Assessment of potential risk factors of infection of Middle East respiratory syndrome coronavirus (MERS-CoV) among health care personnel in a health care setting

Version 1

Date: Version 1

27 January 2014

Contact: mountsa@who.int

World Health Organization

Acknowledgement

This document was adapted from a protocol developed by the Consortium for the Standardization for Influenza Seroepidemiology (CONSISE), a global partnership aiming to develop influenza investigation protocols and standardize seroepidemiology to inform public health policy for pandemic, zoonotic and seasonal influenza. This international partnership was created out of a need, identified during the 2009 H1N1 pandemic, for standardized seroepidemiological data to estimate infection attack rates and severity of the pandemic virus and to inform policy decisions. More information on the CONSISE network can be found on their website: www.CONSISE.tghn.org.

See acknowledgements at the end for individual reviewers.

PROTOCOL SUMMARY

Comprehensive investigations of health care personnel (HCP) who may have been exposed to patients infected with Middle East respiratory syndrome coronavirus (MERS-CoV), diagnosed either prospectively or retrospectively, are essential to understand the risk factors of infection within health care facilities. The risk factors identified from such investigations may provide insights into the potential modes of transmission to inform guidance and policy in infection control in health care facilities, and in directing national and international public health response.

The epidemiological methods to guide data collection for the comprehensive assessment of the HCP are set out in this document. This protocol outlines methods of an analytical epidemiological, virological and serological study involving staff working at the health care facility(ies) where an index patient infected with MERS-CoV virus is being or had been treated.

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 study will be carried out.

CONTENTS

1.0 SCIENTIFIC BACKGROUND & RATIONALE FOR STUDY

The Middle East respiratory syndrome coronavirus (MERS-CoV) was first detected in a patient living in Saudi Arabia in September of 2012 [1]. The virus is thought to be zoonotic in origin although the reservoir(s) and route of transmission to humans remains unclear. Sporadic cases and clusters in health care facilities have been reported in several countries [2-5]. Indeed, the largest proportion of secondary transmission currently appears to have occurred in a health care facility. Identification of the factors that facilitate transmission in health care settings will inform measures to interrupt transmission. Experience with Severe Acute Respiratory Syndrome (SARS) demonstrated that studies of transmission in health care settings were critical to the development of control measures [6].

This investigation, as outlined in this document, will provide data to evaluate risk factors and prevention methods for MERS-CoV infection by comparing exposures of infected (as provided by virologic or serologic confirmation) with HCP not infected (sero-negative study subjects).

Current information on the MERS-CoV and interim guidance on infection prevention and control can be found on the WHO website: http://www.who.int/csr/disease/coronavirus_infections/en/index.html.

1.1 OBJECTIVES

The data collected from this study will be used to characterize the key epidemiological transmission features of MERS-CoV virus and inform strategies for control of transmission, particularly in health care settings.

PRIMARY OBJECTIVES

The primary objectives of this study are to:

- Determine the risk factors for MERS CoV transmission and infection in health care settings
- Assess the extent of MERS-CoV secondary transmission to HCP caring for probable and confirmed patients

SECONDARY OBJECTIVES

Seroepidemiologic investigations, such as the one described below, can provide rich data to assess secondary objectives, including, but not limited to:

- Description of the spectrum of illness and clinical course of disease with MERS-CoV infection
- Quantification of the proportion of asymptomatic to sub-clinical MERS-CoV infections

- Quantification of the proportion of individuals who seroconvert
- Assessment of the effectiveness of infection control measures

2.0 STUDY PROCEDURES

This study uses epidemiological, virological and serological methods applied to HCP exposed to a patient infected with MERS-CoV virus to assess the risk factors for human-to-human transmission of MERS-CoV.

In this study, the exposures of laboratory-confirmed (by RT-PCR) or serologically confirmed health care workers will be compared with those of laboratory- and serologically negative HCP to determine risk factors associated with infection.

It is recommended to start the study with a general interview of HCP, including supervisors and colleagues, to have a better understanding of the potential exposures and existing infection control practices (their proxies, such as direct supervisors/colleagues in the same team, may respond if the affected HCP is unable to participate as a result of critical illness or death), and a visit to the medical facilities to learn more about the management, infrastructure and policies of infection control to develop more concrete hypotheses about the possible exposures HCP may have had to the MERS-CoV (Appendix A). The interview should be used in conjunction with a data collection form to identify all potential study subjects (Appendix B).

A full questionnaire can then be developed. A sample questionnaire has been provided in Appendix C as a starting point.

COMMENT: The timing of this study is critical. Ideally, this study should be conducted as soon a patient with MERS-CoV (the index case) is identified. The current protocol is based on the assumption that the patient with MERS-CoV infection was identified while still in the hospital.

2.1 ETHICAL CONSIDERATIONS

Ethical approval must be sought in accordance with local, regional and national authorities.

