also be able to publish their own data independently. Participation in pooled analysis is not mandatory for any site. Published data from these studies may be used to formulate recommendations on surveillance, diagnostic evaluation and clinical management of pregnant and postpartum women with suspected or confirmed COVID-19 and their newborns. Further, after obtaining agreement from each study site, the use of standardized protocol and harmonized collection of data will allow for pooled analyses, which in turn will contribute to rapid knowledge generation and strengthening the power of the analysis of the data to make recommendations.

Data collected in this study will be stored in password-protected databases. Each participant will be linked to an anonymous study ID, and patient-identifiable information (such as name and address) will be stored in password-protected databases. The location of and responsibility for the database will be determined on a case-to-case basis and dependent on national regulations. The designated data manager will be sent a password-protected copy of the database (anonymized and without any patient identifiers) for data analysis.

Diagnostic test results from the laboratory will be sent directly to the principle investigators so the results can be communicated to the participants. Results of tests will be shared with the participants or their primary care provider.

To protect patient identity, any publications or presentations relating to the study will use only aggregate summary data. The original data collection forms will be stored in a locked storage in accordance with national regulations. An identification log will be used, and this log will be stored in a secure, locked facility within the study country.

All essential study documents, including CRFs, will be electronically archived and retained at WHO for 3 years or for the duration required by the national laws and regulations at local research centres. This is to enable completion of the study, to conduct and complete data curation processes, and to finalize the publication and archival process. An editorial and governing board will be set up with consortium members and following CIOMS guidelines, a governance structure for sharing of analytic harmonized data will be implemented.

COMMENT: The study group will need to provide details on the procedures used for data management, protection and storage in the adaptation of the protocol. Good practice principles that are suggested for local study sites to follow include developing a manual of operations, monitoring study visits, performing visual inspections of paper forms and having a system of data entry that includes checks to ensure accuracy.
5.8.3 Dissemination and utilisation of results, including publication plans

Data sharing agreements will be established with each implementing site. Reporting of pooled results will follow an outlined statistical analysis plan, made available to all participating sites. Any academic publications of pooled results will aim for inclusiveness and equity, and a group author (with alphabetic list of names of participating contributors) as the exclusive author may be considered, following discussion and agreement with participating sites.

Reporting forms of site-specific results is up to individual investigators and should follow STROBE guidelines\(^\text{14}\) for cohort studies and ideally be reported in such a way to allow for comparison of data across different study sites.

At the global level, dissemination will be done in the standard ways to inform clinical management and WHO guideline development work. WHO will work with local partners to develop local dissemination plans, which will be included in site-specific study protocols. Findings from the global pooled analysis will be presented in reports and peer-reviewed publications.

5.8.4 Contributions to gender equality, equity and the human rights agenda

1. How does this research support efforts towards gender equality? The research is designed to describe the potential impact of SARS-CoV-2 on pregnant women.
2. How does it promote and protect human rights – which ones? By describing the potential impact of SARS-CoV-2 infection and COVID-19 on pregnant women, this study may be used in advocating for women’s access to reproductive health and maternal health services.
3. How does it ensure no one is left behind and prioritize the most vulnerable? The study includes all women meeting the inclusion criteria regarding pregnancy and SARS-CoV-2 status, regardless of socioeconomic, racial, religious or gender identity attributes.
4. Will it advance/improve (availability, access and/or quality of care) sexual and reproductive health services, goods, facilities or the underlying determinants? The findings from this study will be used to inform appropriate and necessary sexual and reproductive health and obstetric care for women with SARS-CoV-2 infection.
5. Describe how access to any researched products, interventions, technical solutions, etc., will be provided to in-need populations. Findings from this study will be used to inform guidelines on SARS-CoV-2 infection and pregnancy that may be adopted by national and local governments globally.
6. Are there any foreseeable outcomes of the study/product that might negatively impact human rights or gender equality? None.

5.8.5 Research capacity strengthening

This protocol will be adopted, adapted and implemented by research institutions across the globe, including members of the HRP Alliance who will receive support from their regional partners or the HRP for their

\(^{14}\) The Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies (www.equator-network.org/reporting-guidelines/strobe/).
conduct of the study. The Pregnancy and COVID-19 Research Working Group will provide technical guidance on the study of the implementation, including pooled analysis of data.

5.8.6 Environmental considerations

Environmental impact of this study is low since the data collection follows clinical work.

5.9 Ethical considerations

5.9.1 Informed consent

Written or verbal informed consent and/or assent will be obtained from all study participants. Women will not be included in the study without consent, assent or surrogate consent having been obtained. Best practice recommendations for these processes are described in the protocol. An option for verbal consent via telephone will be available in order to limit the risk of exposure to research staff given the nature of the study. Sites obtaining consent via telephone will create a script for research staff to use, which includes reading the full text of the informed consent form to the prospective participant. Informed consent may also be obtained via online means, in which case the text of the informed consent form – including checkboxes at the end of the form – will be presented online to the prospective participant. The participant will give their consent by checking all relevant checkboxes, indicating that they have read and understood the consent form. Before the first interview with the pregnant woman, the study purpose will be explained, and written or verbal informed consent will be obtained upon study enrolment by a trained investigative team member.

Individuals who are approached for participation in the study and have not reached the age of majority, as determined by local laws, will be included in the study if they provide assent. As per CIOMS guidelines, assessment of a child’s mental capacity to assent should consider the child’s:

1. ability to understand that there is a choice and that choices have consequences;
2. willingness and ability to make a choice, including the option of choosing that someone else make treatment decisions;
3. understanding of the nature and purpose of the procedure;
4. understanding of the risks and side-effects of the procedure;
5. understanding of the alternatives to the procedure and the risks attached to them, and the consequences of no treatment;
6. freedom from pressure.

If allowed by the local ethical review committee, consent of the individual’s parent or guardian may be waived. This can occur because the research involves no more than minimal risk to study participants, as data collection consists of a patient interview and specimen collection. In addition, the waiver of parental/guardian consent will not adversely affect the rights and the welfare of the subjects. In some instances, the research may not be able to be carried out without the waiver of parental consent, for example, if the parent is not present at any of the antenatal care or delivery visits to the facility.

In the context of this study, it may be difficult to distinguish between the researcher and the treating physician; however, research personnel should emphasize this distinction in approaching women for enrolment in the study. If the treating physician and researcher are the same person, utmost caution should be used to differentiate between the treatment of the patient and research. Treating physicians’ involvement
in the enrolment process should emphasize that the woman’s care and treatment is in no way dependent on their participation in the study.

COMMENT: If the study group determines that it will be difficult for participants to differentiate between the researcher’s role as physician and as researcher, they may choose to add additional measures to the consent process. This may include inviting the woman to participate in the study only once and allowing her time to reflect on whether or not she would like to participate in the study.

All women approached for enrolment will be informed that participation is voluntary and that she has the ability to withdraw from the study, without justification, at any time without consequences and the health care she or her newborn receives will not be affected by this action. Participants may withdraw from the study via in-person conversation, telephone or online means. Data that was collected up to the point of participant withdrawal from the study will remain with the study group, unless consent is retroactively withdrawn by the participant in question.

The informed consent form will ask for consent to collect information about the neonate during the birth hospitalization and up to 6 weeks of life. This consent will be collected using the same single consent process of the mother and can be signed by the adult mother. As per local circumstances, sometimes consent from the participant and the father of the neonate may be required for parts of the study concerning the neonate. Only if required by local IRBs, an additional separate consent form will be required and signed by the mother and her partner or a witness of her choice.

In the process of informed consent, participants will be asked to approve the sharing of RT-PCR results (collected for purposes of clinical care) with the research team, review of medical records on the current pregnancy and prior pregnancy history, collection of additional biological samples, as well as the collection of data regarding the outcomes of their pregnancies and neonates, for the intended purpose of the study. In some cases, samples may be drawn and analysed for the purposes of clinical care. If consent is obtained, then the samples and/or test results may be repurposed for use in the research study.

In the case of a cognitively impaired woman, determination of the cognitive level will be done by the managing physician. The managing physician must be someone who is not involved in the research study. In these instances, the individual responsible for enrolling the woman in the study will provide clear information during the informed consent process, emphasizing that the decision of whether or not to participate in the study will not affect care and that the potential risk of harm from study participation is minimal.

Special circumstances:

1. Critically ill patient, unable to consent (family member or responsible party available): If a woman is unable to provide consent due to illness, the family member or other responsible party will be asked to consent on behalf of the patient. If the patient’s responsible party agrees that the patient can participate, the responsible party will sign the consent and be given a copy. If they do not want the patient to participate, they will be thanked for their time and reminded that this decision will not affect their current health care. If the patient who is acutely ill improves and is able to provide consent after their responsible party provides consent, consent will be obtained from the actual study patient once they are able to provide meaningful consent. If the patient does not recover, then the patient’s responsible party will be approached for re-consent. Staff will take into account the sensitivity of the situation, given the death of the patient, in approaching the patient’s surviving family for re-consent.
2. **Critically ill patient, unable to consent (no available representative to make decisions on her behalf):**
   Patients will be approached for consent when they have medically improved to the point that they are able to do so. If they decline at that time, no data collection will follow, and no information will be drawn from their clinical records or specimen. All data collection and specimens will be destroyed.

3. **Patients who have died where informed consent has not been possible to discuss and without a responsible party available:** These patients will not be considered for inclusion in this study.

4. **Inability to read or write:** If the participant giving consent cannot read or write, information will be shared with a witness of her choice and this information will be read to them by a staff member. The witness will be asked to confirm that the woman received all the information about the study, was given the opportunity to ask questions and her questions were answered, and has verbally and voluntarily consented to taking part in the study. The witness must then sign the document stating that (he) was present during the consent process with the participant, the form was read to her, all questions were answered including regarding her rights to leave the study at any point, and she agreed to take part in the study.

**COMMENT:** The study group will need to define parameters of data sharing for both partners outside of the country and for future research endeavours that involve study samples.

In the process of informed consent, participants will be informed that any suspected or confirmed COVID-19 infection may be notified to national authorities under the International Health Regulations (IHR) requirements.

If the study participant agrees, the consent form must be completed legibly, with both the surname and first name, and be dated and signed by the participant (or witness if participant is illiterate) and the member of the investigative team, before any procedure can be performed as part of the current study. The investigative team member is responsible for obtaining the written consent of the participant.

There will be a checkbox on the consent form that explains that the participant has the option to withdraw consent at any time. If she chooses to do so, she will be able to consent or not consent to allowing collected specimens to be used.

After the informed consent form is signed (optional online agreement can be used), one copy will be made and given to the study participant. The original version of the consent form for each participant will be retained by the investigative team and kept in a secure place for a period of time determined by national and local IRB requirements, but at a minimum for 3 years as per WHO Ethical Review Committee requirements.

Information for participant and informed consent form templates for participants (the pregnant woman and her newborn) can be found in Appendix A.

In the event of maternal death prior to study recruitment, the family of the woman may be approached to ask for the possibility of retrieving clinical data from medical records, as well as information from a family member.
5.9.2 Incentives to participate and compensation

The primary benefit of this study is to gain medical knowledge and advance the care and counselling of women who are pregnant or planning pregnancy in a COVID-19 outbreak area. This study is not anticipated to directly benefit pregnant women enrolled in the study nor their infants. Trained health-care workers will provide study participants with additional information on how to protect against COVID-19 infection, the potential modes of COVID-19 transmission and possible risks during pregnancy.

Reimbursement for transportation to the study site will be offered if the visit to the site is for research purposes (as opposed to travel to the site for clinical management of pregnancy or COVID-19 infection). Any additional financial compensation should be determined on a study-by-study basis. This will need to be detailed in the information provided to the participant and during the informed consent process.

COMMENT: The clinical management of patients is not a part of this research protocol. It will be at the discretion of the medical consultant, and medical care will be provided per the standard of care at each recruitment site.

5.9.3 Policy on incidental findings

Ethical approval will be sought in accordance with local, regional, and national regulations. The sponsor and the investigators will be committed to conducting this research in accordance with the World Medical Association (WMA) Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects) adopted by the 64th WHA General Assembly, Fortaleza, October 2013.

Women who test positive for acute COVID-19 infection will be informed on recommended infection prevention and control (IPC) measures in order to limit disease transmission. For women with mild symptoms who are being managed at home, they will be provided with recommendations for home isolation, hand hygiene, respiratory hygiene, movement around the house/utilization of shared spaces and other recommendations as outlined in WHO Home care for patients with COVID-19 presenting with mild symptoms and management of their contacts, published 17 March 2020.15

Pregnant women who do not have COVID-19 infection will be provided with information on recommendations to minimize exposure risk to SARS-CoV-2, including but not limited to proper hand hygiene, recommendations on social distancing (per current local and international guidelines), as well as signs and symptoms of COVID-19 infection, as outlined in WHO COVID-19 risk communication package for health-care facilities published 10 March 2020.16

Investigators should check frequently for updates on recommendations and regulatory guidance, which will be posted on the WHO website. Additionally, investigators should ensure that they are up to date with local regulations and guidelines. WHO will also inform investigators of relevant updates, as they come available.

COMMENT: The study group will need to indicate which IRB has approved the adapted protocol, including the protocol version and date of ethical approval.


5.9.4 Benefits and risks for study subjects

The primary benefit of this study is to improve knowledge, counselling and medical management of women who are pregnant or planning a pregnancy in a COVID-19 outbreak area. The anticipated gained knowledge includes, but is not limited to, the presentation and severity of COVID-19 during pregnancy, prevalence of symptomatic and asymptomatic infections, pregnancy outcomes and potential for teratogenicity and for MTCT. This study is not intended to benefit participants directly because standard medical care will be used for all participants.

All biological specimens will be collected in accordance with current WHO guidance. WHO guidance on proper handling and processing of potentially infectious specimens should be closely adhered to, as outlined in WHO interim guidance Laboratory biosafety guidance related to coronavirus disease (COVID-19), published 19 March 2020, and Laboratory testing for coronavirus disease (COVID-19) in suspected human cases, also published 19 March 2020. WHO reference laboratories should be used, and specimens should be shipped in adherence to protocols outlined in WHO interim guidance document Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus, published 31 March 2020. The 3rd edition of WHO Laboratory biosafety manual, updated in 2004, should also be referenced for additional guidance.

COMMENT: Given the rapidly developing guidance related to SARS-CoV-2, it is recommended that investigators check for updates to these documents prior to study initiation to ensure that current recommendations are being followed.

Individuals in the study will be assigned to study groups based on results of RT-PCR tests for presence of SARS-CoV-2 and/or presence of IgG/IgM via serology testing.

This will require a minimum of two blood draws, which are likely to be performed as part of clinical management of the patient. The first blood draw will be obtained at time of study initiation, and the second blood draw will be obtained just prior to childbirth. If a blood draw is unable to be obtained prior to childbirth, it will be obtained as soon as possible after childbirth during the same hospitalization. The collection of a small amount of venous blood poses minimal risk to the women participating in the study. Results of any testing are the property of each participant and should be provided to each participant as soon as possible.

COMMENT: Both the protocol and informed consent document must explain all tests that will be performed on collected samples, how the results of the tests will be used, and how results will be shared with the participants. This will likely depend on local IRB requirements.

18 WHO. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases (https://apps.who.int/iris/handle/10665/331501).
20 WHO. Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus (https://apps.who.int/iris/handle/10665/331639).
5.9.5 Biobank guidance

Biobank guidance can be found in Appendix H and is based on the CIOMS guidelines on storage of biological specimens. Study sites may choose to save biospecimens locally in their country. In this case, the site should follow CIOMS guidelines with regards to how long the specimens can be stored. Implementing sites should also modify the informed consent forms to include this information regarding storage of samples in local biobanks if this is planned.
6 References


7 Acknowledgements

The continuous input of members of the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP)/Sexual and Reproductive Health (SRH) working group on SARS-CoV-2 and pregnancy research has been invaluable to the development of this generic protocol and is acknowledged. These include:

Moazzam Ali
Mercedes Bonet
Vanessa Brizuela
Megan Foeller
Caron Kim
Loulou Kobeissi
Olufemi Oladapo
Melanie Taylor
Appendix A: Description of investigation and informed consent template

COMMENT: The language of this document is more technical than information sheets and informed consent forms. The text will therefore need to be adapted based on the local setting and IRB requirements.

Part 1: To be completed prior to enrolment

INFORMATION FOR THE WOMAN

Dear Mrs/Ms/Miss,

We are inviting you to participate in the research study entitled:

A prospective longitudinal cohort study of women and newborns diagnosed with SARS-CoV-2 during the course of their pregnancy

This study is being conducted by __________________________, the International Sponsor, __________________________, the local investigator, and several international collaborators including __________________________.

INFORMATION

The purpose of this document is to provide you with written information that is needed for you to make a decision regarding your participation in the study. Please read this document carefully, and please feel free to ask any questions you may have to us or your health-care provider. Additionally, if anything is unclear or if you would like further information, please let us know. You may take additional time to consider participating in this research, and you may discuss this with friends or family prior to making a decision. If you agree to participate in the study, your health-care provider will ask you to fill in, sign and date the consent form in the appropriate spaces.

CONSENT PROCESS

Your participation in the study is completely voluntary. If you chose to participate, you can withdraw your consent at any time, without consequence, ill-feeling or prejudice.

GENERAL BACKGROUND AND RESEARCH OBJECTIVES

As you may know, coronavirus disease 2019 (COVID-19) has been circulating in [region of study] since [time of first detection of COVID-19 into study region]. You are being asked to participate in a study that aims to understand the role of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – the virus that causes COVID-19 – during pregnancy on you and your baby. SARS-CoV-2 is usually transmitted by respiratory droplets. People who become infected with SARS-CoV-2 may have a range of illness, from asymptomatic disease to mild symptoms to severe illness. Symptoms usually consist of fever, shortness of breath or cough.

It is unknown if women who are pregnant experience SARS-CoV-2 infection differently from individuals who are not pregnant. However, one study has shown that SARS-CoV-2 infection during pregnancy is associated with hospitalization, increased risk for intensive care unit admission and receipt of mechanical ventilation, but not with death (1). Additionally, it is not known if pregnant women with SARS-CoV-2 can pass the virus onto their baby, although so far there is no evidence that this occurs. It is unclear if pregnant women who become ill with COVID-19 have higher rates of pregnancy-related complications or health issues in their newborn. The purpose of this study, which we are asking you to consent to participate in, is to answer these questions.
The main objectives of this research study are to:

- describe the symptoms, clinical course and outcomes for pregnant women with COVID-19;
- describe any pregnancy complications or health problems the baby may experience after childbirth, if any, for pregnant women with SARS-CoV-2 infection;
- determine if SARS-CoV-2 infection can be passed from the mother to her baby during pregnancy and, if so, how often this occurs and what it means for the baby;
- estimate the number of pregnant women who may experience SARS-CoV-2 infection with no symptoms or just minimal symptoms.

COMMENT: Briefly describe the location of the study and the anticipated study size. If the option to assess the disease severity of pregnant versus non-pregnant women with SARS-CoV-2 infection is conducted, this should be added to the study objectives.

RESEARCH PROCESS

If you agree to participate in the study, you will be asked questions about your health, pregnancy and medical history, and your life. We will ask for permission to access your past and present medical records.

We will ask to take a sample of amniotic fluid by either amniocentesis prior to delivery (if performed for a separate reason) or during caesarean section. We will also ask to take a small portion of the placenta, a swab of the placenta and a small amount (less than 2 teaspoons) of blood from the umbilical cord after the baby is born and the umbilical cord is cut. Additionally, we will ask to swab the baby’s throat after birth. Tests will be performed to see if the SARS-CoV-2 virus can be identified in these items.

COMMENT: If additional specimens are collected (see Appendix C, Tier 2 and 3 specimens), they should be added and described here.

[Add the following for individuals enrolling into the non-exposed group]:

We would like to draw a small amount (less than 2 teaspoons) of your blood using a needle in your arm. If possible, we will draw these samples with your routine prenatal testing, so you do not have to have any additional blood draws performed. This will be tested for antibodies to SARS-CoV-2 to see if you have already experienced infection (which may be asymptomatic). At the end of pregnancy when you come to maternity unit for childbirth, we will ask to draw approximately 7.5 mL of blood (less than 2 teaspoons) of your blood to, once again, test for antibodies to SARS-CoV-2 to see if you have experienced infection. If possible, we will draw these samples at the same time as the routine testing done during labour, so you do not experience additional blood draws. At the birth, up to 3 ml (approximately ½ teaspoon) will also be collected from your baby. This will be done with a needle and if we are having difficulty in obtaining the blood sample, we will attempt the blood draw no more than two times. The samples collected from you and your baby will be tested for the coronavirus and may be tested for other viral infections as part of your clinical care. Exam findings from the newborn exam will also be collected. Samples will be analysed locally. However, if this is not possible due to lack of local laboratory capacity, then samples may be sent to a neighbouring country for analysis and will be destroyed after analysis is complete.

We will also ask for a follow up visit after childbirth to examine the newborn within 6 weeks following birth. This visit will entail another newborn examination and blood tests for coronavirus and other infections.
COMMENT: The tables below may be adapted to facilitate comprehension of the study visits. As the local team will determine the total number of follow up visits during pregnancy, they will fill in the appropriate number of “follow-up visit” rows. The minimum amount of follow-up visits as stated in the protocol is at least once per trimester until the end of pregnancy. Therefore, the number of follow-up visits is not set as it is dependent on the time point that the woman entered prenatal care and enrolled, as well as the outcome of childbirth (e.g. fewer follow-up visits if the woman was enrolled in the 2nd trimester or if the pregnancy ended earlier than expected).

