INTERNATIONAL JOURNAL OF
MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2021.28290
Int J Med Biochem 2021;4(2):104-20

Research Article

Biosafety risk assessment of a clinical biochemistry laboratory for SARS-CoV2 infection

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Abstract

Objectives: Clinical laboratories are a transfer point for infected patient samples. According to the World Health Organization (WHO) Laboratory Biosafety Guideline, a risk assessment approach is the backbone of laboratory biosafety. In laboratories, risk assessment is recommended at predetermined periods and in the event of new circumstances. On February 12, 2020, the WHO published an interim guidance document, "Laboratory biosafety guidance related to the novel coronavirus (2019-nCoV)" and it was highly recommended that all coronavirus 2019 (COVID-19) testing procedures be performed based on a local risk assessment. This study was designed to evaluate the biosafety risk in a biochemistry laboratory where routine testing of patients diagnosed with COVID-19 is performed.

Methods: Risk assessment for tests performed on analyzers and a complete urinalysis was performed using the risk assessment template included in the subsequent WHO interim guidance document, "Laboratory biosafety guidance related to coronavirus disease (COVID-19)."

Results: The overall initial risk for tests performed on analyzers and a complete urinalysis test was determined to be very high. Processes such as pipetting a sample and checking a sample tube by scanning the barcode during tests performed on analyzers were suspended until additional risk control measures could be implemented. The manual microscopic urinalysis process was also discontinued. To reduce the risk, surgical masks, surgical caps, eye protection, and disposable laboratory coats were added to the previously mandated personal protective equipment. After implementing additional risk control measures, the total residual risk of both processes was graded medium.

Conclusion: Since there is as yet no effective treatment for COVID-19, exposure risk is considered severe. Therefore, the probability of exposure is important in determining the level of risk. Measures put in place reduced the total residual risk.

Keywords: Biosafety, COVID-19, laboratory risk assessment, pandemic

Coronavirus 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in Wuhan, China, in December 2019 [1]. It was declared a pandemic by the World Health Organization (WHO) in March 2020 [2]. The first laboratory-confirmed COVID-19 case in Turkey was announced by the Ministry of Health on March 11, 2020 [3].

COVID-19 is an aerosol transmissible disease, and the infectious dose of SARS-CoV-2 remains unknown. Healthy individuals can also be infected by touching contaminated surfaces and then transferring viral particles to the mucous membranes of the eyes, nose, and mouth (indirect contact or fomite transmission) [4].

Viral respiratory infection is confirmed with the detection of viral nucleic acid in tissue samples, which is indicative of active virus replication [5]. Upper respiratory material (nasopharyngeal and oropharyngeal swab or wash in ambulatory patients) or lower respiratory material (sputum and/or endotracheal aspirate or bronchoalveolar lavage) has been defined by the WHO as the minimum sample for a diagnosis of COVID-19. It

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Submitted Date: November 30, 2020 **Accepted Date:** January 06, 2021 **Available Online Date:** March 22, 2021

has also been reported that SARS-CoV-2 can be detected in blood and stool [6].

Viral RNA in patient specimens (nasopharyngeal swab, sputum, stool samples, etc.) is detected using the polymerase chain reaction (PCR) method, which targets independent regions of the SARS-CoV-2 nucleocapsid gene [7]. Viral RNA is first purified from the sample and then transcribed into DNA, which is amplified in a PCR reaction to produce easily detectable amounts [4]. Several real-time reverse transcriptase PCR assay protocols have been developed and approved by the US Center for Disease Control and Prevention and are now widely used for the diagnosis of COVID-19 [7].

SARS-CoV-2 RNA can be identified in respiratory samples 1 to 2 days before the onset of symptoms and shedding can take up to 7 to 12 days in moderate cases, and up to 2 weeks in severe cases [8]. The viral load in urine, saliva, and stool samples not currently used in the routine diagnosis of COVID-19 has been shown to be almost equal to or greater than the viral load in nasopharyngeal or oropharyngeal swab samples [9]. The viable virus in stool and serum can be detected for nearly 5 weeks after a respiratory sample has tested negative for SARS-CoV-2 RNA [5, 7]. Therefore, the risk of SARS-CoV-2 transmission via stool and blood samples cannot be excluded.

The minimum biosafety level (BSL) for clinical laboratories is BSL 2. While specimen handling for molecular testing would require BSL 2 facilities or the equivalent, culturing the virus would require a minimum of BSL 3 facilities [6]. Clinical laboratories are an transfer point for infected patient samples. Although laboratory divisions such as hematology, biochemistry, and blood bank departments follow BSL 2 blood-born pathogen standards, these units often lack access to equipment such as a certified biological safety cabinet. Also, although lab workers claim that they follow certain practices and take security measures, daily practice observations do not always support these claims [10]. Consequently, it is recommended that clinical laboratories that work with samples such as blood products and urine containing relatively lower virus concentrations (in comparison with a microbiology laboratory where respiratory samples are processed) should also perform a risk assessment to prevent exposure to aerosols and droplets when processing samples that may contain SARS-CoV-2 [11, 12]. As stated in a WHO Laboratory Biosafety Guideline, a risk assessment approach is the backbone of laboratory biosafety [13]. Risk assessment is the process that collects data about workplace hazards and evaluates the possible results of exposure. Appropriate risk control measures are selected and implemented to reduce the risks identified in the evaluation and mitigate residual risk. Laboratory risk assessment is recommended at predetermined periods and in any instance of new circumstances. On February 12, 2020, the WHO published the interim guidance document, "Laboratory biosafety guidance related to the novel coronavirus (2019-nCoV)," which recommended that all procedures related to COVID-19 be performed based on risk assessment [11].

This study is an examination of a biosafety risk assessment performed in a clinical biochemistry laboratory to determine measures to be taken during the COVID-19 pandemic.

Materials and Methods

Risk assessment was performed on analyzers and a complete urinalysis test using the template included in the WHO interim guidance supplement "WHO laboratory biosafety guidance related to coronavirus disease 2019 (COVID-19)" [11].