COMMENT: It is strongly recommended that ethical approval is obtained in advance from relevant ethical or institutional review boards (e.g. national Ministries of Health, Agriculture, etc.) using a generic protocol such as this one before an outbreak occurs. Once an outbreak occurs, the study design, questionnaires, sampling and consent forms can be modified rapidly to the actual situation. This may still have to be resubmitted for ethical approval, but as the generic protocol including this final step has already been approved, this could be a very rapid process, without substantial delay in the investigations.

2.2 STUDY SUBJECT IDENTIFICATION AND SELECTION

2.2.1 SELECTION OF HEALTH CARE PERSONNEL

Every effort will be made to include *all* HCP who may have come in contact with the MERS-CoV confirmed patients (e.g. by means of going through the duty roster, contact tracing, interviews) from the time of first contact with the patient (or patient materials) to 14 days after the last contact.

COMMENT: For the purposes of this protocol specifically designed for MERS-CoV, we recommend that the definition of a contact not be too restrictive so that a large number of potentially exposed HCP are included in the study. Contacts should include, for example, cleaners, clerks, and others who may not have provided care to the patient but who would have been in the general environment.

COMMENT: If the patient was transferred from another health care facility, then the HCP from that facility would need to be recruited for this study.

Health care personnel with potential exposure to the patient should be identified initially by hospital infection control staff. These will include all staff involved in provision of care for an infected patient, including those who may have been present in the same area as the infected patient for other purposes and those who may have had contact with patient body fluids, potentially contaminated items or environmental surfaces. For practical reasons, the study population may comprise all staff working in all hospital facilities involved in provision of care to the infected patient during all or part of the time of potential exposure, including reception area/admission facilities, specialized and supporting services. All categories of potentially exposed staff should be selected, including health care workers, allied health professionals, auxiliary health workers (e.g. cleaning and laundry personnel, x-ray physicians and technicians, clerks, phlebotomists, respiratory therapists, nutritionists, social workers, physical therapists, lab personnel, cleaners, clerks, patient transporters, catering staff, etc.).

COMMENT: The concept of "protected exposure" should be avoided when selecting the study subjects. In particular, wearing personal protective equipment (PPE) should not be considered an exclusion criterion as one of the risk factors to be studied by this protocol is the effectiveness of PPE.

COMMENT: Recommendations are provided for the definition of a HCP contact in terms of space and duration; however, the specific definition of a contact in terms of duration and distance may vary depending on the characteristics of the novel virus, if the protocol is used for viruses other than MERS-CoV. Any variation in the definition of HCP contacts between studies will result in reduced comparability. Definition of a contact in terms of space and time in reporting of the results of this study will aid in comparability between studies.

COMMENT: Background information about the health care setting and those potentially exposed to the patient will be required to be collected before sampling to understand the likely contacts of the MERS-

CoV patients. A data collection tool to help in formulating hypotheses about the exposure and to identify potential subjects for this study is provided in Appendix A.

2.2.2 RECRUITMENT AND FOLLOW UP

After identification of potential participants, informed consent from subjects will be obtained (see 2.2.4 below). At the time of recruitment, combined nasopharyngeal and throat swabs, and, ideally, specimens from the lower respiratory tract (highly recommended, if possible) will be collected for virological confirmation, blood for serological confirmation and a questionnaire will be administered (Appendix C). The recommended clinical specimens may change in the future as more information is learned about the optimal specimens and appropriate timing after exposure to detect MERS-CoV infection.

Subjects will be monitored for symptoms for 14 days after last contact with MERS-CoV patient or patient materials. If symptoms occur, virological testing will be carried out at that time. Specimens to be collected for virological testing include combined nasopharyngeal and throat swabs, and, ideally, specimens from the lower respiratory tract, if possible. Repeat blood collection will be carried out at least 14 days after the last contact with the MERS-CoV patient or patient materials.

2.2.3 INFORMED CONSENT

All potentially exposed HCP will be asked to provide consent by a trained member of the investigation team.

2.2.4 DATA COLLECTION

After enrolment, a brief questionnaire will be administered to those consenting, which will be piloted in advance (Appendix C). Information will be collected on demographics, job duties, symptoms of respiratory disease, use of PPE, and specific exposures to the MERS-CoV confirmed patient. Additional exposure (including exposures to confirmed or suspected human cases in the community and to other potential sources such as animals) questions will be included for all study subjects in the questionnaire.

A template of the study questionnaire for the use of all cases and contacts is provided in Appendix C.

2.2.5 RISKS AND BENEFITS FOR SUBJECTS

This investigation poses minimal risk to participants, involving collection of a small amount of blood and upper (and lower) respiratory tract specimens. The direct benefit to the participant is the early detection of infection to allow appropriate monitoring and early treatment. The primary benefit of the study is indirect in that data collected will help improve and guide efforts to prevent further spread of MERS-CoV to HCP.