**Table A1. Visits and lab tests for unexposed group only**

<table>
<thead>
<tr>
<th>Visit</th>
<th>Questionnaire</th>
<th>Lab tests (control group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolment</td>
<td>Study questionnaire part I</td>
<td>Blood test for SARS-CoV-2 IgG/IgM antibodies (7.5 mL of blood)</td>
</tr>
<tr>
<td>Follow-up visits 1–3 (at ---- weeks)</td>
<td>Study questionnaire part II</td>
<td>Blood test for SARS-CoV-2 IgG/IgM antibodies (7.5 mL of blood)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Comment: include if planning to test for antibodies multiple times during the pregnancy</em></td>
</tr>
<tr>
<td>Childbirth hospitalization</td>
<td>Yes, pregnancy outcome and delivery mode</td>
<td>Blood test for SARS-CoV-2 IgG/IgM antibodies (7.5 mL of blood)</td>
</tr>
<tr>
<td>Post-birth follow-up visit</td>
<td>Study questionnaire part III</td>
<td>No lab tests</td>
</tr>
<tr>
<td>(within 6 weeks following delivery)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Comment: only include Table A1 for the control group.*

**Table A2. Visits and lab tests for exposed group only**

<table>
<thead>
<tr>
<th>Visit</th>
<th>Questionnaire</th>
<th>Lab tests (control group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolment</td>
<td>Study questionnaire part I</td>
<td>No lab tests</td>
</tr>
<tr>
<td>Follow-up visits 1–3 (at ---- weeks)</td>
<td>Study questionnaire part II</td>
<td>No lab tests</td>
</tr>
<tr>
<td>Childbirth hospitalization</td>
<td>Yes, pregnancy outcome and delivery mode</td>
<td>Placental sample</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Umbilical cord blood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amniotic fluid at delivery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baby throat swab</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Baby anal swab</td>
</tr>
<tr>
<td>Post-birth follow-up visit</td>
<td>Study questionnaire part III</td>
<td>No lab tests</td>
</tr>
<tr>
<td>(within 6 weeks following birth)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Comment: only include Table A2 for the study group.*

There is a risk that you may experience some discomfort with the blood draw. Sometimes, a small bruise may appear. Some individuals may feel lightheaded with the blood draw. If this occurs, it is temporary and does not require medical treatment or consultation.
COMMENT: Blood sample/childbirth specimens may require a second informed consent form for collection and, if so, they will need to be signed prior to childbirth. These requirements often depend on local IRB rules and regulations.

RISKS AND BENEFITS OF YOUR PARTICIPATION

This research does not pose any foreseeable risk to you, and no procedures will be performed that are not designed for the purpose of this study. There is no anticipated direct benefit to you or your child by participating in this study. However, this study will help to answer important research questions for other women who experience a pregnancy in a COVID-19 outbreak area.

RESEARCH RESULTS

The results of this research will be shared with national and international organizations, such as the World Health Organization. Data from this research may be presented in scientific conferences or in publications. Your personal data will not be identifiable in any way. Additionally, all study data will remain confidential and coding will be used to remove your first and last name, as well as any other identifying information. Only a small number of key study personnel will be able to access the study data.

COMMENT: If the results of the study will be made available online and there is information on how participants can access this information, this should be added. In addition, there should be additional information inserted by the country team in how the results can be made easily accessible and understood by the lay person (i.e. community meetings, creation of a poster that provides the main results from the study, which is placed in the reception area of the health centres where the research has taken place).

CONFIDENTIALITY AND TREATMENT OF COMPUTERIZED DATA

We will need to enter your data into an electronic data to be able to analyse it and answer the research questions in the study. Your medical data and lifestyle data will be transmitted confidentially and under strict protection only to your doctor or to individuals from the research group or key study personnel in [country of study] or overseas in other countries [name these individuals here].

If, during the study, you decide that you no longer want to participate, the study group will ask for your permission to keep the data you have contributed up to the point you withdraw the study or to destroy all data.

INFORMATION ON YOUR SAMPLES DURING AND AFTER THIS STUDY

COMMENT: This section should only be included if the research team has the capacity for a biobank and has set up a governance structure as detailed in the protocol. The following is a sample section that can be elaborated and adapted to the parameters set up by the research team.

We will also ask you if you would be willing to allow researchers to use any “left over” samples for other research studies. What we mean is, if your samples are not completely used upon completion of this study, they could be stored in a biobank (a storage facility in the study laboratory) and used for other research studies that are looking at SARS-CoV-2 infection. In any future studies, your identity would remain confidential. This future research may be conducted in your country or outside of your country but researchers of the team who collected your samples in the first place will receive priority in the case that multiple researchers are requesting use of the sample. The remaining samples will be stored at [name of national/designated laboratory].
At any time, and without consequence to your participation in the present study or to your medical care, you may choose not to answer certain questions. You may also choose to withdraw your consent for the use of your samples for these other research objectives. This can be done simply by contacting the health-care professional who is supervising your participation in this study.

COMMENT: Ensure to insert the details of how confidentiality will be maintained. Samples stored in the biobank are usually anonymized, de-identified or coded. Please provide the pertinent description based on your team’s decision of how samples will be stored. Examples are given below.

Anonymous data: All personal information that identifies you will be removed, and there will be no link between you and your sample. This would be the process of anonymizing your data.

De-identified data: Your sample will be de-identified, which means that any personal information that identifies you will be removed permanently. There will be nothing that exists which will link you to the sample.

Coded data: All personal identifying information will be replaced with a code which is usually made up of letters, numbers, symbols or a combination of figures. However, a link between this code and you will be kept in a confidential manner. This will be done by having the codes remain with a custodian of the biobank and there will be limited access to the materials by anyone outside of the research team.

The research team needs to decide on the above when setting up their governance structure. Further description of how the samples will be stored should be explained in this information sheet for the patient to make an informed decision.

Measures to protect confidentiality (per CIOMS guidelines):

- how confidentiality of the link between the specimen and personal identifiers is maintained;
- who may have access to the materials for future research and under what circumstances;
- to which other sources of personal information the results of analyses on biological materials may be linked.

Please feel free to ask any questions about the information you have just read/been given or about the study itself.
INFORMED CONSENT OF THE WOMAN

I, undersigned, ___________________________________________ confirm that I have read and understood all the information presented to me, relative to my participation in the study entitled

A prospective longitudinal cohort study of women and newborns diagnosed with coronavirus disease 2019 (COVID-19) during the course of their pregnancy

This study has been described to me, the document “Information for the participant” has been read to me by ________________________________, and I have received answers for all the questions that I asked.

☐ I have read or orally received all the necessary information to understand the topic and enrolment process of the study.

☐ I was able to ask questions and received clear and adequate responses.

☐ I confirm my participation in this study, which includes responding to a questionnaire and allowing the taking of biological samples from me and my newborn baby.

☐ I understand that there are no predicted risks to me or my fetus or newborn in participation in the study.

☐ I have been advised that there is no financial incentive foreseen in this study.

☐ I am aware reimbursement for transportation to the study site will be offered if the visit to the site is for research purposes (as opposed to travel to the site for clinical management of pregnancy or SARS-CoV-2 infection).

☐ I understand that I can withdraw, at any time, my consent to participate in this study, for any reason and without having to justify myself, and without incurring any consequence or prejudice to me or my fetus/baby. I must simply inform the health-care professional in charge of this study through in-person, telephone or online means. If I choose to withdraw from the study, I will be given the option to consent or not consent to allowing samples that have already been collected to be used.

☐ I agree to give access to the study investigators to my past and present clinical data. This clinical data may include biological samples, clinical observations related to the current pregnancy or suspect SARS-CoV-2 infection, and/or prior pregnancy history.
CONSENT TO USE OF PERSONAL DATA

I accept that my personal data will be recorded and computerized by a data manager for the purpose of this study.

I accept that my baby’s personal data will be recorded and computerized by a data manager for the purpose of this study.

I accept that my medical files and the medical files for my baby may be looked at by the appropriate persons implicated in this research study, all of whom will keep my confidential.

CONSENT TO THE USE OF BIOLOGICAL SAMPLES

I accept the use and storage of my biological samples as it has been described by the study group.

I have been informed that my biological samples may be stored even after the end of the study period in order to conduct further research on SARS-CoV-2 infection. Other research teams, national or international, may carry out this research. This authorization will no longer be valid if I withdraw my consent during the study.

SIGNATURES

<table>
<thead>
<tr>
<th>Study participant</th>
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</thead>
<tbody>
<tr>
<td>I freely and voluntarily accept to participate in the study that has been described to me.</td>
</tr>
<tr>
<td>LAST NAME, First name:</td>
</tr>
<tr>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have accurately read or witness the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.</td>
</tr>
<tr>
<td>LAST NAME, First name:</td>
</tr>
<tr>
<td>Contact number:</td>
</tr>
</tbody>
</table>
If the person giving consent cannot read or write, a witness must be present and sign here:

**Witness**

I was present during the consent process with the participant. This form was read to him/her, all questions were answered s(he) agreed to take part in the study.

<table>
<thead>
<tr>
<th>LAST NAME, First name:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Signature:</td>
</tr>
</tbody>
</table>

**Researcher**

I have accurately read or witness the accurate reading of the assent form to the witness, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.

<table>
<thead>
<tr>
<th>LAST NAME, First name:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Signature:</td>
</tr>
</tbody>
</table>

Contact number:

COMMENT: The last page of this document must have the signatures of the researcher and of the person being solicited and must be dated by the hand of the person who has consented in the spaces where indicated.

This information and consent document must be made in two original copies: one copy is to be given to the participant, and one is to be kept for the required legal duration for research documented by the health-care professional in charge of the research, in the research locations at each regional site of the study.
Appendix A1: Consent to the use of biological samples

**COMMENT:** As noted in the protocol, the decision is left to the research team to determine if they have the capacity to store leftover samples (biobank). In the event that leftover samples can be stored, a proper governance structure has to be put in place. Components of that governance structure have been listed in the protocol. A separate consent can be obtained with regards to the biobanking of study samples. The following can be used as a potential sample that will require further details based on the governance structure the research team has set up.

From the samples you provide during this study, a large amount will be used for the analysis planned in this protocol, but there may be some leftover volume of each sample. This consent form is to discuss the storage of these leftover samples in a biobank, which is a storage facility in the study laboratory. The samples can be used to conduct further research on SARS-CoV-2. This future research may be conducted in your country or outside of your country but researchers of the team who collected your samples in the first place will receive priority in the case that multiple researchers are requesting use of the sample. Your sample will not be sold for profit, and any research that uses your sample will have been approved by the proper research governing bodies. This consent for use of samples in future studies will no longer be valid if you withdraw your consent during this current study.

If you agree to have your leftover samples stored and used in future studies, you can decide if you also agree to have your samples included in studies about the impact of human genes on disease.

**COMMENT:** Ensure to check Appendix H for further details on biobanking of specimen. Ensure to insert the details of how confidentiality will be maintained; where and how long the respective specimen would be stored, per CIOMS international guidelines. Note that the transfer of biological materials must be covered by an MTA.

**Measures to protect confidentiality (per CIOMS guidelines):**

- how confidentiality of the link between the specimen and personal identifiers is maintained;
- who may have access to the materials for future research, and under what circumstances;
- to which other sources of personal information the results of analyses on biological materials may be linked.

If you do not agree to have your leftover samples stored and used in future studies, we will destroy the leftover samples after this study is completed.

You have the right to refuse the storage of your samples and also have the right to put restrictions on the use of these samples. This will not impact your care or the current research study.

---


SARS-CoV-2 and pregnancy prospective cohort study
Please indicate below:

1) Do you agree to have your leftover samples stored and used in future studies?
   YES ☐   NO ☐

2) If you agree to have your leftover samples stored and used in future studies, do you understand your sample will be anonymized at the start of the storage time?
   YES ☐   NO ☐

If yes, please note that you will be unable to request destruction of the samples at a later date.

<table>
<thead>
<tr>
<th>Study participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAST NAME, First name:</td>
</tr>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.</td>
</tr>
<tr>
<td>LAST NAME, First name:</td>
</tr>
<tr>
<td>Contact number:</td>
</tr>
</tbody>
</table>
Appendix B: Sample size estimates for individual sites and standardized questionnaires/CRFs

Sample size for site-specific and pooled data
Two approaches were used to determine the required sample sizes for the study:

1. Site-specific sample size calculation is based on a composite adverse pregnancy/neonatal outcome that includes outcomes at each stage of pregnancy, delivery and postpartum (e.g. miscarriage, preterm birth, perinatal death or NICU admission).

2. Pooled data sample size calculation is based on outcome and cohort specific prevalence.

The main components of the sample size determinations are: the study design, which is a prospective cohort study with two groups and predefined outcomes, the statistical analytical methods used to test the study hypothesis, includes likelihood ratio test, generalized linear model (GLM) and possible multilevel modelling. In addition, the significance level $\alpha$ (type I error) is set at 0.05 to protect the null hypothesis or a state in which an incorrect decision is more costly, $P(\text{reject } H_0 | H_0 \text{ is true}) = \alpha$.

The power of the test (or type II error) is the probability of correctly rejecting the null hypothesis when the null hypothesis is false $P(\text{reject } H_0 | H_0 \text{ is false}) = 1 - \beta$, it was set to be 80%. The baseline rate, which is the anticipated outcome(s) rate for the unexposed group, and finally the clinically meaningful relative difference or relative risk.

Once the sample size calculation is determined, several considerations for LFU and seroconversion need to be taken into consideration when determining the required sample size. Also, due to limited human and maternal resources, it may not be feasible to conduct the study under the original ideal specifications; therefore, varying the input parameters to find an appropriate balance between the desired detectable effect, sample size available resources, time and the primary objective of the study, would help in reaching a decision on the “final achievable” sample size. Thus, several scenarios for sample size calculations are presented below for both site-specific and pooled data required sample sizes.

**Site-specific sample size estimate**

1- Outcome (composite adverse outcomes) in the unexposed group ranges between 4% to 50%
2- Relative risk ranges between 1.1 to 1.5 (i.e. an increase between 10% to 50% in the exposed group)
3- Equal group allocation
4- LFU of 10% in both groups
5- Seroconversion of 10% (i.e. 10% of the recruited non-COVID-19 pregnant women will become infected during the study).

Table B1 presents different sample sizes for different parameters. The duration of the recruitment depends on the level of infection (seroprevalence) among pregnant women.
### Table B1. Site-specific sample size estimates

<table>
<thead>
<tr>
<th>RR</th>
<th>P1</th>
<th>P2</th>
<th>N1</th>
<th>N2</th>
<th>N1</th>
<th>N2</th>
<th>N1</th>
<th>N2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>0.04</td>
<td>0.044</td>
<td>39 462</td>
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SARS-CoV-2 and pregnancy prospective cohort study
Generic protocol: Last updated 2 December 2020, version 2.6
Pooled data sample size estimates

All pregnant women and women admitted for delivery or delivered outside the study site in the last 48 hours are eligible for inclusion, therefore, time of enrolment can be divided into THREE periods in relation to the study outcomes:

1. before 22 weeks of gestation (cohort C1)
2. 22+ weeks of gestation (cohort C2)
3. at delivery and 2 days after delivery (cohort C3).

The pooled data sample size will be an outcome and cohort specific and, for each stage, sample size will be determined. As with the size-specific estimates, type I and II errors and allocation values will be the same. However, the LFU and seroconversion will be cohort specific, in addition to the outcome of interest. Attrition due to other outcomes will be used to determine the number of women in each group who are likely to progress to the second stage or to the end of the study to help in estimating the number of additional women to be recruited. Table B2 below gives an example of outcome and cohort specific input parameters and Table B3 provides detailed sample size needed for relative risks of 1.1 to 1.5.

Table B2. Outcome and cohort specific sample size calculation parameters for the pooled data

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Table B3. Sample size calculation for the pooled data with varying relative risks

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23 These numbers are for illustration purposes and could be adjusted as necessary.

24 These numbers are for illustration purposes and could be adjusted as necessary.
Standardised questionnaires/CRFs

Development of the Draft Questionnaires

These questionnaires (also known as CRFs) have been designed by WHO and HRP with contributions from members of the established working groups on COVID-19 and pregnancy research.

Purpose of the generic questionnaire and instructions for use

These questionnaires have been designed to collect the minimum amount of data to address the primary objectives of the generic cohort study of pregnant women. Additional questions may be added to the questionnaire, as determined by the financial and technical capacity of the study group and by the outbreak characteristics. Each questionnaire is designed to be implemented by trained study personnel, without advanced degrees or specialized medical degrees.

COMMENT: By using a standardized protocol, researchers can address many research objectives and will have the opportunity to collaborate with other research sites/countries conducting the same study and potentially will be able to pool data to address the primary research questions of this protocol.
Instructions for completing the questionnaire

When completing the sections of the questionnaire, please ensure that:

- the participant has been given information about the study and the informed consent form has been completed and signed;
- the study ID codes have been assigned for both the pregnant woman and neonate as per study protocol;
- all information should be kept confidential at all times, and no identifiable information is to be recorded on the questionnaires;
- patients’ hospital ID and contact details are recorded on a separate contact list to allow later follow-up by a limited number of key/approved study personnel. The contact forms must be kept separate from the questionnaires at all times and kept in a secure location.

General guidance

- The questionnaire is designed to collect data obtained through patient examinations, through parent/guardian/representative interview (for neonates), and the review of hospital charts. Each questionnaire will state where information should be obtained (i.e. from medical records or patient interview).
- Patient ID codes should be filled in on all pages of the questionnaire (neonate and mother).
- Complete every line of every section, except for where the instructions say to skip a section based on certain responses.
- It is important to indicate when the answer to a particular question is not known. Please mark the “Unknown” box if this is the case. Do not leave the question blank.
- Some sections have open text areas where you can write additional information. To permit standardized data entry, please avoid writing additional information outside of these areas.
- Place an (X) when you choose the corresponding answer. To make corrections, strike through (---) the data you wish to delete and write the correct data above it. Please initial and date all corrections.
- Please keep all sheets for each study participant together, e.g. with a staple or in a folder that is unique to the participant.
- We recommended writing clearly in black or blue ink, using BLOCK CAPITAL LETTERS or completing electronically.
- Do not use abbreviations, write out each letter.
- Complete the heading on each page.
- Use standard medical language.
- Write only one character per box (I_I)
- Numerical values:
  - Align numerical values to the right;
  - Do not add commas or full stops, they will already be present in the form field if appropriate;
  - Do not leave any space empty, enter a zero if necessary:
    - Incorrect: _I_2_I_1_I_I_I
    - Correct: _I_0_I_2_I_1_I
- If the response must be entered into closed tick-boxes, mark the box as follows:
  - Yes ☐ No ☒
- Dates: enter dates in the format Day/Month/Year (DD/MM/YYYY).
- In the case that the data is missing or unknown, leave tick boxes or other spaces empty and enter the codes that follow, as appropriate:
  - NA: Not applicable
  - ND: Not done
  - NK: Not known
For the primary investigators of this study, please contact us if we can help with any questionnaire completion questions, if you have comments and to let us know that you are using the forms. Please contact hrp_covid19pregnancycohort@who.int

**Disclaimer:** These questionnaires are intended for use as a standardized document for the collection of clinical data in studies investigating COVID-19. Responsibility for use of these questionnaires rests with the study investigators. The authors of the questionnaire accept no responsibility for its use in an amended format nor for the use of the questionnaire outside its intended purpose.

**Overview of the CRFs**
The nine CRFs linked to this study (see Fig. B2) are designed to collect data obtained through participant interview, examination and review of hospital notes and other medical records. The data collection period is defined as the period from study enrolment to transfer from study site, death, study exit (i.e. 6 weeks postpartum) or continued hospitalization without possibility to continue data collection. Data may be collected retrospectively if the patient is enrolled into the study after hospitalization or death (with family consent). If CRFs cannot be completed at particular time points (e.g. respondent may be seriously ill, being managed for an obstetric emergency or in labour), attempts should be made to complete them at the soonest opportunity it is reasonable to do so. Note that the schematic below is a simplified general overview that may not reflect the dynamics of participant presentation and data collection in each site. Evidence on MTCT of SARS-CoV-2 is emerging. It is helpful to review Appendices I–L for draft definitions, criteria and scenarios regarding in utero, intrapartum and postnatal transmission of SARS-CoV-2. Appendices K and L contain guides for determining timing of infection and samples for assay.
Figure B2. Simplified schedule of study progression and administration of CRFs

* Investigators can opt to assign study participants into groups based on RDT results. Kindly refer to the WHO guidance on the use of RDTs (www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2-infection-using-rapid-immunoassays). Note that point-of-care immunodiagnostic tests are only recommended for research purposes and not as a basis for clinical decision-making.

** Depending on contextual realities, the frequency of follow-up visits may coincide with the regular schedule of prenatal visits or an alternative schedule. Follow-up visits may be conducted online or via phone to allow for reporting of symptoms or events, as needed.
## Table B4.