In our clinical biochemistry laboratory, an ADVIA Centaur XP immunoassay system (Siemens Healthcare Diagnostics Inc., Deerfield, IL, USA), a Siemens ADVIA chemistry analyzer (Siemens Healthcare Diagnostic Inc., Deerfield, IL, USA), and a DIRUI H-500 urine analyzer (DIRUI Industrial Co. Ltd., Changchun, Jilin China) are used for immunoassay analysis, chemistry analysis, and urine strip analysis, respectively. The urine strip analyzer is semi-automated; microscopic analysis of urine is performed manually. The assessment steps were based on the standard operating procedure and opportunities for potential exposure and/or release for each process. A brief overview of the evaluations is provided in Figure 1 and Figure 2. An initial risk assessment of the laboratory procedures and the overall risk was estimated for each process. The addition of risk control measures was prioritized according to urgency, feasibility/sustainability, delivery and installation time, and availability. Requirements prescribed by international and national regulations, legislation, guidelines, policies, and strategies on biosafety were also included [13, 14]. In addition, the process examines the applicability, availability, and sustainability of the resources available for risk control as well as the level of residual risk with these risk control measures in place. The residual risk after risk control measures was evaluated for each process to determine if that level of risk would be below the tolerance level and whether work should proceed. Step 2 of the WHO risk assessment examines the consequences of exposure and likelihood of exposure. As there is still no effective treatment for COVID-19, the consequences of any exposure to material that is suspected for COVID-19 is categorized as severe. The maximum acceptable residual risk in this case is a medium risk tolerance level. The overall residual risk of the laboratory processes examined with the benefit of risk control measures was estimated. The highest level of risk for any step of the process before risk assessment was considered the initial overall risk for the whole process. Standard operating procedures for tests performed on analyzers and a complete urinalysis were redefined based on the risk assessment (Fig. 3, 4). Finally, a review was scheduled to be performed every 6 months or upon changes in the laboratory (laboratory staff, analyzer, or process) or knowledge of SARS-CoV-2 (Annex 1, 2).

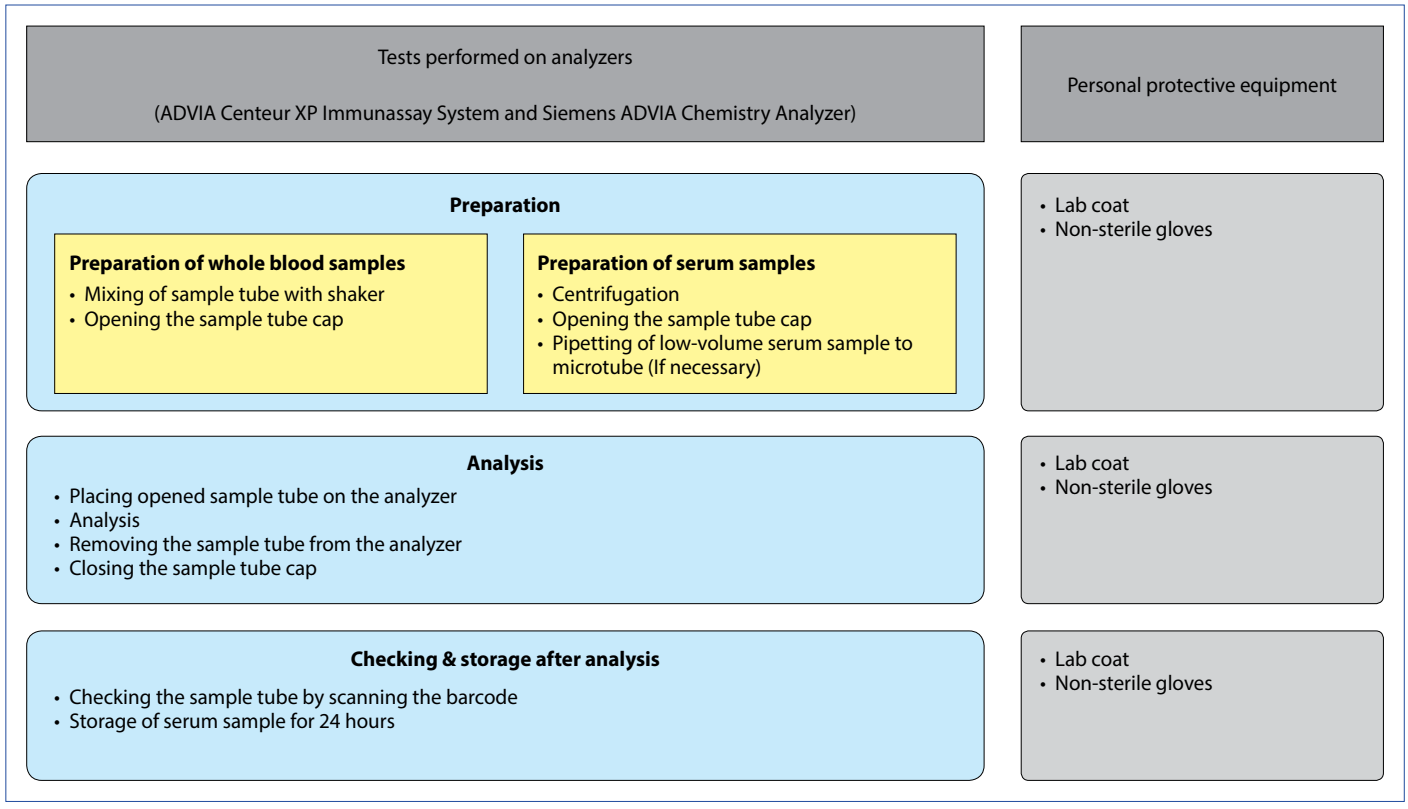

Figure 1. A brief overview of the process for tests performed on analyzers.

