REPUBLIC OF KENYA

MINISTRY OF HEALTH KENYA
NATIONAL COVID-19 GENOMIC SURVEILLANCE STRATEGY

Table of Contents

List of abbreviations

COVID-19	CoronaVirus Disease, 2019
SARS–CoV	Severe Acute Respiratory Syndrome coronavirus
VoCs/VoIs	variants of concern/Variants of Interest
KEMRI	Kenya Medical Research Institute
ILRI	International Livestock Research Institute
NPHL	National Public Health Laboratory
KAVI	Kenya AIDS Vaccine Initiative
WHO	World Health Organization
UoN	University of Nairobi
CDC	Centers for Disease Control and Prevention
DGHT	Division of Global HIV & TB
DLSP	Diagnostic Laboratory Systems Program
MoH	Ministry of Health
CHAI	Clinton Health Access Initiative
DSRU	Disease Surveillance and Response Unit
GF	Global Fund
CEMA	Centre for Epidemiological Modelling and Analysis
DLS	Department of Laboratory Services
MERS-CoV	Middle East Respiratory Syndrome-CoronaVirus
RNA	Ribonucleic Acid
DLS	Department of Laboratory Services
RT-PCR	Real Time Polymerase Chain Reaction
RDT	Rapid diagnostic Testing
GISAID	Global initiative on sharing all influenza data
NCBI	National Center for Biotechnology Information

GoK	Government of Kenya
HIV	Human Immuno Virus
TB	Tuberculosis
USAMRD-K	United States Army Medical Research Directorate-Kenya
CBRD	Centre for Biotechnology Research and Development
JKIA	Jomo Kenyatta International Airport
NP	Nasopharyngeal
OP	Oropharyngeal
VTM	Viral Transport Media
CT	Cycle Threshold
EQA	External Quality Assurance
FastQC	Fast Quality Control
GISRS	Global Influenza Surveillance and Response System
GISAID	Global Initiative on Sharing Avian Influenza Data
ICU	Intensive Care Unit
IATA	International Air Transport Association
WGS	Whole genome sequencing

Foreword

Since the onset of the pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS–CoV-2) also known as COVID-19 in March 2020, the Ministry of Health has developed various guidelines to coordinate effective management of the disease. These includes the National COVID-19 PCR and Rapid antigen testing guidelines. These guidelines ensure that testing for the disease is timely, robust, and reliable.

The SARS–CoV-2 has undergone various genetic mutations that have given rise to new variant strains. Variant strains are identified through sequencing to establish the number, position, and nature of (point) mutations. The set of mutations on a strain can affect its transmission dynamics and the severity of associated disease while other mutations have the potential to make the virus more stable and, this could, in turn, prolong the pandemic. Some of the identified variants of concern (VoC) often disrupt global travel and trade and exert significant strain on healthcare systems, especially in resource-poor settings.

Some of the variants of concern (VOCs) that have been of global worry include the B.1.1.7 (alpha variant) identified in the UK in January 2021, the B.1.351 (Beta variant) initially identified in South Africa in early October 2020, and the P.1 (Gamma variant) first identified among a small population of travelers from Brazil who had visited Japan in January 2021. The Delta variant (B.1.617.2) is the most dominant variant for at least 10 months since December 2020 when it was identified in India. The variant spread to over 85 countries within three months from the date of its identification. This strain caused a significant rise in hospitalized patients and deaths. The latest VoC is the Omicron variant (B.1.1.529), first identified in South Africa and Botswana in November 2021. The Omicron has been reported in at least 16 countries globally in just under one week from the date of initial identification

From the preceding, it is clear that as the COVID-19 pandemic evolves, new variants will continue to emerge and probably spread globally. Given that some variants can negatively impact healthcare, economics, and social interactions, the Ministry of Health (MoH) needs to develop guidelines to coordinate the identification of new variants strains. Currently, sequencing is done in research laboratories such as KEMRI and ILRI. The Ministry of Health plans to launch a sequencing platform at the Department of National Laboratory Services that will act as the National coordination site for SARS-CoV-2 sequencing.

This strategy aims to guide the sequencing of COVID-19 samples nationally. The strategy also seeks to establish a multi-institutional National Whole Genome Sequencing Consortium. While this consortium is currently constituted with a mandate to guide the management of the COVID-19 pandemic, the same strategy shall be used in other future genomic surveillance for similar pandemics. The proposed strategy leverages the existing testing capacity,

available genomic sequencing platforms, and the current expertise in the collaborating laboratories' network. It also seeks to introduce a robust and modern whole genome sequencing platform at the Ministry's Department of Laboratory Services (DLS). The DLS will also coordinate allocation and distribution of sequencing reagents and commodities to sequencing laboratories and coordinate consolidation of referred samples from primary testing facilities to the sequencing laboratories. The DLS will also collate and process data for the Ministry's public health and diagnostic policy formulation.

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Acknowledgments

The Ministry of Health acknowledges all individuals and institutions that participated in the development of this strategy. This strategy will pave the way for resource mobilization from different funding agencies and will be the foundation of a robust multi-disease sequencing strategy in Kenya. It will also ensure sustainable local capability for samples associated with critical pathogens, thus minimizing or eliminating the need to ship samples to third-party facilities outside the country.

Appreciation goes to Dr. John Kiiru (Head, Department of Laboratory Services, MoH), who spearheaded the development of this strategy, and Leonard King'wara (Manager, Genomic Surveillance Unit) who spearheaded the technical write up. Other key players include members of the Genome sequencing consortium that include Dr. Francis Kuria (Ag. Head, Directorate of Public Health), Professor Omu Anzalla (KAVI-University of Nairobi), Prof. Sam Kariuki (Ag. Director-general, KEMRI), Dr. Evans Amukoye (Director Research and Development KEMRI), Prof. Peter Borus (WHO), Dr. George Githinji (KEMRI-Welcome Trust), Prof. Mwangi Thumbi (University of Washington/UoN), Dr. John Waitumbi (KEMRI/US Army Medical Research Directorate-Kenya), Dr. Jane Mwangi, (Branch Chief, Laboratory Services, DGHT, CDC Kenya).

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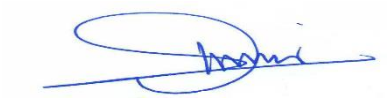

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Background

COVID-19 is a disease caused by a novel coronavirus (SARS-CoV-2) that was initially associated with an outbreak of unusual viral pneumonia in Wuhan, China, before spreading globally to become a pandemic in 2020 (Hu et al., 2020). The SARS-CoV-2 belongs to the Beta coronavirus genus. Human Beta coronaviruses such as the one responsible for the COVID19 pandemic, e.g., SARS-CoV, SARS-CoV-2, and the MERS-CoV, have many similarities. However, the minor differences that arose in their genomic content and expressed phenotypically are responsible for associated pathogenesis (Petrosillo et al., 2020). The SARS-CoV-2 is a single-stranded (positive-sense) RNA virus associated with a nucleoprotein within a protein matrix (capsid). Coronaviruses possess the largest genomes (26.4–31.7 kb) among all known RNA viruses, with G + C contents varying from 32% to 43%. The SARS-CoV2 has four main structural proteins comprising of the Spike (S), Membrane (M), Envelope (E), and Nucleocapsid (N) proteins (Petrosillo et al., 2020).

Due to their fast replication rates and yet to be properly understood mechanisms that they mount in the presence of various selective pressures, genomes of viruses, including those of SARS-CoV-2, constantly change. These genetic variations occur over time and can lead to new variants that may have different phenotypic characteristics. Genomic sequencing allows identifying novel SARS-CoV-2 strains, variants of interest, and variants of concern and monitoring how these change over time. The information generated is critical in understanding how genetic differences affect the characteristics of the virus and how these predict the spread of variants and their impact on healthcare systems (Budd et al., 2020).

Since the COVID-19 pandemic started in Kenya in March 2020, more than 2.6 million human samples have been analyzed as of 12th December 2021. Two hundred fifty-two thousand cases have tested positive from these, and 5,223 of those infected have died. In Kenya,

testing has expanded from the initial single testing site in March 2020 to the 105 sites that use RT-PCR by November 2021. Rapid diagnostic testing introduced during the same period has grown from zero (0) to over 500 testing sites RDTs. The testing sites are spread all over Kenya, the majority of these being in high case-burden counties or along transport corridors where truck drivers require mandatory testing before the exit to neighboring countries. All travelers from Kenya are also tested for COVID-19 before departure, but only passengers arriving from select countries of origin are required to test on arrival. While this may be convenient for passengers, this strategy potentially exposes the country to exotic strains, some of which could be variants of concern. Ports of entry, therefore, remain major potential hotspots for the emergence and spread of variants of interest and variants of concern. Therefore, countries need to include international borders in their genomic surveillance programs.