<table>
<thead>
<tr>
<th>CRF</th>
<th>Descriptive Name</th>
<th>Indications for use and notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRF1</td>
<td>Screening and eligibility assessment</td>
<td><strong>To be completed at first contact with prospective participants</strong></td>
</tr>
<tr>
<td>CRF2</td>
<td>Participant characteristics at enrolment</td>
<td>To be completed at time of enrolment for all participants regardless of test result. This questionnaire is designed to be conducted as an interview with questions directed to the participant. Depending on situation at time of enrolment, it may be conducted at a later date or information retrieved through review of medical records.</td>
</tr>
<tr>
<td>CRF3</td>
<td>Clinical characteristics at enrolment</td>
<td>To be completed at time of enrolment for all participants regardless of test result. If diagnosis of SARS-CoV-2 occurred prior to enrolment, research staff to fill form per review of medical records. Depending on situation at time of enrolment, this form may also be filled at a later date and based on review of medical records.</td>
</tr>
<tr>
<td>CRF4</td>
<td>COVID-19</td>
<td>To be completed for exposed group only at enrolment or verification of seroconversion (i.e. crossover into exposed group), or where needed, for hospitalization due to COVID-19.</td>
</tr>
<tr>
<td>CRF5</td>
<td>Prenatal visit / follow-up information</td>
<td>To be completed for all participants regardless of group (exposed, unexposed, unknown) at every follow-up prenatal visit. These visits should ideally occur once a month. This questionnaire should be filled out by the research staff upon review of the medical record.</td>
</tr>
<tr>
<td>CRF6</td>
<td>Maternal outcomes at delivery or pregnancy termination</td>
<td>To be completed for all participants regardless of group (exposed, unexposed, unknown) at delivery or pregnancy termination. This questionnaire should be filled out by the research staff upon review of the medical record.</td>
</tr>
<tr>
<td>CRF7</td>
<td>Neonatal outcomes between birth and 7 days</td>
<td>To be completed for all participants regardless of group (exposed, unexposed, unknown) at any point between birth and the first 7 days of life (i.e. the perinatal period). This questionnaire should be filled out by the research staff upon review of the medical record. Complete one form per neonate</td>
</tr>
<tr>
<td>CRF8</td>
<td>Neonatal outcomes assessed at 4 weeks of life</td>
<td>To be completed for all participants regardless of group (exposed, unexposed, unknown) at four weeks of life. This questionnaire should be filled out by the research staff upon review of the medical record.</td>
</tr>
<tr>
<td>CRF9</td>
<td>Maternal outcomes at 6 weeks postpartum/study exit</td>
<td>To be completed for all participants regardless of group (exposed, unexposed, unknown) at 6 weeks postpartum or study exit (including death of participant). This questionnaire should be filled out by the research staff upon review of the medical record.</td>
</tr>
</tbody>
</table>
### SCREENING AND ELIGIBILITY ASSESSMENT FORM

**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

**CR1**  
**1/2**  
**V1.0 (16 Nov 2020)**

#### Project ID: **A66012**

#### Center ID: [ ]

#### Screening ID: [ ]

#### Country: [ ]

#### Date of Assessment: [ ]

---

#### VERIFICATION OF ELIGIBILITY

**A. Assessment of Exposure (Assignment based on RT-PCR)**

1. **Confirmed test of SARS-CoV-2 by RT-PCR**
   - before or until 2 days after delivery/pregnancy termination (Note: check medical records. Review of diagnostic result is required for study enrollment)
   - **1 = Yes**
   - **2 = No**

2. **Date of RT-PCR test result**
   - [ ]

3. **Test Result**
   - **1 = Positive**
   - **2 = Negative**
   - **9 = Unknown**

4. **If RT-PCR negative or unknown, conduct antibody (IgG/IgM) testing, or take specimen sample for storing and analysis at a later date**
   - [ ]

5. **Test Result**
   - **1 = Positive**
   - **2 = Negative**
   - **9 = Unknown**

6. **Commercial name of serology test used**

7. **Is serology test positive?**
   - **1 = Yes**
   - **2 = No**

   - **If serology positive**, conduct individual assessment and decide enrollment into exposed group based on level of antibody, gestational age and case history/presenting symptoms

   - **If serology negative**, candidate for unexposed group. Skip to C

   **Note**: If serology test not available, you may enroll participant into unknown group and consider collecting and storing specimen sample for future analysis. Skip to C

**B. Assessment of Exposure (Assignment based on IgG/IgM serology tests)**

8. **Confirmed test of SARS-CoV-2 by serology**
   - before or until 2 days after delivery/pregnancy termination (Note: check medical records. Review of diagnostic result is required for study enrollment)
   - **1 = Yes**
   - **2 = No**

9. **Date of serology test result**
   - [ ]

10. **Commercial name of serology test used**

11. **Is serology test positive?**
    - **1 = Yes**
    - **2 = No**

    **If serology positive**, conduct individual assessment and decide enrollment into exposed group based on level of antibody, gestational age and case history/presenting symptoms

    **If serology negative**, candidate for unexposed group. Skip to C

    **Note**: If serology test not available, you may enroll participant into unknown group and consider collecting and storing specimen sample for future analysis. Skip to C

**C. Other criteria (in addition to assessment of exposure, participants must answer yes to this question)**

12. **Planning to live in the region and attend follow up visits at study site (or catchment health facility) or be followed up by telephone**
    - **1 = Yes**
    - **2 = No**
**SCREENING AND ELIGIBILITY ASSESSMENT FORM**

<table>
<thead>
<tr>
<th>EXCLUSION CRITERIA</th>
<th>COMMENTS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(participant ineligible if 'yes' to any of these questions)</td>
<td></td>
</tr>
<tr>
<td>13. Woman is unable or unwilling to give informed consent or assent, or (where applicable) surrogate consent has not been secured</td>
<td></td>
</tr>
<tr>
<td>14. Woman is planning to move outside of study area during study period</td>
<td></td>
</tr>
<tr>
<td>15. Woman is/was not pregnant at the time of SARS-CoV-2 infection</td>
<td></td>
</tr>
<tr>
<td>16. Woman has not reached the age of majority, as determined by local laws</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ELIGIBILITY DECISION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>17. Does participant meet eligibility criteria for enrollment?</td>
<td></td>
</tr>
<tr>
<td>18. Informed consent obtained</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gestational age at time of enrollment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>20a) weeks</td>
<td></td>
</tr>
<tr>
<td>20b) days</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group Allocation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Exposed</td>
<td></td>
</tr>
<tr>
<td>2 = Unexposed</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
</tbody>
</table>

| Participant ID | |

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A66012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center ID:</td>
<td></td>
</tr>
<tr>
<td>Screening ID:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COMMENTS:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interviewer's name:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>Month</td>
</tr>
</tbody>
</table>
### PARTICIPANT CHARACTERISTICS AT ENROLLMENT FORM

**GENERAL**

1. Date of Assessment/Extraction

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>73</td>
<td>12</td>
<td>2020</td>
</tr>
</tbody>
</table>

**DEMOGRAPHIC INFORMATION**

2. Date of birth (DOB)

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>08</td>
<td>1990</td>
</tr>
</tbody>
</table>

3. If DOB unknown, Age and Birth Year

- 3a) Age
- 3b) Birth Year

4. Area of residence during pregnancy

(Or, enter GPS coordinates)

5. Born in country of current residence?

- 1 = Yes
- 2 = No

5s) If "No", specify country of birth

6. Ethnicity

- 1 = Ethnicity #1
- 2 = Ethnicity #2
- 3 = Ethnicity #3
- 4 = Ethnicity #4
- 5 = Ethnicity #5
- 6 = Ethnicity #6
- 7 = Ethnicity #7
- 8 = Ethnicity #8
- 9 = Ethnicity #9
- 10 = Ethnicity #10
- 99 = Unknown

6s) If "Other", specify

7. Refugee status?

- 1 = Yes
- 2 = No
- 3 = Unknown

8. Gender identity

- 1 = Woman
- 2 = Man
- 3 = Transgender
- 4 = Non-binary
- 5 = Do not wish to respond
- 6 = Other

8s) If "Other", specify

9. What is your marital status?

- 1 = Single
- 2 = Currently married
- 3 = Separated
- 4 = Divorced
- 5 = Widowed
- 6 = Cohabiting
- 7 = Do not wish to respond

10. What is the highest level of schooling attained?

- 1 = No formal schooling
- 2 = Less than primary school
- 3 = Primary school completed
- 4 = Secondary/High school completed
- 5 = College/University completed
- 6 = Post-graduate degree
- 7 = Do not wish to respond

11. Professional category/Occupation

*Comment: Include occupational / professional categories that are appropriate for study context. Select all that apply*

- 1 = Yes
- 2 = No

11a) Government employee
- 11b) Non-government employee
- 11c) Self-employed
- 11d) Student
- 11e) Homemaker/Housewife
- 11f) Retired
- 11g) Daily wage/informal laborer
- 11h) Unemployed (able to work)
- 11i) Unemployed (unable to work)
- 11j) Do not wish to respond
- 11k) Other

11s) If "Other", specify
### INFORMATION ON LIFESTYLE DURING PREGNANCY

The following questions aim to collect information on the pregnancy participants' lifestyle during pregnancy. This is sensitive information and the study group may wish to collect this information at the end of the Part I section.

12. Have you consumed any alcohol within the past 30 days?
   - 1 = Yes
   - 2 = No
   - 3 = Do not wish to answer
   - 9 = Unknown

13. During the past 30 days, did you have at least one standard alcoholic drink?
   - 13a) Number
   - 13b) Do not wish to answer
   - 13c) Unknown

14. During the past 30 days, when you drank alcohol, how many standard drinks on average did you have during one drinking occasion?
   - Standard measures of alcoholic drinks include:
     - 1 can of ordinary beer; a single shot of spirits (e.g., whiskey, gin, vodka, etc.); a glass of wine or a small glass of sherry; a small glass of liqueur or aperitif
   - 14a) Number
   - 14b) Do not wish to answer
   - 14c) Unknown

15. Have you ever smoked any tobacco products, such as cigarettes, cigars, pipes, or vaping?
   - 1 = Yes
   - 2 = No
   - 3 = Do not wish to answer
   - 9 = Unknown

16. Do you currently smoke any tobacco products, such as cigarettes, cigars, pipes, or vaping?
   - 1 = Yes
   - 2 = No
   - 3 = Do not wish to answer
   - 9 = Unknown
   - 16s) If "Yes" to above, do you currently smoke tobacco products (such as cigarettes, cigars, pipes, or vaping) daily?
     - 1 = Yes
     - 2 = No
     - 3 = Do not wish to answer
     - 9 = Unknown

17. On average, how many tobacco products (the equivalent of a cigarette) do you smoke each day/week?
   - 17a) Daily
   - 17b) Weekly

18. Have you ever used any recreational drugs?
   - 1 = Yes
   - 2 = No
   - 3 = Do not wish to answer
   - 9 = Unknown

19. Do you currently use any recreational drugs?
   - 1 = Yes
   - 2 = No
   - 3 = Do not wish to answer
   - 9 = Unknown
   - 19a) Cannabis
   - 19b) Crack
   - 19c) Cocaine
   - 19d) Heroin
   - 19e) Methamphetamine
   - 19f) Opiates / opioids
   - 19g) Other
   - 19s) If "Other", specify

20. During the past 30 days, on how many occasions did you use recreational drugs?
<table>
<thead>
<tr>
<th>MEDICAL HISTORY AND CURRENT CONDITIONS</th>
<th>21c) If &quot;Yes&quot;, specify</th>
<th>21d) If &quot;Yes&quot;, indicate timepoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>21a) Heart disease</td>
<td></td>
<td>1. Prior to current pregnancy</td>
</tr>
<tr>
<td>21b) Lung disease</td>
<td></td>
<td>2. During current pregnancy</td>
</tr>
<tr>
<td>21c) Blood disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21d) Kidney disease</td>
<td></td>
<td></td>
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<tr>
<td>21e) Liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21f) Neurological disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21g) Thyroid disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21h) Endocrine disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21i) Immunosuppression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21j) Type 1 or Type 2 diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21k) Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21l) Malaria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21m) Dengue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21n) Chikungunya</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21o) Zika</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21p) Influenza</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21q) HIV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21r) Syphilis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21s) Hepatitis A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21t) Hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21u) Hepatitis C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21v) Hepatitis D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21w) Hepatitis E</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21x) Toxoplasmosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21y) Rubella</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21z) CMV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>an) Kaposi's Simplex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ab) Other medical condition/infection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SARS-CoV-2 and pregnancy prospective cohort study
Generic protocol: Last updated 2 December 2020, version 2.6
# A66012: SARS-CoV-2 and pregnancy prospective cohort study

## Generic protocol

Last updated 2 December 2020, version 2.6

## Particiant characteristics at enrollment form

<table>
<thead>
<tr>
<th>Project ID</th>
<th>Center ID</th>
<th>Participant ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>A66012</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Medications during this pregnancy

22. Medications that have been or are in use during the current pregnancy and taken regularly or as prescribed

<table>
<thead>
<tr>
<th>1 = Yes</th>
<th>2 = No</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

22s) If "Yes", specify generic name (s)

22si) specify

- Fever or pain treatment
- Aspirin
- Anticonvulsants
- Antihypertensives
- Anti-nausea
- Antivirals
- Antibiotics
- Intermittent preventive treatment
- Medications for diabetes mellitus
- Prenatal vitamins/micronutrients
- Iron Supplement
- Folic acid supplement
- Other prescribed or routine medications

### Immunization history

Provide information on immunizations ever received, including during current pregnancy. The list of options should be revised based on contextual norms and depending on availability of records.

Where multiple (booster) doses have been received, indicate dates for each dose

23. Immunized?

<table>
<thead>
<tr>
<th>1 = Yes</th>
<th>2 = No</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

23s) If "Yes", date of last dose

23si) specify

- Pneumococcal vaccine?
- Meningococcal vaccine?
- MMR vaccine?
- Varicella (chickenpox) vaccine?
- DPT vaccine?
- Poliomyelitis vaccine?
- Seasonal influenza vaccine?
- Hepatitis B vaccine?
- Hepatitis A vaccine?
- BCG vaccine?
- Inactivated typhoid vaccine?
- Rabies vaccine?
- Yellow fever vaccine?
- Other vaccinations?

If yes, specify

Note: list should be revised per context e.g. tick-borne encephalitis; Japanese encephalitis
### OBSTETRIC HISTORY

*Excluding the current pregnancy and regardless of whether the pregnancy resulted in a live birth, please indicate*

24. Number of past pregnancies

25. Number of previous pregnancies beyond 22 weeks gestation

26. Number of previous vaginal deliveries

27. Number of previous cesarean deliveries

### COMMENTS:

**Interviewer's name:**

**Signature:**

**Date:**

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>
## PARTICIPANT CHARACTERISTICS AT ENROLLMENT FORM

<table>
<thead>
<tr>
<th>Project ID: A66012</th>
<th>Center ID</th>
<th>Participant ID:</th>
<th>Date of the end of the pregnancy: Day Month Year</th>
</tr>
</thead>
</table>

1. Number of fetuses (1-9)  
2. What was the outcome of the pregnancy?  
   1 = Livebirth  
   2 = Spontaneous abortion  
   3 = Induced abortion  
   4 = Missed abortion  
   5 = Stillbirth  
   6 = Ectopic pregnancy  
3. Gestational age at birth/termination of pregnancy:  
   3a) Weeks  
   3b) Days  
4. Mode of delivery:  
   1 = Vaginal delivery  
   2 = Spontaneous  
   3 = Instrumental (vacuum/forceps)  
   4 = Planned cesarean delivery  
   5 = Emergency cesarean delivery  

Following section should be repeated separately for each fetus/baby indicated in question 1.

5. Fetus/Baby Number (1-9)  
6. Gender of Baby:  
   1 = Male  
   2 = Female  
   3 = Non-binary  
   4 = Do not wish to respond  
7. Weight of baby at delivery:  
   from card Kg  
   from recall Kg  
8. If weight unknown, estimate size of baby:  
   1 = Very large  
   2 = Larger than average  
   3 = Average  
   4 = Smaller than average  
   5 = Very small  
   9 = Don’t know  
9. If live birth, current status:  
   1 = Alive  
   9 = Unknown  
10. If born alive and now dead, how old was the baby when he/she died?:  
   Years  
   Months  
   Days
### GENERAL

1. Date of Assessment/Extraction

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

### CURRENT PREGNANCY

2. Number of fetuses (1-9)

3. Dating of pregnancy
   - 1 = Yes
   - 2 = No
   - 3a) LMP
   - 3b) LMP consistent with ultrasound during pregnancy
   - 3c) First trimester ultrasound
   - 3d) Second trimester ultrasound
   - 3e) Third trimester ultrasound
   - 3f) ART (artificial reproductive technology)
   - 3fs) If "yes", date

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

- 3g) Unknown
- 3h) Other
  - 3hs) If "Other", specify

### Pregnancy complications, diagnoses or symptoms in relation to the current pregnancy and prior to COVID-19 diagnosis if this has occurred

- Note: ask of all women, regardless of test result status
- Note that this form needs to be repeated at all (bi)monthly follow up visits until termination/delivery irrespective of COVID-19

5. Gestational hypertension
   - 1 = Yes
   - 2 = No
   - 9 = Unknown
   - 5s) If "Yes", specify
     - 5si) Non-proteinuric hypertension
     - 5sii) Pre-eclampsia / eclampsia
     - 5siii) Unspecified / don’t know

6. Anemia (Hb < 11 g/dL)
   - 1 = Yes
   - 2 = No
   - 9 = Unknown

7. Hyperemesis
   - 1 = Yes
   - 2 = No
   - 9 = Unknown

8. Fetal growth restriction
   - 1 = Yes
   - 2 = No
   - 9 = Unknown

9. Placental previa/accreta/percreta
   - 1 = Yes
   - 2 = No
   - 9 = Unknown

10. Embolic disease
    - 1 = Yes
     - 2 = No
     - 9 = Unknown

11. Placental abruption
    - 1 = Yes
     - 2 = No
     - 9 = Unknown
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. Preterm labor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Preterm premature rupture of membranes (&lt;37 weeks) (PPROM)</td>
<td></td>
<td></td>
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<tr>
<td>14. Bleeding during pregnancy</td>
<td></td>
<td></td>
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<tr>
<td>15. Vaginal watery discharge</td>
<td></td>
<td></td>
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<tr>
<td>16. Headaches</td>
<td></td>
<td></td>
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<tr>
<td>17. Vision changes</td>
<td></td>
<td></td>
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<tr>
<td>18. Right upper quadrant (abdominal) pain</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>19. Decreased or no fetal movement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Hemorrhage (&gt;500 ml of blood loss)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21. Liver disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. Other complications/diagnoses/symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23. Was ultrasound performed?</td>
<td></td>
<td></td>
<td>go to question 34</td>
</tr>
<tr>
<td>24. Fetal growth restriction &lt;10th centile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. Oligohydramnios (SDP &lt;2cm)</td>
<td></td>
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</tr>
<tr>
<td>26. Ultrasound abnormalities (if performed)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20s) If &quot;Yes&quot;, specify</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21si) Obstetric cholestasis</td>
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<td></td>
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<tr>
<td>21sii) Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21siii) Abortion-related</td>
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<td></td>
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</tr>
<tr>
<td>20sii) Postpartum haemorrhage</td>
<td></td>
<td></td>
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<tr>
<td>20siii) Antepartum/intrapartum</td>
<td></td>
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</table>

**CLINICAL CHARACTERISTICS AT ENROLLMENT FORM**

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A66012</th>
<th>Center ID:</th>
<th>Participant ID:</th>
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<tbody>
<tr>
<td>Country:</td>
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### CLINICAL CHARACTERISTICS AT ENROLLMENT FORM

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<th>Center ID:</th>
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<td>A66012</td>
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**Country:**

<table>
<thead>
<tr>
<th>Item</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>26. Polyhydramnios (SDP &gt;8cm)</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>25s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>27. Echogenic bowel</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>26s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>28. Ventriculomegaly (≥ 10 mm)</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>27s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>29. Effusion</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>28s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>30. Cardiomegaly</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>29s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>31. Ascites</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>30s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>32. Hydrops fetalis</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>31s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
<tr>
<td>33. Other/Suspected anomaly</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>32s) If &quot;Yes&quot;, specify gestational age</td>
<td></td>
</tr>
</tbody>
</table>

**CLINICAL INFORMATION AT ENROLLMENT**

(Note: complete all boxes with 9s in case of unknown value)

<table>
<thead>
<tr>
<th>Item</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>34. Current body weight</td>
<td>kg</td>
</tr>
<tr>
<td>35. Height</td>
<td>m</td>
</tr>
<tr>
<td>36. Body temperature</td>
<td>°C</td>
</tr>
<tr>
<td>37. Respiratory rate</td>
<td>breaths/minute</td>
</tr>
<tr>
<td>38. Heart rate</td>
<td>beats/minute</td>
</tr>
<tr>
<td>39. Urinary Glucose</td>
<td></td>
</tr>
<tr>
<td>1 = (+)</td>
<td></td>
</tr>
<tr>
<td>2 = (++)</td>
<td></td>
</tr>
<tr>
<td>3 = (+++)</td>
<td></td>
</tr>
<tr>
<td>4 = Negative</td>
<td></td>
</tr>
<tr>
<td>40. Urinary Protein</td>
<td></td>
</tr>
<tr>
<td>1 = (+)</td>
<td></td>
</tr>
<tr>
<td>2 = (++)</td>
<td></td>
</tr>
<tr>
<td>3 = (+++)</td>
<td></td>
</tr>
<tr>
<td>4 = Negative</td>
<td></td>
</tr>
<tr>
<td>41. Arterial blood pressure (Systolic / Diastolic)</td>
<td>mmHg</td>
</tr>
<tr>
<td>42. Pulse</td>
<td>beats/minute</td>
</tr>
</tbody>
</table>
### CLINICAL CHARACTERISTICS AT ENROLLMENT FORM

**Project ID:** A66012  
**Center ID:**  
**Participant ID:**  
**Country:**  

<table>
<thead>
<tr>
<th>42. Pulse oximetry</th>
<th>%</th>
<th>62. ESR</th>
<th>mm/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>43. Fetal heart rate</td>
<td>beats/minute</td>
<td>63. Total bilirubin</td>
<td>mg/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>64. D-dimer</td>
<td>ng/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65. Urea (BUN)</td>
<td>g/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66. Ferritin</td>
<td>ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>67. Lactate</td>
<td>mg/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68. IL-6</td>
<td>pg/mL</td>
</tr>
</tbody>
</table>

**LABORATORY RESULTS AT ENROLLMENT**

*Note: Specify unit of measurement for each parameter. Modify list as relevant for the context. Complete all boxes with 9s in case of unknown value.*

<table>
<thead>
<tr>
<th>44. Haemoglobin</th>
<th>g/L</th>
<th>49. Potassium</th>
<th>mEq/L = mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>50. Platelets</td>
<td>mm3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>G/L (= x 10^9/L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51. Procalcitonin</td>
<td>ng/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ng/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>52. APTT/APTR</td>
<td>seconds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>53. CRP</td>
<td>mg/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>54. PT</td>
<td>seconds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55. LDH</td>
<td>IU/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>56. INR</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>57. Creatinine Kinase</td>
<td>RI/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>58. ALT/SGPT</td>
<td>IU/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60. Troponin</td>
<td>ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>61. AST/SGOT</td>
<td>IU/L</td>
</tr>
</tbody>
</table>

**COMMENTS:**

*Interviewer's name:  
Signature:  
Date:  Day  Month  Year*
**COVID-19 FORM**

### GENERAL

1. Date of Assessment/Extraction

   Day Month Year

### PREGNANCY STATUS AT TIME OF SARS-CoV-2 INFECTION

_These questions pertain to the time that the participant was symptomatic and diagnosed with COVID-19_

