AANVRAAGFORMULIER

Deadline voor indiening: 14 mei 2020 (14:00 u)

LEES ALSTUBLIEFT ALLE INSTRUCTIES IN BIJLAGE "TOELICHTING INDIENING PROJECTIDEE" VAN DE OPROEPTEKST ZORGVULDIG!

Wanneer u het formulier heeft ingevuld:

1. **Zet het formulier om naar een PDF file en controleer de details**
2. **Upload het complete formulier als een bijlage bij uw indiening in Projectnet (Let op: dit zijn twee verschillende links, gebruik maar 1 van de 2!)**

ProjectNet: Aandachtsgebied 1 (voorspellende diagnostiek en behandeling)
ProjectNet: Aandachtsgebied 2 (zorg en preventie)

BASISGEGEVENS (voorpagina)

NAAM VAN DE HOOFDAANVRAGER:

(10)(2e)

ORGANISATIE:

Radboudumc, Nijmegen

PROJECTTITEL:

Protection from airborne virus transmission in the care for corona patients

DATASTEWARD:

Wie is de datasteward die de open science en FAIR data planning in uw project ondersteunt? Zie de webinars op de ZonMw website om de datastewards te informeren en ondersteunen.

☒ Ik betrek een datasteward bij mijn project:
Naam: (10)(2e)
Instituut: Radboudumc
E-mail: (10)(2e)@radboudumc.nl
Was aanwezig bij de webinar: ☒ Ja ☐ Nee

☐ Ik heb nog geen datasteward.

Summary (remove when submit)
Healthcare workers who are taking care of corona patients have a high risk of infection. In addition to large droplets and splashes that contribute to an infection risk by direct contact and through surface contamination transmission can also occur when inhaling droplets and aerosols. To prevent the exposure to the SARS-CoV-2 virus healthcare workers wear respiratory protection equipment (RPE) such as a respirator often combined with a face shield. The most adequate type of RPE solutions is not well supported by research in the clinical setting. During this project we will study the emission of droplets and aerosols during normal breathing, speaking and coughing by patients and we will characterize the emissions from aerosol-generating medical procedures. Source measurements will be done close to the patient to study virus load by qPCR in small, intermediate and large droplets. The dispersion of airborne droplets and aerosols will be studied by collection of air samples at different distances in the room. Again, virus loads will be determined as a function of distance from the source. This information will be used to calibrate laboratory set-up to test efficiency of RPE solutions. A second use of this data is the construction of an exposure model to describe the transmission from the source to the receptor. This exposure model can be used to make informed decisions on mitigation of virus transmission contributing factors at the source (medical procedures) in the indoor environment (ventilation) and at the receptor (RPE solutions). We expect that the results of this research will inform decisions on adequate measures to reduce exposures to the virus in the interest of healthcare worker protection already in the first 6 months. Later in the project we will deliver data that can be used to derive a risk based safe level of virus in the air at the workplace. **(Word count 1887)**

DONDERZOEKSVOORSTEL **max 3 pagina's A4** (inclusief literatuurreferenties)	(voorpagina met basisgegevens niet meegerekend - font type Arial 10 pts)

1. PROBLEEMSTELLING EN DOELSTELLING(EN):

The method of transmission of SARS-CoV-2 has been a subject of much discussion since the virus was first reported. The WHO advice on SARS-CoV-2 infection prevention and control for health care workers is based on transmission through respiratory droplets and contact and until now only assumes the possibility for airborne transmission during aerosol-generating procedures [WHO, 2020). It is important to determine the role of airborne transmission of SARS-CoV-2 to be able to provide optimal respiratory protection equipment (RPE) used to protect health care workers from airborne transmission of the virus.
Currently, the use of type FFP2 or N95 respirators is considered good practice, especially in aerosol-generating procedures in COVID-19 (suspected) patients [WHO, 2020].
Research question 1 (RQ1): Is FFP2 is the only type of RPE that offers adequate protection to health workers during the care and treatment of patients with respiratory symptoms. This question is relevant and urgent during the current COVID-19 pandemic in view of the continuing (imminent) shortage of RPE, in particular respirators such as FFP2. For immediate use we would like to compare this option with that of the type IIR surgical mask and study combining RPE with face shields to also protect from large droplets and splashes.
Research question 2 (RQ2): To what extent are healthcare workers exposed to inhalable droplets (in size ranging down to aerosols) and how can this exposure be quantitatively characterized with respect to inhalable virus load supported by measurements and model simulations relevant to the care for patients in a clinical setting?
Research questions 3 (RQ3): RQ1 and RQ2 can feed in a risk-based approach to define the adequate protection of worker's health as soon as a safe virus load threshold has been established in cohort studies in populations of healthcare workers (such as the COCON study that is already funded by ZonMw). This research could then lead to a health-based occupational exposure levels OELs