Countries need to have active genomic surveillance programs because mutations in SARS-COV-2 can confer characteristics that can impact detection of the virus, case management, and the general trends of the pandemic. Some of these negative outcomes on variants of concern include but are not limited to the following;

1. Variant strains may spread more quickly in the community and, in turn, seriously overwhelm healthcare systems (Benton et al., 2021).
2. Variant strains may cause more severe disease in certain vulnerable populations and contribute to high mortality rates, especially in resource-poor settings (McCarthy et al., 2021).
3. Variant strains may evade detection by specific diagnostic tests due to mutations on genes targeted by various detection kits (McCarthy et al., 2021).
4. Variant strains may exhibit decreased susceptibility to therapeutics such as antivirals drugs and vaccines, especially those that elicit monoclonal antibodies (Planas et al., 2021).
5. Certain variants may persist longer in natural hosts or carriers, therefore, increasing the chances of spread.

Currently, five main variants have been reported globally:

1. The United Kingdom (UK) identified a variant with many mutations in 2020, which is known as B.1.1.7 (alpha variant). This variant strain spreads more easily and faster than other variants. In January 2021, experts in the UK reported that this variant might be associated with an increased risk of death compared to other variants (Mascola et al., 2021)strains.
2. In South Africa, another variant known as B.1.351 (Beta variant) emerged independently of B.1.1.7. Originally detected in early October 2020, B.1.351 shares some mutations with B.1.1.7 (Liu et al., 2021).
3. A variant strain called P.1 (Gamma variant) emerged in Brazil. This strain was first identified among travelers from Brazil who were tested during routine screening at an airport in Japan in early January 2021. This variant contains a set of additional mutations that may affect its ability to be recognized by antibodies(Fujinoetal.,2021).
4. The Delta Variant (formerly known as the Indian variant and officially referred to as B.1.617.2) was first identified in India in late 2020. The variant spread to over 85 countries in less than 3 months. This strain is now the dominant strain globally and has caused a significant rise in the number of hospitalized patients and those who have died from COVID-19 globally (Salimi-Jeda et al., 2021).
5. The B.1.1.529 (Omicron) infection was from a specimen collected on November 9th, 2021, but the first confirmation of the variant was from South Africa on November 24th, 2021. This variant has many mutations, some of which are concerning. Preliminary evidence suggested an increased risk of reinfection with this variant compared to other Variants of concern. The number of cases of this variant appears to be increasing in almost all provinces in South Africa and has now been reported in 12 countries worldwide in under a week. Several laboratories have indicated the strain is poorly detectable using kits based on the S gene, where most mutations are localized.

Some variants seem to spread more easily and quickly than others, which may lead to more cases of COVID-19. An increase in cases and

deaths significantly strains healthcare systems, especially in developing countries where resources may be scarce. This underpins the importance of genomic surveillance in resource-poor settings. poor resource settings

Justification for the strengthening of Genomic Surveillance

RNA viruses accumulate genetic changes at high evolutionary rates than other pathogens (Duffy, 2018). Such mutations may result from adaptations to selective pressures induced by antivirals, vaccines, or host immunity, among other factors. Following the emergence of variants of concern and variants of interest, many countries have initiated or scaled up their genomic surveillance, leading to an unprecedented number of viral genomes deposited in publicly accessible databases (Brito et al., 2021). The leading genome data platform for COVID-19, the GISAID database, now has over 2,400,000 genome sequences as of Dec 2021, while NCBI has over 969,500 such sequences (Brito et al., 2021). However, there are striking differences in genomic surveillance's spatial and temporal intensity worldwide.

Kenya and a few other developing countries are currently in the process of upscaling their genomic surveillance. KEMRI, CDC, ILRI, and The Walter Reed Project currently support sequencing for SARS-COV-2. In this regard, Kenya is currently consolidating expertise and resources to increase its genome capabilities sequencing to realize the following objectives:

1. A robust genome surveillance strategy can identify variant strains (VoC and VoI) circulating locally or globally.
2. Identify risk factors associated with the acquisition and spread of various strains by merging the sequencing data to the patient metadata.

3. Identify the potential effect of the identified point mutations on the current COVID-19 countermeasures in place

4. Jointly collaborate in providing global SARS CoV-2 sequence data that can potentially aid the development of other countermeasures.

Methodology for coming up with the SARS CoV2 surveillance strategy

To develop the Kenya SARS-CoV-2 Genomic Surveillance Strategy, an online workshop, consultative meetings, and email exchanges between various stakeholders have occurred since July 7th, 2021. Technical expertise was drawn from the US CDC, The Department of Laboratory Services, Disease surveillance, and a network of sequencing laboratories. The current version of the strategy heavily borrows from the Global Action Plan on SARS-CoV-2 from Africa CDC, The European Union, and the WHO. The overall goals and objective of the Kenyan SARS CoV-2 genomic surveillance strategy aligned the responses on seven strategic pillars as outlined below:

I. Assessment of the current sequencing capacity
II. Resource mapping for genome surveillance
III. Sampling, sample selection, shipment, and processing
IV. Sample archival
V. Quality assurance and standardization of sequencing procedures
VI. Data analysis, interpretation, and dissemination.
VII. Utilization and uptake of sequencing data

Current genome surveillance capacity on COVID-19 in Kenya

Genomic data published from Kenya has primarily been generated at KEMRI-Welcome Trust, CDC, ILRI, and The Walter Reed Project. However, this data is only restricted to samples collected from the catchment areas of each sequencing facility and may therefore lack a national outlook. Furthermore, most sequences published so far have been generated using the Oxford Nanopore sequencing platform, which has some inherent sequencing depth weaknesses. While the nanopore technology has significantly improved, there is a need to utilize other robust platforms such as those based on Illumina, PacBio, Ion torrent, and related technologies that give a deeper sequencing capability which in turn significantly improves the accuracy of identification of variants based on single (point) mutations.

The Ministry of Health wishes to support other sequencing sites to improve current sequencing technologies and increase national sequencing outputs. There is also a need for the Ministry of Health to strengthen DLS to participate in genomic surveillance by installing and commissioning a sequencing pipeline at the DLS (National Public

Health Laboratories) in Nairobi. Another site that will require support to increase capacity for genomic surveillance includes the University of Nairobi and other GoK laboratories in KEMRI. Considering that the DLS houses the National Reference Laboratory, there is a need for this facility to play a more critical role in quality assurance, country-wide sample consolidation, and distribution to other sequencing laboratories across Kenya and act as centralized data analysis and dissemination point. Further, DLS is better placed to consolidate sequencing reports generated from all other sequencing sites to synthesize such data for onward transmission to the Ministry for public health policy formulation.

In order to launch a robust yet sustainable genome sequencing strategy, the Ministry is seeking to expand national genomic surveillance using two approaches:

1. Expand the panel of collaborators that can support the Ministry in upscaling the scope of the national COVID-19 genome surveillance strategy
2. Launch a high-capacity WGS sequencing pipeline at the NPHL by improving the existing Sanger and Ion-torrent technologies, to include Illumina, Nanopore, and MGI technologies. The NPHL can also use the same sequencing pipeline for genomic surveillance of other pathogens such as influenza viruses, HIV, malaria, TB, etc. Similar sequencing platforms across the sequencing consortium network ease commodity and reagent forecasting and quantification plan.

The current national sequencing potential as of May 2021 is as detailed in the table below:

Laboratory	Type of platform	Samples per run	**Number of runs per week**	**Total samples per week***
KEMRI WellcomeTrust Kilifi-	Illumina MiSeq** , Nanopore	370	4	740

Walter Reed (USAMRD-K), Kisumu	Illumina MiSeq	90	1	90
KAVI-UON, Nairobi	Nanopore	60	1	60
KEMRI-CDC(DLSP)Kisumu	Sanger method**	48	2	96
KEMRI-CBRD, Nairobi	Illumina MiSeq, Nanopore	390	2	390
KEMRI-CDC(DLSP)Nairobi	Illumina MiSeq	90	1	90
ILRI	Illumina MiSeqs and (Nextseq 550, Oxford Nanopore)**	480	2	960
DLS	(Ion-Torrent PGEM and Illumina MiSeq)**	300	2	600

* This capability includes RNA extraction, sequencing, and bioinformatics
** The current output of these platforms is below the expected output due to ti unavailability of reagents or because the platform is under construction. Once these bottlenecks are removed, the current national capacity for sequencing can be increased. The sequencing platform at DLS is currently not operational, but a requisition has been placed through the Global Fund. We anticipate that DLS will be capable of sequencing 600 samples every week should these be acceptable.

The DLS has included a budget for reagents in the Global Fund application to support sequencing based on the Ion Torrent WGS equipment currently available in the facility. With support to this facility , it will be capable of processing at least 200-400 samples per week (from RNA extraction, sequencing, and bioinformatics analysis). Extra

output at DLS can be realized by supporting the KAVI-UON, Nairobi facilities, other high throughput testing laboratories at KEMRI, PCR, and Antigen testing sites.