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Gestational age at time of COVID-19 diagnosis</td>
<td></td>
</tr>
<tr>
<td>2a) Weeks</td>
<td></td>
</tr>
<tr>
<td>2b) Days</td>
<td></td>
</tr>
<tr>
<td>3. Post-partum at time of diagnosis?</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>3s) If &quot;Yes&quot;, specify number of days post-partum at time of diagnosis</td>
<td></td>
</tr>
<tr>
<td>4. Was diagnosis made at time of labor/delivery?</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>5. Was diagnosis made post-abortion?</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>5s) If &quot;Yes&quot;, specify number of days post-abortion</td>
<td></td>
</tr>
<tr>
<td>6. Was diagnosis made at point of miscarriage?</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>7. Number of fetuses (1-9)</td>
<td></td>
</tr>
<tr>
<td>8. Date of diagnostic test result</td>
<td>Day Month Year</td>
</tr>
</tbody>
</table>

### 9. Type of test conducted

<p>| | |</p>
<table>
<thead>
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<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9a) RT-PCR</td>
<td></td>
</tr>
<tr>
<td>9b) Serology</td>
<td></td>
</tr>
<tr>
<td>9bs) If &quot;Serology&quot;, commercial name of test used</td>
<td></td>
</tr>
</tbody>
</table>

### COVID-19 SYMPTOMS

_Please answer the following questions about being infected with COVID-19. (Note: These questions pertain to the time that the participant was diagnosed with SARS-CoV-2.)_

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>10. Date of symptom onset type</td>
<td></td>
</tr>
<tr>
<td>1 = Known</td>
<td></td>
</tr>
<tr>
<td>2 = Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>10s) If &quot;Known&quot;, date (i.e. first/earliest symptom)</td>
<td>Day Month Year</td>
</tr>
<tr>
<td>11. Which of the following symptoms did you experience?</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
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<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>11a) None</td>
<td></td>
</tr>
<tr>
<td>11b) Fever</td>
<td></td>
</tr>
<tr>
<td>11c) Confusion</td>
<td></td>
</tr>
<tr>
<td>11d) Shortness of breath</td>
<td></td>
</tr>
<tr>
<td>11e) Diarrhea</td>
<td></td>
</tr>
<tr>
<td>11f) Muscle pains</td>
<td></td>
</tr>
<tr>
<td>11g) Nausea or vomiting</td>
<td></td>
</tr>
<tr>
<td>11h) Chills</td>
<td></td>
</tr>
<tr>
<td>11i) Headache</td>
<td></td>
</tr>
<tr>
<td>11j) Chest pain</td>
<td></td>
</tr>
<tr>
<td>11k) Loss of smell</td>
<td></td>
</tr>
<tr>
<td>11l) Loss of taste</td>
<td></td>
</tr>
<tr>
<td>11m) Sore throat</td>
<td></td>
</tr>
<tr>
<td>11n) Runny/stuffy nose</td>
<td></td>
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</tbody>
</table>
### COVID-19 FORM

**Project ID:** A66012

**Center ID:**

**Participant ID:**

**Country:**

<table>
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</tbody>
</table>

**11ae) Cough**

- 11aes) If "Yes", specify
  - 11aesii) Cough with sputum production
  - 11aesii) Cough with haemoptysis

- 11af) Bleeding
  - 11afs) If "Yes", specify site

- 11ag) Other symptoms
  - 11ags) If "Yes", specify

**12. For how many days did you have (or have you had) symptoms of COVID-19?**

1 = Yes
2 = No

- 12a) No day of symptoms
- 12b) Days

**13. Which of the following symptoms were still present 2 weeks (or more) after you had a positive Covid-19 test?**

1 = Yes
2 = No

- 13a) Not applicable- Diagnosed less than 2 weeks ago

- 13b) None
- 13c) Fever
- 13d) Confusion
- 13e) Shortness of breath
- 13f) Diarrhea
- 13g) Muscle pain
- 13h) Nausea or vomiting
- 13i) Chills
- 13j) Headache
- 13k) Chest pain
- 13l) Loss of smell
- 13m) Loss of taste
- 13n) Sore throat
- 13o) Runny/stuffy nose
- 13p) Abdominal pain
- 13q) Tingling sensation
- 13r) Dizziness
- 13s) Inability to walk
- 13t) Constrictions
- 13u) Decreased fetal movement
- 13v) Wheezing
- 13w) Sore throat
- 13x) Skin rash
- 13y) Seizures
- 13z) Joint pain
- 13aa) Fatigue/malaise
- 13ab) Lower chest indrawing
- 13ac) Conjunctivitis
- 13ad) Skin ulcers
- 13ae) Lymphadenopathy
- 13af) Cough
  - 13afs) If "Yes", specify
    - 13afsi) Cough with sputum production
    - 13afsii) Cough with haemoptysis

- 13ag) Bleeding
  - 13ags) If "Yes", specify site

- 13ah) Other symptoms
  - 13ahs) If "Yes", specify

---

**SARS-CoV-2 and pregnancy prospective cohort study**

**Generic protocol: Last updated 2 December 2020, version 2.6**
14. Have symptoms resolved
   1 = Yes  2 = No  3 = Not applicable - Diagnosed less than two weeks ago
   9 = Unknown
   14a) If "Yes" all symptoms, date
       Day  Month  Year

   14b) If "No", specify persisting symptoms

LABORATORY FINDINGS DURING SARS-CoV-2 INFECTION
Note: Specify unit of measurement for each parameter.
Modify list as relevant for the context. Complete all boxes with 9s in case of unknown value

15. Haemoglobin
    g/L  g/dL

16. Creatinine
    mg/L  μmol/L

17. WBC Count
    mm3  (× 10^9/L)

18. Sodium
    mEq/L = mmol/L

19. Haematocrit
    %

20. Potassium
    mEq/L = mmol/L

21. Platelets
    mm3  (× 10^9/L)

22. Procalcitonin
    ng/mL  μg/L

23. APTT/APTR
    seconds

24. CRP
    mg/L

25. PT
    seconds

26. LDH
    IU/L

27. INR

28. Creatinine Kinase
    IU/L

29. ALT/SGPT
    IU/L

30. Troponin
    ng/mL  μg/L

31. AST/SGOT
    IU/L

32. ESR
    mm/hr

33. Total bilirubin
    mg/dL  μmol/L

34. D-dimer
    mg/mL  μg/L

35. Urea (BUN)
    g/dL  mg/dl

36. Ferritin
    mg/mL  μg/L

37. Lactate
    mg/dl  mmol/L

38. IL-6

HOSPITALIZATION

39. Were you admitted to the hospital anytime after being diagnosed with COVID-19?
   1 = Yes  2 = No  3 = Not applicable
   9 = Unknown
   39s) If "Yes", date admitted
       Day  Month  Year

   39sii) If dates unknown, specify number of days

40. What was the reason for admission?
   1 = Yes  2 = No
   40a) Pregnancy-related?
   40as) If "Yes", specify reason
### COVID-19 FORM

**Project ID:** A66012

**Center ID:**

**Participant ID:**

#### 40b) COVID-19 related?

- [ ] Yes
- [ ] No
- [ ] Other reason?

#### 40bs) If “Yes”, specify reason

#### 40c) Other reason?

#### 40cs) If “Yes”, specify reason

- [ ] Do not know

#### VITAL SIGNS ON ADMISSION

*(Note: complete all boxes with 9s in case of unknown value)*

41. Temperature °C

42. Maternal Heart rate beats per min

43. Respiratory rate breaths/min

44. Arterial BP systolic mmHg

45. Severe dehydration

1. Yes
2. No
9. Unknown

46. Ecternal capillary refill time > 2 seconds

1. Yes
2. No
9. Unknown

47. Alert

1. Yes
2. No

48. Voice

1. Yes
2. No

49. Pain

1. Yes
2. No

50. Unresponsive

1. Yes
2. No

51. Oxygen Saturation %

52. GCS/15

53. Fetal heart rate beats per min

#### DIAGNOSTIC/PATHOGEN TESTING

54. Chest X-ray/CT performed?

1. Yes
2. No
9. Unknown

54a) If “Yes”, infiltrates present?

1. Yes
2. No
9. Unknown

55. Was pathogen testing done during this illness episode?

1. Yes
2. No
9. Unknown

56. Influenza virus

1. Positive
2. Negative
3. Not done

57. Sternal capillary refill time > 2 seconds

1. Yes
2. No
9. Unknown
### Presenting Symptoms on Admission

<table>
<thead>
<tr>
<th>57. Coronavirus</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
<td></td>
</tr>
<tr>
<td>2 = Negative</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
<tr>
<td>57s) If &quot;Positive&quot;, type</td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>57si) MERS-CoV</td>
<td></td>
</tr>
<tr>
<td>57sii) SARS-CoV-2</td>
<td></td>
</tr>
<tr>
<td>57siii) Other</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>58. Other respiratory pathogen</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
<td></td>
</tr>
<tr>
<td>2 = Negative</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
<tr>
<td>58s) If &quot;Positive&quot;, specify</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>59. Viral haemorrhagic fever</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
<td></td>
</tr>
<tr>
<td>2 = Negative</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
<tr>
<td>59s) If &quot;Positive&quot;, specify virus</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>60. Other pathogen of public health interest detected</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>60s) If &quot;Yes&quot;, specify</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>61. Falciparum malaria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
<td></td>
</tr>
<tr>
<td>2 = Negative</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>62. Non-falciparum malaria</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
<td></td>
</tr>
<tr>
<td>2 = Negative</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>63. HIV</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
<td></td>
</tr>
<tr>
<td>2 = Negative</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>64. Symptoms on admission</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
</tbody>
</table>

64a) Fever
64b) Confusion
64c) Shortness of breath
64d) Runny/stuffy nose
64e) Abdominal pain
64f) Diarrhea
64g) Muscle pains
64h) Nausea or vomiting
64i) Joint pain
64j) Fatigue/malaise
64k) Chills
64l) Headache
64m) Chest pain
64n) Contractions
64o) Vaginal bleeding
64p) Wheezing
64q) Loss of smell
64r) Loss of taste
64s) Sore throat
64t) Skin rash
64u) Seizures
64v) Skin ulcers
64w) Lymphadenopathy
64x) Lower chest indrawing
64y) Conjunctivitis
64z) Tingling sensation
64aa) Dizziness
64ab) Inability to walk
64ac) Decreased fetal movement
64ad) Cough
64ads) If "Cough", specify
   64adsi) Cough with sputum production
   64adsii) Cough with haemoptysis
64ae) Other symptoms
64aes) If "Yes", specify

---
## MEDICATION AND SUPPORTIVE CARE DURING HOSPITALIZATION

65. At any time during hospitalization or at discharge, did the patient receive  
   1 = Yes  
   2 = No  
   9 = Unknown

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Oral/orogastric fluids?</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B. Intravenous fluids?</strong></td>
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<tr>
<td><strong>C. Antiviral?</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>C(i). Ribavirin</strong></td>
<td></td>
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<tr>
<td><strong>C(ii). Lopinavir/Ritonavir</strong></td>
<td></td>
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<tr>
<td><strong>C(iii). Neuraminidase inhibitor</strong></td>
<td></td>
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<tr>
<td><strong>C(iv). Interferon alpha</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>C(v). Interferon beta</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>C(vi). Remdesivir</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>C(vii). Favipiravir</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>D. Corticosteroids</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>D(i). Oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D(ii). Intravenous</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>D(iii). Inhaled</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>D(iv). specify agent and maximum dose</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>E. Antibiotic</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>E(i). Oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>E(ii). Intravenous</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>E(iii). Inhaled</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>E(iv). specify agent and maximum dose</strong></td>
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<tr>
<td><strong>F. Antifungal agent</strong></td>
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</tr>
<tr>
<td><strong>F(i). Oral</strong></td>
<td></td>
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<td></td>
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<tr>
<td><strong>F(ii). Intravenous</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>F(iii). Inhaled</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>F(iv). specify agent and maximum dose</strong></td>
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</tr>
<tr>
<td><strong>G. Antimalarial agent</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>G(i). Oral</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>G(ii). Intravenous</strong></td>
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<td></td>
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<tr>
<td><strong>G(iii). Inhaled</strong></td>
<td></td>
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<tr>
<td><strong>G(iv). specify agent and maximum dose</strong></td>
<td></td>
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<tr>
<td><strong>H. Experimental agent</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>H(i). Oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>H(ii). Intravenous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>H(iii). Inhaled</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>H(iv). specify agent and maximum dose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>I. Systemic anticoagulants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>I(i). Oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>I(ii). Intravenous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>I(iii). Inhaled</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>I(iv). specify agent and maximum dose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

65j) Immunotherapy  
   65(j) If "Yes", specify  
   65(i). Convalescent plasma  
   65(ii). Monoclonal antibodies  
   65(iii). Interferons  
   65(iv). duration of treatment (days)

65k) Angiotensin converting enzyme inhibitors (ACE inhibitors)  
   65(k). If "Yes", specify

65l) Angiotensin II receptor blockers (ARBs)  
   65(l). If "Yes", specify

65m) Systemic anticoagulants  
   65(m). If "Yes", specify

65n) Other medications received  
   65(n) If "Yes", please list all others

---

**SARS-CoV-2 and pregnancy prospective cohort study**

Generic protocol: Last updated 2 December 2020, version 2.6

---

80
66. At any time during hospitalization, did the patient receive or undergo

1 = Yes
2 = No
9 = Unknown

66a) ICU or high dependency unit (HDU) admission

66as) If "Yes", Date of ICU/HDU admission

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

66asi) If "Yes", Date of ICU/HDU discharge

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

66b) Oxygen therapy

66bs) If "Yes", total duration in days

<table>
<thead>
<tr>
<th>Flow Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5 L/min</td>
</tr>
<tr>
<td>6-10 L/min</td>
</tr>
<tr>
<td>11-15 L/min</td>
</tr>
<tr>
<td>&gt;15 L/min</td>
</tr>
</tbody>
</table>

66bsi) If "Yes", 02 flow

66bsii) If "Yes", 02 flow

66bsiii) If "Yes", 02 flow

66bsiv) If "Yes", 02 flow

66bsv) Unknown

66bsvi) Source oxygen Piped

66bsvii) Source oxygen Cylinder

66bsviii) Source oxygen Concentrator

66bsix) Source oxygen Unknown

66bsx) Interface Nasal prongs

66bsxi) Interface HF nasal cannula

66bsxii) Interface Mask

66bsxiii) Interface Mask with reservoir

66bsxiv) Interface CPAP/NIV mask

66bsxv) Interface Unknown

66c) Non-invasive ventilation (e.g. BIPAP, CPAP)

66d) Any type of invasive ventilation

66ds) If "Yes", total duration in days

66dsi) If "Yes", specify PEEP (cm H2O)

66dsii) If "Yes", specify FiO2 (%)

66dsiii) Plateau pressure (cm H2O)

66dsiv) Plateau PaCO2

66dsv) Plateau PaO2

66e) Extracorporeal (ECMO) support

66es) If "Yes", total duration in days

66f) Prone position

66fs) If "Yes", total duration in days

66g) Inotropes/vasopressors

66gs) If "Yes", specify

66gsi) If "Yes", total duration in days

66h) Renal replacement therapy (RRT) or dialysis

66i) Tocolysis

66if) If "Yes", specify

66ifs) If "Yes", specify

66is) If "Yes", specify

66j) If "Yes", specify

66jfs) If "Yes", specify

66jis) If "Yes", specify
**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

**COVID-19 FORM**

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A 6 6 0 1 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center ID:</td>
<td></td>
</tr>
<tr>
<td>Participant ID:</td>
<td></td>
</tr>
<tr>
<td>Country:</td>
<td></td>
</tr>
</tbody>
</table>

**66j) Induction of labour**
**66k) Casearean section**
**66i) Blood transfusion**
**66ls) If "Yes", specify blood product transfused**

**66ls) If "Yes" specify units of each component transfused**

**66m) Other forms or treatment or interventions received**
**66ms) If "Yes", please list all others**

**COMPLICATIONS**

<table>
<thead>
<tr>
<th>67. At any time during hospitalization, did the patient experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
</tr>
<tr>
<td>67a) Shock</td>
</tr>
<tr>
<td>67d) Anaemia</td>
</tr>
<tr>
<td>67g) Pneumonia</td>
</tr>
<tr>
<td>67j) Stroke: intracerebral haemorrhage</td>
</tr>
<tr>
<td>67l) Vaginal bleeding</td>
</tr>
<tr>
<td>67n) Endocarditis</td>
</tr>
<tr>
<td>67p) Acute renal injury</td>
</tr>
<tr>
<td>67r) Liver dysfunction</td>
</tr>
<tr>
<td>67t) Acute respiratory distress syndrome (ARDS)</td>
</tr>
<tr>
<td>67u) Other</td>
</tr>
<tr>
<td>67us) If &quot;Other&quot;, specify</td>
</tr>
</tbody>
</table>

**OUTCOME OF HOSPITALIZATION**

**68. Outcome**

1 = Discharged alive  
2 = Transfer/Referral to another facility  
3 = Death  
4 = Palliative Discharge  
9 = Unknown

**69. If discharged alive, ability to self-care at discharge versus before illness**

1 = Same as before illness  
2 = Worse than before illness  
3 = Better than before illness  
9 = Unknown

**70. Outcome/Discharge date**

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

**PREGNANCY STATUS AT DISCHARGE**

**71. Pregnancy outcome/status at discharge**

1 = Yes  
2 = No  
71a) Not yet delivered  
71b) Livebirth  
71c) Spontaneous abortion  
71d) Induced abortion  
71e) Missed abortion  
71f) Stillbirth  
71g) Ectopic pregnancy  
71h) Post-abortion or postpartum on admission

(Note: If postpartum on admission and discharge at 6 weeks post-partum, fill CRF 9: Maternal outcomes at 6 weeks post-partum/study exit)
A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

COVID-19 FORM

**Project ID:** A66012  |  **Center ID:**  |  **Participant ID:**

**Country:**

72. Delivery or Pregnancy termination during admission?
- 1 = Yes
- 2 = No
- 72s) If "Yes", date of delivery or pregnancy termination

(Note, If yes, fill CRF 6: Maternal outcomes at delivery or pregnancy Termination and, where applicable, CRF 7: Neonatal outcomes between birth and 7 days)

**MATERNAL STATUS AT DISCHARGE**

73. Maternal death at discharge
- 1 = Yes
- 2 = No  if "No", go to Q75

74. What was the underlying cause of death
- 1 = Yes
- 2 = No
- 74a) Obstetric hemorrhage
- 74b) Hypertensive disorder
- 74c) Acute respiratory infection
- 74d) Complications related to COVID-19
- 74ds) If "Yes", specify

74e) Obstetric related infection
- 74f) Unsafe abortion
- 74g) Ectopic pregnancy
- 74h) Unanticipated complications of management (e.g. anaesthesia-related complications)
- 74i) Other direct cause
- 74j) Other indirect cause (e.g. severe anaemia)
- 74k) Coincidental cause (e.g. motor vehicle accident)
- 74l) Other
- 74ls) If "Other", specify

74m) Unknown

(Note: If maternal death at discharge, fill CRF 9: Maternal outcomes at 6 weeks post-partum/study exit)

**BIOSPECIMEN COLLECTION AND RESULTS**

75. Umbilical cord blood. Specimen obtained and SARS-CoV-2 RNA RT-PCR Result
- 1 = No
- 2 = Positive
- 3 = Negative
- 9 = Unknown
- 75s) If "Positive" or "Negative" or "Unknown", date specimen obtained

76. Placenta. Specimen obtained and SARS-CoV RNA RT-PCR Result
- 1 = No
- 2 = Positive
- 3 = Negative
- 9 = Unknown
- 76s) If "Positive" or "Negative" or "Unknown", date specimen obtained

77. Amniotic fluid. Specimen obtained and SARS-CoV RNA RT-PCR Result
- 1 = No
- 2 = Positive
- 3 = Negative
- 9 = Unknown
- 77s) If "Positive" or "Negative" or "Unknown", date specimen obtained

78. Breast milk. Specimen obtained and SARS-CoV RNA RT-PCR Result
- 1 = No
- 2 = Positive
- 3 = Negative
- 9 = Unknown
- 78s) If "Positive" or "Negative" or "Unknown", date specimen obtained
### A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

**Generic protocol: Last updated 2 December 2020, version 2.6**

<table>
<thead>
<tr>
<th>Project ID: A66012</th>
<th>Center ID:</th>
<th>Participant ID:</th>
</tr>
</thead>
</table>

#### COVID-19 FORM

**World Health Organization**

**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

**CR4**

**page 10/10**

**V1.0 (16 Nov 2020)**

---

#### COMMENTS:

**Interviewer's name:**

**Signature:**

**Date:**

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
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</table>

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79. Vaginal swab. Specimen obtained

and SARS-2-CoV RNA RT-PCR Result

1 = No
2 = Positive
3 = Negative
9 = Unknown

79s) If "Positive" or "Negative" or "Unknown", date specimen obtained

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
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</table>

80. Feces/Anal swab. Specimen obtained

and SARS-2-CoV RNA RT-PCR Result

1 = No
2 = Positive
3 = Negative
9 = Unknown

80s) If "Positive" or "Negative" or "Unknown", date specimen obtained

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
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</table>

81. Fetal tissue (in the case of fetal death/induced abortion). Specimen obtained and

SARS-2-CoV RNA RT-PCR Result

1 = No
2 = Positive
3 = Negative
9 = Unknown

81s) If "Positive" or "Negative" or "Unknown", date specimen obtained

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Prenatal Visit / Follow Up Information Form

**General**

1. Date of Assessment/Extraction
   - Day [ ]
   - Month [ ]
   - Year [ ]

#### Current Pregnancy

*(Note: in the case of recent pregnancy loss, collect data based on latest pregnancy)*

2. Current gestational age
   - 2a) Weeks [ ]
   - 2b) Days [ ]

3. If post-partum, number of weeks/days since delivery
   - 3a) Weeks [ ]
   - 3b) Days [ ]

4. Pregnancy complications, diagnoses or symptoms in relation to the current pregnancy
   *(Note: ask of all women, regardless of test result status)*
   - 4a) Gestational diabetes [ ]
   - 4b) Gestational hypertension
     - 4bs) If "Yes", specify
       - 4bsi) Non-proteinuric hypertension [ ]
       - 4bsii) Pre-eclampsia / eclampsia [ ]
       - 4bsiii) Unspecified / don't know [ ]
   - 4c) Anemia (Hb < 11 g/dL) [ ]
   - 4d) Hyperemesis [ ]
   - 4e) Fetal growth restriction [ ]
   - 4f) Placental previa/accreta/percreta [ ]
   - 4g) Embolic disease [ ]
   - 4h) Placental abruption [ ]
   - 4i) Preterm labor [ ]
   - 4j) Preterm premature rupture of membranes (< 37 weeks) (PPROM) [ ]
   - 4k) Bleeding during pregnancy [ ]
   - 4l) Vaginal watery discharge [ ]
   - 4m) Headaches [ ]
   - 4n) Vision changes [ ]
   - 4o) Right upper quadrant (abdominal) pain [ ]
   - 4p) Decreased or no fetal movement [ ]

5. Any changes to medical conditions / infections/chronic conditions since enrollment into study?
   - 5a) Hemorrhage (>500 ml of blood loss) [ ]
   - 5b) If "Yes", specify
     - 5bs) Antepartum/intrapartum [ ]
     - 5bsi) Postpartum haemorrhage [ ]
     - 5bsii) Abortion-related [ ]
   - 5c) Liver disease
     - 5cs) If "Yes", specify
       - 5csi) Obstetric cholestasis [ ]
       - 5csii) Other [ ]
       - 5csiii) If "Other", specify

   - 5d) Other complications/diagnoses/symptoms [ ]
   - 5ds) If "Yes", specify

#### Current Conditions

5. Any changes to medical conditions / infections/chronic conditions since enrollment into study?
   - 5a) Hemorrhage (>500 ml of blood loss) [ ]
   - 5b) If "Yes", specify
     - 5bs) Antepartum/intrapartum [ ]
     - 5bsi) Postpartum haemorrhage [ ]
     - 5bsii) Abortion-related [ ]
   - 5c) Liver disease
     - 5cs) If "Yes", specify
       - 5csi) Obstetric cholestasis [ ]
       - 5csii) Other [ ]
       - 5csiii) If "Other", specify

   - 5d) Other complications/diagnoses/symptoms [ ]
   - 5ds) If "Yes", specify

---

SARS-CoV-2 and pregnancy prospective cohort study
Generic protocol: Last updated 2 December 2020, version 2.6

---
## CURRENT CONDITIONS

5) Medical conditions / infections/chronic conditions since enrollment into study?