2.2.6 CONFIDENTIALITY

HCP and controls will be assigned a study identification number by hospital staff for labelling of study questionnaires and clinical specimens. The link to specific individuals will be maintained by the hospital and the Ministry of Health (or equivalent) and will not be disclosed to any other research personnel.

COMMENT: If shared by the implementing organization, data provided to WHO or any agency supporting data analysis will include only the study identification number.

2.2.7 PREVENTION OF MERS-COV TRANSMISSION IN FRONT-LINE STAFF

Before study implementation, front-line staff, including all study personnel, will be trained in infection control procedures (standard, contact, droplet or airborne precautions). These procedures include proper hand hygiene and the correct use of surgical or respiratory face masks, if necessary, not only to minimize their own risk of infection when in close contact with patients in a health care setting, during home visits and elsewhere, but also to minimize the risk of spread among other HCP and their household members.

2.3 SAMPLE SIZE CONSIDERATIONS

For this study, the overall sample size will be determined by the number of HCP in contact with the confirmed MERS-CoV patient(s). Every effort will be made to include *all* HCP who have been and are in contact with confirmed MERS-CoV patients.

2.4 SPECIMEN COLLECTION AND LABORATORY EVALUATIONS

2.4.1 SPECIMEN COLLECTION, TRANSPORTATION

WHO lab guidance on specimen collection and transportation can be found at: http://www.who.int/csr/disease/coronavirus_infections/LaboratoryTestingNovelCoronavirus_21Dec12.pdf

Additional records will be kept for each biological sample, including the time of collection, the conditions for transportation and the time of arrival at the study laboratory.

2.4.2 LABORATORY PROCEDURES

VIROLOGIC TESTING

MERS-CoV case definitions can be found at: http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/MERS-CoV_confirmed.html.

As of 3 July 2013, one of the following conditions must be met to consider a case as laboratory-confirmed:

- positive RT-PCR or other validated molecular assays for at least two different specific targets on the MERS-CoV genome

OR

- one positive RT-PCR assay for a specific target on the MERS-CoV genome and an additional different PCR product sequenced, confirming identity to known sequences of the new virus.

A positive PCR assay for a single specific target without further testing is considered *presumptive* evidence of MERS-CoV infection. Final classification of cases will depend on clinical and epidemiological information combined with laboratory data. Member States are requested to immediately notify WHO.

See full details for virologic laboratory testing of MERS-CoV can be found here: http://www.who.int/csr/disease/coronavirus_infections/LaboratoryTestingNovelCoronavirus_21Dec12.pdf.

SEROLOGIC TESTING

COMMENT: Serologic assays for MERS-CoV are currently in development by a small number of laboratories around the world. Here we provide details of the only published serologic testing available for MERS-CoV [7,8]. Investigators are encouraged to check current scientific literature for newer information on serological testing.

COMMENT: Only a limited number of laboratories have the facilities for MERS-CoV serologic testing and therefore collaboration between countries without current capacity and designated reference laboratories is possible. Collaboration is up to the discretion of Member States carrying out the research, but WHO strongly supports such collaborations and will facilitate this collaboration and possible shipment for testing, if required.

The following laboratory assay results are currently available for defining a case as MERS-CoV antibody positive (full details can be found in [7,8]). However, as more research findings on the improvement of serological assay become available, guidance will be updated accordingly.

- Screening for antibodies reactive to MERS-CoV by indirect immunofluorescence assay (IFA) described in [7,8]

- More specific secondary serologic testing should be done using microneutralization or ELISA-based assays using appropriately timed sera (ideally, paired acute and convalescent sera)[7,8]

COMMENT: Although a four-fold rise in titre is generally thought to be indicative of seroconversion for most standardized serological assays for other pathogens, MERS-CoV assays have not yet been

standardized. However, the analysis of data from this study will compare rates of seropositivity or presumptive seroconversion to those without. The relationship will depend on a statistical association to determine potential risk factors rather than the absolute value of an individual test. Therefore, for the purposes of this study, a positive test will be determined by the specific laboratory doing the assay. It will likely depend on a combination of results from multiple tests and cut-off values designating a "positive" result set by the laboratory based on the results of experience with the particular assay.

3.0 STUDY ENDPOINTS & STATISTICAL ANALYSES

The following section discusses the endpoints – that is, what can be measured and calculated using the data collected in this study – for the primary objectives, including statistical advice.

3.1 STUDY OUTCOME MEASURES

3.1.1 PRIMARY ENDPOINTS

The following will be assessed as study endpoints corresponding to the study's primary objectives as outlined above.