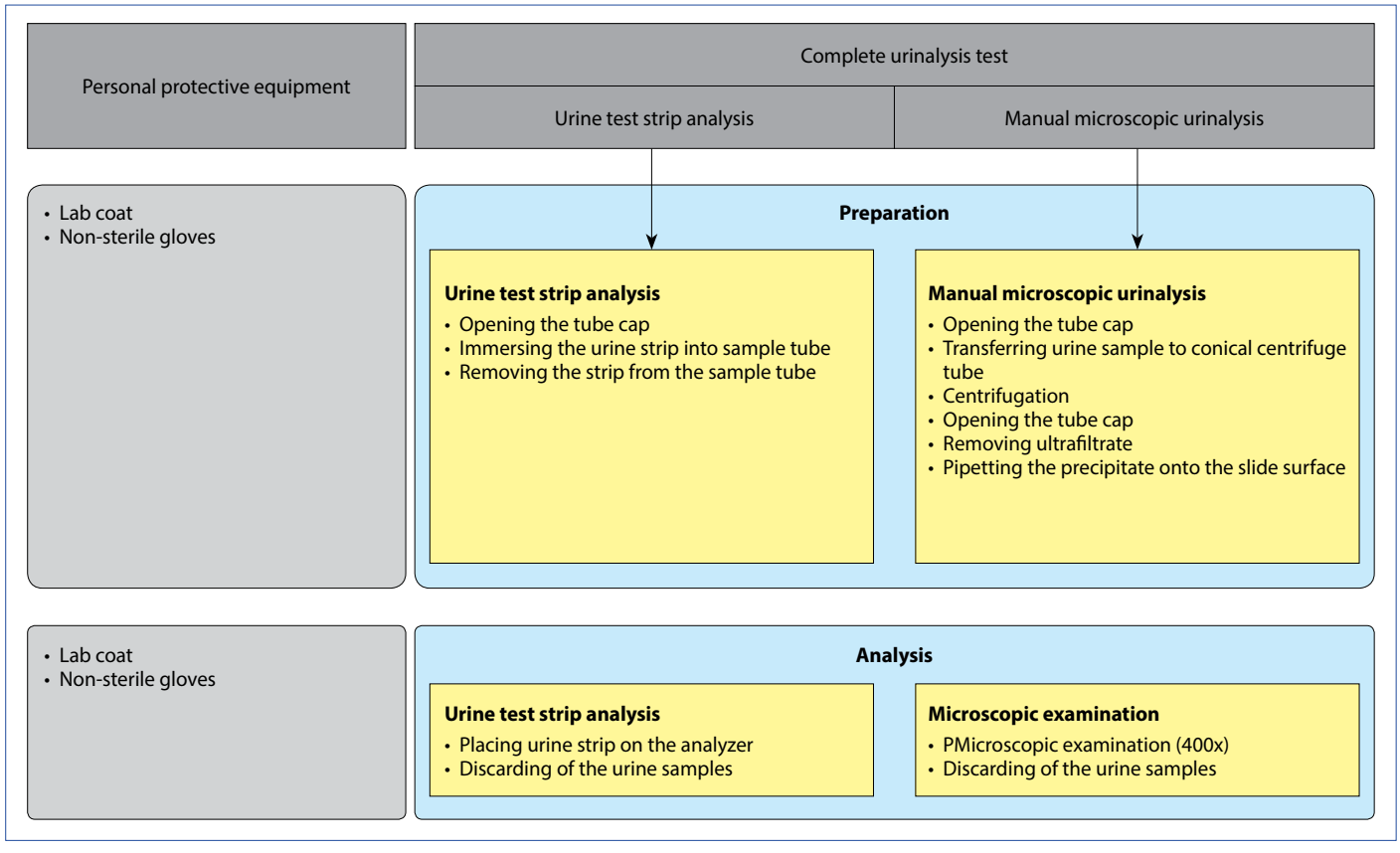

Figure 2. A brief overview of the process for a complete urinalysis test.

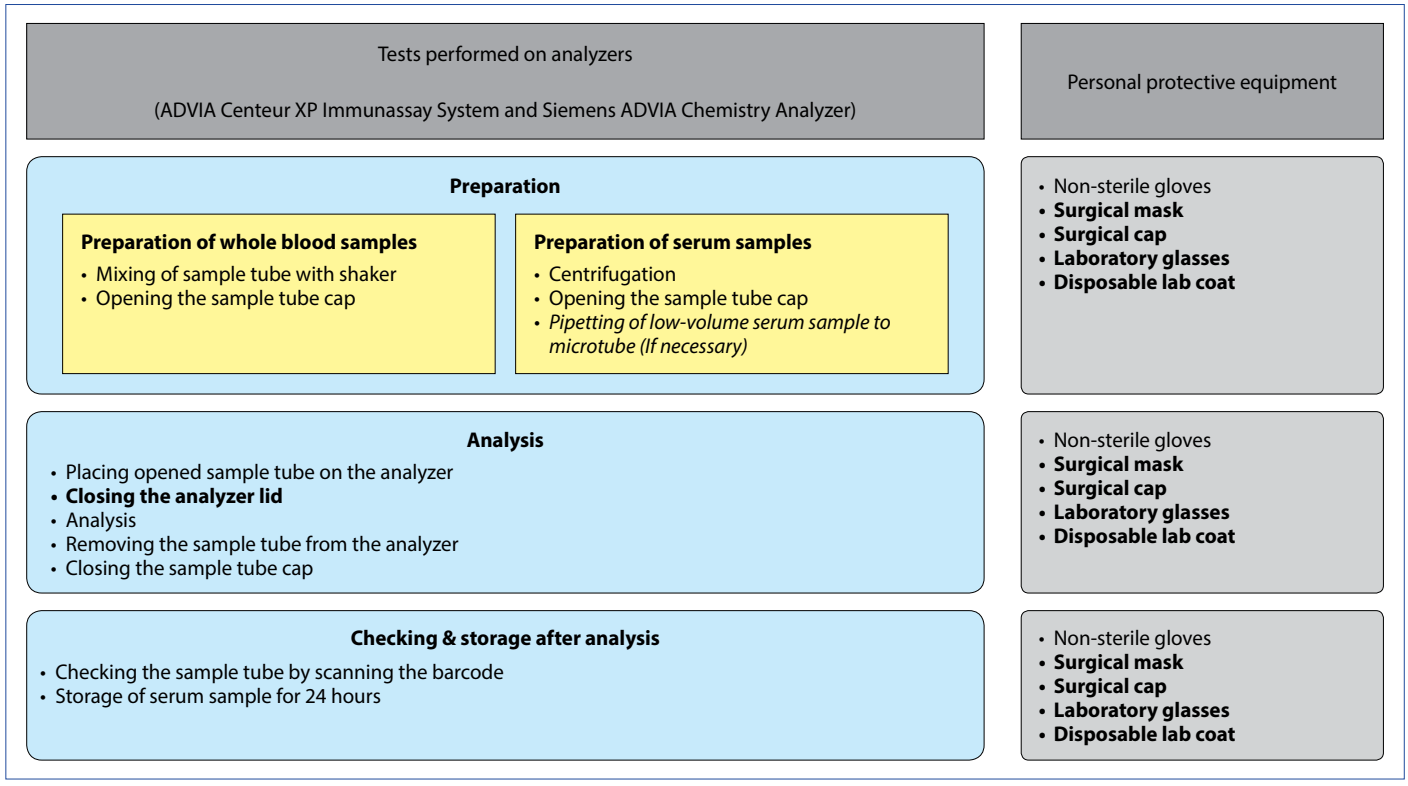

Figure 3. A brief overview after implementation of risk control measures for tests performed on analyzers. Discontinued steps are presented in italic font and new biosafety steps are in bold font.