Sources of samples for Genome surveillance

In the proposed National genome Surveillance, samples will be submitted from diverse locations and categories of sample collection sites as outlined in the next section below. However, the aim is to collect samples with detailed demography and the patient's COVID-19 clinical history to facilitate data analysis linking the genome to the patient's presentation and outcome. The proposed category of populations to be sampled are as follows; -

Category 1 sites: Key international ports of entry such as airports and road border point crossings: the following testing sites will be included in this list: - JKIA airport, Wilson Airport, Kisumu, and Mombasa international airports, and any other airport that handles international travelers. Lunga-Lunga, Lamu, Tana River, Garissa, Wajir, Mandera, Marsabit, Kitale, Busia, Kisumu, Migori, Narok, Namanga, Illasit (Oloitoktok), Taita Taveta that have border points will also be included in this category. Since entry points are key channels through which new variant strains can be introduced, at least 65% of all positive samples that meet sequencing criteria per **ANNEXES KENSEQC003** collected from such sites will be sequenced.

Category 2 sites. At least 5% of all positive samples from testing locations in the following high case burdens regions (as of July 2021) will also be submitted: - Nairobi, Kiambu, Nakuru, Mombasa, Machakos, Uasin Gishu, Kisumu counties.

Category 3 samples: All positive samples of healthcare workers, port (health) workers, teachers, refugee camps, and other cadres of populations at increased risk due to interaction with large populations will be included. These samples will be collected from all over the country

Category 4 Samples: Wastewater surveillance, especially from prison and school settings. The MOH may not necessarily conduct

environmental sampling and testing, but positive samples obtained by researchers may be included in the sequencing pool.

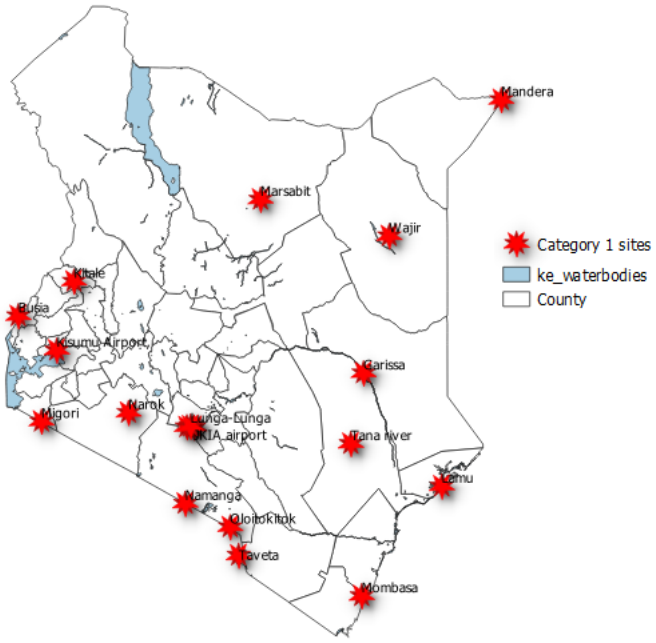


Figure 1. **Proposed sources of positive samples that will be submitted for the National COVID-19 Genomic Surveillance**

Type of samples to be collected

From each individual identified for sampling, n asopharyngeal (NP) and o ropharyngeal (OP) swabs will be collected into a single tube of Viral Transport Media (VTM). Another set of NP and OP samples will also be collected from patients who turn positive using rapid antigen tests (RDTs). Samples from those who turn negative using the RDTs but have symptoms characteristic of COVID-19 disease will be subjected to RT-PCR for confirmation . Only RT-PCR-positive samples with a cycle threshold (CT) value of less than 30 will be submitted for genome sequencing. The positive samples will be shipped to the NPHL for sorting and distribution to other sequencing laboratories. Positive samples identified in participating sequencing laboratories will not be shipped to the NPHL but will be sequenced in the primary laboratory that conducted the PCR. In case many samples are collected (e.g., during a spike) and not all samples can be sequenced due to

budgetary constraints, samples to be shipped to sequencing laboratories will undergo another round of selection based on the following criteria;

1. Availability and diversity of case metadata regarding age, gender, occupation, clinical symptoms, vaccination status, if exposed before travel history, etc. Attempts to include samples from cases with different metadata categories
2. Geolocation of where the samples were collected and where the cases live and/or work. This will allow the Ministry to identify transmission pathways of various variants and determine the possibility of community transmission of variants of interest.
3. Positive samples of cases who had a previous COVID-19 infection. The sequencing data will reveal the identity of the re-infecting strain if a previous strain is known
4. Samples from cases with a breakthrough infection (those that get a second infection after receiving vaccination) will be of special interest.
5. Samples of cases who have had a recent international travel history will be of special interest because the sequence data may reveal the role of global travel pathways for the dissemination of variant strains
6. Samples from people with severe outcomes such as hospitalization, need for oxygen supplementation, and those who die will also be of special interest because such sequences may identify more virulent strains that could call for special national pandemic surveillance measures.
7. Samples from special categories of populations such as healthcare workers, teachers, and hospitality industry workers will be of special interest because such populations have the potential to spread to a larger population than people from other job and occupational cadres.

The samples will be transported to the DLS in cooler boxes and then documented for distribution to the sequencing facilities using standard shipment guidelines for SARS-COV-2. The number of samples submitted to each sequencing laboratory will depend, among other factors, on the sequencing capability of the facility and the

availability of reagents. Pre-shipment and sample handling can be found in **ANNEXES KENSEQC003**

Expansion of Biorepository capacity at DLS

Since the DLS will be receiving and consolidating samples from different sites before shipping them to other sequencing laboratories, this facility needs to handle COVID-19 samples short-term and long-term. Regarding this requirement, a budget for a biorepository facility - procurement of large capacity deep freezers and fridges and data management software - were- factored into the Ministry of Health Global Fund application. The CDC also supports the DLS in developing a robust sample archival and retrieval facility system.

Scope of sampling

Based on the current sequencing capabilities in the country coupled with the proposed launching of a sequencing pipeline at the DLS , it is expected that Kenya can sequence between 1000 and 1500 samples per week. It is also probable that as the pandemic continues, more sequencing facilities will join the consortium. This will increase the country's capacity to sequence more samples if need be. Rather than initiate a mass sequencing initiative, the MoH will use targeted genomics (number and types of samples selected to be sequenced) that can provide critical information on the following issues: -

1. The diversity of variants in circulation
2. Predicted impact of the variant strains on community transmission and predicted type of strain that can exert serious pressure on (weak) healthcare systems.
3. Derivation of linkages between sequence data and symptoms observed in the source patient, relative associated severity of the infection or mortalities, and the type of underlying conditions of patients positive with variant strains
4. Patterns of metadata where different viral clades are implicated in successive reinfection of the same patient, location of the cadre of patients
5. Whether novel or variant strains are associated with infection among vaccinated individuals

The size of the samples to be sequenced will depend on

1. The prevailing local and global prevalence of the disease

2. The prevailing positivity rates of the disease
3. The number and size of clusters and hotspots of the disease
4. The total combined capacity of the sequencing laboratories

Preparation and purification of RNA for sequencing

Viral RNA will be extracted and purified using a spin-column and/or magnetic bead extraction platform that will include appropriate controls following the manufacturer's instructions. The NPHL will also acquire an automated extractor to expedite the extraction process while minimizing errors.

Sequencing strategy

Kenya will adopt uniform genome sequencing strategies (standardized wet-lab and dry lab processes) across all laboratories to ensure that data generated in different sequencing laboratories are comparable and reproducible. Sanger sequencing strategies will be used on a need arising basis. The majority of the sequencing sites will utilize the Illumina platforms for sequencing, while nanopore technology will be available in a limited number of sites. The DLS will use the Illumina and the Ion torrent platform currently installed at DLS.

In order to strengthen the sequencing strategies, various items have been earmarked for financing

I. Strengthening of specimen referral to ensure expanded diagnostic network for both COVID-19 diagnostic and genomic surveillance. This integrated sample referral is also funded by Global fund
II. Improving the bio-banking capabilities through increased storage and development of an electronic sample archival and retrieval system supported by CDC
III. Optimization of Genomic Sequencing laboratory processes through standardization of sample processing, RNA extraction, and sequencing protocols
IV. Development of genomic data dashboard and setting report sharing turn-around time

Quality assurance

In order to ensure that data generated from various sequencing sites and platforms are of high quality, the following quality assurance strategies will be utilized:

1. Samples will be maintained under the right cold-chain temperatures during sampling, storage, and transport. Samples will only be transported by a courier trained on the minimum requirements for shipment of samples targeted for sequencing and on biosafety and biosecurity of such specimens.
2. Samples that do not meet the minimum criteria for sequencing will be rejected. This criterion will include the integrity of the cold chain and the sample packaging and labeling.
3. The DLS will coordinate an External Quality Assurance (EQA)/inter-lab comparison for all sequencing sites. In this arrangement, the DLS will send aliquots of blinded samples to all sequencing laboratories to compare the generated data quality.
4. Laboratories using the same sequencing platform will use similar RNA extraction and sequencing protocols.