<p>| | | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5s) If "Yes", specify

5si) If "Yes", date of diagnosis or symptom onset

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

- a) Heart disease
- b) Lung disease
- c) Blood disease
- d) Kidney disease
- e) Liver disease
- f) Neurological disease
- g) Thyroid disease
- h) Endocrine disease
- i) Immunosuppression
- j) Hypertension
- k) Type 1 or Type 2 diabetes
- l) Malaria
- m) Dengue
- n) Chikungunya
- o) Zika
- p) Influenza
- q) HIV
- r) Syphilis
- s) Hepatitis A
- t) Hepatitis B
- u) Hepatitis C
- v) Hepatitis D
- w) Hepatitis E
- x) Toxoplasmosis
- y) Rubella
- z) Cytomegalovirus
- aa) Herpes Simplex
- ab) Other medical condition/infection

## CLINICAL INFORMATION AT FOLLOW-UP VISIT

(Note: complete all boxes with 9s in case of unknown value)

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>

6. Current body weight kg

7. Height m

8. Body temperature °C °F

9. Respiratory rate breaths/min

10. Heart rate beats/min

11. Urinary Glucose

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>

1 = (+) 3 = (+++)
2 = (++) 4 = Negative
9 = Unknown/not done
### PRENATAL VISIT / FOLLOW UP INFORMATION FORM

#### Project ID:

A66012

#### Center ID:


#### Participant ID:


#### Country:


### LABORATORY RESULTS AT FOLLOW-UP VISIT

*Note: Specify unit of measurement for each parameter. Modify list as relevant for the context. Complete all boxes with 9s in case of unknown value.*

<table>
<thead>
<tr>
<th>Test</th>
<th>Unit</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. Urinary Protein</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>13. Arterial blood pressure</td>
<td>mmHg</td>
<td></td>
</tr>
<tr>
<td>14. Pulse</td>
<td>beats/min</td>
<td></td>
</tr>
<tr>
<td>15. Pulse oximetry</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>16. Haemoglobin</td>
<td>g/L</td>
<td></td>
</tr>
<tr>
<td>17. Creatinine</td>
<td>mg/L</td>
<td></td>
</tr>
<tr>
<td>18. WBC Count</td>
<td>mm³</td>
<td></td>
</tr>
<tr>
<td>19. Sodium</td>
<td>mEq/L = mmol/L</td>
<td></td>
</tr>
<tr>
<td>20. Haematocrit</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>21. Potassium</td>
<td>mEq/L = mmol/L</td>
<td></td>
</tr>
<tr>
<td>22. Platelets</td>
<td>mm³</td>
<td></td>
</tr>
<tr>
<td>23. Procalcitron</td>
<td>ng/mL, μg/L</td>
<td></td>
</tr>
<tr>
<td>24. APTT/APTR</td>
<td>seconds</td>
<td></td>
</tr>
<tr>
<td>25. CRP</td>
<td>mg/L</td>
<td></td>
</tr>
<tr>
<td>26. PT</td>
<td>seconds</td>
<td></td>
</tr>
<tr>
<td>27. LDH</td>
<td>IU/L</td>
<td></td>
</tr>
<tr>
<td>28. INR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29. Creatinine Kinase</td>
<td>IU/L, UKAT/L</td>
<td></td>
</tr>
<tr>
<td>30. ALT/SGPT</td>
<td>IU/L</td>
<td></td>
</tr>
<tr>
<td>31. Troponin</td>
<td>μg/L</td>
<td></td>
</tr>
<tr>
<td>32. AST/SGOT</td>
<td>IU/L</td>
<td></td>
</tr>
<tr>
<td>33. ESR</td>
<td>mm/hr</td>
<td></td>
</tr>
<tr>
<td>34. Total bilirubin</td>
<td>mg/L</td>
<td></td>
</tr>
<tr>
<td>35. D-dimer</td>
<td>ng/mL, μg/L</td>
<td></td>
</tr>
<tr>
<td>36. Urea (BUN)</td>
<td>mg/dL, mmol/L</td>
<td></td>
</tr>
<tr>
<td>37. Ferritin</td>
<td>μg/mL</td>
<td></td>
</tr>
<tr>
<td>38. Lactate</td>
<td>mg/dL, mmol/L</td>
<td></td>
</tr>
<tr>
<td>39. IL-6</td>
<td>pg/mL</td>
<td></td>
</tr>
</tbody>
</table>

#### COVID-19 SYMPTOMS

*Please answer the following questions about experiencing any of the following symptoms. (Note: These questions pertain to the period since the last follow-up visit of the participant)*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>40a) None</td>
<td></td>
</tr>
<tr>
<td>40b) Fever</td>
<td></td>
</tr>
<tr>
<td>40c) Confusion</td>
<td></td>
</tr>
<tr>
<td>40d) Shortness of breath</td>
<td></td>
</tr>
<tr>
<td>40e) Diarrhea</td>
<td></td>
</tr>
<tr>
<td>40f) Muscle pains</td>
<td></td>
</tr>
<tr>
<td>40g) Nausea or vomiting</td>
<td></td>
</tr>
<tr>
<td>40h) Chills</td>
<td></td>
</tr>
<tr>
<td>40i) Headache</td>
<td></td>
</tr>
<tr>
<td>40j) Chest pain</td>
<td></td>
</tr>
<tr>
<td>40k) Loss of smell</td>
<td></td>
</tr>
<tr>
<td>40l) Loss of taste</td>
<td></td>
</tr>
<tr>
<td>40m) Sore throat</td>
<td></td>
</tr>
<tr>
<td>40n) Runny/stuffy nose</td>
<td></td>
</tr>
<tr>
<td>40o) Abdominal pain</td>
<td></td>
</tr>
</tbody>
</table>

---

SARS-CoV-2 and pregnancy prospective cohort study

Generic protocol: Last updated 2 December 2020, version 2.6
A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

PRENATAL VISIT / FOLLOW UP INFORMATION FORM

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V1.0 (16 Nov 2020)

Project ID: A66012
Center ID: 
Participant ID: 

Country: 

40p) Tingling sensation
40q) Dizziness
40r) Inability to walk
40s) Contractions
40t) Decreased fetal movement
40u) Wheezing
40v) Sore throat
40w) Skin rash
40x) Seizures
40y) Joint pain
40z) Fatigue/malaise
40aa) Lower chest indrawing
40ab) Conjunctivitis
40ac) Skin ulcers
40ad) Lymphadenopathy
40ae) Cough
40aes) If "Yes", specify
40aesi) Cough with sputum production
40aesii) Cough with haemoptysis
40af) Bleeding
40afs) If "Yes", specify site
40ag) Other symptoms
40ags) If "Yes", specify

41. For how many days did you have (or have you had) these symptoms?
   1 = Yes  2 = No
41a) No day of symptoms
41b) Days

SARS-CoV-2 TEST RESULT

42. SARS-CoV-2 test result at follow up visit
   a) Type of Test
      1=RT-PCR  3=Ag-RDT
      2=Serology  4=Not performed
   b) Commercial name of Test: 

   d) Date of result
      Day  Month  Year

   e) Test Result
      1=Positive  2=Negative  9=Unknown

   f) If positive, is participant already assigned to exposed group?
      1 = Yes  2 = No

      Note: If No, assess participants' clinical history, presenting complaints and consider repeating test to determine sero-conversion.

   g) Is sero-conversion reasonably established?
      1 = Yes  2 = No

      Note: A participant who was previously SARS-CoV-2 positive and assigned to the exposed group and has a negative test result in a follow-up visit should not be re-assigned to the unexposed group.

COMMENTS:

Interviewer's name: 
Signature: 

Date:  Day  Month  Year
### MATERNAL OUTCOMES AT DELIVERY OR PREGNANCY TERMINATION FORM

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A 6 6 0 1 2</th>
<th>Center ID:</th>
<th>Participant ID:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### GENERAL

1. Date of Assessment/Extraction

#### CURRENT PREGNANCY

2. Date of Delivery or Pregnancy termination

3. Gestational age at delivery/pregnancy termination
   - 3a) Weeks
   - 3b) Days

4. Pregnancy complications/diagnosis/symptoms at time of delivery/pregnancy termination
   - 1 = Yes
   - 2 = No
   - 9 = Unknown
   - 4a) Gestational diabetes
   - 4b) Gestational hypertension
     - 4bs) If "Yes", specify
     - 4bsi) Non-proteinuric hypertension
     - 4bsii) Pre-eclampsia / eclampsia
     - 4bsiii) Unspecified / don't know
   - 4c) Anemia (Hb < 11 g/dL)
   - 4d) Hyperemesis
   - 4e) Fetal growth restriction
   - 4f) Placental previa/accreta/percreta
   - 4g) Placental abruption
   - 4h) Preterm labor
     - 4i) Preterm premature rupture of membranes (< 37 weeks) (PPROM)
   - 4j) Decreased or no fetal movement
   - 4k) Bleeding during pregnancy
   - 4l) Vaginal watery discharge
   - 4m) Headaches
   - 4n) Vision changes
   - 4o) Right upper quadrant (abdominal) pain
   - 4p) Liver disease
     - 4ps) If "Yes", specify
     - 4psii) Obstetric cholestasis
     - 4psiii) Other
     - 4psiii) If "Other", specify

4q) Hemorrhage during pregnancy
   (>500ml of blood loss)
   - If "Yes", specify
     - 4rsi) Antepartum hemorrhage
     - 4rsii) Intrapartum hemorrhage
     - 4rsiii) Abortion-related hemorrhage
   - 4r) Embolic disease
   - 4s) Anaesthetic complication
   - 4t) Bacterial infection
   - 4u) Other complications/diagnoses/symptoms
     - 4us) If "Yes", specify

5. Status on presentation
   - 1 = Pregnant not in labor
   - 2 = Pregnant in labor
   - 3 = Recent pregnancy termination (post abortion/miscarriage)

6. Indication for admission
   - 1 = Yes
   - 2 = No
   - go to Q7
   - if yes, complete
     - 6a) Scheduled induction of labor
     - 6b) Scheduled cesarean delivery
     - 6c) Indication for emergency cesarean delivery
       - 6cs) If "Yes", specify indication

6d) Hemorrhage (>500ml of blood loss)

6e) Vaginal bleeding

6f) Obstruction of labour

6g) Fever
   - 6gs) If "Yes", specify
     - C°
     - F°

6h) Other
   - 6hs) If "Other", specify

SARS-CoV-2 and pregnancy prospective cohort study
Generic protocol: Last updated 2 December 2020, version 2.6
# Signs and Symptoms

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

### Sub-Signs

- **7a) Vaginal watery discharge**
- **7b) Vaginal bleeding**
- **7c) Headaches**
- **7d) Vision changes**
- **7e) Right upper quadrant (abdominal) pain**
- **7f) Decreased or no fetal movement**
- **7g) High blood pressure**
  - **7gs) If "Yes", specify blood pressure**
    - **systolic mmHg**
    - **diastolic mmHg**
- **7h) Low blood pressure**
  - **7hs) If "Yes", specify blood pressure**
    - **systolic mmHg**
    - **diastolic mmHg**
- **7l) Uterine contractions**
- **7j) Fetal distress**
  - **7js) If "Yes", specify fetal heart rate**
    - **beats/min**
- **7k) Fever**
  - **7ks) If "Yes", specify temperature**
    - °C
    - °F

### Indication for Childbirth

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

### Suspected or Verified SARS-CoV-2 Infection

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

### Pregnancy Outcome

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
</tr>
</tbody>
</table>

### Fetal Presentation at Delivery

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Cephalic</td>
</tr>
<tr>
<td>2</td>
<td>Transverse</td>
</tr>
<tr>
<td>3</td>
<td>Breech</td>
</tr>
<tr>
<td>4</td>
<td>Unknow</td>
</tr>
</tbody>
</table>

### Amniotic Fluid at Delivery

<table>
<thead>
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Clear</td>
</tr>
<tr>
<td>2</td>
<td>Meconium-stained</td>
</tr>
<tr>
<td>3</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

### Mode of Delivery

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vaginal</td>
</tr>
<tr>
<td>2</td>
<td>Spontaneous</td>
</tr>
<tr>
<td>3</td>
<td>Instrumental (vacuum/forceps)</td>
</tr>
<tr>
<td>4</td>
<td>Planned Cesarean delivery</td>
</tr>
<tr>
<td>5</td>
<td>Emergency Cesarean delivery</td>
</tr>
</tbody>
</table>

### Pregnancy Near-Miss Markers

1. **13a) Acute cyanosis**
2. **13b) Oxygen saturation <90% for > 60 minutes**
3. **13c) Use of continuous vasoactive drugs**
4. **13d) Gasiing**
5. **13e) PaO2/FiO2 <200 mmHg**
6. **13f) Hysterectomy following infection or haemorrhage**
7. **13g) Respiratory rate >40/min or <6/min**
8. **13h) Creatinine ≥ 300 micromol/l or ≥ 2.5 mg/dl**
9. **13i) Transfusion ≥ 5 units red cells**
10. **13j) Shock**
11. **13k) Bilirubin > 100 micromol/l or > 6.0 mg/dl**
12. **13l) Intubation and ventilation for ≥ 60 minutes not related to anesthesia**
13. **13m) Oliguria non-responsive to fluids diuretics**
14. **13n) pH <7.1**
### MATERNAL OUTCOMES AT DELIVERY OR PREGNANCY TERMINATION FORM

<table>
<thead>
<tr>
<th>PROTOCOL</th>
<th>Project ID: A66012</th>
<th>Center ID:</th>
<th>Participant ID:</th>
</tr>
</thead>
</table>

#### 13. MATERNAL OUTCOMES AT DELIVERY OR PREGNANCY TERMINATION FORM

- **13a)** Dialysis
- **13b)** Clotting failure
- **13c)** Lactate >5
- **13d)** Cardiopulmonary resuscitation (CPR)
- **13e)** Loss of consciousness lasting ≥ 12 hours
- **13f)** Acute thrombocytopenia (<50,000 platelets)
- **13g)** Loss of consciousness and absence of pulse/heartbeat
- **13h)** Loss of consciousness and the presence of glucose and ketone bodies in urine
- **13i)** Stroke
- **13j)** Uncontrollable fit/total paralysis
- **13k)** Jaundice in the presence of preeclampsia

#### LABORATORY DATA ON ADMISSION

**Note:** Specify unit of measurement for each parameter. Modify list as relevant for the context. Complete all boxes with 9s in case of unknown value.

- **14. Haemoglobin**
  - g/L
  - g/dL

- **15. Creatinine**
  - g/L
  - g/dL

- **16. WBC Count**
  - mg/L
  - μmol/L

- **17. Sodium**
  - mmol/L
  - g/L (×10^{-6} L)

- **18. Haematocrit**
  - mL/L

- **19. Potassium**
  - %

- **20. Platelets**
  - mL/L

- **21. Procalcitonin**
  - g/L
  - g/L (×10^{-6} A)

- **22. APTT/APTR**
  - seconds

- **23. CRP**
  - mg/L

- **24. PT**
  - seconds

- **25. LDH**
  - IU/L

- **26. INR**

- **27. Creatinine Kinase**
  - L/L

- **28. ALT/SGPT**
  - L/L

- **29. Troponin**
  - g/L

- **30. AST/SGOT**
  - g/L

- **31. ESR**
  - mm/hr

- **32. Total bilirubin**
  - mg/L
  - μmol/L

- **33. D-dimer**
  - mg/L
  - μg/L

- **34. Urea (BUN)**
  - g/L

- **35. Ferritin**
  - ng/mL

- **36. Lactate**
  - mg/dL
  - mmol/L

- **37. IL-6**
  - pg/mL

---

World Health Organization

A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

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V1.0 (16 Nov 2020)

SARS-CoV-2 and pregnancy prospective cohort study

Generic protocol: Last updated 2 December 2020, version 2.6
### BIOSPECIMEN COLLECTION AND RESULTS

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Collection Status</th>
<th>SARS-CoV-2 RNA RT-PCR Result</th>
<th>Date Specimen Obtained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilical cord blood</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
<tr>
<td>Placenta</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
<tr>
<td>Breast milk</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Collection Status</th>
<th>SARS-CoV-2 RNA RT-PCR Result</th>
<th>Date Specimen Obtained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal swab</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
<tr>
<td>Feces/Anal swab</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
<tr>
<td>Fetal tissue (in case of fetal death/induced abortion)</td>
<td>Specimen obtained</td>
<td>1 = No, 2 = Positive, 3 = Negative, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
</tbody>
</table>

### MATERNAL STATUS/OUTCOMES

<table>
<thead>
<tr>
<th>Status/Outcome</th>
<th>Date of Discharge or Referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Discharge, 2 = Referral, 3 = Death, 9 = Unknown</td>
<td>Day Month Year</td>
</tr>
</tbody>
</table>

**Note:** If discharge or referral occurs, skip to Q48.
A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

MATERNAL OUTCOMES AT DELIVERY OR PREGNANCY TERMINATION FORM

Project ID: A66012  Center ID:  Participant ID:  
Country:  

47. Discharge with newborn(s)?  
1 = Yes  2 = No  9 = Unknown  
47s) If "No", specify reason  

If Maternal death  
48) date of death  
Day Month Year  

49) Specify cause of death  
1 = Yes  2 = No  
a) Obstetric hemorrhage  
b) Hypertensive disorder  
c) Acute respiratory infection  
d) Complications related to COVID-19  
49ds) If "Yes", specify  
e) Obstetric related infection  
f) Unsafe abortion  
g) Ectopic pregnancy  
h) Unanticipated complications of management (e.g. anaesthesia-related complications)  
i) Other direct cause  
j) Other indirect cause (e.g. severe anaemia)  
k) Coincidental cause (e.g. motor vehicle accident)  
l) Other  
ls) If "Other", specify  
m) Unknown  

Note: Also fill CRF 9- Maternal outcomes at 6 weeks post-partum/study exit

SARS-CoV-2 TEST RESULT

50. SARS-CoV-2 test result at follow up visit  
a) Type of Test  
1=RT-PCR  3=Ag-RDT  
2=Serology  4=Not performed  
go to End

b) Commercial name of Test:  

d) Date of result  
Day Month Year  
e) Test Result  
1=Positive  2=Negative  9=Unknown  
f) If positive, is participant already assigned to exposed group?  
1 = Yes  2 = No  
Note: If No, assess participants' clinical history, presenting complaints and consider repeating test to determine sero-conversion.  
g) Is sero-conversion reasonably established?  
1 = Yes  Re-assign to exposed group and complete CR4 form  
2 = No  
Note: A participant who was previously SARS-CoV-2 positive and assigned to the exposed group and has a negative test result in a follow-up visit should not be re-assigned to the unexposed group

COMMENTS:  

Interviewer's name:  
Signature:  

Date:  
Day Month Year  

World Health Organization

SARS-CoV-2 and pregnancy prospective cohort study
Generic protocol: Last updated 2 December 2020, version 2.6
# A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

## NEONATAL OUTCOMES BETWEEN BIRTH AND 7 DAYS FORM

### GENERAL

<table>
<thead>
<tr>
<th>1. Date of Assessment/Extraction</th>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

### CHILDBIRTH INFORMATION

<table>
<thead>
<tr>
<th>2. Date of birth</th>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>3. Time of birth</th>
<th>24hs clock</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>4. Gestational age at delivery/termination</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>4a) Weeks</td>
<td></td>
</tr>
<tr>
<td>4b) Days</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Place of birth</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Health facility</td>
<td></td>
</tr>
<tr>
<td>2 = Home</td>
<td></td>
</tr>
<tr>
<td>3 = Other</td>
<td></td>
</tr>
<tr>
<td>5s) If &quot;Other&quot;, specify</td>
<td></td>
</tr>
</tbody>
</table>