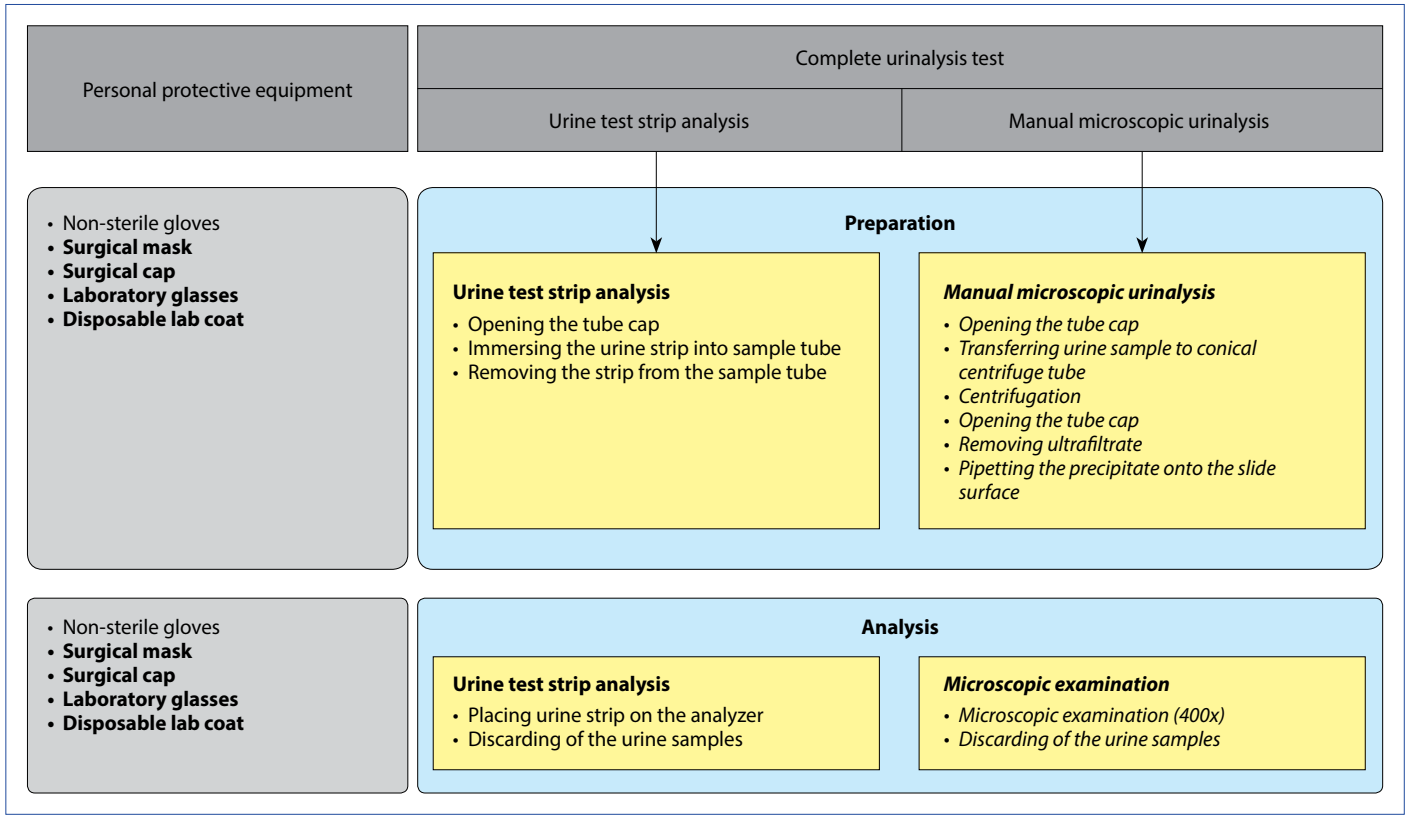

Figure 4. A brief overview after implementation of risk control measures for a complete urinalysis test. Discontinued steps are presented in italic font and new biosafety steps are in bold font.

Results

Examination of tests performed on analyzers revealed that the opening or closing of a sample tube cap, pipetting of specimens, placing opened sample tubes on the analyzer, analysis procedures, removing the sample tube from the analyzer, and checking sample tubes by scanning barcodes were steps with the risk of generating aerosols that could include SARS-CoV-2.

The initial risk classification for pipetting a specimen was very high, while it was graded high for the analysis step, and medium for opening or closing the sample tube cap, placing opened samples tube on the analyzer, removing the sample tube from the analyzer, and checking the sample tube by scanning the barcode (Table 1). The overall initial risk for the analyzer testing process was determined to be very high. It was decided that additional risk control measures were necessary. The steps of pipetting the specimen and checking the sample tube by scanning the barcode were discontinued (Table 2). To reduce the risk of contact, surgical masks, surgical caps, eye protection, and disposable laboratory coats were added to the previously used personal protective equipment.

Table 1. The initial risk assessment for tests performed on analyzers

		Likelihood of exposure/release		
		Unlikely	**Possible**	**Likely**
Consequence of exposure/release	Severe	Medium	High	Very high
	Moderate	Low	Medium	High
	Negligible	Very low	Low	Medium
Laboratory activity/procedure		Initial risk (very low, low, medium, high, very high)	Is the initial risk above the tolerance level? (yes/no)	Priority (high/medium/low)
Opening or closing the sample tube cap		Severe x Unlikely=Medium	No	Low
Pipetting of specimen		Severe x Likely=Very high	Yes	High
Placing opened sample tube on the analyzer		Severe x Unlikely=Medium	No	Low
Analysis		Severe x Possible=High	Yes	High
Removing the sample tube from the analyzer		Severe x Unlikely=Medium	No	Low
Checking the sample tube by scanning the barcode		Severe x Unlikely=Medium	No	Low
Select the overall initial risk		☐ Very low ☐ Low	☐ Medium ☐ High	☑ Very high
Should work proceed without additional risk control measures?		☐ Yes	☑ No	

Table 2. The risk assessment for tests performed on analyzers after the adoption of control measures

Laboratory activity/procedure	**Selected risk control measure(s)**	**Residual risk (very low, low, medium, high, very high)**	**Is the residual risk above the tolerance level? (yes/no)**	**Are risk control measures available, effective and sustainable? (yes/no)**
Opening or closing the sample tube cap	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Pipetting of specimen	Discontinued	-	No	-
Placing opened sample tube on the analyzer	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Analysis	Analyzer lid closed; surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Removing the sample tube from the analyzer	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Checking the sample tube by scanning the barcode	Discontinued	-	No	-
Overall residual risk	☐ Very low ☐ Low	☑ Medium	☐ High	☐ Very high