Sequence preparation and bioinformatics

Consensus sequences will be assembled using various bioinformatic software compatible with the sequencing assays in place. Curated bioinformatic analysis pipelines will be used to perform FASTQC generation, genome assembly, cleaning, demultiplexing, alignment, assembly, variant calling, and annotation. Detailed quality control of the resulting genomes will be done using manual and automated methods. Detailed analysis of mutations will be conducted and visualized using various software such as Webclades (v0.4.2). Viral lineages will be assigned using lineage tools such as the Pangolin toolkit (v2). The sequencing consortium will work towards standardizing sequencing protocols as well as the informatics tool used in all participating laboratories, and data will be projected through a common dashboard hosted by DLS

Submission of sequence data to DLS

While each sequencing laboratory will conduct sequencing and bioinformatics independently, all sequencing laboratories will submit their findings to the DLS for consolidation, interpretation of sets, and archival of all the FASTQC files. The data sent to the DLS Bioinformatics center will include an excel line list of all samples

received and sequenced, dates of sample collection, raw sequences, the platform used for RNA extraction and sequencing, key findings on strains identified, and a red flag for strains showing unique mutations that may signal the emergence of novel strains that have not been reported before. A technical committee comprising representatives from each sequencing laboratory will review the sequence data quality and identify unique patterns or data sets suitable for public policy formulation by the Ministry of Health. The committee will compile a report advising the Director-General for Health on the expected impact of various variants identified through whole-genome sequencing.

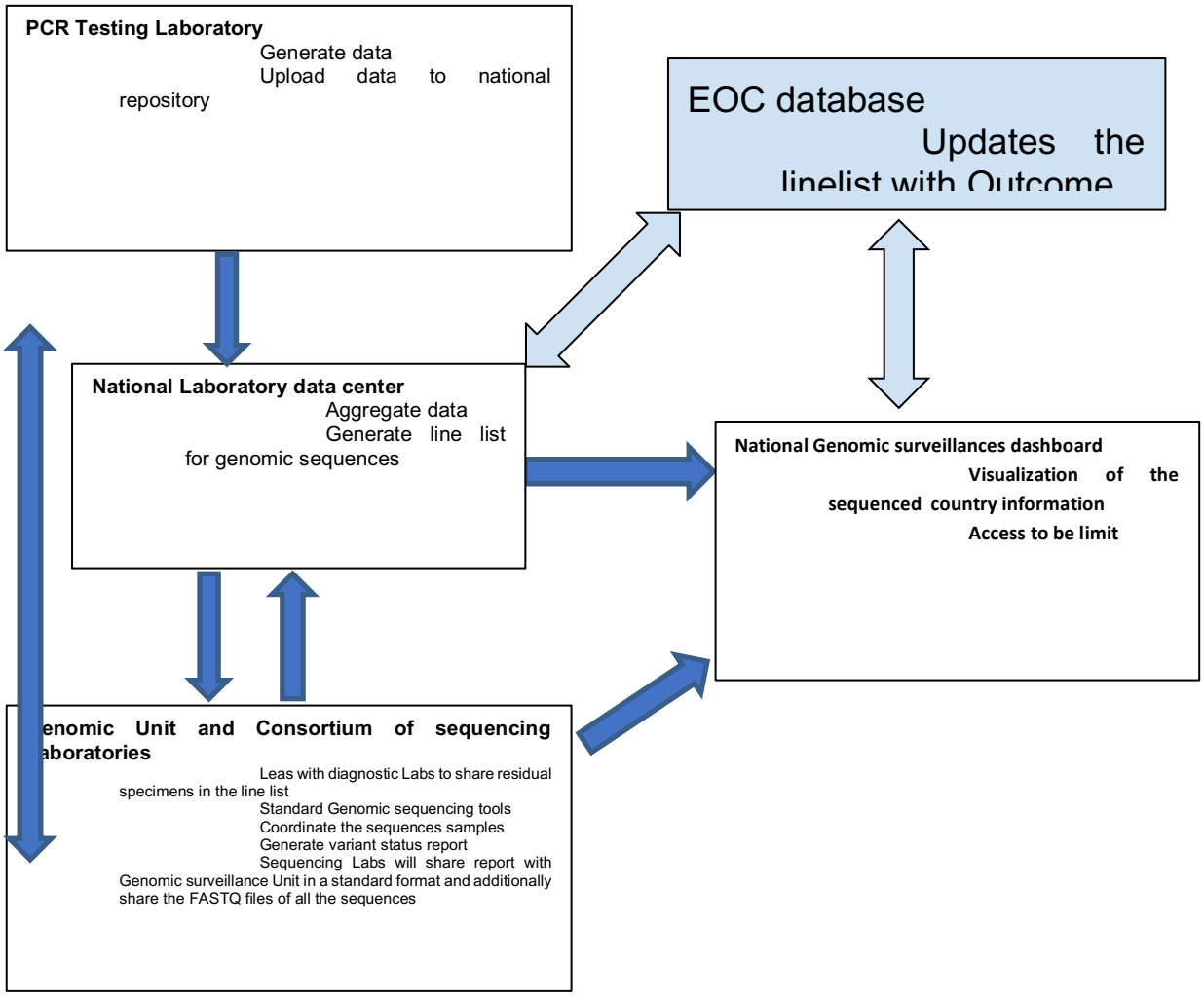
Data management

Sequencing laboratories will receive metadata related to samples earmarked for sequencing using a secure electronic format to ensure confidentiality and privacy. Each laboratory will assemble and clean sequence data generated in their facility. The final sequence file will be sent to the DLS for further cleaning and bioinformatic analysis if need be and for data mining for information that may inform the formulation of public policy by the Ministry. The DLS will employ two genome scientists to query and clean all genomic data in coordination with sequencing facilities before this data is assigned to various clades or strain types and before submission to international databases. The budget for these two genome scientists will be supported through Global Fund. The genome data will be submitted to the Global Influenza Surveillance and Response System (GISRS) platform and deposited in the Global Initiative on Sharing Avian Influenza Data (GISAID) database. Where applicable, sequence data will also be submitted at ENA, NCB, and the Centre for Epidemiological Modelling and Analysis (CEMA) at the University of Nairobi. All data generated regarding sequencing of COVID-19 and other pathogens of national security importance will only be released after permission from the office of the Director-General of Health. After the data is officially released and deposited in relevant databases, researchers on the subject matter will be free to publish the data in peer-reviewed journals further. All persons participating in the sequencing consortium will sign a non-disclosure agreement with the Ministry of health. However, this agreement will not make scientific findings opaque but ensure that the consortium works in a synergistic and coordinated manner.

The synthesis that will be done on sequencing data will be used to inform specific interventions, including

1. Determining community transmission dynamics of variant and strains of concern
2. Determining the impacts of variant strains on pandemic management, the strain on the healthcare system, and general strain on the economy
3. Analyzing the catalog of mutation accumulated in different strains and determine if such mutations impact the precision of diagnostic kits to identify positive cases
4. Determining if there are significant associations between patient metadata and acquisition of new strains and their transmission efficiency.

Data flow



Utilization of sequence data

The primary use of genomic sequence data will not be for patient care. It will be used to shed critical light on the evolution of the pandemic, risk factors associated with acquisition and spread of variant strains and strains of concern, and to predict the potential impact of variant strains on healthcare systems that include the severity of the disease, risk of hospitalization and death. The data will enable Ministry to identify and determine the types and proportions of variant strains circulating locally and how this data compares to global data. The information generated will guide Kenya's public health response to the COVID 19 pandemic and other related threats that may emerge.

Training and collaboration amongst sequencing laboratories

Different sequencing facilities will form a national sequencing consortium that will generate public health policy formulation data. While some sequencing facilities may have extra resources supporting sequencing, the DLS will equitably allocate and distribute sequencing reagents for public health needs to all sequencing laboratories. MoH will also organize Webinars and training workshops for the sequencing consortium. The participating laboratories will also be allowed to publish their findings in journals of international reputation while ensuring that all stakeholders and funding agents are sufficiently acknowledged in such publications.

Funding and sustainability options for a sequencing pipeline at the DLS

While the Global Fund will heavily support the initial sequencing initiative, the Ministry of Health has already started playing an active role through the launching of an integrated sample referral system that will allow shipment of samples from the field to the testing laboratories, from testing laboratories to DLS and from DLS to different sequencing laboratories. The Ministry of Health will consolidate resources to ensure that the sequencing equipment procured at the DLS and that the bioinformatic pipeline launched is sustainable. It is also the objective of the Ministry to make the DLS genome

sequencing pipeline, the DLS biorepository, and the Bioinformatics center a multi-disease genome surveillance Centre of excellence. The Ministry will also ensure that the sequencing consortium assembled for COVID-19 sequencing will be interactive and supported with the required training needs. This consortium's research and innovation component will closely work with relevant research institutions to address issues around reducing the cost of testing and assessing the effectiveness of various COVID-19 countermeasures. The consortium will also ensure that Kenya can sequence all critical pathogens eliminating the need to ship samples to other countries.

GUIDELINE ON SHIPMENT OF SARS-COV-2 POSITIVE SAMPLES TO SEQUENCING LABORATORIES.