### 8. If "Performed", specify

- 1 = Yes
- 2 = No

8a) Standard
8b) MTCT screening

### 9. SARS-CoV-2 Test

- 1 = RT-PCR
- 2 = Serology
- 3 = Not performed

9 = Unknown

**skip to 13**

### 10. Commercial name of test:

### 11. Result

- 1 = Positive
- 2 = Negative
- 9 = Unknown

### 12. Date of the test

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
</table>

### 13. Apgar scores

- a) 1 min
- b) 5 min
- c) 10 min

### 14. Respiratory distress

- 1 = Yes
- 2 = No
- 9 = Don’t know

### 15. NICU admission

- 1 = Yes
- 2 = No

15s) If "Yes", number of days

---

**SARS-CoV-2 and pregnancy prospective cohort study**

**Generic protocol: Last updated 2 December 2020, version 2.6**
### NEONATAL OUTCOMES BETWEEN BIRTH AND 7 DAYS FORM

**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A66012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country:</td>
<td></td>
</tr>
<tr>
<td>Center ID:</td>
<td></td>
</tr>
<tr>
<td>Participant ID:</td>
<td></td>
</tr>
<tr>
<td>Birth order</td>
<td></td>
</tr>
</tbody>
</table>

#### 16. Neonatal complications
- **1** = Yes  
- **2** = No

**If "Yes", check all that apply**
- 17a) Ventilator support
- 17b) Seizures
- 17c) Hypoxic ischemic encephalopathy
- 17d) Sepsis
- 17e) Other
  - 17es) If "Other", specify

#### 17. Neonatal outcome
- 1 = Discharged
- 2 = Referral to specialist /other hospital
- 3 = Death

**If discharged**
- 19a) Date of discharge

**If referral,**
- 20a) Date of referral
- 20s) specify

**If death**
- 21a) Date of death

#### 21b. If neonate died, what was the primary cause of death?
- 1 = Yes
- 2 = No

**i) Preterm**

**ii) Low birth weight**

**iii) Birth asphyxia**

**iv) Infection COVID-19**

**v) Infection Bacteraemia/Septicemia**

**vi) Infection HIV**

**vii) Other infection**

  - viis) If "Other", specify

**viii) Complications from COVID-19**

  - viiis) If “Yes”, specify

**ix) Birth trauma**

**x) Congenital/birth defects**

**xi) Other**

  - xis) If “Other”, specify

**xii) Unknown**

### NEONATAL PHYSICAL EXAM AT BIRTH

**Note:** complete all boxes with 9s in case of unknown value.

#### 22. Temperature
- \( ^\circ C \)
- \( ^\circ F \)

**22a. Temperature taken**
- 1 = Oral
- 2 = Tympanic
- 3 = Rectal
- 4 = Axillary
- 5= Other

**22as) If "Other", specify**
### Neonatal Outcomes between Birth and 7 Days Form

**Project ID:** A66012  
**Center ID:**  
**Participant ID:**  
**Birth order:**

**23. Respiratory rate**  
breaths/min

**24. Heart rate**  
beats/min

**25. Blood pressure**  
systolic mmHg  
diastolic mmHg

**26. Peripheral O2 saturation (SpO2)**  
%

**27. Birth weight**  
grms

**28. Length**  
cm

**29. Head circumference**  
cm

**30. Cord blood arterial pH**  
cm

**31. Cord blood arterial base excess**  
cm

**32. Cardiovascular system**  
1 = Normal  
2 = Abnormal  
3 = Murmur  
4 = Other  
9 = Unknown  
32s) If "Other" specify

**33. Respiratory system**  
1 = Normal  
2 = Abnormal  
3 = Murmur  
4 = Other  
9 = Unknown  
33s) If "Abnormal", describe

**34. Gastrointestinal system**  
1 = Normal  
2 = Abnormal  
3 = Murmur  
4 = Other  
9 = Unknown  
34a) Jaundice  
34b) Hepatomegaly  
34c) Hernia  
34d) Gastrochisis  
34e) Omphalocele  
34f) Splenomegaly  
34g) Abdominal tenderness  
34h) Other  
35hs) If Other, specify

**35. Seizure**  
1 = Yes  
2 = No  
3 = General  
4 = Focal  
9 = Unknown  
35s) If "Yes", describe

**36. Paralysis**  
1 = Yes  
2 = No  
3 = General  
4 = Ascending  
9 = Unknown  
36s) If "Yes", describe

**37. Hypotonia (floppiness)**  
1 = Yes  
2 = No  
9 = Unknown
### NEONATAL OUTCOMES BETWEEN BIRTH AND 7 DAYS FORM

#### Project ID: A66012 Center ID: [ ] Participant ID: [ ]

#### Country: [ ] Birth order [ ]

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
<th>Date of Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>38. Stiffness or spasticity or increased tone of limbs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>39. Arthrogryposis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40. Other neurological signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41. Other abnormal movements (e.g. writhing movements)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42. Tonic neck reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43. Moro reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>44. Rooting reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45. Sucking reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>46. Grasp reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>47. Babinski reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48. Rash</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49. Oedema</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50. Fever</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51. Eye redness/conjunctivitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52. Other condition</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

52ss) If "Yes", describe

---

**NOTE:**

- Day: [ ]
- Month: [ ]
- Year: [ ]

---

**SARS-CoV-2 and pregnancy prospective cohort study**

**Generic protocol: Last updated 2 December 2020, version 2.6**
### NEONATAL OUTCOMES BETWEEN BIRTH AND 7 DAYS FORM

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A66012</th>
<th>Center ID:</th>
<th>Participant ID:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth order</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### NEONATAL LABORATORY EXAMINATION

58. Specimen obtained and SARS-2-CoV RNA RT-PCR Result

<table>
<thead>
<tr>
<th></th>
<th>1 = Positive</th>
<th>2 = Negative</th>
<th>3 = Not done</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>58a) Neonatal throat swab at birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58as) Date specimen obtained</td>
<td>Day</td>
<td>Month</td>
<td>Year</td>
<td>If Positive or Negative or Unknown</td>
</tr>
<tr>
<td>58b) Neonatal anal swab at birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58bs) Date specimen obtained</td>
<td>Day</td>
<td>Month</td>
<td>Year</td>
<td>If Positive or Negative or Unknown</td>
</tr>
</tbody>
</table>

#### NEONATAL FEEDING, SEPARATION, CONTACT, MORBIDITY

59. Please indicate time point for which questions are being asked or data is being extracted

<table>
<thead>
<tr>
<th></th>
<th>1 = Between birth and day 2 post-delivery</th>
<th>2 = Between day 2 and day 7 post-delivery</th>
<th>3 = Not done</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>60. Has the baby been put to the breast?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61. If &quot;No&quot;, why was the baby not put to the breast?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>62. Has the baby been given breastmilk from a cup, bottle, spoon, tube or other method?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Specific Laboratory Examination

53. Fundoscopy

<table>
<thead>
<tr>
<th></th>
<th>1 = Normal</th>
<th>2 = Abnormal</th>
<th>3 = Not done</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>53) If &quot;Abnormal&quot;, specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

54. Red reflex or chorioretinitis

<table>
<thead>
<tr>
<th></th>
<th>1 = Present</th>
<th>2 = Absent</th>
<th>3 = Not done</th>
<th>9 = Unknown</th>
</tr>
</thead>
</table>

55. Cataract

<table>
<thead>
<tr>
<th></th>
<th>1 = Normal</th>
<th>2 = Abnormal</th>
<th>3 = Not done</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>55) If &quot;Abnormal&quot;, specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

56. Hearing test

<table>
<thead>
<tr>
<th></th>
<th>1 = Normal</th>
<th>2 = Abnormal</th>
<th>3 = Not done</th>
<th>9 = Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>56) If &quot;Abnormal&quot;, specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

57. Newborn blood screening

<table>
<thead>
<tr>
<th></th>
<th>1 = Positive</th>
<th>2 = Negative</th>
<th>3 = Not done</th>
<th>57a) Hypothyroidism</th>
<th>57b) Phenylketonuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>61) If &quot;Other&quot;, specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

62) If "Unknown", skip to Q65
### 63. If "Yes", was the breastmilk your own milk or someone else's milk?
- 1 = Own milk
- 2 = Someone else's milk
- 9 = Unknown

### 64. If "Yes", why was the baby given breastmilk from a cup, bottle, spoon, tube, or other method?
- 1 = Baby unwell
- 2 = Mother unwell
- 3 = Problems with breastmilk supply or with breasts
- 4 = Hospital policy for COVID-19
- 5 = Usual hospital policy
- 6 = Other

64s) If "Other", specify

### 65. Did the mother (or caregiver) give the baby any other foods or fluids?
- 1 = Yes
- 2 = No
- 9 = Unknown

### 66. Was the baby ever been put on the mother's chest?
- 1 = Yes
- 2 = No
- 9 = Unknown

66s) If "No", skip to Q68

### 67. If yes, was the baby's bare skin touching the mother's bare skin?
- 1 = Yes
- 2 = No
- 9 = Unknown

### 68. How long is/was the baby on the bare skin of the mother's chest?
- 1 = All the time
- 2 = Occasionally
- 3 = No
- 4 = Other

68s) If "Other", specify

### 69. Where did the baby sleep?
- 1 = In a cot near the mother's bed
- 2 = In a cot outside the mother's room
- 3 = In the mother's bed
- 4 = Other

69s) If "Other", specify

### 70. If outside of mother's room, why was this?
- 1 = Baby unwell
- 2 = Mother unwell
- 3 = Problems with breastmilk supply or with breasts
- 4 = Hospital policy for COVID-19
- 5 = Usual hospital policy

### 71. Did the child have any of the following problems?
- 1 = Yes
- 2 = No

71a) Poor feeding
71b) Convulsions or fits
71c) Fast breathing
71d) Severe chest indrawing
71e) Not moving spontaneously/by self
71f) Temperature >37.5C
71g) Temperature <35.5C
71h) Jaundice or yellow colour in skin or eyes
71i) Nasal congestion/runny nose
71j) Vomiting
71k) Diarrhea
71l) Skin rash
71m) Skin peeling from hands, feet, or lips
71n) Enlarged lymph nodes
71o) Red eyes
71p) Discharge or fluid coming from eyes
71q) Any other symptom

71qs) If "Yes", specify

---

71qsi) If "Yes", and the child was not in a health facility, did the mother seek care for the illness or problem?
- 1 = Yes
- 2 = No
- 9 = Unknown
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/No</th>
<th>Date/Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>71qsi) If &quot;Yes&quot;, did the baby receive any of the following</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiia) Antibiotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiib) Medicine but name unknown</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiic) Help with breathing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiid) Admission to intensive care unit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiie) Oxygen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiie) Medicine for COVID-19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiies) If &quot;Yes&quot; specify</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiif) Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71qsiifs) If &quot;Other&quot;, specify</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72. Any congenital anomalies?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72a) None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72b) Neural tube defects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72bs) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72c) Microcephaly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72cs) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72d) Congenital malformations of ear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72ds) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72e) Congenital heart defects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72es) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72f) Orofacial clefts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72fs) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72g) Congenital malformations of digestive system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72gs) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72h) Congenital malformations of genital organs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>73hs) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>73i) Abdominal wall defects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72is) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72j) Chromosomal abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72js) If &quot;Yes&quot;, date assessed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

SARS-CoV-2 and pregnancy prospective cohort study

Generic protocol: Last updated 2 December 2020, version 2.6
### NEONATAL OUTCOMES BETWEEN BIRTH AND 7 DAYS FORM

**Project ID:** A66012

**Center ID:**

**Participant ID:**

**Country:**

**Birth order**

| 72k) Genetic abnormalities |  
|----------------------------|---
| 72ks) If "Yes", date assessed |  
| Day | Month | Year |

| Unknown |

| 72l) Reduction defects of upper and lower limbs |  
|-------------------------------|---
| 72ls) If "Yes", date assessed |  
| Day | Month | Year |

| Unknown |

| 72m) Talipes equinovarus/clubfoot |  
|-------------------------------|---
| 72ms) If "Yes", date assessed |  
| Day | Month | Year |

| Unknown |

| 72n) Others |  
|-----------------|---
| 72ns) If "Other", specify |  
|  

| 72nsi) date assessed |  
|-----------------|---
| Day | Month | Year |

| Unknown |

**COMMENTS:**

**Interviewer's name:**

**Signature:**

**Date:**

### World Health Organization

A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2

**Generic protocol: Last updated 2 December 2020, version 2.6**
### General

1. Date of Assessment/Extraction

### Neonatal Physical Exam

**Note:** Complete all boxes with 9s in case of unknown value.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Temperature</td>
<td><strong>°C</strong></td>
</tr>
<tr>
<td></td>
<td><strong>°F</strong></td>
</tr>
<tr>
<td>3. Temperature taken</td>
<td><strong>Oral</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Tympanic</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Rectal</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Axillary</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>3s) If &quot;Other&quot;, specify</td>
<td></td>
</tr>
<tr>
<td>4. Respiratory rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>breaths/min</strong></td>
</tr>
<tr>
<td>5. Heart rate</td>
<td><strong>beats/min</strong></td>
</tr>
<tr>
<td>6. Blood pressure</td>
<td><strong>systolic mmHg</strong></td>
</tr>
<tr>
<td></td>
<td><strong>diastolic mmHg</strong></td>
</tr>
<tr>
<td>7. Peripheral O2 saturation (SpO2)</td>
<td><strong>%</strong></td>
</tr>
<tr>
<td>8. Weight</td>
<td><strong>grams</strong></td>
</tr>
<tr>
<td>9. Length</td>
<td><strong>cm</strong></td>
</tr>
</tbody>
</table>

### Neonatal Complications

11. Neonatal complications

1 = Yes  
2 = No  
11a) ventilator support  
11b) Seizures  
11c) Hypoxic ischemic encephalopathy  
11d) Sepsis  
11e) Other  
11es) If "Other", specify  

### Cardiovascular System

12. Cardiovascular system

1 = Normal  
2 = Abnormal  
3 = Murmur  
4 = Other  
9 = Unknown  
12s) If "Other" or "Abnormal", specify  

### Respiratory System

13. Respiratory system

1 = Normal  
2 = Abnormal  
9 = Unknown  
13s) If "Abnormal", describe
<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A 6 6 0 1 2</th>
<th>Center ID:</th>
<th>Participant ID:</th>
<th>Birth order</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Country:</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>14. Gastrointestinal system</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Normal</td>
<td></td>
</tr>
<tr>
<td>2 = Abnormal</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>14a) Jaundice</td>
<td></td>
</tr>
<tr>
<td>14b) Hepatomegaly</td>
<td></td>
</tr>
<tr>
<td>14c) Hernia</td>
<td></td>
</tr>
<tr>
<td>14d) Gastrochisis</td>
<td></td>
</tr>
<tr>
<td>14e) Omphalocele</td>
<td></td>
</tr>
<tr>
<td>14f) Splenomegaly</td>
<td></td>
</tr>
<tr>
<td>14g) Abdominal tenderness</td>
<td></td>
</tr>
<tr>
<td>14h) Other</td>
<td></td>
</tr>
<tr>
<td>14hs) If &quot;Other&quot; or &quot;Abnormal&quot;, specify</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>15. Seizure</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>15s) If &quot;Yes&quot;, describe</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>16. Paralysis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>3 = General</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
<tr>
<td>16s) If &quot;Yes&quot;, describe</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>17. Hypotonia (floppiness)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18. Stiffness or spasticity or increased tone of limbs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>19. Arthrogryposis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
<tr>
<td>9 = Unknown</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>20. Other neurological signs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
</tbody>
</table>

<p>| 21. Other abnormal movements                  |   |</p>
<table>
<thead>
<tr>
<th>(e.g. writhing movements)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>22. Tonic neck reflex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Present</td>
<td></td>
</tr>
<tr>
<td>2 = Absent</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>23. Moro reflex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Present</td>
<td></td>
</tr>
<tr>
<td>2 = Absent</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>24. Rooting reflex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Present</td>
<td></td>
</tr>
<tr>
<td>2 = Absent</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>25. Sucking reflex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Present</td>
<td></td>
</tr>
<tr>
<td>2 = Absent</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>26. Grasp reflex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Present</td>
<td></td>
</tr>
<tr>
<td>2 = Absent</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>27. Babinski reflex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Present</td>
<td></td>
</tr>
<tr>
<td>2 = Absent</td>
<td></td>
</tr>
<tr>
<td>3 = Not done</td>
<td></td>
</tr>
</tbody>
</table>
### NEONATAL OUTCOMES ASSESSED AT 4 WEEKS OF LIFE FORM

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A 6 6 0 1 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center ID:</td>
<td></td>
</tr>
<tr>
<td>Participant ID:</td>
<td></td>
</tr>
<tr>
<td>Birth order</td>
<td></td>
</tr>
</tbody>
</table>

#### 28. Rash
1 = Yes
2 = No
9 = Unknown
28s) If "Yes", date of onset

#### 29. Oedema
1 = Yes
2 = No
9 = Unknown
29s) If "Yes", date of onset

#### 30. Fever
1 = Yes
2 = No
9 = Unknown
30s) If "Yes", date of onset

#### 31. Eye redness/conjunctivitis
1 = Yes
2 = No
9 = Unknown
31s) If "Yes", date of onset

#### 32. Other condition
1 = Yes
2 = No
9 = Unknown
32s) If "Yes", date of onset

#### 33. Fundoscopy
1 = Normal
2 = Abnormal
9 = Unknown
4 = Not done
33s) If "Abnormal", specify

#### 34. Red reflex or chorioretinitis
1 = Present
2 = Absent
9 = Unknown
4 = Not done

#### 35. Cataract
1 = Normal
2 = Abnormal
9 = Unknown
4 = Not done
35s) If "Abnormal", specify

#### 36. Hearing test
1 = Normal
2 = Abnormal
9 = Unknown
4 = Not done
36s) If "Abnormal", specify

#### 37. Newborn blood screening
1 = Positive
2 = Negative
3 = Not done
37a) Hypothyroidism
37b) Phenylketonuria
## NEONATAL FEEDING, SEPARATION, CONTACT, MORBIDITY

38. Please indicate time point for which questions are being asked or data is being extracted
   1 = In the last 24 hours
   2 = Between 1 and 4 weeks post-delivery

39. Has the baby been ever put to the breast?
   1 = Yes  
   2 = No  
   9 = Unknown
   *If "Yes", skip to Q41
   *If "Unknown", skip to Q41

40. If "No", why was the baby never put to the breast?
   1 = Baby unwell
   2 = Mother unwell
   3 = Problems with breastfeeding supply or with breasts
   4 = Hospital policy for COVID-19
   5 = Usual hospital policy
   6 = Other
   40s) If "Other", specify

41. Has the baby been given breast milk from a cup, bottle, spoon, tube or other method?
   1 = Yes
   2 = No  
   9 = Unknown
   *If "No", skip to Q44
   *If "Unknown", skip to Q44

42. If "Yes", was the breast milk mother’s milk or someone else’s milk?
   1 = Mother’s milk
   2 = Someone else’s milk
   9 = Unknown

43. If "Yes", why was the baby given breast milk from a cup, bottle, spoon, tube, or other method?
   1 = Baby unwell
   2 = Mother unwell
   3 = Problems with breastfeeding supply or with breasts
   4 = Hospital policy for COVID-19
   5 = Usual hospital policy
   6 = Other
   43s) If "Other", specify

44. Did the mother (or caregiver) give the baby any other foods or fluids?
   1 = Yes
   2 = No
   9 = Unknown

45. Was the baby ever been put on the mother’s chest?
   1 = Yes
   2 = No  
   9 = Unknown
   *If "No", skip to Q48
   *If "Unknown", skip to Q48

46. If "Yes", was the baby’s bare skin touching the mother’s bare skin?
   1 = Yes
   2 = No  
   9 = Unknown

47. How long is/was the baby on the bare skin of the mother’s chest?
   1 = All the time
   2 = Occasionally
   3 = Other
   9 = Unknown
   47s) If "Other", specify

48. Where does the baby sleep?
   1 = In a cot near the mother’s bed
   2 = In a cot outside the mother’s room
   3 = In the mother’s bed
   4 = Other
   48s) If "Other", specify

49. If outside of mother’s room, why?
   1 = Baby unwell
   2 = Mother unwell
   3 = Problems with breastfeeding supply or with breasts
   4 = Hospital policy for COVID-19
   5 = Usual hospital policy
NEONATAL OUTCOMES ASSESSED AT 4 WEEKS OF LIFE FORM

50. Does the child have any of the following problems?
   1 = Yes
   2 = No
   50a) Convulsions or fits
   50b) Fast breathing
   50c) Severe chest indrawing
   50d) Not moving spontaneously/by self
   50e) Temperature >37.5C
   50f) Temperature <35.5C
   50g) Jaundice or yellow colour in skin or eyes
   50h) Nasal congestion/runny nose
   50i) Vomiting
   50j) Diarrhea
   50k) Skin rash
   50l) Skin peeling from hands, feet, or lips
   50m) Enlarged lymph nodes
   50n) Red eyes
   50o) Discharge or fluid coming from eyes
   50p) Any other symptom
       50ps) If "Yes", specify

51) If "Yes", and the child was not in a health facility, did you seek care for the illness or problem?
   1 = Yes
   2 = No
   52) If "Yes", did your baby receive any of the following
   1 = Yes
   2 = No
   52a) Antibiotics
   52b) Medicine but name unknown
   52c) Help with breathing
   52d) Admission to intensive care unit
   52e) Oxygen
   52f) Medicine for COVID-19
       52fs) If "Yes", specify

52g) Other
       52gs) If "Other", specify

53. Did neonate die?
   1 = Yes
   2 = No
   9 = Unknown
   53s) If "Yes", date of death
       Day
       Month
       Year

54. If neonate died, what was the primary cause of death?
   1 = Yes
   2 = No
   54a) Preterm
   54b) Low birth weight
   54c) Birth asphyxia
   54d) Infection
   54e) COVID-19
   54f) Bacteraemia/Septicemia
   54g) HIV
   54h) Other
       54hs) If "Other", specify

54i) Complications from COVID-19
       54is) If "Yes", specify

54j) Birth trauma
   54k) Congenital/birth defects
   54l) Other
       54ls) If "Yes", specify