Table 3. The initial risk assessment for a complete urinalysis test

		Likelihood of exposure/release				
		Unlikely		**Possible**		**Likely**
Consequence of exposure/ release	Severe	Medium		High		Very high
	Moderate	Low		Medium		High
	Negligible	Very low		Low		Medium
Laboratory activity/procedure		Initial risk (very low, low, medium, high, very high)		Is the initial risk above the tolerance level? (yes/no)		Priority (high/ medium/low)
Immersing the urine strip into sample tube, removing the strip from the sample tube		Severe x Unlikely=Medium		No		Low
Transferring urine sample to conical centrifuge tube (pipetting)		Severe x Likely=Very high		Yes		High
Opening the tube cap		Severe x Unlikely=Medium		No		Low
Pipetting		Severe x Likely=Very high		Yes		High
Removing ultrafiltrate		Severe x Likely=Very high		Yes		High
Pipetting the precipitate onto the slide surface		Severe x Likely=Very high		Yes		High
Microscopic examination of stained slides		Severe x Possible=High		Yes		High
Discarding of the urine samples		Severe x Unlikely=Medium		No		Low
Select the overall initial risk		☐ Very low	☐ Low	☐ Medium	☐ High	☑ Very high
Should work proceed without additional risk control measures?		☐ Yes	☑ No			

As a result, the general residual risk for tests performed on an analyzer was reduced to medium (Table 2). A summary of the standard operating procedures following the addition of risk control measures is shown in Figure 3.

The risk of generating aerosols containing SARS-CoV-2 was identified in the urine test strip analysis process steps of opening the tube cap, immersing the urine strip into a sample tube, removing the strip from a sample tube, and disposal of the sample. During the manual microscopic urinalysis, transferring the urine sample to a conical centrifuge tube (pipetting), opening the tube cap, removing ultrafiltrate, pipetting the precipitate onto the slide surface, microscopic examination of stained slides, and discarding the sample were determined to be the steps with the most risk.

The initial risk rating was very high for the transfer and removal of ultrafiltrate, while microscopic examination of stained slides was considered a high risk, and opening the tube cap, immersing the urine strip into a sample tube, removing the strip from the sample tube, and disposal were classified as a medium risk (Table 3). The overall initial risk for a complete urinalysis test was very high. Additional risk control measures were considered necessary (Table 3). The manual microscopic urinalysis process was discontinued. Once additional risk control measures were implemented, the total residual risk of the process for a complete urinalysis was evaluated as medium level (Table 4). A summary of the revised standard operating procedures is shown in Figure 4.

Discussion

Since there is currently no effective treatment for COVID-19, determining the probability of exposure is important. In our risk assessment of analyzer testing, the greatest possibility of aerosolization was in the steps of opening and closing the tube cap, pipetting for transfer, placing the sample tube on the device, analysis (pipetting), and barcode scanning of the tube. The overall initial risk of the process was determined to be very high. To reduce the risk, surgical masks, surgical caps, eye protection, and disposable laboratory coats were added to the personal protective equipment already in use. Measures were implemented to reduce contact between the laboratory workers and the patient samples. The pipetting process (transfer of patient samples with low sample volume to a microtube) and barcode scanning of the sample tubes were eliminated and insufficient samples were rejected. It was also decided that the procedures for the final check of the patient samples would be performed using only the laboratory information system. It was observed that the lid of the sample pipetting area of the analyzer remained open during daily practice. As a result of closing the lid of the analyzer, the risk of the analysis process decreased from high to medium due to reduced exposure to aerosolization that may occur by pipetting inside the instrument. The final residual risk rating after applying risk control measures related to analyzer testing was medium.

In our laboratory, urine microscopic examination and strip analysis are performed manually. These processes were evalu-

Table 4. The risk assessment for a complete urinalysis test after the adoption of control measures

Laboratory activity/ procedure	Selected risk control measure(s)	Residual risk (very low, low, medium, high, very high)	Is the residual risk above the tolerance level? (yes/no)	Are risk control measures available, effective and sustainable? (yes/no)
Immersing the urine strip into sample tube, removing the strip from the sample tube	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Transferring urine sample to conical centrifuge tube (pipetting)	Discontinued	-	No	-
Opening the tube cap	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Pipetting	Discontinued	-	No	-
Removing ultrafiltrate	Discontinued	-	No	-
Pipetting the precipitate onto the slide surface	Discontinued	-	No	-
Microscopic examination of stained slides	Discontinued	-	No	-
Discarding of the urine samples	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	Severe x Unlikely=Medium	No	Yes
Overall residual risk	☐ Very low ☐ Low	☑ Medium	☐ High	☐ Very high

ated separately in the risk assessment of the complete urinalysis test process. In the urine test strip analysis process, opening the tube cap, immersing and removing the urine strip from a sample tube, and disposal were determined to be steps that could generated aerosols. Transferring the urine sample into a conical centrifuge tube, opening the tube cap, removing the ultra-filtrate, pipetting the precipitate onto the slide surface, and microscopic examination procedures were the steps that could lead to aerosolization of SARS-CoV-2 in the manual microscopic analysis. Pipetting was found to be a high risk step due to high exposure probability. The remaining steps were evaluated as medium risk. The overall initial risk of a complete urinalysis test was considered very high.

Human coronaviruses other than SARS-CoV and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) are classified in Risk Group 2 according to Appendix B of the US National Institute of Health Guideline for Research Involving Recombinant or Synthetic Nucleic Acid Molecules [15]. SARS-CoV and MERS-CoV cause severe lower respiratory tract disease and are classified in Risk Group 3.

At the time of writing, the SARS-CoV-2 risk group has not yet been identified. The US Centers for Disease Control and Prevention guideline recommends that some standard practices used in the laboratory during the manipulation of potentially infected samples be performed in a certified class 2 biosafety cabinet (BSC), and at least within a BSL 2 laboratory [12].

Our laboratory includes microbiology and biochemistry departments. There is 1 BSC 2A cabinet in the microbiology department and it is in constant use by that staff. It is also not possible to transfer patient samples to a different unit for pipetting due to the physical conditions of the laboratory. Therefore, steps that could result in aerosol formation, such as pipetting performed by the biochemistry department, cannot be performed in the BSC 2A cabinet.

Pipetting is used in many steps of the manual microscopic examination process. In addition, accidents such as leakage between the coverslip or cracking of the coverslip are not uncommon during microscopic examination in daily practice. In such cases, there is typically 15 to 20 cm between the urine sample and the nose of the examiner. Transmission of SARS-CoV-2 through respiratory droplets and direct contact has been widely acknowledged, but viral shedding in urine has also been reported, and infection through infected urine remains a possibility [16].

The urine strip analysis panel performed in our laboratory includes leukocyte esterase and hemoglobin analyses. In a previous study, our performance of urine strip analysis was classified as good [17]. Therefore, the manual microscopic evaluation analysis process of a complete urinalysis test was suspended temporarily because the risk level could not be reduced.