This guideline outlines the critical components to be considered when shipping samples from the primary screening lab to the sequencing laboratory

1. **Shipping address**

   The address of the recipient and the consigner will be indicated in the packing. The name and email of the contact person from the consigner laboratory will also be indicated.

2. **Sample details**

The required sample type is a nasopharyngeal or Oropharyngeal swab (NP/OP). A sample volume of at least 1mL. Volumes larger than 1mL are ideal because these allow PCR repeats in case of initial failure. Appropriate shipping conditions will be observed if extracted RNA is required when the raw sample is used up. Samples will be shipped in externally threaded cryovials labeled with a unique ID.

3. **Shipment**

Samples will be triple packaged, the containers sealed and labeled based on the IATA protocol/guidelines. The samples will preferably be shipped within 4 hours in the cold chain (+4^{0}C. Dry Ice and should reach the sequencing laboratory within 36 hours.)

Patient metadata primarily accompanying the samples will be shared on password-protected electronic data; however, hard copy metadata will be acceptable on a case-by-case basis. The meta-data to include are:

- Collection date and Geographic details: County Sub-county & Health Facility
- Sample type: OP or NP or both
- Demographic information
- Data on whether the sample is from reinfection or first infection
- Details of the primary screening laboratory

- Laboratory results from the primary screening laboratory and Diagnostic method used (e.g., antigen RDT), name of PCR kit, and the realized Ct value.
- Patient demographic details: Age, gender, nationality, etc.
- Patient status: Asymptomatic, symptomatic, ICU, deceased, etc
- Reason for testing (patient management, travel, etc.)
- Travel history
- Vaccination status, including vaccination dates and names, complete or incomplete doses

Upon receipt, the samples will be analyzed for the suitability, and parameters to be considered will include

- Completeness of metadata
- Well labeled vials with sample details
- Packaging integrity (broken packages, spilled packages, etch)
- Length of shipment to reception
- Compromised cold-chain during shipments

The receiving laboratory will confirm the sample integrity through PCR resting or RNA quantification procedure before sequencing commences.

ANNEXES KENSEQC001

Data Sharing Agreement for the National Sequencing Consortium

Background

Countries need to have active genomic surveillance programs because mutations in SARS-COV-2 can confer characteristics that can impact detection of the virus, case management, and the general trends of the pandemic. Variant strains may spread more quickly in the community and, in turn, seriously overwhelm healthcare systems. Other variant strains may cause more severe disease in certain vulnerable populations and contribute to high mortality rates, especially in resource-poor settings. Variant strains may evade detection by specific diagnostic tests due to mutations on genes targeted by various detection kits. Variant strains may exhibit decreased susceptibility to therapeutics such as antivirals drugs and vaccines, especially those that elicit monoclonal antibodies. Certain variants may persist longer in natural hosts or carriers, therefore, increase the chances of spread

In order to identify variant strains, strains of interest and strains of concern, genomic laboratories conduct (whole genome) sequencing of the Viral RNA. Kenya and a few other developing countries are currently in the process of upscaling their genomic surveillance. KEMRI, CDC, ILRI, and The Walter Reed Project currently support sequencing for SARS-COV-2. Kenya is currently consolidating expertise and resources to increase its genome capabilities sequencing to realize the following objectives:

1. A robust genome surveillance strategy can identify variant strains (VoC and VoI) circulating locally or globally.
2. Identify risk factors associated with the acquisition and spread of various strains by merging the sequencing data to the patient metadata.
3. Identify the potential effect of the identified point mutations on the current COVID-19 countermeasures in place
4. Jointly collaborate in providing global SARS CoV-2 sequence data that can potentially aid the development of other countermeasures.

In order to develop a robust sequencing platform, the Ministry of Health has identified various laboratories and stakeholders that will form the National Sequencing Consortium. This consortium will generate sequencing data, cleaned and curate the data and develop a scientific synthesis that can be used by the Ministry of health to formulate Public Health Policies.

Since sequencing data seriously impact public health policies including travel restrictions, lockdowns, mobilization of resources to support healthcare systems, there is a need to develop a framework that will ensure that

1. All facilities involved in (genomic) sequencing generate robust high-quality data devoid of errors

2. All sequencing activities are properly coordinated in order to ensure that sequencing resources and reagents are used efficiently
3. Data generated from sequencing facilities are protected from unintended use by unauthorized persons and that this data is released in a coordinated fashion that may not lead to public confusion and panic
4. That data is properly handled in order to ensure that patient privacy and confidentiality is not compromised

The purpose of this agreement is to provide a framework that will guide how data generated by facilities included in the National Sequencing Consortium is shared, transmitted and published.

Composition of the National Sequencing Consortium

1. Only laboratories approved to conduct COVID-19 testing and sequencing will be incorporated into the National Sequencing Consortium
2. Diagnostic and research Laboratories wishing to join the National Sequencing Consortium will make a written application to the Office of the Director-General for Health
3. Facilities wishing the join the National Sequencing Consortium must meet the following minimum requirements
    a. Must demonstrate the capacity to conduct genome sequencing by having the right sequencing platforms and equipment
    b. Must have the right computational capacity to conduct genome analysis
    c. Must have the right capacity to generate, transmit and archive sequence data
    d. Must be able to secure data privacy and to provide security for stored data

Facilities that were active in sequencing or participated in the development of the National Sequencing Strategy will automatically be members of the National Sequencing Consortium. These members include the laboratories in ILRI, KEMRI, KEMRI-Welcome Trust (Kilifi), CDC Nairobi, CDC Kisumu, The DLS laboratories, KEMRI-Walter Reed project (Kisumu), UoN-KAVI, and WHO US Army Medical Research Directorate-Kenya, University of Washington, Centre for Epidemiological Modelling and Analysis (CEMA)/UoN. This list will be updated on a regular basis depending on how many other facilities meet the criteria to join the National Sequencing Consortium.

Responsibility of Members of National Sequencing Consortium

1. The Laboratory manager of the participating facility will be responsible for data generation quality, security, analysis, transmission a d archival
2. Under no circumstances should personal data be processed in any way that is unsecure or left unattended.

3. It is the responsibility of the sender to ensure that the method is secure and that they have the correct contact details for the receiver.
4. It is the responsibility of the Consortium member laboratory to ensure that the data generated or transferred is scientifically accurate

Exit from the National Sequencing Consortium

Facilities may cease to be members of the National Sequencing Consortium due to

1. Voluntary decision to stop testing and/or sequencing COVID-19 samples
2. Breaching the non-disclosure and data sharing agreement
3. Not being able to generate quality sequencing data as determined by a peer-reviewed External Quality Assurance assessment that is agreed by the members of the National Sequencing Consortium
4. Upon exit from the National Sequencing Consortium, the sequencing facility will
    a. Cease to conduct any sequencing of COVID-19 samples
    b. Cease transmitting and receiving COVID-19 sequencing data
    c. Cease to receive support for reagents, kits, and commodities meant to support COVID-19 sequencing
    d. Transfer or release of unused sequencing commodities meant for sequencing to active laboratories within the National Sequencing Consortium.

Scope of privileged data sets

The scope of data covered by this agreement includes

1. The names of participants
2. Addresses of the participants
3. Diagnostic test results of the participants
4. Location of work or aboard of the participants
5. Raw and processed sequencing data
6. Synthesized sequence data identifying variant strains and strains of interest

Data Security

1. The data will be generated through secure systems that ensure privacy and confidentiality of the data and the participants/patients
2. The data will be held in the primary facility where it is generated in secure and password-encrypted electronic and hard copy files
3. The data will only be made available to people directly involved in the National Sequencing Consortium
4. Data shared electronically through email will only be transmitted in secure emails and files transferred on email will be password encrypted
5. Hard copy files will only be transferred using a secure courier

Sharing of sequencing data within the National Sequencing Consortium

1. The primary raw and curated data generated in a sequencing facility shall remain under the custody of that laboratory. The facility will retain the first of initial use of this data for publication upon the data being released publicly by the Ministry of health
2. A copy of the data will be shared with the DLS data Centre and Genomic unit for archival upon cleaning and proper curation by the primary laboratory
3. While members of the consortium will be free to publish their primary data, the Ministry will encourage and facilitate sharing of different data sets between different facilities and also, the amalgamation of all data into a single data set to larger publications that will be co-authored by members of the consortium
4. After the data is shared with the Ministry of Health and publicly released, the primary laboratory will be free to upload this data into international databases such as GSAID, NCBI etc.

Method of transmitting data to the Ministry of Health

The report to the Director-General of Health will contain the following summary

1. Epidemic week related to the sequencing report
2. General sequence quality in terms of coverage
3. The identity of the strains, variant strains, strains of interest, or strain of concern detected in various samples
4. Predicted effects of various mutations, if any, on the virulence of the strains, its transmissibility, possibility of immune escape, effects on vaccine efficacy, effect on the accuracy of various diagnostic kits to detect strains with various mutations

A copy of this report will also be copied to the Head, Department of Laboratory Services for further analysis and synthesis

Modes and strategies for Data protection

The confidentiality of data pertaining to individuals will be protected as follows:

a. The data recipient will not release the names of individuals or information that could be linked to an individual, nor will the recipient present the results of data analysis (including maps) in any manner that would reveal the identity of individuals.
b. The data recipient will not release individual addresses, nor will the recipient present the results of data analysis (including maps) in any manner that would reveal individual addresses.
c. Both parties shall comply with all aspects of the laws of Kenya governing the confidentiality of the information that is the subject of this Agreement.

