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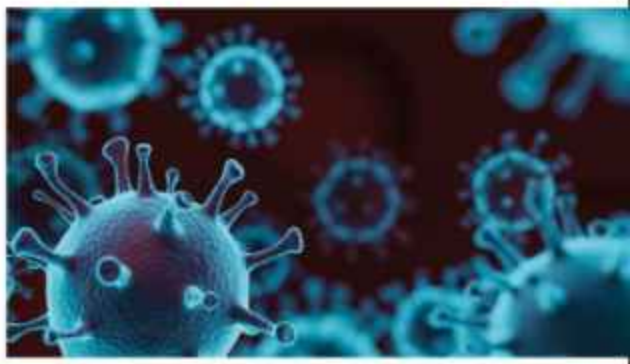

A COLLABORATIVE RESEARCH PROJECT ON "CONTROL OF TUBERCULOSIS AND GLANDERS"

The progress and future activities of the project in NCCD

B.Buyankhishig, *MD, PhD, Local PI of the project,*
Consultant of National Reference TB Laboratory, NCCD

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Project Output 1:

The function of laboratory diagnosis for zoonotic diseases is enhanced in Mongolia through the development of LAMP /immunochromatography-based novel rapid diagnostic methods (kits) for detecting *M.bovis and B.Mallei* as well as updating existing disease diagnostic systems.

The plan outlines 10 activities in NCCD to Outcome 1:

- Ongoing – 3
- Delayed implementation – 1
- The activity is planned to be implemented in later year -6

Progress of Activities for Output 1:

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1.6. Updating of the diagnostic flow for tuberculosis including detection of *M. bovis* as well as of the methods for detecting drug-resistant *M. tuberculosis* in NCCD.

- ✓ Requests for lab.reagents and equipment for the conventional detection method of *M. bovis* were submitted to the JICA in Mongolia (1.6.1).
- ✓ Orders were placed in the first quarter of 2021 and will be delivered in the first quarter of 2022 (1.6.2)

Stop TB Partnership
GLOBAL DRUG FACILITY

Global Drug Facility
Chemin du Pommier 40
1218 Le Grand-Saconnex, Geneva, Switzerland

QUOTE
GDF Order Number: MNG/IH/21/11400
Project / Activity Number: 11295-014-99

Quote Date: 14 May 2021
Quote Expiry (*): 12 August 2021
Contact: Andres, Mr Cedric
Cedrica@stoptb.org

Client institution:
East Plaza, 5th Floor, 39th building, 15th khoroo, Peace Avenue, Bayanzurkh District,
Ulaanbaatar, Mongolia
Ulaanbaatar
Mongolia

Client institution contact:
Likhamsuren Jantasan
likhamaa@aids.mn

Dispatched to:
Tuberculose Surveillance and Research
National Center for Communicable Diseases
Namyanju Street
, Ulaanbaatar
Bayanzurk District
Mongolia

Dispatch to contact:
Dr Danjaad Enkhmandakh
NTP Manager
976-11-451169
enkhmandakh_0625@yahoo.com

Product Code	Product Name	Quantity	Units	Unit Price (USD)	Total Price (USD)	Supplier / Manufacturer	Volume (m3 (*))	Weight Kg (*)	Delivery requirement
106585	Moxifloxacin - lyophilized drug for laboratory use	4	Box(es) of 6	90.000	360.00	BD Europe	0.002	0.64	Cool cargo (+2-8°C)
106313	Ofloxacin 10 g - for laboratory use	4	Box(es) of 1	295.150	1,180.60	TTM	0.002	1.60	Cool cargo (+2-8°C)
106315	Protionamid 2 g - for laboratory use	4	Box(es) of 1	165.900	663.60	TTM	0.002	1.60	Cool cargo (+2-8°C)
106316	Ethionamide 5 g - for laboratory use	3	Box(es) of 1	135.200	405.60	TTM	0.001	1.20	Cool cargo (+2-8°C)
106653	Linezolid 25 g - for laboratory use	4	Box(es) of 1	516.950	2,067.80	TTM	0.002	1.60	Cool cargo (+2-8°C)
106560	Levofloxacin 1 g - for laboratory use	4	Box(es) of 1	43.750	175.00	TTM	0.002	1.20	General cargo
106654	Clofazimine 1 g - for laboratory use	4	Box(es) of 1	111.300	445.20	TTM	0.002	1.20	General cargo
			Totals:	**USD**	**5,297.80**		**0.012**	**9.04**	

Progress of Activities for Output 1:

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1.6. Updating of the diagnostic flow for tuberculosis including detection of M.bovis as well as of the methods for detecting drug-resistant M.tuberculosis in NCCD.