3.2 STATISTICAL ANALYSES

3.2.1 FOR PRIMARY OBJECTIVES

The primary objective of this study is to assess the frequency of infection (virological and serological) among exposed HCP

- Virologic infection = % of total subjects included in study who are RT-PCR positive
- Immunologic infection = % of total subjects included in study who are seropositive (see section 2.4.2 for definition of seropositivity)

COMMENT: Depending on your study sample size, reporting of these rates may be done by reporting overall infection rates or by subtype (e.g. by occupational group or job duty, by age, gender, etc.).

RISK FACTORS FOR INFECTION

One way to measure risk factors for infection is to compare the exposures (e.g. characteristics, behaviours, practices) of subjects who are seropositive or virologically positive (combining the two into a "infected" group) versus study subjects who are negative serologically and virologically.

The reported practices among seropositive and seronegative subjects will be compared using appropriate statistical tests, e.g. bivariate associations between risk factors being infected will be

determined by chi-square statistics or 2-sided Fisher's exact test and expressed as odds ratios with 95% confidence intervals. Multivariate logistic regression will be used to further analyse the associations.

COMMENT: Univariate statistical analysis by logistic regression could be used to test the significance of each predictor on the outcome of infection. Multivariate logistic regression can be used to identify independent risk factors (after adjusting for known or potential confounders) or a combination of risk factors associated with the odds of infection.

COMMENT: Alternatively, Mantel-Haenszel matched-pair analysis (McNemar test) can be used to estimate the strength and statistical significance of associations between exposures and infection.

4.0 REPORTING OF FINDINGS

COMMENT: Any deviation from the study methodology should be reported to aid in the interpretation of findings. The timely dissemination of results of this study are critical in understanding transmission of the MERS-CoV virus to inform guidance for policy to direct national and international public health response.

REFERENCES

1. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA (2012) Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 367: 1814-1820.

2. Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeah AA, et al. (2013) Hospital Outbreak of Middle East Respiratory Syndrome Coronavirus. New England Journal of Medicine 2013 Jun 19. [Epub ahead of print].

3. Guery B, Poissy J, el Mansouf L, Séjourné C, Ettahar N, et al. (2013) Clinical features and viral diagnosis of two cases of infection with Middle East Respiratory Syndrome coronavirus: a report of nosocomial transmission. The Lancet 381: 2265-2272. doi: 2210.1016/S0140-6736(2213)60982-60984. Epub 62013 May 60930.

4. Hijawi B, Abdallat M, Sayaydeh A, Alqasrawi S, Haddadin A, et al. (2013) Novel coronavirus infections in Jordan, April 2012: epidemiological findings from a retrospective investigation. Eastern Mediterranean Health Journal 19: S12-S18.

5. The WHO MERS-CoV Research Group. State of Knowledge and Data Gaps of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Humans. PLOS Currents Outbreaks. 2013 Nov 12. Edition 1. doi: 10.1371/currents.outbreaks.0bf719e352e7478f8ad85fa30127ddb8

6. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J (2012) Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. PLoS One 7: e35797. doi: 35710.31371/journal.pone.0035797. Epub 0032012 Apr 0035726.

7. Buchholz U, Müller MA, Nitsche A, Sanewski A, Wevering N, et al. (2013) Contact investigation of a case of human novel coronavirus infection treated in a German hospital, October-November 2012. Euro Surveill 2013;18(8):pii=20406 Available online: http://wwweurosurveillanceorg/ViewArticleaspx?ArticleId=20406

8. Corman VM, Müller MA, Costabel U, Timm J, Binger T, et al. (2012) Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. Euro Surveill 2012;17(49):pii=20334 Available from: <http://wwweurosurveillanceorg/ViewArticleaspx?ArticleId=20334>.

ACKNOWLEDGEMENTS

Many people were involved in the creation and revision of this protocol. These include: Maria D Van Kerkhove, Anthony W Mounts, Sergey Eremin, Cota Vallenas, Julia Fitzner, Tim Uyeki, John Wood, Othmar Engelhardt, Jeffery Cutter, Salah Al Awaidi, Susan I Gerber, Pasi Penttinen, Julien Baute and Elizabeth Bancroft.

APPENDIX A QUESTIONS TO THE HEALTH CARE INFECTION CONTROL OR ADMINISTRATION STAFF

Note, these questions, while not part of the actual analysis, are important for hospital officials and administrators to consider when evaluating the preparedness of their facility to manage cases of MERS-CoV or other serious transmissible diseases.