The unknown properties of the pathogen of the current pandemic present several difficulties and concerns. Laboratories should be aware that any sample may contain high-risk pathogens and therefore a safe environment for laboratory staff is essential. This requires the support of not only laboratory experts, but the administrative and working staff as well [13, 18].

Communication is a vital point in risk assessment and control. The measures to be taken will only be as effective as the employees' awareness of risk. The technicians working in our biochemistry laboratory had no experience working in a laboratory with high-risk pathogens. Therefore, their awareness of the use of personal protective equipment was not at a sufficient level. After completing the risk assessment, detailed in-service training was provided for all laboratory staff, including the revised standard operating procedures.

Conclusion

The risk assessment process has established steps; however, it should not be forgotten that it is subjective and the results of one process are not a recipe that can be used for each process or each laboratory. This study examined a risk assessment applied to routine laboratory processes during the COVID-19 pandemic. The tools used and the results may be useful to other clinical laboratories as a means to transfer recommended risk assessment guidelines to daily practice.

Conflict of Interest: The authors declare no conflict of interest.

Ethics Committee Approval: Not applicable.

Financial Disclosure: The authors have nothing to disclose.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept – N.Z., O.Z.; Design – N.Z., O.Z.; Supervision – N.Z., O.Z.; Funding – None; Materials – N.Z.; Data collection &/or processing – N.Z.; Analysis and/or interpretation – N.Z., O.Z.; Literature search – N.Z., O.Z.; Writing – N.Z., O.Z.; Critical review – O.Z.

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Annex 1. World Health Organization risk assessment tool used for tests performed on analyzers.

Risk Assessment Template

Although a qualitative approach to combining likelihood and severity parameters in a risk matrix is provided as a risk evaluation method here, it is important to note that quantitative (for example, simple numerical scoring schemes to complex mathematical models) and hybrid (semi-quantitative) methods can also be used for risk evaluation. Laboratories should use a risk evaluation/assessment method that best meets their unique needs, without excluding the possibility of developing customized evaluation approaches, scoring methods and definitions of the parameters.

While this template was primarily developed for biosafety risk assessment, it can also be used for general safety risk assessment of laboratory activities, especially when the biosafety and general safety risks are interlinked, for example, sample collection and transport, where appropriate and applicable.

Institution/Facility name	Kemalpasa State Hospital
Laboratory name	Clinical Biochemistry Laboratory
Laboratory manager/Supervisor	Dr. Nergiz Zorbozan/Specialist of Medical Biochemistry
Project titles/Relevant standard operating procedures (SOPs)	Tests Performed on auto analyzers
Date	March 11, 2020

STEP 1. Gather information (hazard identification)

Instructions: Provide a brief overview of the laboratory work and summarize the laboratory activities to be conducted that are included in the scope of this risk assessment.

Describe the biological agents and other potential hazards (for example, transmission, infectious dose, treatment/preventive measures, pathogenicity).	SARS-CoV-2; • Aerosol transmission, infectious dose unknown, treatment NA, vaccine NA
Describe the laboratory procedures to be used (for example, culturing, centrifugation, work with sharps, waste handling, frequency of performing the laboratory activity).	• Centrifugation • Opening the sample tube cap • Pipetting of low-volume serum sample to microtube (if necessary) • Placing opened sample tube on the analyzer • Analysis • Removing the sample tube from the analyzer • Closing the sample tube cap • Checking the sample tube by scanning the barcode
Describe the types of equipment to be used (personal protective equipment (PPE), centrifuges, autoclaves, biological safety cabinets (BSCs)).	Automatic pipette Centrifuge Autoanalyzer Disposable gloves Lab coat
Describe the type and condition of the facility where work is conducted.	Routine biochemistry laboratory of a secondary healthcare center where COVID-19 cases are also treated. Tests are performed daily.
Describe relevant human factors (for example, competency, training, experience and attitude of personnel).	Patient samples are processed by 8 technicians. Three technicians have been working in the same laboratory for 2 years and the remaining staff for at least 5 years.
Describe any other factors that may affect laboratory operations (for example, legal, cultural, socioeconomic).	Technicians have no experience working with high-risk pathogens with aerosol transmission. Therefore, their awareness of the use of personal protective equipment is inadequate. In general, except for extraordinary situations, the use of personal protective equipment is not given enough attention.

STEP 2. Evaluate the risks

Instructions: Describe how exposure and/or release could occur.

What potential situations are there in which exposure or release could occur?	Aerosols, including SARS-CoV-2, can be generated during the opening and closing of a sample tube cap, pipetting of specimen, placing opened sample tube on the analyzer, analysis (due to pipetting), and checking the sample tube by scanning the barcode.
What is the likelihood of an exposure/release occurring? • Unlikely: not very possible to occur in the near future • Possible: feasible to occur in the near future • Likely: very possible to occur in the near future	Likely
What is the severity of the consequences of an exposure/release (negligible, moderate, severe)?	The consequences of an exposure are severe because to date there is no effective therapy or vaccine for COVID-19.

Instructions: Evaluate the risk and prioritize the implementation of risk control measures. Circle the initial (inherent) risk of the laboratory activities before additional risk control measures have been put in place.

Note:

• When assigning priority, other factors may need to be considered, for example, urgency, feasibility/sustainability of risk control measures, delivery and installation time and training availability.

• To estimate the overall risk, take into consideration the risk ratings for the individual laboratory activities/procedures, separately or collectively as appropriate for the laboratory.

		Likelihood of exposure/release		
		Unlikely	**Possible**	**Likely**
Consequence of exposure/release	Severe	Medium	High	Very high
	Moderate	Low	Medium	High
	Negligible	Very low	Low	Medium
Laboratory activity/procedure		Initial risk (very low, low, medium, high, very high)	Is the initial risk above the tolerance level? (yes/no)	Priority (high/medium /low)
Opening or closing the sample tube cap		S x U=Medium	No	Low
Pipetting of specimen		S x L=Very high	Yes	High
Placing opened sample tube on the analyzer		S x U=Medium	No	Low
Analysis		S x P=High	Yes	High
Removing the sample tube from the analyzer		S x U=Medium	No	Low
Checking the sample tube by scanning the barcode		S x U=Medium	No	Low
Select the overall initial risk.		☐ Very low ☐ Low	☐ Medium ☐ High	☑ Very high
Should work proceed without additional risk control measures?		☐ Yes ☑ No		

STEP 3. Develop a risk control strategy	
Instructions: List any requirements that have been prescribed by international and national regulations, legislation, guidelines, policies and strategies on biosafety and biosecurity.	
Describe the measures required by national legislation or regulations (if any).	-
Describe the measures advised by guidelines, policies and strategies (if any).	It is advised that laboratory procedures that can generate aerosols are to be done in a biological safety cabinet in the World Health Organization document, "Laboratory biosafety guidance related to the novel coronavirus (2019-nCoV)."