In framework updating of the diagnostic flow for tuberculosis as well as of the methods for detecting drug-resistant *M. tuberculosis*:

- The GeneXpert MTB/RIF testing is used at the frontline of TB diagnosis.
- At national level, 41 TB laboratories are provided the equipment by the government policy

GeneXpert MTB/RIF machine based on real-time PCR for the detection of *M. tuberculosis* complex, *but not identified subspecies including M. bovis*

Progress of Activities for Output 1:

NATIONAL CENTER FOR COMMUNICABLE DISEASES

1.6. Updating of the diagnostic flow for tuberculosis including detection of *M. bovis* as well as of the methods for detecting drug-resistant *M. tuberculosis* in NCCD.

- ✓ As part of the TB care service, 197 *M. tuberculosis* were isolated from a sample of 2004 suspected extra-pulmonary TB in a liquid medium from November 2020 to October 2021. *M. bovis* can be identified in further (1.6.1).

Progress of Activities for Output 1:

NATIONAL CENTER FOR COMMUNICABLE DISEASES

1.6. Updating of the diagnostic flow for tuberculosis including detection of *M. bovis* as well as of the methods for detecting drug-resistant *M. tuberculosis* in NCCD.

- ✓ Determining next-generation genome sequencing (NGS), 2 pieces Oxford Nanopore's MinION Sequencing Device and with MinION mk1b MinION Flow Cell received on August 9, 2021 at the NCCD TB Reference Laboratory (1.6.3).
- ✓ SOP for the performance of WGS has been prepared.
- ✓ Laboratory procedure for Deeplex Myc-TB is in progress in RIT.

Progress of Activities for Output 1:

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1.6. Updating of the diagnostic flow for tuberculosis including detection of *M. bovis* as well as of the methods for detecting drug-resistant *M. tuberculosis* in NCCD.

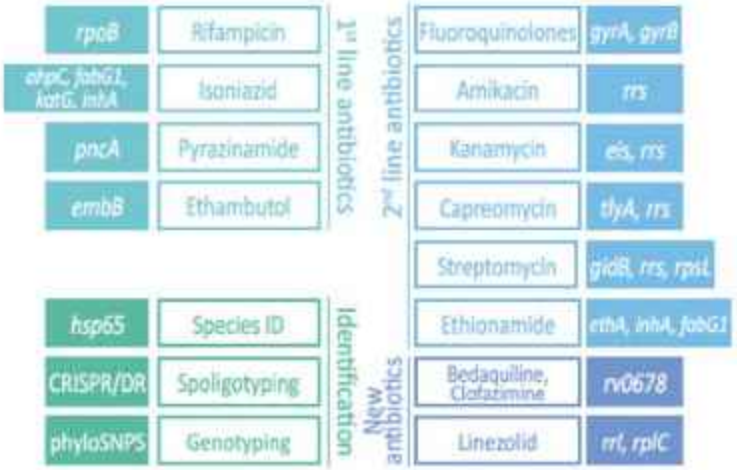

Figure 3. Genes or genes regions amplified and sequenced via the Deeplex® Myc-TB assay.