1.1 Is there an infection prevention and control (IPC) program in the health care facility?	☐ Yes	☐ No	☐ Unknown
1.2 Is an infection control professional working at the facility?	☐ Yes	☐ No	☐ Unknown
1.3 Have any HCP been infected with MERS-CoV in your health care facility?	☐ Yes	☐ No	☐ Unknown
1.4 Is infection control education and training provided to HCP?	☐ Yes	☐ No	☐ Unknown
1.4.1 If 1.4 = yes, does the training include prevention of respiratory pathogen exposure?	☐ Yes	☐ No	☐ Unknown
1.4.2 If yes, how often is training for respiratory pathogens mandated for HCP? On employment? Every year? As needed?			
1.5 Was IPC information on this specific emerging infection provided to HCP?	☐ Yes	☐ No	☐ Unknown
1.6 Is there a policy in the hospital to prevent transmission of respiratory infection?	☐ Yes	☐ No	☐ Unknown
1.7 Is there a triage system in place to early detect cases and isolate them?	☐ Yes	☐ No	☐ Unknown
1.8 Are there policies and procedures for screening and work restrictions for exposed or ill HCP?	☐ Yes	☐ No	☐ Unknown
1.9. Are there safe procedures for laboratory submission of specimens for MERS-CoV testing?	☐ Yes	☐ No	☐ Unknown
1.10 Are there negative-pressure airborne infection isolation rooms or well ventilated isolation rooms that are functioning correctly and appropriately monitored for airflow and exhaust handling?	☐ Yes	☐ No	☐ Unknown
1.11 Are PPE and other infection control supplies (e.g. hand hygiene supplies) available in sufficient quantities?	☐ Yes	☐ No	☐ Unknown

APPENDIX B HOSPITAL PERSONNEL

Identify HCP who had potential exposure to MERS-CoV patients

ID of HCP completing table: _____

Date (dd/mm/yyyy)	Name of HCP	Name/ID of MERS-CoV patient HCP cared for	Date of admission of MERS-CoV patient (dd/mm/yyyy)	Hospital unit where potentially exposed*

*Intensive care unit, emergency department, surgical theatre, etc.

COMMENT: Add more lines as needed.

APPENDIX C QUESTIONNAIRE

Questionnaire for Assessment of potential risk factors of infection of MERS-CoV among health care personnel in a health care setting

The following questionnaire should be used for **all subjects** included in the investigation. This questionnaire is divided into sections: **General questions, Exposure questions**, **Symptom and Course of Disease questions and Background Demographic questions** and represents the minimum questions that should be asked of all subjects. We encourage the user to keep these sections in the recommended order and to add additional exposure questions that are relevant to your cultures, situation, contexts, and understanding of the situation in your country.

Each subject should be allocated a unique identification number.

COMMENT: Once questionnaire is finalized, full instructions and skip patterns should be added. Comments throughout the questionnaire are highlighted in purple text.

COMMENT: Note that adding multiple choice answers will allow for easier data analysis.

COMMENT: The questions provided below are meant to be a guide for the investigation. However, this questionnaire will need revision to be appropriate for the health care facility where this investigation will take place.

SECTION 1 GENERAL QUESTIONS

Subject name (First/Given): _____ (Last/Family) _____

Study ID Number |____|____|____|____|____|____|
Country ID Study ID Number

COMMENT: Use a 2-letter country ID and 4-digit study ID number. Put this study ID number on all pages of questionnaire.

Residence (City, Province): _____

Subject is a (circle one): Case Neighborhood control Hospital control

If case, when was the symptom onset (dd/mm/yyyy): ____/____/____

If control, for which case is the subject a control (provide identification number of case):
Case Study ID Number |____|____|____|____|____|____|
Country ID Study ID Number

Sex (circle one): Male Female

Date of interview (dd/mm/yyyy): ____/____/____

Place of interview (city, province): _____

Person answering questions is: subject relative (specify relationship: _____) acquaintance

Language used for interview: English Arabic Other, please specify_____

Name of interviewer: _____

Contact information of interviewer (including institution and phone number): _____

_____

General questions

1.1. Place of primary residence (address): _____

1.1.1. Do you have homes elsewhere? Y/N/UK

1.1.2. If yes, please specify where: _____

1.2. Date of birth: ____/____/_____ (dd /mm /yyyy)

General occupational questions

1.3. What is your occupation? (circle all that apply):

A=doctor B=health care student C=nurse D=respiratory therapist E=laboratory technician F=phlebotomist G=radiologist H=x-ray technician I=physical/occupational therapist J=morgue staff K=ambulance staff L=admissions clerk M=ward clerk N=auxiliary health worker O=health volunteer P=community health worker Q=patient transport R=catering staff S=housekeeping staff/cleaner

T=Other, specify _____

1.3.1. If doctor, please indicate speciality (circle):

A= emergency department doctor B= anaesthesiologist C=intensivist D= surgeon

E=general internist F=cardiologist G=pulmonologist H=infectious disease

specialist I=house officer in training (specify department_____)

1.3.2. If nurse, in which department/speciality were you working when the MERS-CoV patient was in hospital? (e.g. emergency department, medical ward, intensive care unit, etc.)?