1. The data recipient will not release data to a third party without prior approval from the data provider or the express authority of the Office of Director-General for Health.

2. The data recipient/generator will not share, publish, or otherwise release any findings or conclusions derived from the analysis of data obtained from the data provider without prior approval from the data provider or the express authority of the Office of Director-General for Health.

Submission of data to international, local and public databases

1. The data will only be submitted to databases accessible to persons not within the National Sequencing Consortium only after proper cleaning and curation
2. The data will only be submitted to databases accessible to persons not within the National Sequencing Consortium only after a report of the same is shared with the Office of Director-General for Health and authority of release issued

Issue of authority to release data generated by the National Sequencing Consortium

1. The Office of Director-General for Health will issue authority to release sequencing data through a written format that include a phone message, an email, or a telephone call
2. A public declaration or release of sequence data by the Ministry of health will include verbal, written, and media updates on sequencing data or an update of circulating strains and variants
3. Sequencing data will be assumed in the public domain after it's publicly released by the Office of Director-General for Health or any other relevant unit in the Ministry of Health.

Duration of Agreement

This agreement is valid from the day of receipt of the sequencing samples until the content is made publicly available through the Ministry mechanisms that include public pronouncements, dissemination through digital media, publications and communique. At the end of the duration of this data agreement, all parties will ensure that the data released does not contain metadata that may compromise the identity, safety and privacy of the participants.

Sections on data protection shall survive termination of the duration of this agreement.

IN WITNESS WHEREOF, both the Ministry of Health, through its duly authorized representative, and The participating member of the National Sequencing Consortium [**Name.**], through its duly authorized representative, have hereunto executed this Data Sharing Agreement as of the last date below written.

Signatures

[Ministry of Health]	**[Name of Facility In-charge, Member National Sequencing Consortium]**
_____	_____
Signature	Signature
_____	_____
Printed Name	Printed Name
_____	_____
Title	Title
_____	_____
Date	Date

ANNEXES KENSEQC002

Biological Material Transfer Agreement, dated for the Transfer of Biological Materials of Clinical Nature between Non-Profit Institutions and an Implementing Letter for the Transfer of Biological Material

Subject matter	MATERIAL: Original material, progeny, and unmodified derivatives. The material shall not include (a) modifications, or (b) other substances created by the recipient through the use of the material which is not modifications, progeny, or unmodified derivatives.
Summary of use(s)	The MATERIAL is to be used: solely for teaching and academic research purposes; will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects without the written consent of the provider; only at the recipient organization and only in the recipient scientist's laboratory under the direction of the recipient scientist or others working under his/her direct supervision; and will not be transferred to anyone else within the RECIPIENT organization without the prior written consent of the PROVIDER.
Purpose or background	The transfer of biological material between non-profit institutions.
Contact details	Name of custodian**:**_____ Name of alternative custodian;_____

	Institution of the custodian:_____
	Laboratory or diagnostic unit of the custodian _____
	The physical address of the custodial facility_____
	Email of the main custodian _____ and alternative custodian _____
Custody of the UBMTA	The telephone contact of the main custodian XXX and alternative custodian _____
	Genomic Surveillance Unit at DLS will serve as the repository for signed UBMTA Master Agreements and will maintain a list of signatory institutions:

Upon execution of an Implementing Letter in the form attached which specifies the materials to be transferred, this organization agrees to be bound by the terms of the attached Uniform Biological Material Transfer Agreement ("UBMTA") published by the Ministry of Health as of December 22nd, 2021.

Attachments:

UBMTA

Implementing Letter

Organization:_____
_____

Address:_____
_____

Authorized Official (custodian and of the Biological materials or their representatives :_____

Title:_____
_____

Signature:_____
_____

Date:_____
_____

Please return an executed copy of this Master Agreement to**: Genomic Surveillance Unit at Department of National Lab Services**

Genomic Surveillance Unit at Department of National Lab Services will be maintaining signed originals and the official list of signatory organizations.

THE UNIFORM BIOLOGICAL MATERIAL TRANSFER AGREEMENT
(22nd December 2021)

I. Definitions:
1. PROVIDER: Organization providing the ORIGINAL MATERIAL. The name and address of this party will be specified in an implementing letter.

2. PROVIDER SCIENTIST or organization: The name and address of this party as specified in the implementing letter.

3. RECIPIENT: Organization receiving the ORIGINAL MATERIAL. The name and address of this party as specified in the implementing letter.

4. RECIPIENT SCIENTIST: The name and address of this party as specified in the implementing letter.

5. ORIGINAL MATERIAL: The description of the material being transferred as specified in the implementing letter.

6. MATERIAL: ORIGINAL MATERIAL, PROGENY, and UNMODIFIED DERIVATIVES. The MATERIAL shall not include (a) MODIFICATIONS, or (b) other substances created by the RECIPIENT through the use of the MATERIAL which is not MODIFICATIONS, PROGENY, or UNMODIFIED DERIVATIVES.

7. PROGENY: Unmodified descendant from the MATERIAL, such as the original biological sample, the virus from virus, cell from cell, or organism from organism.

8. UNMODIFIED DERIVATIVES: Substances created by the RECIPIENT which constitute an unmodified functional subunit or product expressed by the ORIGINAL MATERIAL. Some examples include subclones of unmodified cell lines, purified or fractionated subsets of the ORIGINAL MATERIAL, proteins expressed by DNA/RNA supplied by the PROVIDER, or monoclonal antibodies secreted by a hybridoma cell line.

9. MODIFICATIONS: Substances created by the RECIPIENT which contain/incorporate the MATERIAL.

10. COMMERCIAL PURPOSES: The sale, lease, license, or other transfer of the MATERIAL or MODIFICATIONS to a for-profit organization. COMMERCIAL PURPOSES shall also include uses of the MATERIAL or MODIFICATIONS by any organization, including RECIPIENT, to perform contract research, to screen compound libraries, to produce or manufacture products for general sale, or to conduct research activities that result in any sale, lease, license, or transfer of the MATERIAL or MODIFICATIONS to a for-profit organization. However, industrially sponsored academic research shall not be considered a use of the MATERIAL or MODIFICATIONS

for COMMERCIAL PURPOSES per se, unless any of the above conditions of this definition are met.

11. NONPROFIT ORGANIZATION(S): A university or other institution of higher education or a research organization as described in relevant Acts of Parliament of Kenya or any nonprofit scientific or educational organization qualified under relevant Acts of parliament in Kenya. As used herein, the term also includes government agencies.

II. Terms and Conditions of this Agreement

1. The PROVIDER retains ownership of the MATERIAL, including any MATERIAL contained or incorporated in MODIFICATIONS.
2. The RECIPIENT retains ownership of (a) MODIFICATIONS (except that, the PROVIDER retains ownership rights to the MATERIAL included therein), and (b) those substances created through the use of the MATERIAL or MODIFICATIONS, but which are not PROGENY, UNMODIFIED DERIVATIVES or MODIFICATIONS (i.e., do not contain the ORIGINAL MATERIAL, PROGENY, UNMODIFIED DERIVATIVES). If either 2 (a) or 2 (b) results from the collaborative efforts of the PROVIDER and the RECIPIENT, joint ownership may be negotiated.

3. The RECIPIENT and the RECIPIENT SCIENTIST agree that the MATERIAL:
(a) is to be used solely for teaching and (academic) research purposes;

(b) will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects without knowledge and the written consent of the PROVIDER;

(c) is to be used only at the RECIPIENT organization and only in the RECIPIENT SCIENTIST's laboratory [Custodian) under the direction of the RECIPIENT SCIENTIST or others working under his/her direct supervision; and

(d) will not be transferred to anyone else within the RECIPIENT organization without the prior written consent of the PROVIDER.

4. The RECIPIENT and the RECIPIENT SCIENTIST agree to refer to the PROVIDER any request for the MATERIAL from anyone other than those persons working under the RECIPIENT SCIENTIST's direct supervision. To the extent supplies are available, the PROVIDER or the PROVIDER SCIENTIST agrees to make the MATERIAL available,

under a separate implementing letter to this Agreement or other agreement having terms consistent with the terms of this Agreement, to other scientists (at least those at NONPROFIT ORGANIZATION(S)) who wish to replicate the RECIPIENT SCIENTIST's research; provided that such other scientists reimburse the PROVIDER for any costs relating to the preparation and distribution of the MATERIAL.