2. PLAN VAN AANPAK:

The project plan consists of three steps:
Step-1: Clinical study: acquire data in a clinical setting as input for improvement of a laboratory set-up and provide data for exposure modelling.
Step-2: Laboratory set-up: further development of an existing laboratory set-up for testing RPE and face shields
Step-3: Source and dispersion modelling: Information from steps 1 and 2 will feed into an exposure model to simulate source strength, dispersion and protection scenarios

In **step-1** we will collect two types of air samples (near- and far-field) in a room used for the care for corona patients (Pan et al., 2019). Close to the patient we will collect near-field samples of 5-min in the breathing zone (30 cm from nose-mouth) at a flow of 3.5 L/min using Anderson three stage-cascade impactors to characterize the patient as a emission source during normal, breathing, speaking and cough. We will also characterize emission of planned aerosol–generating medical procedures such as Bilevel Positive Airway Pressure (BiPAP), Continuous Positive Airway Pressure (CPAP), Nasal High Flow (NHF) and sputum extraction. For this we will use a cascade impactor to differentiate between large, intermediate and small droplets (approximate ranges >5, 1-5, and <1 µm). In total we will collect 10 replicates of each condition. In each of these samples we will measure the concentration of viable virus. In parallel we will perform in situ measurements of the aerosol emissions using a Spraytec system (Malvern). For multiple far-field measurements at 1.5 m from the floor (number of measurements and distances to be determined in a predetermined grid) air samples will be collected using liquid impingers to collect airborne virus at a high flow (12.5 L/min, to compensate for the much lower expected concentrations). At the patient the virus load in each of the size fractions will be determined by QPCR. We will also invite 20 patients who are recovering from a confirmed COVID-19 infection to participate in *in situ* measurements with the Spraytec system of the emitted aerosols while normal breathing, speaking and coughing. In parallel an air sample will be collected with the cascade impactor to provide material for virus testing by QPCR. For the direct involvement of

patients. approval will be requested from the ethics board. In addition, we will interview the staff involved in patient care about their work practices and the use of protective equipment with emphasis on RPE. We will also collect contextual information in the patient care environment such as: room dimensions and lay-out, temperature/relative humidity characteristics, air exchange rate, ventilation system and air flow characteristics using helium filled soap bubbles (HFSB). From the analysis for the air samples and the particle size distribution we will calculate the virus load stratified by droplet size (>5, 1-5 and <1 µm), based on the data from the cascade-impactor measurements.

In **step-2** of this project we would like to simulate droplet and aerosol emissions using a laboratory model using water and artificial saliva with a fluorescent marker. For this research we will optimize an improvised laboratory set-up that we have used during the early phase of the crisis in March/April 2020. Briefly, we use a Savilex X cross flow nebulizer with open outlet to generate a spray of small to large droplets ranging in size from <1 to 100 µm. This spray is directed towards an anatomically correct head (Sheffield head). On this dummy head we will then place different RPE solutions with and without face shield that was developed at the Radboudumc Reshape Center by (10)(2e) In the position of the mouth a membrane filter is placed for collection of a sample of the (small and large) droplets that may penetrate through the filter material of the respirator or by-pass the protection by side-seal leakage (so-called total inward leakage). This leakage will be quantified using a known concentration of a fluorescent marker to the spray. This marker is selected based on a high-water solubility and low vapor pressure, so even if the water would completely evaporate from the smaller aerosols, the non-volatile tracer could still be detected on the membrane filter with high sensitivity (<5 ng on the filter). We will standardize and monitor temperature and relative humidity conditions and (low) air velocity-controlled environment at standardized distances (e.g. 30, 60 and 90 cm). Initially, we used water as a model and in the project, we will do some verification measurements with a reconstituted artificial saliva to see to what extent the liquid rheology and viscosity would affect the particle size distribution of the generated spray of pure water. These measurements will be done using the Spraytec instrument and using Phase-Doppler Particle Analyser (TSI) in an existing measurement set-up of (10)(2e) at the WUR. These measurement data will also be used to model the airflow and the trajectories of water droplets and aerosols of different sizes in **step-3**.

In **step-3** the data collected in **step-1** and **step-2** will be used to parameterize three models: a source strength model (S), a dispersion model (D) and a receptor protection model (RP). The S model describes the emissions from the (a) normal breathing, talking and coughing patient and (b) from the aerosol-generating medical procedures in part based on experimental and modelling work performed in the laboratory of (10)(2e) TU Twente. Based on the data collected in sample grid of far-field samples and the contextual data of the ventilation systems and air flow data we will perform dispersion modelling for different particle sizes based on the PDPA measurements and existing modelling expertise of (10)(2e) WUR. In collaboration with (10)(2e) of NLR Netherlands Aerospace Center/DNW German Dutch Wind Tunnels we will study how adding a face shield would change the air flow pattern of the RPE at different air velocities due to turbulence caused by the edges of the face shield and which may lead to optimization of the face shield design. This will be described in the receptor protection (RP) model. With a suite of these three models an overall SDRP model is constructed that allows risk-based calculations in real life setting leading to informed decisions regarding mitigation strategies at the source. If this is not possible measures will be taken to reduce dispersion and if this does not lead to an appropriate level of protection a proper level of RPE can be defined in accordance with the occupational hygiene strategy (Deziel et al., 2020).