_____

1.4. Do you work in other hospitals? Y/N

1.4.1. If yes, in which hospital(s) do you work? _____

SECTION 2 EXPOSURE QUESTIONS

EXPOSURE TO MERS-COV PATIENTS

2.1. What was the date of admission of the MERS-CoV patient? ____/____/_____ (dd/mm/yyyy)

2.2. What was the date of your first exposure to MERS-CoV patient? ____/____/_____ (dd/mm/yyyy)

2.3. What was the date of your last exposure to MERS-CoV patient? ____/____/_____ (dd/mm/yyyy)

2.4. Circle all specific health care settings where your exposure to the MERS-CoV confirmed patient occurred or may have occurred:

A=reception area B=emergency ward C=intensive care unit D=inpatient room/ward

F=surgical suite/theatre (operating room) G=maternity ward H=radiology/imaging

I=laboratory J=morgue K=outpatient facility/clinic L= transport patient

N= recovery room L=other (specify) _____

2.5. Circle all specific exposures that you have had with the MERS-CoV confirmed patient at any time:

A=taking vital signs B=performing physical exam C= conducting medical procedures

D=placing intravascular device E=placing urinary catheter F=drawing blood

G=collecting respiratory specimens for lab H=performing x-ray I=changing linen

J=bathing K=feeding K=lifting, positioning M=emptying bedpan N=providing medication

O=providing injection P=conducting surgery Q= haemodialysis R=processing clinical specimens

S = taking medical history T=caring for body after death

U=other, specify _____

COMMENT: Other exposures may be added as necessary

2.6. Were you present in the same room when any of the following procedures were carried out on the MERS-CoV infected patient?

Procedures	**Were you present? (Yes/No)**	**Did you perform? (Yes/No)**
2.6.1 Endotracheal intubation		
2.6.2 Bronchoscopy		
2.6.3 Airway suction		
2.6.4 Sputum induction		
2.6.5 High-flow oxygen		
2.6.6 Autopsy		
2.6.7 Tracheotomy		
Cardiopulmonary resuscitation (CPR) with 2.6.8 Mouth-to-mouth ventilation 2.6.9 Ventilation using bag/mask		
2.6.10 Non-invasive ventilation		
2.6.11 Manual ventilation		
2.6.12 High frequency oscillatory ventilation		
2.6.13 Oxygen mask		
2.6.14 Defibrillation		
2.6.15 Insertion of nasogastric tube		
2.6.16 Collection of sputum samples		
2.6.17 Chest physiotherapy		
2.6.18 Nebulizer treatment		

COMMENT: Other procedures may be added as necessary

2.7. At time of exposure(s), were hand hygiene facilities and supplies available and accessible? Y/N/UK

2.7.1. If yes, which facilities and supplies:

1=running (tap) water 2=soap 3=paper towels 4=hand antiseptic
5=other (specify) _____

2.8. Was hand hygiene performed according to the WHO 5 moments?

1=always (100% of time) 2=often (>50% of time) 3=infrequent (<50% of time) 4=unsure

2.9. Was hand hygiene performed after removing PPE?

1=always (100% of time) 2=not always 3=never

2.10. What is the longest total amount of time that you were exposed to the case-patient on any one shift (include time in the patient's room or checking patient or handling patient's bedding/equipment/fluids) (check one):

A=less than 1 hour B=1-2 hours C=3-4 hours D=5 or more hours

2.11. During the course of the MERS-CoV patient's stay in hospital, what was the total duration of time spent in the patient's room or checking patient or handling patient's bedding/equipment/fluids?

A=less than 1 hour B=1-2 hours C=3-4 hours D=5 or more hours

2.12. What was the closest distance on any one shift from the MERS-CoV patient?

A=Less than 1 meter B=1- 2 meters C=More than 2 meters

2.13. Was there a direct contact with blood, body fluids, excretions, secretions of the index patient? Y/N/UK

2.13.1. If yes, with what body fluid or excretion did you come into contact?

A=blood B=sputum C=urine D=faeces E=other (specify)_____

2.13.2. If yes, what was the nature of contact?

A=touched bare skin B=got in eye C=got in mouth D=penetrating injury (e.g. needle stick or scalpel cut) E=on clothing or PPE F=other (Describe: _____)

2.14. When in contact with the MERS-CoV patient, how often did you use the following? At time of exposure, was PPE used?

	Close direct contact	**For room entry**	**For aerosol-generating procedures**
2.14.1 Gloves	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant
2.14.2 Gown	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant
2.14.3 Eye protection[1]	1=always	1=always	1=always

1 face shield or goggles or eye visor

	2=not always 3=never 4=not relevant	2=not always 3=never 4=not relevant	2=not always 3=never 4=not relevant
2.14.4 Medical mask	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant
2.14.5 Particulate respirator[2]	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant
2.14.6 Other[3] (specify here: _____)	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant
2.14.6 Other[4] (specify here: _____)	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant
2.14.6 Other[5] (specify here: _____)	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant	1=always 2=not always 3=never 4=not relevant

2.15. Did you receive infection control education and training? Y/N/UK

2.15.1. If yes, did the training include prevention of respiratory pathogen exposure? Y/N/UK

2.16. Was IPC information on MERS CoV infection provided to you? Y/N/UK

SECTION 3 SIGNS, SYMPTOMS AND COURSE OF DISEASE QUESTIONS

The following questions address the symptoms you experienced during (specify time period of interest, which should include at least a two-week period after last exposure to the patient). If the subject had no symptoms, skip to section 4.