Instructions: Describe the resources available for risk control and consider their applicability, availability and sustainability in the local context including management support.	
Are resources sufficient to secure and maintain potential risk control measures?	There is no class IIA biological safety cabinet available in our laboratory for relocation of aerosol-generating steps.
What factors exist that may limit or restrict any of the risk control measures?	-
Will work be able to proceed without any of the risk control measures; are there alternatives?	Work cannot proceed without risk control measures.

STEP 4. Select and implement risk control measures

Instructions: Describe where and when risk control measures are needed, the level of residual (remaining) risk when these risk control measures are in place, and an assessment of the availability, effectiveness and sustainability of the risk control measures.

Laboratory activity/procedure	Selected risk control measure(s)	Residual risk (very low, low, medium, high, very high)	Is the residual risk above the tolerance level? (yes/no)	Are risk control measures available, effective and sustainable? (yes/no)
Opening or closing the sample tube cap	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes
Pipetting of specimen	Discontinued	-	No	-
Placing opened sample tube on the analyzer	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes
Analysis	Analyzer lid closed. Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes
Removing the sample tube from the analyzer	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes
Checking the sample tube by scanning the barcode	Discontinued	-	No	-

Instructions: Evaluate the residual risk that remains after risk control measures have been selected to determine if that level of risk is now below the tolerance level and whether work should proceed.

Circle the residual risk of the laboratory activities after risk control measures are in place.

		Likelihood of exposure/release		
		Unlikely	**Possible**	**Likely**
Consequence of exposure/release	Severe	Medium	High	Very high
	Moderate	Low	Medium	High
	Negligible	Very low	Low	Medium
Overall residual risk:		☐ Very low ☐ Low	☑ Medium ☐ High	☐ Very high

If the residual risk is still above the risk tolerance level, further action is necessary such as additional risk control measures, based on the initial risk evaluated in STEP 2, redefining the scope of work such that it falls below the risk tolerance level with existing risk control measures in place or identifying an alternative laboratory with appropriate risk control strategies already in place that is capable of conducting the work as planned.

Should work proceed with selected risk control measures?	☑ Yes ☐ No
Approved by (Name and title)	Dr. Nergiz Zorbozan/Specialist of Medical Biochemistry
Approved by (Signature)	
Date	March 11, 2020

Instructions: Describe how to communicate risks and risk mitigation strategies to personnel. Provide a mechanism of communication within the laboratory. Describe the process and timeline for ensuring that all identified risk control measures are purchased, have associated SOPs and training has been completed before starting the laboratory work.	
Communication of the hazards, risks and risk control measures	Training for laboratory personnel on risks and risk-mitigation strategies was arranged.
Purchase (and budgeting) of risk control measures	-
Operational and maintenance procedures	The transfer of low-volume serum samples to microtube was suspended.
Training of personnel	Training on the revised operational procedures was planned.

STEP 5. Review risks and risk control measures

Instructions: Establish a periodic review cycle to identify: changes in laboratory activities, biological agents, personnel, equipment or facilities; changes in knowledge of biological agents or processes; and lessons learnt from audits/inspections, personnel feedback, incidents and/or near misses.	
Frequency of the review	Every 6 months or upon significant change
Person to conduct the review	Dr. Nergiz Zorbozan/Specialist of Medical Biochemistry
Describe updates/changes	Risks will be reviewed when the COVID-19 conditions in our region have changed.
Personnel/procedures to implement the changes	Lab. Tech. Hakan Acay
Reviewed by (Name and title)	
Reviewed by (Signature)	
Date	

Annex 2. World Health Organization risk assessment tool used for urinalysis.

Risk Assessment Template

Although a qualitative approach to combining likelihood and severity parameters in a risk matrix is provided as a risk evaluation method here, it is important to note that quantitative (for example, simple numerical scoring schemes to complex mathematical models) and hybrid (semi-quantitative) methods can also be used for risk evaluation. Laboratories should use a risk evaluation/assessment method that best meets their unique needs, without excluding the possibility of developing customized evaluation approaches, scoring methods and definitions of the parameters.

While this template was primarily developed for biosafety risk assessment, it can also be used for general safety risk assessment of laboratory activities, especially when the biosafety and general safety risks are interlinked, for example, sample collection and transport, where appropriate and applicable.

Institution/Facility name	Kemalpasa State Hospital
Laboratory name	Clinical Biochemistry Laboratory
Laboratory manager/Supervisor	Dr. Nergiz Zorbozan/Specialist of Medical Biochemistry
Project titles/Relevant standard operating procedures (SOPs)	Urine test strip analysis
	Manual microscopic urinalysis
Date	March 11, 2020

STEP 1. Gather information (hazard identification)

Instructions: Provide a brief overview of the laboratory work and summarize the laboratory activities to be conducted that are included in the scope of this risk assessment.

Describe the biological agents and other potential hazards (for example, transmission, infectious dose, treatment/preventive measures, pathogenicity).	SARS-CoV-2; • Transmission by aerosols, infectious dose unknown, treatment NA, vaccine NA
Describe the laboratory procedures to be used (for example, culturing, centrifugation, work with sharps, waste handling, frequency of performing the laboratory activity).	**Urine test strip analysis** • Opening the tube cap • Immersing the urine strip into the sample tube • Removing the strip from the sample tube **Manual microscopic urinalysis** • Opening the tube cap • Transferring urine sample to conical centrifuge tube • Centrifugation • Removing ultrafiltrate • Pipetting the precipitate onto the slide surface
Describe the types of equipment to be used (personal protective equipment (PPE), centrifuges, autoclaves, biological safety cabinets (BSCs)).	Automatic pipette Centrifuge Disposable gloves Lab coat Microscope Strip analyzer
Describe the type and condition of the facility where work is conducted.	Routine clinical biochemistry laboratory of a secondary healthcare center where COVID-19 cases are also treated. Tests are performed daily.
Describe relevant human factors (for example, competency, training, experience and attitude of personnel).	Patient samples are processed by 8 technicians. Three technicians have been working in the laboratory for 2 years and the remainder for at least 5 years.
Describe any other factors that may affect laboratory operations (for example, legal, cultural, socioeconomic).	Technicians have no experience working with high-risk, aerosol-transmissible pathogens. Therefore, their awareness of the use of personal protective equipment is inadequate. In general, except for extraordinary situations, the use of personal protective equipment is not given enough attention.