5.(a) The RECIPIENT and/or the RECIPIENT SCIENTIST shall have the right, without restriction, to distribute substances created by the RECIPIENT through the use of the ORIGINAL MATERIAL only if those substances are not PROGENY, UNMODIFIED DERIVATIVES, or MODIFICATIONS.
(b) Under a separate implementing letter to this Agreement (or an agreement at least as protective of the PROVIDER's rights), the RECIPIENT may distribute MODIFICATIONS to NONPROFIT ORGANIZATION(S) for research and teaching purposes only.

(c) Without written consent from the PROVIDER, the RECIPIENT, and/or the RECIPIENT, SCIENTIST may NOT provide MODIFICATIONS for COMMERCIAL PURPOSES. It is recognized by the RECIPIENT that such COMMERCIAL PURPOSES may require a commercial license from the PROVIDER and the PROVIDER has no obligation to grant a commercial license to its ownership interest in the MATERIAL incorporated in the MODIFICATIONS. Nothing in this paragraph, however, shall prevent the RECIPIENT from granting commercial

licenses under the RECIPIENT's intellectual property rights claiming such MODIFICATIONS, or methods of their manufacture or their use.

6. The RECIPIENT acknowledges that the MATERIAL is or may be the subject of a patent application. Except as provided in this Agreement, no express or implied licenses or other rights are provided to the RECIPIENT under any patents, patent applications, trade secrets or other proprietary rights of the PROVIDER, including any altered forms of the MATERIAL made by the PROVIDER. In particular, no express or implied licenses or other rights are provided to use the MATERIAL, MODIFICATIONS, or any related patents of the PROVIDER for COMMERCIAL PURPOSES.

7. If the RECIPIENT desires to use or license the MATERIAL or MODIFICATIONS for COMMERCIAL PURPOSES, the RECIPIENT agrees, in advance of such use, to negotiate in good faith with the PROVIDER to establish the terms of a commercial license. It is understood by the RECIPIENT that the PROVIDER shall have no obligation to grant such a license to the RECIPIENT and may grant exclusive or non-exclusive commercial licenses to others, or sell or assign all or part of the rights in the MATERIAL to any third party(ies), subject to any pre-existing rights held by others and obligations to the Federal Government.

8. The RECIPIENT is free to file a patent application(s) claiming inventions made by the RECIPIENT through the use of the MATERIAL but agrees to notify the PROVIDER upon filing a patent application claiming MODIFICATIONS or method(s) of manufacture or use(s) of the MATERIAL.

9. Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. The PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT

THE USE OF THE MATERIAL WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS.

10. Except to the extent prohibited by law, the RECIPIENT assumes all liability for damages that may arise from its use, storage, or disposal of the MATERIAL. The PROVIDER will not be liable to the RECIPIENT for any loss, claim or demand made by the RECIPIENT, or made against the RECIPIENT by any other party, due to or arising from the use of the MATERIAL by the RECIPIENT, except to the extent permitted by law when caused by the gross negligence or willful misconduct of the PROVIDER.

11. This agreement shall not be interpreted to prevent or delay publication of research findings resulting from the use of the MATERIAL or the MODIFICATIONS. The RECIPIENT SCIENTIST agrees to provide appropriate acknowledgment of the source of the MATERIAL in all publications.

12. The RECIPIENT agrees to use the MATERIAL in compliance with all applicable statutes and regulations, including Public Health Service and National Institutes of Health regulations and guidelines such as, for example, those relating to research involving the use of animals or recombinant DNA.

13. This Agreement will terminate on the earliest of the following dates: (a) when the MATERIAL becomes generally available from third parties, for example, through reagent catalogs or public depositories or (b) on completion of the RECIPIENT's current research with the MATERIAL, or (c) on thirty (30) days written notice by either party to the other, or (d) on the date specified in an implementing letter, provided that:
(i) if termination should occur under 13(a), the RECIPIENT shall be bound to the PROVIDER by the least restrictive terms applicable to the MATERIAL obtained from the then-available resources; and

(ii) if termination should occur under 13(b) or (d) above, the RECIPIENT will discontinue its use of the MATERIAL and will, upon the direction of the PROVIDER, return or destroy any remaining MATERIAL. The RECIPIENT, at its discretion, will also either destroy the MODIFICATIONS or remain bound by the terms of this agreement as to they apply to MODIFICATIONS; and

(iii) in the event the PROVIDER terminates this Agreement under 13(c) other than for breach of this Agreement or for a cause such as an imminent health risk or patent infringement, the PROVIDER will defer the effective date of termination for a period of up to one year, upon request from the RECIPIENT, to permit completion of research in progress. Upon the effective date of termination, or if requested, the deferred effective date of termination, RECIPIENT will discontinue its use of the MATERIAL and will, upon the direction of the PROVIDER, return or destroy any remaining MATERIAL. The RECIPIENT, at its discretion, will also either destroy the MODIFICATIONS or remain bound by the terms of this agreement as they apply to MODIFICATIONS.

14. Paragraphs 6, 9, and 10 shall survive termination.

15. The MATERIAL is provided at no cost, or with an optional transmittal fee solely to reimburse the PROVIDER for its preparation and distribution costs. If a fee is requested by the PROVIDER, the amount will be indicated in an implementing letter.

IMPLEMENTING LETTER

The purpose of this letter is to provide a record of the biological material transfer, to memorialize the agreement between the PROVIDER SCIENTIST or organization (identified below) and the RECIPIENT SCIENTIST (identified below) to abide by all terms and conditions of the Uniform Biological Material Transfer Agreement ("UBMTA") 22nd December 2021 and to certify that the RECIPIENT (identified below) organization has accepted and signed an unmodified copy of the UBMTA. The RECIPIENT organization's

Authorized Official also will sign this letter if the RECIPIENT SCIENTIST is not authorized to certify on behalf of the RECIPIENT organization. The RECIPIENT SCIENTIST (and the Authorized Official of the RECIPIENT, if necessary) should sign both copies of this letter and return one signed copy to the PROVIDER. The PROVIDER SCIENTIST will forward the material to the RECIPIENT SCIENTIST upon receipt of the signed copy from the RECIPIENT organization.

Please fill in all of the blank lines below:

Nature and description of ORIGINAL MATERIAL being transferred

Nature	quantity

Purpose of this transfer

Intended use of materials being transferred

Justification of this transfer (e.g., unavailability of resources, techniques, and equipment to perform similar tests and research requested for in this transfer by the transferring organization)

If applicable,

1. Approval details of the research that collected the biological materials being transferred {_____}

Period of keeping of the biological materials being transferred

These biological materials will be kept in the recipient organization for a period of _____ after the initial date of transfer. Upon expiry of this period,

1. The recipient and source organization will review an extension for the keep YES _____ NO _____
2. The original materials will be destroyed in line with international protocols for the destruction of such materials YES_____ NO _____
3. The original materials will be returned to the source country YES _____ NO _____
4. The proposal that collected these materials sufficiently addressed the issues of intellectual property rights arising from intended and unintended use of materials being transferred YES _____NO_____

Please fill the following sections

1. The biological materials being transferred were obtained from an approved research project YES {_____ NO {_____}.
2. The approval number of this study was {_____}.

3. This study was approved by the following Institutional approved review board {_____**}**.
4. The biological materials being transferred were obtained from patients of participants who gave informed consent for collection of their samples YES {_____} NO {_____}.

1. PROVIDER: Organization providing the ORIGINAL MATERIAL:

Organization:_____
_____

Address:
_____
_

_____
_____

2. RECIPIENT: Organization receiving the ORIGINAL MATERIAL:

Organization:
_____

Address:
_____
_

_____
_____

3. ORIGINAL MATERIAL (Enter description):

_____
_____

_____
_____

_____
_____

_____

_____

4. Termination date for this letter (optional):

5. Transmittal Fee to reimburse the PROVIDER for preparation and distribution costs (optional).

Amount:_____

_____

This Implementing Letter is effective when signed by all parties. The parties executing this Implementing Letter certify that their respective organizations have accepted and signed an unmodified copy of the UBMTA, and further agree to be bound by its terms, for the transfer specified above.