2 N95 or equivalent (e.g. FFP 2)

3 This may include both other PPE (e.g. N99, PAPR, FFP3) and attempts to use surrogate respiratory protection (scarves, head scarves, veils and similar parts of traditional garments)

4 This may include both other PPE (e.g. N99, PAPR, FFP3) and attempts to use surrogate respiratory protection (scarves, head scarves, veils and similar parts of traditional garments)

5 This may include both other PPE (e.g. N99, PAPR, FFP3) and attempts to use surrogate respiratory protection (scarves, head scarves, veils and similar parts of traditional garments)

3. Did you experience any signs or symptoms during (specify time period of interest)? Y/N

   If the subject had no symptoms, skip to section 4.

   3.1. When did you first start experiencing symptoms? (DD/MM/YYYY): ____/___/_____

   3.2. What were your symptoms on the first day of illness? (DD/MM/YYYY): ____/___/_____

3.2.1.	Dry cough	1 Yes	0 No	9 Don't know	
3.2.2.	Productive cough	1 Yes	0 No	9 Don't know	
3.2.3.	Phlegm	1 Yes	0 No	9 Don't know	
3.2.4.	Runny nose	1 Yes	0 No	9 Don't know	
3.2.5.	Sore throat	1 Yes	0 No	9 Don't know	
3.2.6.	Fever	1 Yes	0 No	9 Don't know	if yes, max. temp: ____°C
3.2.7.	Shortness of breath	1 Yes	0 No	9 Don't know	
3.2.8.	Muscle pain	1 Yes	0 No	9 Don't know	
3.2.9.	Diarrhoea	1 Yes	0 No	9 Don't know	
3.2.10.	Chest pain	1 Yes	0 No	9 Don't know	
3.2.11.	Vomiting	1 Yes	0 No	9 Don't know	
3.2.12.	Rash	1 Yes	0 No	9 Don't know	

   3.3. Did you become ill rather suddenly or slowly? Suddenly/slowly

   3.4. Symptoms during the course of disease:

3.4.1.	Dry cough	1 Yes	0 No	9 Don't know; How many days?___	
3.4.2.	Productive cough	1 Yes	0 No	9 Don't know; How many days?__	
3.4.3.	Phlegm	1 Yes	0 No	9 Don't know; How many days?___	
3.4.4.	Runny nose	1 Yes	0 No	9 Don't know; How many days?___	
3.4.5.	Sore throat	1 Yes	0 No	9 Don't know; How many days?___	
3.4.6.	Fever	1 Yes	0 No	9 Don't know; How many days?___ if yes, max. temp: ____°C or ____°F	
3.4.7.	Shortness of breath	1 Yes	0 No	9 Don't know; How many days?___	
3.4.8.	Muscle pain	1 Yes	0 No	9 Don't know; How many days?___	
3.4.9.	Diarrhoea	1 Yes	0 No	9 Don't know; How many days?___	

3.4.10.	Chest pain	1 Yes	0 No	9 Don't know; How many days?___
3.4.11.	Vomiting	1 Yes	0 No	9 Don't know; How many days?___
3.4.12.	Rash	1 Yes	0 No	9 Don't know; How many days?___
3.4.13.	Bloody urine	1 Yes	0 No	9 Don't know; How many days?___

3.5. Did you seek medical care? Y/N

3.6. Were you hospitalized during the course of your illness? Y/N

3.6.1. If yes, when were you hospitalized (DD/MM/YYYY): ____/___/_____

3.6.2. If yes, in which hospital did you receive treatment(s)? _____

SECTION 4 BACKGROUND INFORMATION AND MEDICAL HISTORY

Personal living situation

4.1. What is your current marital status? (circle)

Single Married

Divorced Other, please specify_____

4.2. How many people live in your household with you (one household is defined as sharing a single kitchen)?

4.2.1. Children aged less than 18 years old: _____

4.2.2. Adults aged 18 years and older: _____

4.3. Do you have persons working in your household? Y/N/UK

If yes,

4.3.1. How many? _____

4.3.2. Do they live in your house? Y/N

4.3.3. What nationality(/nationalities) are they? _____

4.4. What type of dwelling do you live in? (circle)

Apartment detached house other (please specify: _____)

4.4.1. Do you have air-conditioning in your house? Y/N/UK

4.4.2. What is the size of your family living space (square meters)?: _____ sq meters

Background Medical History

The following questions address your medical history and other background questions.