Deeplex Myc-TB
Amplicon deep sequencing directly from clinical specimen

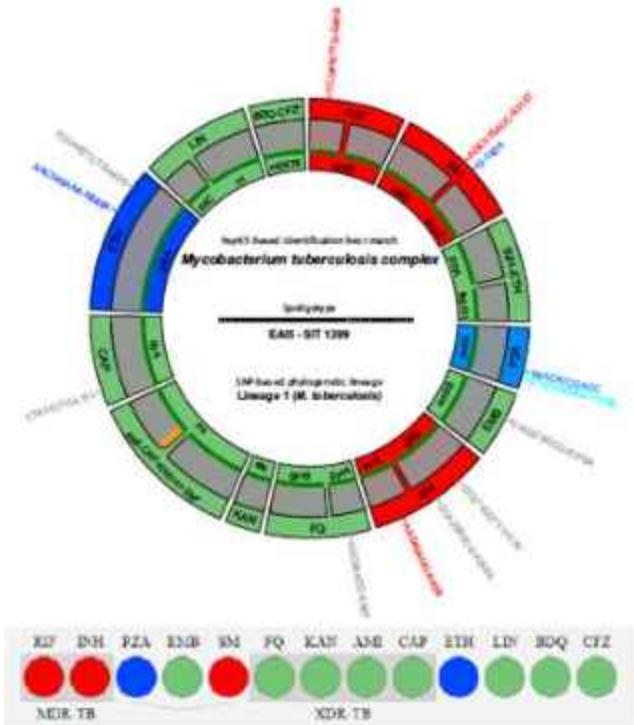

Figure 1. **The Deeplex® web app** (Top) **Deeplex® map** showing mutations associated (red) or unassociated (or synonym, grey) with antibiotic resistance of MTBC along with yet-to-be characterized mutations (blue). Information on mycobacterial identification is shown in the center of the map. (Bottom) **Resistotype** of an identified MTBC strain showing its predicted resistance pattern to 13 anti-tuberculosis drugs/drug classes.

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Project Output 2:

The epidemics of tuberculosis and glanders as zoonotic diseases in human are evaluated using molecular epidemiological techniques.

The plan outlines 8 activities in NCCD to Outcome 2:

- Ongoing – 2
- The activity is planned to be implemented in later -6

Progress of Activities for Output 2:

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2.1 Molecular-epidemiological evaluation of the epidemics of *M. bovis* Infection in human.

- ✓ Received QuantiFERON TB Gold Plus tube and QuantiFERON TB Gold Plus to detect latent TB infection. The training will be followed by a comparative assessment of conventional and new methods.
- ✓ The activity is planned to be implemented in 2022–2023 ***(2.1.3)***

Progress of Activities for Output 2:

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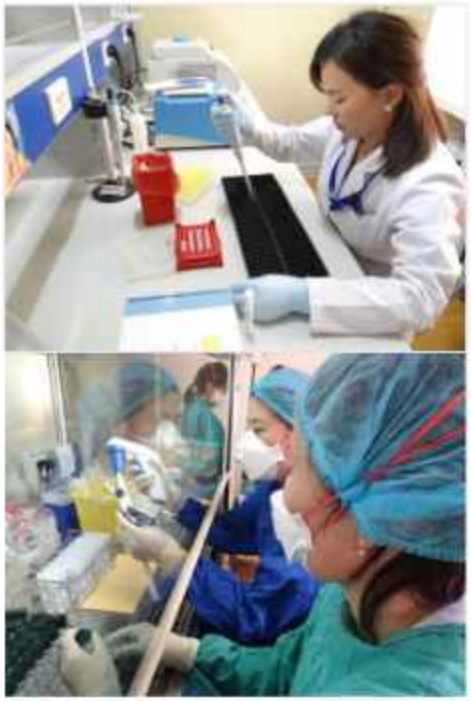
2.2 Molecular-epidemiological evaluation of the emergence of drug-resistant (multidrug-resistant) *M. tuberculosis* in human

- ✓ DST is performed by molecular and conventional methods in direct samples and isolated strains
- ✓ A total of 1,028 people were tested for DST by molecular methods (LPA and Xpert MTB/RIF), of which 85.0% were susceptible, 9.0% were RIF resistant, and 14.8% were resistant to isoniazid.
- ✓ In the first 9 months of 2021, 110 people were tested DST for MGIT and solid medium, with a susceptible of 72.7% and any resistance of 28.2%. ***(2.2.1)***



Progress of Activities for Output 2:

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2.5 Epidemiological evaluation of the epidemics of *B. mallei* Infection in human

- ✓ Project meetings are being held between the institutes. An agreement is being drafted to exchange information, samples, and to share the laboratory in the study. Currently, researchers are working to share experiences ***(2.5.1).***

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Project Output 3:

The epidemics of tuberculosis and glanders as zoonotic diseases in livestock are evaluated using seroepidemiological and molecular epidemiological/ seroepidemiological techniques, respectively.

No planned activities at NCCD

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Project Output 4:

A platform for One-Health approach-based infectious disease control is functioning for the practical application of research outcomes including risk analyses of tuberculosis and glanders as zoonotic diseases.