PROVIDER SCIENTIST

Name:_____

_____

Title:_____

_____

Address:_____

_____

_____

_____

Signature:_____

_____

Date:_____

_____

RECIPIENT SCIENTIST

Name:_____
_____

Title:_____
_____

Address:_____
_____

_____
_____

Signature:_____
_____

Date:_____
_____

RECIPIENT ORGANIZATION CERTIFICATION

Certification: I hereby certify that the RECIPIENT organization has accepted if authorized by the RECIPIENT organization):

Authorized
Official:_____

Title:_____

Address:_____

_____

Signature:_____

Date:_____

ANNEXES KENSEQC003

Specimen Referral Standard Operating Procedure (SOP) for Genomic Surveillance of SARS-COV-2

I. PROCEDURE

A. Acceptable specimen types for sequencing are :

a. At least 500uL of upper and lower respiratory specimens in viral transport media (VTM), including nasopharyngeal, oropharyngeal, nasal middle-turbinate, and anterior nares (nasal swab)
b. Only those samples which are positive for SARS-CoV-2 by RT PCR preferably with a Ct value of 30 or less should be packaged & transported. If Ct values are not available, specimens that are positive for SARS-CoV-2 by another testing modality may be sent.
c. Only specimens that have not previously been sequenced.
d. Only send samples with complete metadata as in the attached

B. Potential considerations for screening of the new Variants Of concerns (VOCs)

a. All SARS-CoV-2 positive specimens collected through screening of International travellers
b. All SARS-CoV-2 positive specimens from people who are either participating in vaccine trials or have been vaccinated
c. All SARS-CoV-2 positive samples from people with a prior history of infection and confirmed re-infection
d. Representative and randomly selected SARS-CoV-2 positive specimens by RT PCR

C. Request for submission

- Select the VTM or RNA extracts residual specimens
    - Ensure the specimens have not been freeze-thawed for more than once
    - Ensure laboratory documented rejection criteria are adhered to . A d etailed SOP for specimen rejection will be shared with all COVID-19 testing laboratories
    - Prepare the shipment log and document the meta-data required. Kindly get in touch with leonard.kingwara@gmail.com for clarification on the same
- Once samples are selected for sequencing, please complete the National Laboratory Services (NLS) SARS-CoV-2 sequencing submission form.
    - To be developed
- Send the completed form electronically to leonard.kingwara@gmail.com
- The NLS team will review and provide feedback within 24 hours of submission of the electronic form
- Shipment instructions will be shared with the Shipping lab? immediately approval is done by NLS

D. Preparation for shipment

- **Shipping documentation**
    - The shipping laboratory will be required to provide the following paperwork before shipping the samples:
        - T he completed request form in C above
        - Material Transfer Agreement with the recipient institution ANNEXES KENSEQC002
        - The Material transfer agreement will be waived if the shipping institution is from a public health facility under the department of National Laboratory Services
- **List of supplies needed for shipping specimens on dry ice**

- Leak-proof primary container, 1.5ml tubes with O-rings (e.g NUNC vials, Sarstedt Tubes, etc) are preferred. If not available use 1.5ml tubes and wrap the cap with parafilm
- Leak-proof secondary container
- Absorbent material, enough to absorb all liquid in package
- Biohazard Label
- Pipette tips (1000uL tips)
- PPEs to aliquot and pack the samples
- Packaging boxes and dry ice (will be provided by the courier agent)
- Techni Ice

- **Safety Procedures**
  -
  - Specimens should be packed and transported according to International Air Transport Association (IATA) regulations and in compliance with regulations for UN3373 Biological Substance, Category B.
  - The packaging consists of three layers as follows.
    - **Primary container:** A labelled primary watertight, leak-proof receptacle containing the specimen. The receptacle is wrapped in enough absorbent material to absorb all fluid in case of breakage.
    - **Secondary container:** A second durable, watertight, leak-proof receptacle to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be placed in the secondary container to absorb the total volume of liquid in all primary containers. Bubble wrap can be used to cushion multiple primary receptacles, if necessary.
    - **Outer shipping package:** The secondary receptacle is placed in an outer shipping package which protects it and its contents from outside influences such as physical damage/stress and water while o n transit. Dry ice/Techni Ice should be placed between the Outer package and the secondary container. Never place dry ice in the secondary container.

E. Sample shipment

- The NLS team will engage or reserve a designated courier to arrange the collection of the specimens as soon as possible.
- NLS team will notify the requesting lab on the booking and assist with the required documentations
- The courier agent will provide who? with the “JOB NUMBER” and will attach the required documentations.
- Once documentations are completed, the courier agent will schedule a collection date and time and communicate with NLS, the sending and recipient labs/NLS.
- The courier agent will provide Techni ice, packaging and labelling materials required to comply with international transport regulations.
- Once picked up, the courier agent is expected to provide status update of the sample using a courier tracking system for specimen tracking
- When specimens are delivered, the recipient lab/DLS will provide a status update on the sequencing and sequencing results will be sent back within 14 days of shipment.

F. Questions?

a. For technical questions regarding the packing of specimens please contact any IATA certified Infectious Substance Shipper. Detailed booklet will be shared with the facilities shipping the specimens
b. For samples shipment related questions, please contact veraonwonga@gmail.com.and rukiasarahmdd@gmail.com
c. For general questions on genomic-based surveillance for SARS-CoV-2 and technical guidance on sampling strategy, please contact leonard.kingwara@gmail.com and kyirow@gmail.com

Request/Questions related to	Responsible	Contact
• Genomic-based surveillance for SARS-CoV-2 and technical guidance on sampling strategy	Dr. John Ndemi Kiiru Leonard Kingwara	kyirow@gmail.com leonard.kingwara@gmail.com
• Data management: data sharing, dashboard		
Samples shipment		
• SARS-CoV-2 sequencing submission form	Vera Onuonga Morangi	veraonwonga@gmail.com
• Assistance on specimen shipment details	Rukia Madada	rukiasarahmdd@gmail.com

FORCASTING AND QUANTIFICATION OF SARS CoV2 GENOMIC SURVEILLANCE NEEDS

Capacity building	Cost per Unit	Total Need	Total cost	Requested in GF	Pending Gap as at Dec 20212	Comments
Training of Laboratory staff (Specimen referral and collection)	KES 60,000	500	KES 30,000,000	0	KES 30,000,000.00	Yearly recurring request
Training of Laboratory staff (Sequencing and Bio-informatics)	KES 140,000	10	KES 1,400,000	0	KES 1,400,000.00	Yearly recurring request
Human Resource	KES 3,000,000	3	KES 9,000,000	2	KES 3,000,000.00	Yearly recurring request
Total Initial Investments			**KES 40,400,000**		**KES 34,400,000.00**	

Equipment need	Cost per Unit	Total Need	Total cost	Requested in GF	Pending Gap as at Dec 20212	Comments
Illumina Sequencing platform	KES 10,000,000	2	KES 20,000,000	1	KES 10,000,000.00	One off investment

MGIC	KES 14,000,000	1	KES 14,000,000	0	KES 14,000,000.00	One off investment
Nanopore (Grid-Ion)	KES 7,000,000	1	KES 7,000,000	0	KES 7,000,000.00	One off investment
Nanopore (Mini-Ion)	KES 3,000,000	4	KES 12,000,000	0	KES 12,000,000.00	One off investment
Extractors (Sentosa)	KES 10,000,000	5	KES 50,000,000	2	KES 30,000,000.00	One off investment
Total Initial Investments			**KES 103,000,000**		**KES 73,000,000.00**	

Reagents and Consumables need	Cost per Unit	Total Need	Total cost	Requested in GF	Pending Gap as at Dec 20212	Comments
MagMAX™ Viral/Pathogen Nucleic Acid Isolation Kit	KES 465,500	10	KES 4,655,000	2	KES 3,724,000.00	Yearly recurring request
COVIDSeq Test (3072 Samples)	KES 9,200,000	5	KES 46,000,000	1	KES 36,800,000.00	Yearly recurring request
8 IDT for Illumina-PCR Indexes Sets 1-4 (384 Indexes)	KES 650,000	140	KES 91,000,000	28	KES 72,800,000.00	Yearly recurring request
Qubit dsDNA HS Assay Kit, Thermo Fisher Scientific	KES 20,000	150	KES 3,000,000	30	KES 2,400,000.00	Yearly recurring request
MiSeq reagent kit V3 (600 cycles)	KES 1,500	500	KES 750,000	100	KES 600,000.00	Yearly recurring request
LunaScript RT superMix Kit	KES 45,000	20	KES 900,000	0	KES 900,000.00	Yearly recurring request
Q5 Hot Start High Fidelity DNA Polymerase	KES 71,000	20	KES 1,420,000	0	KES 1,420,000.00	Yearly recurring request
SQK-RBK 004 Rpid Barcoding Kit Oxford Nanopore	KES 75,000	20	KES 1,500,000	0	KES 1,500,000.00	Yearly recurring request
MinION Flow cell r9.4.1Oxford Nanopore Technologies	KES 120,000	20	KES 2,400,000	0	KES 2,400,000.00	Yearly recurring request
Conumables bundle package	KES 65,000	20	KES 1,300,000	0	KES 1,300,000.00	Yearly recurring request
COVIDSeq Test (3072 Samples) consumables	KES -		KES -	0	KES -	Yearly recurring request
Vella Sentosa Iron TorRENT PGEM End to end Kit	KES 15,000	3000	KES 45,000,000	1000	KES 30,000,000.00	Yearly recurring request
Total Initial Investments			**KES 197,925,000**		**KES 153,844,000.00**	

ICT need	Cost per Unit	Total Need	Total cost	Requested in GF	Pending Gap as at Dec 20212	Comments
Computing space	KES 4,500,000	1	KES 4,500,000	0	KES 4,500,000.00	One off investment
Laptops	KES 200,000		KES -	0	KES -	Yearly recurring request
Softwares	KES 1,000,000	2	KES 2,000,000	0	KES 2,000,000.00	Yearly recurring request
Total Initial Investments			**KES 6,500,000**		**KES 6,500,000.00**	