Smoking

4.5. Do you currently smoke tobacco? Y/N/UK

Daily -----> go to question 4.9

Less than daily -----> go to question 4.7

Not at all -----> go to question 4.7

Don't know -----> go to question 4.7

4.6. Have you smoked tobacco daily in the past?

Yes-----> go to question 4.8

No-----> go to question 4.9

Don't know-----> go to question 4.9

4.7. In the past, have you smoked tobacco on a daily basis, less than daily, or not at all?

COMMENT: Interviewer, if respondent has done both "daily" and "less than daily" in the past, check "daily"

Daily

Less than daily

Not at all

Don't know

4.8. Do you consume alcoholic beverages? Y/N/UK

4.8.1 If yes, how frequently? (circle all that apply)

Every day

Less than every day but at least weekly

Less than weekly but at least monthly

On rare occasions (less than once per month)

4.9. Does any hereditary disease run in your family? Y/N/UK

4.9.1 If yes, please specify: _____

4.10. Do you have any of the following pre-existing chronic diseases?:

4.10.1. Diabetes? Y/N/UK

4.10.1.1. If yes, do you use insulin?: Y/N/UK

4.10.2. Emphysema, chronic bronchitis or other chronic lung disease besides asthma? Y/N/UK

4.10.2.1. If yes, do you take medications for treatment? Y/N/UK (if yes, specify: _____)

4.10.3. Asthma? Y/N/UK

4.10.3.1. If yes, which of the following have been used for treatment in the last month

(circle all that apply):

handheld Inhalers oral medications to open airways

oral steroids home nebulizer treatment to open airways

other (specify): _____

4.10.4. Kidney failure? Y/N/UK

4.10.4.1. If yes, are you receiving dialysis? Y/N/UK

4.10.5. Chronic liver disease, such as hepatitis? Y/N/UK

4.10.6. Heart disease? Y/N/UK

4.10.6.1. If yes, please specify _____

4.10.7. Is your immune system compromised for any reason? Y/N/UK

4.10.7.1. If yes, describe specific condition: _____

4.10.8. History of cancer treatment in the last year? Y/N/UK

4.10.8.1. If yes, please indicate the type of cancer: _____

4.10.8.2. If yes, circle all treatments received:

chemotherapy radiation

other, please specify _____

4.10.9. Blood disorder, such as chronic anaemia? Y/N/UK

4.10.9.1. If yes, describe specific condition: _____

4.11. Are you taking steroids? Y/N/UK

4.12. What medications do you regularly take? _____

4.13. What herbal medications do you take regularly? _____

4.14. If female, are you pregnant? Y/N/UK

4.14.1. How many weeks? _____ weeks

4.15. If female, have you recently had a baby? Y/N/UK

4.15.1. If yes, date of delivery (dd/mm/yyyy): ____/____/___

SECTION 5 NON-HOSPITAL RELATED EXPOSURE QUESTIONS

The remaining questions collect general information on non-hospital related exposures.

5.1. In the last six months, have you had contact *outside the hospital setting* with a sick person experiencing severe respiratory symptoms?

5.1.1. If yes, on what date was the last time you were exposed to this person? (dd/mm/yyyy): ____/____/___

5.1.2. If yes, in what setting did this exposure occur (e.g. home, place of worship, other)? _____

5.2. In the last six months, did you travel to other countries?

5.2.1. If yes, when and where did you travel?

5.2.1.1. Town name and country: _____

5.2.1.1.1. Dates travelled: _____ to _____

5.2.1.2. Town name and country:

5.2.1.2.1. Dates travelled: _____ to _____

5.3. In the last six months, have you had any direct physical contact with the following animals? (circle all that apply)

camel goat horse sheep

cattle dog cat

chickens, ducks or geese other birds

Other, please specify _____

5.3.1. If you circled any animals, when was the date of last exposure to the animal(s)?

Species:_____ Date of last exposure (dd/mm/yyyy)___/____/____

Species:_____ Date of last exposure (dd/mm/yyyy)___/____/____

Species:_____ Date of last exposure (dd/mm/yyyy)___/____/____

Species:_____ Date of last exposure (dd/mm/yyyy)___/____/____

5.4. During the past six months, how often, on average, did you consume any of the following products (indicate with an X in the appropriate cells):

	At least once per week	Less than once per week but more than once per month	Less than once per month but several times in the year	Never	Unknown
Fresh fruit					
Dried fruits					
Fresh salad					
Unpasteurized milk products					
Raw meat products					