3. HAALBAARHEID VAN HET PROJECT:

TIJDSSCHEMA
Month 1-6: optimizing the current laboratory set-up for total inward leakage to test RPE solutions in response to imminent shortage in anticipation of a potential second wave of hospital admissions, where our results will support informed decisions for adequate use of RPE solutions.
Month 7-12: collection of air samples in the clinical care for corona patients
Month 13-18: calibrating laboratory set-up with conditions realistically reflecting the clinical practice and testing relevant RPE solutions combined with facemasks
Month 19-24: constructing a theoretical-numerical model to simulate exposure scenarios, taking into account source characteristics (droplet size distribution) of patients and aerosol-generating medical

procedures, ambient temperature and humidity conditions, and air ventilation and flow conditions.
MOTIVATIE HAALBAARHEID
This line of research started during the crisis when the Radboudumc was facing imminent shortage to protect healthcare workers during aerosol generating medical procedures and has been used to inform decisions in the Raboudumc. Our preliminary results were also shared with the OMT and the FMS (Wertheim et al., 2020). The test procedure was based on available knowledge and equipment (van Dijk et al., 2011; Scheepers et al. 2015, Scheepers et al. 2017). The laboratory set-up was based on a worst-case exposure scenario and designed as a 'stress test' for RPEs. Data collected in the clinic will be used to improve the set-up technically to achieve better reproducibility and also secure the possibility that our tests can be independently verified by other researchers. We will also calibrate our settings using clinical practice in the care of corona patients for external calibration, e.g. particle size distributions of certain aerosol-generating medical procedures, air flows in the rooms, more realistic time patterns and more realistic distances from the bed of the patient. For adequate communication of the project and its results to all stakeholders and the public we will work together with (10)(2e) of Schuttelaar & Partners.

4. RELEVANTIE VOOR DE PRAKTIJK:

Onderbouw de relevantie aan de hand van de in de subsidieoproep benoemde relevantiecriteria
Our test facility for determination of the total inward leakage is a contribution to the Landelijk Test Team Mondkapjes commissioned by the Ministry of EZK to independently perform conformity tests (based on the EN149:2009 standard) on FFP2-equivalend RPE solutions provided by Productie NL, a consortium of industrial partners who are producing FFP2 respirators in The Netherlands.
The results from our measurements will inform decisions regarding the RPE solutions that are tested so our results can immediately be used for decisions on RPE use policy, regarding current shortages in RPE supplies.
Second, we expect to generate knowledge that can support better understanding of the role of droplet and aerosol transmission in a clinical setting and the development of models to support risk calculations based on real-life exposure scenarios in hospitals and other settings for patient care such as nurseries.
Third, this research will also provide leads to develop additional methods to evaluate RPE for certification specifically for droplet and aerosol exposures.
We will share data with prof. P. Bluyssen and her team who are studying airborne transmission of SARS-CoV-2 in non-medical settings such as classrooms and offices at the TU Delft (proposal 'Beyond 1.5m: measures to reduce airborne transmission' (main applicant (10)(2e) TU Delft) that will be submitted in the same ZonMw COVID-19 call).

5. DEELNAME VAN DE STAKEHOLDER(S) (e.g. patiënten, zorgprofessionals, etc.):

?? Prof. dr. (10)(2e) (10)(2e), expert groep infectiepreventie Federatie Medisch Specialisten
Beroepsvereniging Verzorgenden Verpleegkundigen (V&VN) **[nog te benaderen, wie kan dit op zich namen?]**
?? Dr. (10)(2e) (10)(2e)
?? Drs. (10)(2e) (10)(2e)
?? Prof. dr. Maarten Honing, Landelijk Test Team Mondkapjes (ProQaris, TNO, Kalibra, TU Delft, Radboudumc, Ministerie EZK)
?? Prof. dr. Frans Russel, DECOS, Netherlands Health Council
?? Dr. ir. Atze Boerstra, ABB Binnenmilieu [en bestuurslid Ventilatie Installatietechniek]

6. LITERATUURREFERENTIES (optioneel):

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3. (10)(2e) (10)(2e), Wu CY. Collection, particle sizing and detection of airborne viruses. J Appl Microbiol. 2019;127(6):1596-1611. doi:10.1111/jam.14278
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