STEP 2. Evaluate the risks

Instructions: Describe how exposure and/or release could occur.

What potential situations are there in which exposure or release could occur?	Aerosols, including SARS-CoV-2, can be generated during opening the tube cap, immersing the urine strip into the sample tube, removing the strip from the sample tube, transferring the urine sample to the conical centrifuge tube, opening the tube cap, removing the ultrafiltrate, pipetting the precipitate onto the slide surface, microscopic examination, discarding the urine samples.
What is the likelihood of an exposure/release occurring? • Unlikely: not very possible to occur in the near future • Possible: feasible to occur in the near future • Likely: very possible to occur in the near future	Likely
What is the severity of the consequences of an exposure/release (negligible, moderate, severe)?	The consequences of an exposure are severe because there is currently no effective therapy or vaccine for COVID-19.

Instructions: Evaluate the risk and prioritize the implementation of risk control measures. Circle the initial (inherent) risk of the laboratory activities before additional risk control measures have been put in place.

Note:

• When assigning priority, other factors may need to be considered, for example, urgency, feasibility/sustainability of risk control measures, delivery and installation time and training availability.

• To estimate the overall risk, take into consideration the risk ratings for the individual laboratory activities/procedures, separately or collectively as appropriate for the laboratory.

		Likelihood of exposure/release		
		Unlikely	**Possible**	**Likely**
Consequence of exposure/release	Severe	Medium	High	Very high
	Moderate	Low	Medium	High
	Negligible	Very low	Low	Medium
Laboratory activity/procedure		Initial risk (very low, low, medium, high, very high)	Is the initial risk above the tolerance level? (yes/no)	Priority (high/medium /low)
Immersing the urine strip into the sample tube, removing the strip from the sample tube		S x U=Medium	No	Low
Transferring the urine sample to the conical centrifuge tube (pipetting)		S x L=Very high	Yes	High
Opening the tube cap		S x U=Medium	No	Low
Pipetting		S x L=Very high	Yes	High
Removing ultrafiltrate		S x L=Very high	Yes	High
Pipetting the precipitate onto the slide surface		S x L=Very high	Yes	High
Microscopic examination of stained slides		S x P=High	Yes	High
Discarding the urine samples		S x U=Medium	No	Low
Select the overall initial risk.		☐ Very low ☐ Low	☐ Medium ☐ High	☑ Very high
Should work proceed without additional risk control measures?		☐ Yes ☑ No		

STEP 3. Develop a risk control strategy

Instructions: List any requirements that have been prescribed by international and national regulations, legislation, guidelines, policies and strategies on biosafety and biosecurity.

Describe the measures required by national legislation or regulations (if any).	-
Describe the measures advised by guidelines, policies and strategies (if any).	The World Health Organization document, "Laboratory biosafety guidance related to the novel coronavirus (2019-nCoV)" advises that aerosol-generating laboratory procedures are to be performed in a biological safety cabinet.

Instructions: Describe the resources available for risk control and consider their applicability, availability and sustainability in the local context including management support.

Are resources sufficient to secure and maintain potential risk control measures?	We have no class IIA biological safety cabinet available in our biochemistry laboratory for relocation of aerosol-generating steps.
What factors exist that may limit or restrict any of the risk control measures?	-
Will work be able to proceed without any of the risk control measures; are there alternatives?	Work cannot proceed without risk control measures.

STEP 4. Select and implement risk control measures

Instructions: Describe where and when risk control measures are needed, the level of residual (remaining) risk when these risk control measures are in place, and an assessment of the availability, effectiveness and sustainability of the risk control measures.

Laboratory activity/procedure	**Selected risk control measure(s)**	**Residual risk (very low, low, medium, high, very high)**	**Is the residual risk above the tolerance level? (yes/no)**	**Are risk control measures available, effective and sustainable? (yes/no)**
Immersing the urine strip into sample tube, removing the strip from the sample tube	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes
Transferring the urine sample to a conical centrifuge tube (pipetting)	Discontinued	-	No	-
Opening the tube cap	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes
Pipetting	Discontinued	-	No	-
Removing ultrafiltrate	Discontinued	-	No	-
Pipetting the precipitate onto the slide surface	Discontinued	-	No	-
Microscopic examination of stained slides	Discontinued	-	No	-
Discarding the urine samples	Surgical mask, surgical cap, laboratory glasses, disposable lab coat	S x U=Medium	No	Yes

Instructions: Evaluate the residual risk that remains after risk control measures have been selected to determine if that level of risk is now below the tolerance level and whether work should proceed.

Circle the residual risk of the laboratory activities after risk control measures are in place.

		Likelihood of exposure/release				
		Unlikely		**Possible**		**Likely**
Consequence of exposure/release	Severe	Medium		High		Very high
	Moderate	Low		Medium		High
	Negligible	Very low		Low		Medium
Overall residual risk:		☐ Very low	☐ Low	☑ Medium	☐ High	☐ Very high

If the residual risk is still above the risk tolerance level, further action is necessary such as additional risk control measures, based on the initial risk evaluated in STEP 2, redefining the scope of work such that it falls below the risk tolerance level with existing risk control measures in place or identifying an alternative laboratory with appropriate risk control strategies already in place that is capable of conducting the work as planned.

Should work proceed with selected risk control measures?	☑ Yes ☐ No
Approved by (Name and title)	Dr. Nergiz Zorbozan/Specialist of Medical Biochemistry
Approved by (Signature)	
Date	March 11, 2020

Instructions: Describe how to communicate risks and risk mitigation strategies to personnel. Provide a mechanism of communication within the laboratory. Describe the process and timeline for ensuring that all identified risk control measures are purchased, have associated SOPs and training has been completed before starting the laboratory work.

Communication of the hazards, risks and risk control measures	Training for laboratory personnel on risks and risk-mitigation strategies was planned.
Purchase (and budgeting) of risk control measures	-
Operational and maintenance procedures	Fresh microscopic examination was discontinued.
Training of personnel	Training for the laboratory technicians on the revised operational procedures was arranged.

STEP 5. Review risks and risk control measures

Instructions: Establish a periodic review cycle to identify: changes in laboratory activities, biological agents, personnel, equipment or facilities; changes in knowledge of biological agents or processes; and lessons learnt from audits/inspections, personnel feedback, incidents and/or near misses.

Frequency of the review	Every 6 months or upon significant change.
Person to conduct the review	Dr. Nergiz Zorbozan/Specialist of Medical Biochemistry
Describe updates/changes	Risks will be reviewed when the COVID-19 conditions in our region have changed.
Personnel/procedures to implement the changes	Lab. Tech. Hakan Acay
Reviewed by (Name and title)	
Reviewed by (Signature)	
Date	