55. Any congenital anomalies?
   1 = Yes
   2 = No
   55a) None
   55b) Neural tube defects
       55bs) If "Yes", date assessed
       Day
       Month
       Year
       Unknown
### NEONATAL OUTCOMES ASSESSED AT 4 WEEKS OF LIFE FORM

<table>
<thead>
<tr>
<th>Microcephaly</th>
<th>Abdominal wall defects</th>
<th>Chromosomal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>55c) Microcephaly</td>
<td>55i) Abdominal wall defects</td>
<td></td>
</tr>
<tr>
<td>55cs) If &quot;Yes&quot;, date assessed</td>
<td>55i) Abdominal wall defects</td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
<td>Year</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Congenital malformations of ear</th>
<th>Congenital malformations of ear</th>
<th>Chromosomal abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>55d) Congenital malformations of ear</td>
<td>55j) Chromosomal abnormalities</td>
<td></td>
</tr>
<tr>
<td>55ds) If &quot;Yes&quot;, date assessed</td>
<td>55j) Chromosomal abnormalities</td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
<td>Year</td>
</tr>
<tr>
<td>Unknown</td>
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<table>
<thead>
<tr>
<th>Congenital heart defects</th>
<th>Congenital heart defects</th>
<th>Genetic abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>55e) Congenital heart defects</td>
<td>55k) Genetic abnormalities</td>
<td></td>
</tr>
<tr>
<td>55es) If &quot;Yes&quot;, date assessed</td>
<td>55k) Genetic abnormalities</td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
<td>Year</td>
</tr>
<tr>
<td>Unknown</td>
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</table>

<table>
<thead>
<tr>
<th>Orofacial clefts</th>
<th>Orofacial clefts</th>
<th>Genetic abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>55f) Orofacial clefts</td>
<td>55l) Reduction defects of upper and lower limbs</td>
<td></td>
</tr>
<tr>
<td>55fs) If &quot;Yes&quot;, date assessed</td>
<td>55l) Reduction defects of upper and lower limbs</td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
<td>Year</td>
</tr>
<tr>
<td>Unknown</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Congenital malformations of digestive system</th>
<th>Congenital malformations of digestive system</th>
<th>Reduction defects of upper and lower limbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>55g) Congenital malformations of digestive system</td>
<td>55m) Talipes equinovarus/clubfoot</td>
<td></td>
</tr>
<tr>
<td>55gs) If &quot;Yes&quot;, date assessed</td>
<td>55m) Talipes equinovarus/clubfoot</td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
<td>Year</td>
</tr>
<tr>
<td>Unknown</td>
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</table>

<table>
<thead>
<tr>
<th>Congenital malformations of genital organs</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>55h) Congenital malformations of genital organs</td>
<td>55n) Others</td>
</tr>
<tr>
<td>55hs) If &quot;Yes&quot;, date assessed</td>
<td>55n) Others</td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
</tr>
<tr>
<td>Unknown</td>
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<table>
<thead>
<tr>
<th>Others</th>
<th>Others</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>55n) Others</td>
<td>55n) Others</td>
<td>55n) Others</td>
</tr>
<tr>
<td>55ns) If &quot;Other&quot;, specify</td>
<td>55ns) If &quot;Other&quot;, specify</td>
<td>55ns) If &quot;Other&quot;, specify</td>
</tr>
<tr>
<td>Day</td>
<td>Month</td>
<td>Year</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## SARS-CoV-2 Test Result

56. Laboratory analyses of the neonate  
   1 = Performed  go to Q57  
   2 = Not performed  go to Q58

57. If "Performed", specify  
   1 = Yes  
   2 = No  
   a) Standard  
   b) MTCT screening

58. SARS-CoV-2 Test  
   1 = RT-PCR  
   2 = Serology  
   3 = Not performed  go to End  
   4 = Ag-RDT  
   5 = Unknown

59. Commercial name of test: 

   ____________________________
   ____________________________

60. Result  
   1 = Positive  
   2 = Negative  
   9 = Unknown

61. Date of the test  
   Day  |  Month  |  Year

---

**Comments:**

Interviewer's name:  
Signature:  

Date:  
   Day  |  Month  |  Year

---

**World Health Organization**

**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

NEONATAL OUTCOMES ASSESSED AT 4 WEEKS OF LIFE FORM

**Project ID:**  
**Center ID:**  
**Participant ID:**  
**Birth order:**  

---

SARS-CoV-2 and pregnancy prospective cohort study  
Generic protocol: Last updated 2 December 2020, version 2.6
### Project ID:
A66012

**World Health Organization**

**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

**MATERNAL OUTCOMES AT 6 WEEKS POST-PARTUM / STUDY EXIT FORM**

**CR9**

page 1/1

V1.0 (16 Nov 2020)

---

**Project ID:** A66012  
**Country:**  
**Center ID:**  
**Participant ID:**

---

**1. Date of Assessment/Extraction**

Day  Month  Year

**2. Status of the mother**

1 = Alive  
2 = Dead

2s) If "Dead", explain cause of death

---

**3. Has the woman had any of the following postpartum complications**

1 = Yes  
2 = No  
9 = Unknown

3a) Infection or endometritis  
3b) Fever  
3c) Postpartum haemorrhage  
3d) Postpartum preeclampsia/hypertension

---

**3e) Other cardiovascular complications**

**3f) Maternal blood transfusion**

**3g) Perineal pain**

**3h) Mastitis**

**3i) Other**

3is) If "Other", specify

---

**4. Was the woman readmitted to the hospital since discharge?**

1 = Yes  
2 = No  
9 = Unknown

4s) If "Yes", specify

---

**5. Any maternal medical visit since discharge?**

1 = Yes  
2 = No  
9 = Unknown

5s) If "Yes", specify

---

**MEDICAL HISTORY AND INFECTIONS**

**6. Any updates to medical history or infections?**

1 = Yes  
2 = No  
9 = Unknown

6s) If "yes" please specify

---

| a) Heart disease | b) Lung disease | c) Blood disease | d) Kidney disease | e) Liver disease | f) Neurological disease | g) Thyroid disease | h) Endocrine disease | i) Immunosuppression | j) Hypertension | k) Type 1 or Type 2 diabetes | l) Malaria | m) Dengue | n) Chikungunya | o) Zika | p) Influenza | q) HIV | r) Syphilis | s) Hepatitis A | t) Hepatitis B | u) Hepatitis C | v) Hepatitis D | w) Hepatitis E | x) Toxoplasmosis | y) Rubella | z) Cytomegalovirus | aa) Herpes Simplex | ab) Other medical condition/infection |
|-----------------|----------------|-----------------|------------------|-----------------|-----------------------|------------------|------------------|-------------------|----------------|-------------------------|----------|--------|-------------|------|--------|------|-------|----------|----------|--------|--------|--------|--------|-----------|---------|-----------|-----------|-----------------|

---

**Interviewer's name:**  
**Signature:**  
**Date:**

Day  Month  Year
Appendix C: Biological sampling algorithm

For the exposed group of pregnant women, the following specimens will be collected as shown in Table C1.

Table C1.

<table>
<thead>
<tr>
<th>Tier sampling approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1: minimum sample set</td>
</tr>
<tr>
<td>Tier 2: comprehensive sampling set</td>
</tr>
<tr>
<td>Tier 3: samples to be taken dependent on resources</td>
</tr>
</tbody>
</table>

| Pregnant women with RT-PCR confirmed SARS-CoV-2 infection or evidence of seroconversion during pregnancya |
|-------------------------------------------------|-------------------------------------------------|
| Timing of collection                           | Specimen                                         |
| Childbirth specimens                           | Amniotic fluid samples                          |
| Cord blood                                     | Directly obtain from segment of cord at time of | 0.5 mL or 1 swab                                 |
| Placenta (2)                                   | Placental sampling (umbilical cord, chorionic   | 1 cm sections                                   |
| Maternal blood                                 | villi, amniotic membrane)                       | PCR                                             |
| Specimens following birthc                     | Maternal breast milk                             | 0.5 mL (need to confirm)                        |
| Neoprenatal throat swab                        | Neonatal throat swab immediately following      | 1 swab                                          |
| Neoprenatal anal swab                          | Neonatal anal swab immediately following        | 1 swab                                          |

*Participants must have confirmed SARS-CoV-2 by RT-PCR prior to enrolment.
*If collected for other purposes.
*If any RT-PCR tests result positive from specimens collected following birth, it is recommended to continue testing specimens every 24–72 hours, if feasible, until specimens test negative by 2 consecutive swabs separated by at least 24 hours.

To perform real time RT-PCR on specimens, country-specific protocols should be followed, if available:

- US CDC protocol for SARS-2-CoV RT-PCR

• Other country-specific protocols are available on the WHO website.

Standard safety procedures for handling and processing specimens will be followed, in addition to WHO specific guidance for SARS-2-CoV.26

To perform **ELISA antibody testing for SARS-2-CoV IgG/IgM**, the following protocol is available in:

• A serological assay to detect SARS-CoV-2 seroconversion in humans (4).

It is helpful to review Appendices I–L for draft definitions, criteria and scenarios regarding in-utero, intrapartum and postnatal transmission of SARS-CoV-2. Appendices K and L contain guides for determining timing of infection and samples for assay.

Appendix D: Options for variations in study design

**Option 1:** Disease severity in pregnant versus non-pregnant women (see Fig. D1)

**Figure D1: Disease severity**

- **Objective:** To determine if COVID-19 is more severe in pregnant women compared with non-pregnant women of reproductive age.

**Study population**

- **Inclusion criteria:** RT-PCR for SARS-CoV-2, ability to review clinical records/hospitalization course and diagnostic evaluation for COVID-19 infection.

- **Exclusion criteria:** Inability to review clinical records/hospitalization course or diagnostic evaluation for COVID-19 to confirm infection.

**Pregnancy status**

- **Pregnancy status** will be confirmed if there is recent sonographic evidence of pregnancy, confirmation of fetal heart rate (e.g. fetal doppler) or recent urine pregnancy test/blood pregnancy test. For non-pregnant
group, it is preferred to confirm non-pregnant status through recent urine/blood pregnancy test and/or verbal confirmation from the study participant.

**Recruitment**

- Consecutive prospective recruitment is recommended in a health-care setting where the screening or symptomatic testing of SARS-CoV-2 is ongoing. Study enrolment should not occur until after a positive SARS-CoV-2 test has resulted.

- Matching is recommended between the study groups on the following characteristics as they are known to impact disease severity of SARS-CoV-2 infection:
  1. age (<18, 18–24, 25–29, 30–34, 35–39, 40–45)
  2. gestational age
  3. body mass index (<18.5, 18.6–24.9, 25–29.9, 30–34.9, 35–39.9, 40+)
  4. comorbidities (specifically, type 1 or type 2 diabetes mellitus, chronic hypertension, chronic kidney disease, asthma/chronic obstructive pulmonary disease/obstructive sleep apnoea).

**Data collection**

Data to be collected at enrolment:

- **Pregnant women**: Please see protocol.
- **Non-pregnant women**:
  - demographic information
  - socioeconomic history (as indicated by wealth index)
  - medical and obstetric history
  - medical history
  - medication use
  - immunization history (in particular, seasonal influenza and bacille Calmette–Guérin (BCG) vaccines)
  - social history (substance use/abuse)
  - signs and/or symptoms of COVID-19 (hospitalization, laboratory studies, clinical characteristics and disease course)
  - laboratory evaluation (blood and nasopharyngeal samples)
  - specifically, confirmation of prior SARS-CoV-2 infection by RT-PCR and serology.

**Table D1. Sample data collection**

<table>
<thead>
<tr>
<th>Clinical variables for data collection (during acute COVID-19 illness)</th>
<th>Pregnant women</th>
<th>Non-pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized patients:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presenting signs/symptoms (if available)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care unit admission (Y/N)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubation (Y/N)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supplemental oxygen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressor support (Y/N)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childbirth during acute COVID-19 illness (Y/N)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

27 This list is suggestive and subject to revisions.
Cardiac manifestation:
- Myocardial infarction (Y/N)
- Cardiomyopathy (Y/N)
- Arrhythmia (Y/N)
- Other (Y/N)

Neurological manifestation:
- Seizures (Y/N)
- Haemorrhagic or ischaemic stroke (Y/N)
- Coma (Y/N)
- Other (Y/N)

Thrombotic manifestation:
- Deep vein thrombosis (Y/N)
- Pulmonary embolism (Y/N)
- Arterial thrombosis (Y/N)
- Other (Y/N)
- Coagulopathy (Y/N)

Laboratory data (white blood cells including differential to analyse individual cell lines, Hgb/Hct, platelets, lactate, procalcitonin, fibrinogen, pH) *if collected (obtained as deemed necessary by healthcare provider)

Treatment (antibiotics, antivirals, investigational therapeutics)

Death (Y/N)
If yes, please specify cause of death as listed on the death certificate

Non-hospitalized patients:
- Presenting signs/symptoms (if available)
- Duration of signs/symptoms (if available)
- Treatment (if available)

* Note: see Appendix E for questionnaires for non-pregnant individuals with SARS-CoV-2 infection.

Option 2: Nested case control (for sites with limited antibody testing ability)

Purpose: This study design is for study sites who have limited ability to perform antibody testing for all individuals enrolled into the cohort and who are not assessed as exposed upon cohort entry. It allows for antibody testing to be conducted on only a proportion of individuals from the unexposed cohort (this proportion should be determined based on the testing capability of the study site).

Cases: All or a random sample of women in the cohort experiencing selected outcomes, these women would be SARS-CoV-2 tested to assess exposure status unless they have a confirmed positive exposure status.

Controls: A randomly drawn matching number of controls from the cohort (controls as in women without any outcome of interest (i.e. a pregnancy/delivery without registered events deviating from a “normal” course). These women would be tested to assess exposure status, unless they are already tested positive.

The odds ratios (instead of relative risk) for adverse outcomes would be analysed between cases (adverse outcome) and controls (non-adverse outcome) in relation to their exposure status. This would generate odds ratios for e.g. pre-term birth when exposed/infected with SARS-CoV-2 versus non-exposed/non-infected.

This design option can be considered in areas where antibody testing may be limited.

Data collection:
- The general protocol should be followed for the full cohort, random sample.
- The following lab tests can be collected on a **randomly selected proportion** for the selected **unexposed** cases and controls (see Table D2):

**Table D2.**

<table>
<thead>
<tr>
<th>Timing of collection</th>
<th>Specimen</th>
<th>Method</th>
<th>Minimum volume</th>
<th>Test</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>At time of enrolment</td>
<td>Maternal blood</td>
<td>Standard blood draw (preferred: with routine prenatal lab tests)</td>
<td>To be determined</td>
<td>ELISA (4)</td>
<td>To be determined</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If deemed medically necessary by health-care provider</td>
<td>Nasopharyngeal swab</td>
<td>Per standard testing procedures</td>
<td>10 mL → 5 mL for RT-PCR, 5 mL for biobank</td>
<td>PCR</td>
<td></td>
</tr>
<tr>
<td>On admission to maternity unit for childbirth</td>
<td>Maternal blood</td>
<td>Standard blood draw (preferred: with routine lab tests on admission to maternity unit)</td>
<td>To be determined</td>
<td>ELISA (4)</td>
<td>To be determined</td>
</tr>
<tr>
<td>A. Verification of non-pregnant status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Participant attestation that she is not pregnant at time of COVID-19 disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Recent negative blood or urine pregnancy test within the last 2 weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 = Yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 = No</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Assessment of Exposure (Assignment based on RT-PCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Confirmed test of SARS-CoV-2 by RT-PCR</td>
</tr>
<tr>
<td>(Note: check medical records. Review of diagnostic result is required for study enrollment)</td>
</tr>
<tr>
<td>1 = Yes</td>
</tr>
<tr>
<td>2 = No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Date of RT-PCR test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Test Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
</tr>
<tr>
<td>2 = Negative</td>
</tr>
<tr>
<td>9 = Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. If RT-PCR negative or unknown, conduct antibody (IgG/IgM) testing, or take specimen sample for storing and analysis at a later date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of serology test result</td>
</tr>
<tr>
<td>Day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. Test Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Positive</td>
</tr>
<tr>
<td>2 = Negative</td>
</tr>
<tr>
<td>9 = Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8. Commercial name of serology test used</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>9. Is serology test positive?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
</tr>
<tr>
<td>2 = No</td>
</tr>
</tbody>
</table>

If serology positive, conduct individual assessment and decide enrollment into exposed group based on level of antibody, contact history and case history/presenting symptoms.

If serology negative, candidate for unexposed group. Skip to C.

Note: If RT-PCR negative or unknown and antibody test not available, you may enroll participant into unknown group and consider collecting and storing specimen sample for future analysis. Skip to C.

<table>
<thead>
<tr>
<th>C. Assessment of Exposure (Assignment based on IgG/IgM serology tests)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Confirmed test of SARS-CoV-2 by serology</td>
</tr>
<tr>
<td>(Note: check medical records. Review of diagnostic result is required for study enrollment)</td>
</tr>
<tr>
<td>1 = Yes</td>
</tr>
<tr>
<td>2 = No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>11. Date of serology test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>12. Commercial name of serology test used</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>13. Is serology test positive?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Yes</td>
</tr>
<tr>
<td>2 = No</td>
</tr>
<tr>
<td>9 = Unknown</td>
</tr>
</tbody>
</table>

If serology positive, conduct individual assessment and decide enrollment into exposed group based on level of antibody, contact history and case history/presenting symptoms.

If serology negative, candidate for unexposed group. Skip to C.

Note: If serology test not available, you may enroll participant into unknown group and consider collecting and storing specimen sample for future analysis. Skip to C.
### SARS-CoV-2 and pregnancy prospective cohort study

**A66012 - A prospective cohort study investigating maternal pregnancy and neonatal outcomes for women and neonates infected with SARS-CoV-2**

**SCREENING AND ELIGIBILITY ASSESSMENT**

**FORM NON-PREGNANT WOMEN**

<table>
<thead>
<tr>
<th>Project ID:</th>
<th>A</th>
<th>6</th>
<th>6</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**D. Other criteria (in addition to assessment of exposure, participants must answer yes to this question)**

14. Planning to live in the region and present at study site (or catchment health facility) or be followed up by telephone
   1. Yes
   2. No

**EXCLUSION CRITERIA**

(participant ineligible if "yes" to any of these questions)

15. Woman is unable or unwilling to give informed consent or assent, or (where applicable) surrogate consent has not been secured
   1. Yes
   2. No

16. Woman is planning to move outside of study area during study period
   1. Yes
   2. No

17. Woman is/was pregnant at the time of SARS-CoV-2 infection
   1. Yes
   2. No

18. Woman has not reached the age of majority, as determined by local laws
   1. Yes
   2. No

**ELIGIBILITY DECISION**

19. Does participant meet eligibility criteria for enrollment?
   1. Yes
   2. No

    *If eligibility is confirmed, the woman can be enrolled in the study*

20. Informed consent obtained
   1. Yes
   2. No

21. Date of enrollment
    Day | Month | Year
    --- | --- | ---

22. Age at time of enrollment
   20(a) years
   20(b) months

23. Group Allocation
   1 = Exposed
   2 = Unexposed
   9 = Unknown

24. Participant ID

---

**Interviewer's name:**

**Signature:**

**Date:**

Day | Month | Year
--- | --- | ---

---

*SARS-CoV-2 and pregnancy prospective cohort study*  
*Generic protocol: Last updated 2 December 2020, version 2.6*
### Appendix F: Specimen storage, preservation and shipment

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Collection materials</th>
<th>Storage temperature until testing</th>
<th>Recommended temperature for shipment according to expected shipment time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngeal (NP) swab</td>
<td>Dacron or polyester flocked swabs</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 5 days or −70 °C (dry ice) if &gt; 5 days</td>
</tr>
<tr>
<td>Tissue (placental)</td>
<td>Sterile container with saline or viral transport medium</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 24 hours or −70 °C (dry ice) if 24 hours 5 days</td>
</tr>
<tr>
<td>Serum</td>
<td>Serum separator tubes (collect 3–5 mL of whole blood)</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 5 days or −70 °C (dry ice) if &gt; 5 days</td>
</tr>
<tr>
<td>Whole blood</td>
<td>Collection tube</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 5 days or −70 °C (dry ice) if &gt; 5 days</td>
</tr>
<tr>
<td>Stool or anal swab</td>
<td>Stool container or Dacron or polyester flocked swabs</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 5 days or −70 °C (dry ice) if &gt; 5 days</td>
</tr>
<tr>
<td>Breastmilk</td>
<td>Sterile container</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 5 days or −70 °C (dry ice) if &gt; 5 days</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>Sterile container or Dacron or polyester flocked swabs</td>
<td>2–8 °C</td>
<td>2–8 °C ≤ 5 days or −70 °C (dry ice) if &gt; 5 days</td>
</tr>
</tbody>
</table>
Appendix G: Sample tables for study outcomes

**Primary outcome 1:** Determine if COVID-19 infection in pregnancy increases the risk of adverse pregnancy or neonatal outcomes.

**Table G1. Sample table for primary pregnancy outcome 1**

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Entire cohort</th>
<th>COVID-19 positive</th>
<th>COVID-19 negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth &lt; 37 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm birth &lt; 32 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premature preterm rupture of membranes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placental abruption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antepartum haemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postpartum haemorrhage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caesarean section</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal distress (defined by healthcare provider)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal growth restriction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stillbirth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscarriage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preeclampsia/eclampsia/gestational hypertension/HELLP (i.e. hemolysis, elevated liver enzymes, and a low platelet count)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chorioamnionitis/endometritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Near miss criteria (one or more)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table G2. Sample table for primary neonatal outcome 1

<table>
<thead>
<tr>
<th>Neonatal outcomes</th>
<th>Entire cohort</th>
<th>COVID-19 positive</th>
<th>COVID-19 negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small for gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very small for gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extremely small for gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large for gestational age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apgar &lt;7 at 5 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NICU admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay &gt;4 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory distress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator support</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID-19 infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoxic ischaemic encephalopathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal death</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Primary outcome 2:** To estimate the risk of mother-to-child-transmission of SARS-CoV-2 virus during pregnancy, intrapartum, postpartum or during breastfeeding among mother-neonate pairs with confirmed SARS-CoV-2 infection in pregnancy.