The plan outlines 3 activities in NCCD to Outcome 4:

- Ongoing – 1
- The activity is planned to be implemented in later year - 2

Progress of Activities for Output 4:

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4.2. Risk assessment of *M. bovis* infection as a zoonotic disease

- ✓ The risk assessment protocol is developing for assessment in two types. The first design is in a retrospective type and the second is done in the prospective. In retrospective study, we will use the results of molecular epidemiological studies in isolated cultures of TB prevalence survey. Prospective study we will use referral specimens of extrapulmonary suspect TB will be evaluated using L-J medium with sodium pyruvate and L-J with glycerol and MGIT.
- ✓ We are working to complete the risk assessment protocol by the end of this year.
- ✓ The activity is planned to be implemented in 2022–2023.

Progress of Activities for Output 4:

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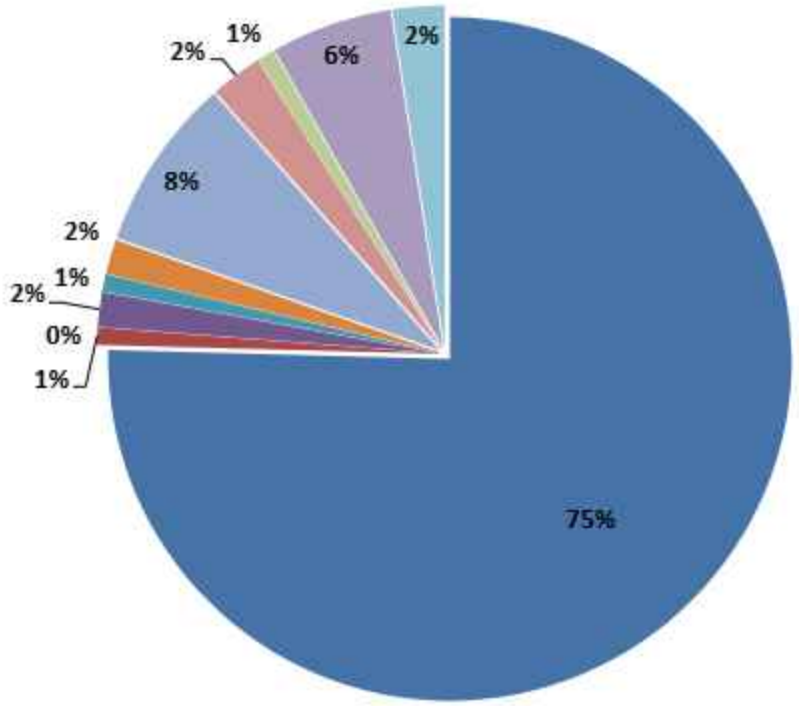
4.2. Risk assessment of *M. bovis* infection as a zoonotic disease

- ✓ Retrospective risk assessment of *M. bovis* infection in the community.
- ✓ WGS analysis of TB prevalence survey isolates (2014).
- ✓ No isolation of animal lineage (n=122).



- lineage2 East-Asian Beijing RD105lineage2.2 East-Asian (Beijing) Beijing-RD207 RD105;RD207lineage2.2.1 East-Asian (Beijing) Beijing-RD181 RD105;RD207;RD181
- lineage2 East-Asian Beijing RD105lineage2.2.1 East-Asian (Beijing) Beijing-RD181 RD105;RD207;RD181lineage4 Euro-American LAM;T;S;X;H Nonelineage4.9 Euro-American (H37Rv-like) T1 None
- lineage2 East-Asian Beijing RD105lineage4.3 Euro-American (LAM) mainly-LAM Nonelineage4.3.3 Euro-American (LAM) LAM;T RD115
- lineage4 Euro-American LAM;T;S;X;H None
- lineage4 Euro-American LAM;T;S;X;H Nonelineage4.1 Euro-American T;X;H Nonelineage4.1.2 Euro-American (X-type) T;H Nonelineage4.1.2.1 Euro-American (X-type) T1;H1 RD182
- lineage4 Euro-American LAM;T;S;X;H Nonelineage4.2 Euro-American H;T;LAM Nonelineage4.2.1 Euro-American (TUR) H3;H4 None
- lineage4 Euro-American LAM;T;S;X;H Nonelineage4.3 Euro-American (LAM) mainly-LAM Nonelineage4.3.3 Euro-American (LAM) LAM;T RD115
- lineage4 Euro-American LAM;T;S;X;H Nonelineage4.5 Euro-American H;T RD122
- lineage4 Euro-American LAM;T;S;X;H Nonelineage4.7 Euro-American (mainly T) T1;T5 None
- lineage4 Euro-American LAM;T;S;X;H Nonelineage4.8 Euro-American (mainly T) T1;T2;T3;T5 RD219

Progress of Activities for Output 4:

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4.3. Risk assessment of *B. mallei* infection as a zoonotic disease

- ✓ Due to the SARS-CoV-2 pandemic, NCCD TB specialists were mobilized for COVID-19 pandemic response. We are working to complete the risk assessment protocol by the end of this year.

