Proposal (title)	1st WHO International Standard for SARS-CoV-2 RNA		
Proposer (name of Institution)	NIBSC	**Principal contact**	Giada Mattiuzzo
Rationale	Severe acute respiratory syndrome coronavirus -2 (SARS-CoV-2) previously known as novel coronavirus 2019 (nCOV-2019) is the aetiological agent of the Coronavirus Disease 2019 (COVID-19). It causes mild symptoms in most cases, however ~10% cases are requiring medical intervention, with a small percentage progressing to severe pneumonia and death. The World Health Organization declared COVID-19 a Public Health Emergency of International Concern on 30th January 2020, and a Pandemic on 11th March 2020. As of 31st March 2020, there are over 850,000 confirmed cases and 42,000 deaths. Accurate diagnosis of the infection is essential not only for patient treatment, but also to contain the outbreak and to inform governmental quarantine and isolation procedures. The WHO has published in their technical guidance for novel coronavirus 2019 a list of in-house developed molecular assays. A common reference reagent will facilitate development, assessment of assays and allow for comparability of the assays, including determining the limit of detection, and ultimately the most reliable result.		
Anticipated uses and users	Standardisation of diagnostic assays based on nucleic acid amplification techniques (NAT) (e.g. PCR, quantitative PCR, digital PCR, etc) for identification of SARS-CoV-2 in: Clinical and public health laboratories Vaccine manufacturers - Vaccine studies Assay Kit manufacturers Research laboratories		
Source/type of materials	High titer of SARS-CoV-2 will be grown at NIBSC within CL3 lab and the virus in the supernatant will be inactivated by a validated treatment, with minimal disruption of the RNA. We have already received the England/2/20 from PHE, and another isolate will be also made available. In the study, an alternative preparation will be also included. SARS-CoV-2 RNA packaged inside lentiviral particles. These chimeric constructs will be designed to be safe, non-infectious, non-replicative. Single nucleotide mutations will be introduced in the SARS-CoV-2 sequences to prevent the production of any viral protein. This approach has already been applied for the International Reference Reagent for Ebola virus RNA established by ECBS in 2015.Particles have already been produced.		

Outline of proposed collaborative study	Collaborative study will involve 20+ laboratories worldwide, performing nucleic acid amplification technology (NAT) based assays for SARS-CoV-2, and representing control laboratories, manufacturers, clinical and academic laboratories. The aim will be to assess the suitability of different preparations to serve as the International Standard for use in the harmonisation of SARS-CoV-2 diagnostics assays by: • characterisation of the candidate preparations in terms of reactivity/specificity in different assay systems. • assessing each preparation's potency i.e. readout in a range of typical assays performed in different laboratories		
Issues raised by the proposal	Validated inactivation protocol is not available and will need optimisation- may take time. Commutability- the lentivirus vector (LVV) system has not been compared to the real virus. A collaborative study to include both preparations will be very useful to provide more insight into this approach.		
Action required	ECBS to endorse proposal		
Proposer's project reference		**Date proposed:**	31 March 2020
CONSIDERATIONS FOR ASSIGNMENT OF PRIORITIES (TRS932)			
Approval status of medicine or in vitro diagnostic method	Several licensed drugs are under investigation to be re-purposed for COVID-19 treatment. Clinical trials are taking place 44 vaccine candidate have been developed and 2 of them are in phase I.		
Number of products or methods	Commercial kits and in-house assays are available and have been published. Mainly these assays are based on reverse transcriptase polymerase chain reaction (RT-PCR) assay.		
Public health importance	The World Health Organization declared COVID-19 a Public Health Emergency of International Concern on 30th January 2020, and a Pandemic on 11th March 2020		
Global importance	The World Health Organization declared COVID-19 a Public Health Emergency of International Concern on 30th January 2020, and a Pandemic on 11th March 2020. Proposed standard is essential for evaluation of vaccines and other biologicals developed for prevention and control of COVID-19 disease.		

Global need from regulatory & scientific considerations	Clinical symptoms of COVID-19 are not specific, an accurate diagnosis is essential for early identification of the disease, to respond and control outbreak. Furthermore, a reference material will assure harmonisation in the evaluation of vaccine/treatments in clinical studies.
ECBS outcome	[BLANK]

Running Title: 1st SARS-CoV-2 RNA standard