**Primary outcome 3:** To describe viral presence and persistence in the placenta as well as breast milk and other bodily fluids

**Primary outcome 4:** To characterize the clinical course and disease spectrum of COVID-19 infection during pregnancy
Table G3. Sample table for primary outcome 4

<table>
<thead>
<tr>
<th>Maternal clinical variables for data collection (during acute COVID-19 infection)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospitalized patients:</strong></td>
</tr>
<tr>
<td>Duration of hospitalization</td>
</tr>
<tr>
<td>Presenting signs/symptoms (if available)</td>
</tr>
<tr>
<td>Intensive care unit admission (Y/N)</td>
</tr>
<tr>
<td>Intubation (Y/N)</td>
</tr>
<tr>
<td>Supplemental oxygen</td>
</tr>
<tr>
<td>Vasopressor support (Y/N)</td>
</tr>
<tr>
<td>Childbirth during acute COVID-19 infection (Y/N)</td>
</tr>
<tr>
<td><strong>Cardiac manifestation:</strong>    Myocardial infarction, cardiomyopathy, arrhythmia (Y/N)</td>
</tr>
<tr>
<td><strong>Neurologic manifestation:</strong>    seizures, haemorrhagic or ischaemic stroke, coma, other (Y/N)</td>
</tr>
<tr>
<td><strong>Thrombotic manifestation:</strong>     deep vein thrombosis, pulmonary embolism, arterial thrombosis, other (Y/N)</td>
</tr>
<tr>
<td>Coagulopathy (Y/N)</td>
</tr>
<tr>
<td>Laboratory data (white blood cells including differential to analyse individual cell lines, Hgb/Hct, platelets, lactate, procalcitonin, fibrinogen, pH) if collected (obtained as deemed necessary by health-care provider)</td>
</tr>
<tr>
<td>Treatment (antibiotics, antivirals, investigational therapeutics)</td>
</tr>
<tr>
<td>Maternal death (Y/N)</td>
</tr>
<tr>
<td><strong>Non-hospitalized patients</strong></td>
</tr>
<tr>
<td>Presenting signs/symptoms (if available)</td>
</tr>
<tr>
<td>Duration of signs/symptoms (if available)</td>
</tr>
<tr>
<td>Treatment (if available)</td>
</tr>
</tbody>
</table>
Appendix H: Biobank guidance

According to the CIOMS guidelines on storage of biological specimens, the following are key components to the governance structure that the research team should take into account and adhere to:

**Responsible body:**
- name of the legal entity the samples will be entrusted
- name of the body that will review research proposals for future use of the material

**Setting the parameters for storage:**
- types of research that will be pursued (in broad terms)
- types of research that will be excluded or included only after recontacting the donor for consent
- how the quality of the material is controlled
- length of time: samples cannot be stored for an indefinite amount of time; term of validity for the biobank should align with the national guidelines

**Protection of the donor:**
- how authorization from the donor was obtained and how the donor can retract this authorization
- how the rights and welfare of individuals from whom the materials were collected are not adversely affected

**Measures to protect confidentiality:**
- how confidentiality of the link between the specimen and personal identifiers is maintained*
- who may have access to the materials for future research, and under what circumstances
- to which other sources of personal information the results of analyses on biological materials may be linked

*In relation to this, consideration has to be taken into how the samples will be stored. Samples can be anonymized, de-identified or coded.

Anonymous data: All personal identifying information have not been retained and cannot be retrieved. Therefore, there is no link between the sample and the participant which will be a matter of consideration for the participant and research team when discussing the point in time when the participant can withdraw their samples.

De-identified data: This is permanent removal of any personal identifying information and no code exists to link the sample to the participant. Therefore, as in the case above, this is a matter of consideration for the participant and research team when discussing the point in time when the participant can withdraw their samples.

Coded data: Personal identifying information has been replaced with letters, numbers, symbols or a combination of figures. However, a link between this code and the participant is retained. If coded, then the participant needs to understand that the key to the code will remain with the custodian of the biobank.

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*SARS-CoV-2 and pregnancy prospective cohort study

Generic protocol: Last updated 2 December 2020, version 2.6
and there is limited access of the materials of third parties. Unlike the other two situations, this scenario allows a broader period of time that the participant can request withdrawal of their samples.

Taking the above into account, the research team needs to decide on the above when setting up their governance structure. Further description of how the samples will be stored should be explained in the information sheet for the patient to make an informed decision.

**Considerations for re-contacting and/or disseminating future findings:**

- circumstances in which donors need to be recontacted
- procedure for determining whether unsolicited findings should be disclosed, and if so, how they should be managed
- appropriate mechanisms for keeping donors informed of research outcomes
- how participatory engagement with patient groups or the wider community is organized
Appendix I: Draft criteria for defining in utero transmission of SARS-CoV-2

NOTE: These draft criteria have been informed by an ongoing expert consultation process convened by HRP on MTCT of SARS-CoV-2. The information in this section are early extracts of this consultation process and are subject to revision and finalization.

Certain assumptions have been made in order to develop these criteria for defining MTCT of SARS-CoV-2. These include:

1. possibility of transmission at different stages of pregnancy
2. in utero/peripartum/postnatal (breast milk)
3. maternal infection: timing of infection, confirmed infection
4. laboratory results of the women: timing and type of samples, type of laboratory test
5. clinical status of the infant at/close to birth: presence of symptoms
6. laboratory results of the infant: timing and type of samples (sterile versus non-sterile tissues/fluid), type of test, confirmatory test
7. contamination/transient colonization: persistence on multiple tests

Intrauterine transmission (IUT) is presumed to have occurred if there is evidence of both early presumably in utero SARS-CoV-2 exposure AND persistence of SARS-CoV-2 in the infant. The definitions and specimen guidelines cover the assessment of IUT for two major pregnancy outcomes (born alive and stillbirth), and four time periods: at birth; from birth to 24 hours; between 24 hours and 7 days; and from 7 to 14 days. Using the definitions presented below, IUT may be classified as either confirmed, possible or unlikely.

Figure I1. Schematic of possibilities: IUT of SARS CoV-2 in live births

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29 Final definitions and guide will be made available on the WHO website.
Figure I2. Confirmed IUT of SARS CoV-2 in live births

1. Mother positive NP RT-PCR sample or IgM (14 days before delivery to 2 days after birth)

   **AND**

2. Evidence of early presumably in utero infant viral exposure (any one of below)
   - Newborn (age <24 hr) blood positive
   - Placenta fetal side swab or placental tissue positive
   - Amniotic fluid (C/S, before ROM) positive
   - Newborn (age <24 hr) NP positive

   **AND**

3. Evidence viral persistence or immune response in infant (any one of below)
   - Newborn (age >24 hr) blood positive
   - Newborn (age <7 days) IgM positive
   - Newborn (age >24 hr) NP positive

   If only evidence of early infection and persistence is positive NP, then infant must also have symptoms to be considered confirmed

**CONFIRMED intrauterine transmission**
- Mother positive + in utero viral exposure + late infection and viral persistence

Note: C/S, caesarean section; NP, Nasopharyngeal; ROM, rupture of membranes.
Figure I3. Possible IUT of SARS CoV-2 in live births

1. Mother positive
   NP RT-PCR sample or IgM (14 days before delivery to 2 days after birth)

   AND

2. Evidence of early presumably in utero infant viral exposure
   (any one of below)
   - Newborn (age <24 hr) blood positive
   - Placenta fetal side swab or placental tissue positive
   - Amniotic fluid (C/S, before ROM) positive
   - Newborn (age <24 hr) NP positive

   AND

3. Evidence viral persistence or immune response in infant
   (any one of below)
   - Newborn (age >24 hr) blood positive
   - Newborn (age <7 days) IgM positive
   - Newborn (age >24 hr) NP positive

   Blood, placenta or amniotic fluid positive and persistence tests (item 3) not done and infant has symptoms

   NP positive age >24 hr and other tests not done and infant does not have symptoms

   IgM positive at age <7 days and other tests negative or not done and confirmed by 2nd IgM positive at age >7 days
Figure I4. Unlikely IUT of SARS-CoV-2 in live births

1. Mother positive NP RT-PCR sample or IgM (14 days before delivery to 2 days after birth)

AND

2. Evidence of early presumably in utero infant viral exposure (any one of below)

- Newborn (age <24 hr) blood positive
- Placenta fetal side swab or placental tissue positive
- Amniotic fluid (C/S, before ROM) positive
- Newborn (age <24 hr) NP positive

AND

3. Evidence viral persistence or immune response in infant (any one of below)

- Newborn (age >24 hr) blood positive
- Newborn (age <7 days) IgM positive
- Newborn (age >24 hr) NP positive

Placenta or amniotic fluid or blood positive and persistence tests (item 3) not done and infant does not have symptoms

One or more positive early and persistence (item 3) tests negative

Only positive NP at <24 hrs and persistence tests (item 3) not done

IgM positive at age <7 days and other tests negative or not done

Unlikely intrauterine transmission
Figure I5. Possibilities for IUT of SARS-CoV-2 in stillbirths

- IUT of SARS-CoV-2 (stillbirth)
- Evidence of early presumably in utero infant viral infection
- Mother positive (NP RT-PCR or IgM) 14 days before delivery to 2 days after birth
- AND

- IUT confirmed (mother positive and fetal tissue positive)
- IUT possible (placenta positive without fetal tissue testing)
- IUT unlikely (placenta positive and fetal tissue negative on testing)

Note: Confirmed infection requires detection of SARS-CoV-2 in fetal tissue.
Appendix J: Draft criteria for defining intrapartum and postnatal transmission of SARS-CoV-2

NOTE: These draft criteria have been informed by an ongoing expert consultation process convened by HRP on MTCT of SARS-CoV-2. The information in this section are early extracts of this consultation process and are subject to revision and finalization.

Certain assumptions have been made in order to develop these criteria for defining MTCT of SARS-CoV-2. These include:

1. Possibility of transmission at different stages of pregnancy
2. in utero/peripartum/postnatal (breast milk)
3. maternal infection: timing of infection, confirmed infection
4. laboratory results of the women: timing and type of samples, type of laboratory test
5. clinical status of the infant at/close to birth: presence of symptoms
6. laboratory results of the infant: timing and type of samples (sterile vs non-sterile tissues/fluid), type of test, confirmatory test
7. contamination/transient colonization: persistence on multiple test

The following pages include draft guidelines and definitions for peripartum (i.e. intrapartum/early ≤24 hours postpartum) and postnatal horizontal transmission including through breast milk.

Peripartum transmission
Peripartum (intrapartum/early ≤24 hours) transmission is presumed to have occurred if there is evidence of both lack of early exposure AND infection with persistence of SARS-CoV-2 in the infant after early period.

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30 Final definitions and guide will be made available on the WHO website.
PERIPARTUM (INTRAPARTUM/EARLY <24HRS) TRANSMISSION

1. Mother positive NP RT-PCR sample or IgM (14 days before delivery to 2 days after birth)

2. LACK of evidence of early presumably in utero infant viral exposure (≥1 test done, and all tests done are negative)
   - Newborn (age <24 hr) blood negative
   - Placenta fetal side swab or placental tissue negative
   - Amniotic fluid (C/S, before ROM) negative
   - Newborn (age <24 hr) NP negative RT-PCR
   - Newborn (age <7 days) IgM negative

3. Evidence LATER infection and viral persistence or immune response in infant (any one of below)
   - Newborn (age 7–14 days) IgM positive and confirmed by 2nd IgM positive test
   - Newborn (age >24 hr) NP positive and confirmed by 2nd NP positive at age 1–7 days

CONFERMED peripartum transmission
   - Mother positive
   - in utero viral exposure
   - late infection and viral persistence

POSSIBLE peripartum transmission
   - No early tests done (item 2 not done)
   - and positive confirmed late testing (item 3)
1. Mother positive NP RT-PCR sample or IgM (14 days before delivery to 2 days after birth)

2. LACK of evidence of early presumably in utero infant viral exposure (≥1 test done, and all tests done are negative)
   - Newborn (age <24 hr) blood negative
   - Placenta fetal side swab or placental tissue negative
   - Amniotic fluid (C/S, before ROM) negative
   - Newborn (age <24 hr) NP negative RT-PCR
   - Newborn (age <7 days) IgM negative

3. Evidence LATER infection and viral persistence or immune response in infant (any one of below)
   - Newborn (age 7–14 days) IgM positive and confirmed by 2nd IgM positive test
   - Newborn (age >24 hr) NP positive and confirmed by 2nd NP positive at age 1–7 days

CONFIRMED peripartum transmission
- Mother positive + in utero viral exposure + late infection and viral persistence

UNLIKELY peripartum transmission
- Single IgM positive at age 7–14 days with negative 2nd confirmatory IgM test or no other testing done
- Single NP positive at age >24 hr with negative 2nd confirmatory NP test or no other testing done
Postnatal horizontal transmission

Postnatal horizontal transmission is presumed to have occurred if there is evidence of both lack of early exposure AND infection and persistence of SARS-CoV-2 in the infant after the peripartum period.

Figure J3.

1. Mother positive
   NP RT-PCR sample or IgM
   (14 days before delivery to 2 days after birth)

2. LACK of evidence of peripartum infant viral exposure
   (≥1 test done, and all tests done are negative)
   - Infant NP negative in any samples obtained at age <7 days
   - Newborn blood, placenta and amniotic fluid (C/S, before ROM) negative if done
   - Infant IgM in any samples at age <14 days negative if done

3. Evidence SUBSEQUENT infection with viral persistence or immune response in infant
   (any one of below)
   - Infant IgM positive at age >14 days and confirmed by 2nd IgM positive test
   - Infant NP positive at age >7 days and confirmed by 2nd NP positive test

CONFIRMED postnatal transmission
   Mother positive +
   no peripartum exposure +
   subsequent infection and viral persistence

POSSIBLE postnatal transmission
   No early tests done (item 2 not done)
   and positive confirmed late testing (item 3)
POSTNATAL HORIZONTAL TRANSMISSION

1. Mother positive
NP RT-PCR sample or IgM
(14 days before delivery to 2 days after birth)

2. LACK of evidence of peripartum infant viral exposure
(≥1 test done, and all tests done are negative)

   Infant NP negative in any samples obtained at age <7 days

   Newborn blood, placenta and amniotic fluid (C/S, before ROM) negative if done

   Infant IgM in any samples at age <14 days negative if done

3. Evidence SUBSEQUENT infection with viral persistence or immune response in infant
(any one of below)

   Infant IgM positive at age >14 days and confirmed by 2nd IgM positive test

   Infant NP positive at age >7 days and confirmed by 2nd NP positive test

CONFIRMED postnatal transmission
   Mother positive +
   no peripartum exposure +
   subsequent infection and viral persistence

UNLIKELY peripartum transmission
   Single IgM positive at age >14 days with negative 2nd confirmatory IgM test or no other testing done

   Single NP positive at age >7 days with negative 2nd confirmatory NP test or no other testing done
**Breast milk transmission**: Breast milk transmission will be difficult to document as breastfeeding infant will likely be exposed to an environment with SARS-CoV-2 (mother, household) so ruling out horizontal acquisition will be difficult.

Figure J5.

1. **Mother positive NP RT-PCR sample or IgM**
   (14 days before delivery to 2 days after birth)

2. **LACK of evidence of infection prior to breastfeeding**
   (must have at least 1 negative test before breastfeeding)
   - ALL infant sample negative in any samples obtained prior to ingestion + breast milk

3. **Breastmilk confirmed positive for SARS-CoV-2**
   - ≥2 breast milk samples positive

4. **Positive breast milk ingested in environment where horizontal transmission unlikely/minimized**

5. **Initially uninfected infant has confirmed infection**
   - Negative IgM converts to positive IgM following breast milk ingestion
   - Negative infant NP or faecal specimen become positive, confirmed by second specimen following breast milk ingestion

Note: This category is so difficult. Scenarios for possible or unlikely breast milk transmission could not be developed. If mother first becomes infected with SARS-CoV-2 after childbirth while breastfeeding, it will be extremely difficult to distinguish infant exposure/acquisition horizontally from mother/environment versus breast milk acquisition.
Appendix K: Potential testing of live birth for determination of infection timing\textsuperscript{31}

NOTE: These draft criteria have been informed by an ongoing expert consultation process convened by HRP on MTCT of SARS-CoV-2. The information in this section are early extracts of this consultation process and are subject to revision and finalization.

Figure K1.

<table>
<thead>
<tr>
<th>If possible, additional maternal specimens:</th>
<th>If possible, birth specimens:</th>
<th>Birth–24 hours:</th>
<th>24 hours–7 days:</th>
<th>7–14 days:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal</td>
<td>Placental swab (fetal side)/ biopsy for PCR/ histology</td>
<td>Neonatal NP swab</td>
<td>Infant NP swab</td>
<td>Neonatal NP swab</td>
</tr>
<tr>
<td>Rectal</td>
<td>Amniotic fluid (CS prior to ROM)</td>
<td>Neonatal blood PCR</td>
<td>Infant blood PCR</td>
<td>Neonatal blood swab</td>
</tr>
<tr>
<td>Optional:</td>
<td>Umbilical cord sample</td>
<td>Neonatal blood IgM</td>
<td>Infant blood IgM</td>
<td>Neonatal blood IgM</td>
</tr>
<tr>
<td>Breastmilk</td>
<td>Cord blood for PCR, IgM</td>
<td>Optional:</td>
<td>Optional:</td>
<td>Optional:</td>
</tr>
<tr>
<td>Blood</td>
<td></td>
<td>Neonatal rectal</td>
<td>Infant rectal</td>
<td>Infant rectal</td>
</tr>
</tbody>
</table>

To confirm in utero infection if testing positive from birth to 24 hours (or positive birth specimen) To confirm peripartum infection when birth test is negative and 24 hours–7 days test positive

\textsuperscript{31} Final definitions and guide will be made available on the WHO website.
Appendix L: Potential samples to test for timing of SARS-COV-2 perinatal infection

NOTE: These draft criteria have been informed by an ongoing expert consultation process convened by HRP on MTCT of SARS-CoV-2. The information in this section are early extracts of this consultation process and are subject to revision and finalization.

Table L1.

<table>
<thead>
<tr>
<th>Maternal SARS-CoV-2 (in addition to positive nasopharyngeal)</th>
<th>Fetal/neonatal SARS-CoV-2 testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antenatal</strong></td>
<td>• Optional</td>
</tr>
<tr>
<td></td>
<td>- Amniotic fluid RT-PCR (if done for other purpose)</td>
</tr>
<tr>
<td><strong>1st trimester miscarriage</strong></td>
<td>• Products of conception RT-PCR or other viral identification (EM, culture)</td>
</tr>
<tr>
<td>• Vaginal swab RT-PCR</td>
<td>• Placenta swab (fetal side preferred) or biopsy RT-PCR or other viral identification (EM, culture)</td>
</tr>
<tr>
<td>• Optional</td>
<td>• Umbilical cord for RT-PCR or other viral identification (EM, culture)</td>
</tr>
<tr>
<td>- Blood RT-PCR</td>
<td>• Umbilical cord blood RT-PCR</td>
</tr>
<tr>
<td><strong>2nd trimester miscarriage/stillbirth</strong></td>
<td>• Fetal tissues RT-PCR or other viral identification (EM, culture)</td>
</tr>
<tr>
<td>• Vaginal swab RT-PCR</td>
<td>• Placenta histology when possible</td>
</tr>
<tr>
<td>• Optional</td>
<td>• Placenta histology when possible</td>
</tr>
<tr>
<td>- Blood RT-PCR</td>
<td>• Placenta histology when possible</td>
</tr>
<tr>
<td><strong>Intrapartum/immediately postpartum:</strong></td>
<td>• Placenta histology when possible</td>
</tr>
<tr>
<td>• Vaginal swab RT-PCR</td>
<td>• When possible:</td>
</tr>
<tr>
<td>• Rectal swab RT-PCR</td>
<td>- Amniotic fluid (prior to rupture membrane with caesarean section aspirate through intact membrane after uterine incision)</td>
</tr>
<tr>
<td>• Optional</td>
<td>- Placenta swab (fetal side preferred) or biopsy RT-PCR or other viral identification (EM, culture)</td>
</tr>
<tr>
<td>- Blood RT-PCR</td>
<td>- Umbilical cord for RT-PCR or other viral identification (EM, culture)</td>
</tr>
<tr>
<td><strong>Live birth</strong></td>
<td>- Umbilical cord blood RT-PCR and/or SARS-CoV-2 IgM (must be confirmed with peripheral blood)</td>
</tr>
<tr>
<td><strong>Postpartum:</strong></td>
<td>• Placenta histology when possible</td>
</tr>
<tr>
<td>• Optional</td>
<td>• Placenta histology when possible</td>
</tr>
<tr>
<td>- Breast milk (if positive, must confirm with at least one more sample) RT-PCR or cytotoxicity/infectivity assay</td>
<td>• Placenta histology when possible</td>
</tr>
</tbody>
</table>

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32 Final definitions and guide will be made available on the WHO website.

SARS-CoV-2 and pregnancy prospective cohort study

Generic protocol: Last updated 2 December 2020, version 2.6
### Birth to 24 hours for SARS-CoV-2 testing:
- Respiratory sample for RT-PCR
- Peripheral blood for RT-PCR
- Peripheral blood for SARS-CoV-2 IgM
- Optional:
  - Neonatal rectal swab for RT-PCR

### 24 hours–7 days for SARS-CoV-2 testing:
- Respiratory sample for RT-PCR
- Blood for SARS-CoV-2 IgM
- Optional
  - Blood for RT-PCR
  - Rectal swab for RT-PCR

### 14 days for SARS-CoV-2 RT-PCR (if test at birth negative or not done and test at age 24 hours–7 days positive):
- Respiratory sample for RT-PCR
- SARS-CoV-2 IgM

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**Note:** EM, electron microscopy.

- **a** To confirm *in utero* infection if birth specimen positive; to determine peripartum (intrapartum/early postnatal transmission) if birth specimen is negative.

- **b** To confirm intrapartum/early postnatal transmission when birth testing negative and 24 hour-7 days test positive.

*Note: Table L1 has been modified from (4).*
Appendix references