Progress of Activities for Output 4:

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4.5. To hold symposiums and/or joint seminars on project collaborative research at least once a year.

- ✓ Two technical committee meetings - 2 times(October 21' 2020 and August 29' 2021)
- ✓ Scientific Zoom meetings -5 times (Dates: 4th Aug 2020: 10th Sept 2020: 20th May 2021: 28th June 2021:13th Aug., 2021)
- ✓ The inter-institute research team meetings -3 times
- ✓ Brief introduction of SATREPS project at the 2nd International Conference on "SEEKING WAYS TO ELIMINATE TUBERCULOSIS IN ASIA" in 2019.

Achievements of Output

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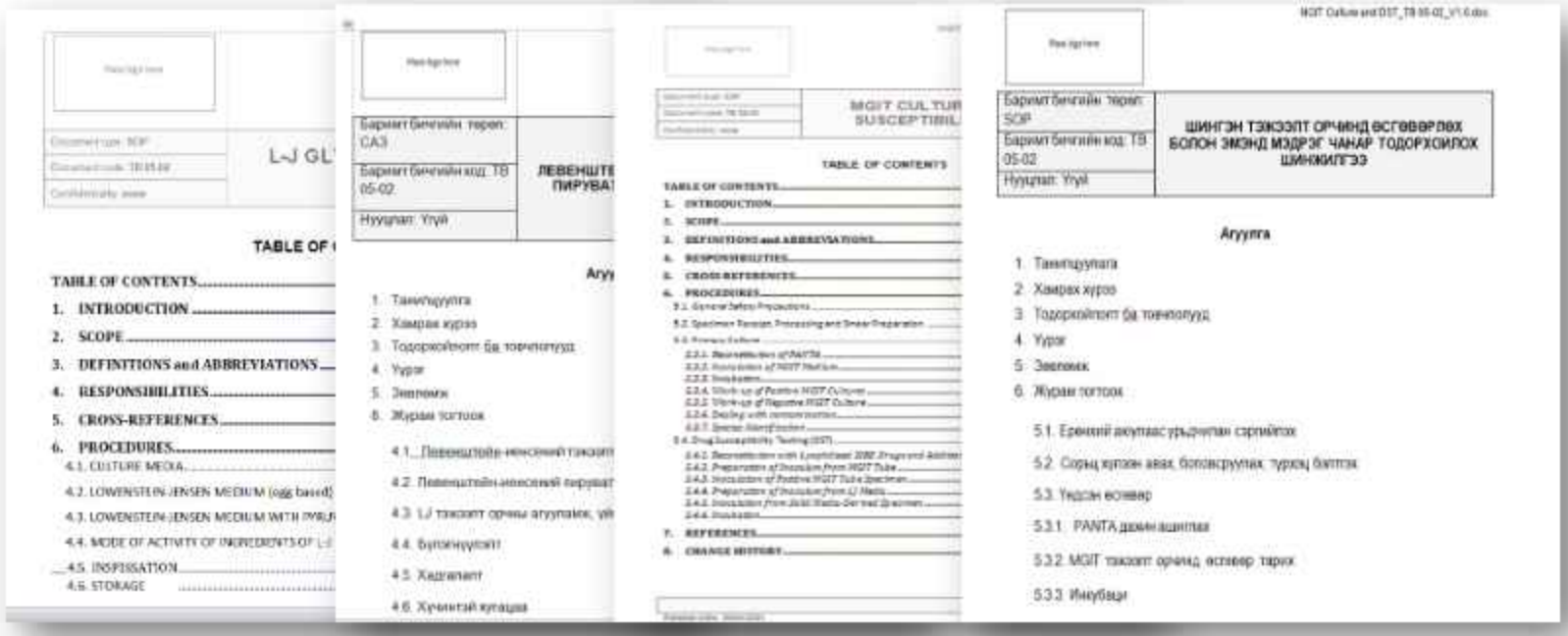
Output 1.

1. Other products (i.e. SOP, protocol, guideline)
   - SOP for Culture examination has been prepared by English and Mongolian.



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1. INTRODUCTION
2. SCOPE
3. DEFINITIONS and ABBREVIATIONS
4. RESPONSIBILITIES
5. CROSS-REFERENCES
6. PROCEDURES

Баримт бичгийн төрөл: SOP

Баримт бичгийн код: ТВ 05-02

Нууцлал: Үгүй

ШИНГЭН ТЭЖЭЭЛТ ОРЧИНД ӨСГӨВӨРЛӨХ БОЛОН ЭМЭНД МЭДРЭГ ЧАНАР ТОДОРХОЙЛОХ ШИНЖИЛГЭЭ

Агуулга

1. Танилцуулга
2. Хамрах хүрээ
3. Тодорхойлолт ба товчилуулт
4. Үүрэг
5. Зэвлэмж
6. Журам тогтоох

5.1. Ерөнхий анхаарах урьдчилан сэргийлэх

5.2. Сорьц хүлээн авах, боловсруулах, түүвэр бэлтгэх

5.3. Үндсэн ажиллагаа

5.3.1. PANTA давин ашиглах

5.3.2. MGIT тэжээлт орчинд өсгөвөр тариа

5.3.3. Инкубаци

Achievements of Output

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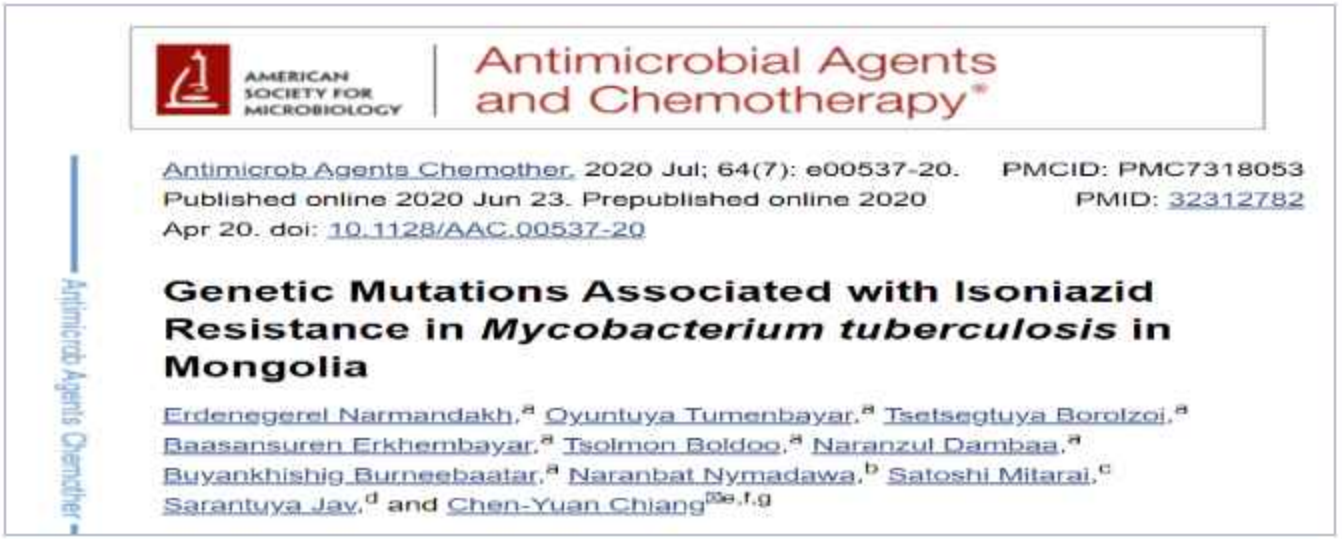
Output 2.

1. Published paper
   - Narmandakh E, Tumenbayar O, Borolzoi T, Erkhembayar B, Bold T, Dambaa N, Burneebaatar B, Nyamdavaa N, Mitarai S, Jav S, Chiang CY. Genetic mutations associated with isoniazid resistance in Mycobacterium tuberculosis in Mongolia. Antimicrobial Agent Chemother 2020 Apr 20. pii: AAC.00537-20. doi: 10.1128/AAC.00537-20.



AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

Antimicrob Agents Chemother. 2020 Jul; 64(7): e00537-20. PMCID: PMC7318053
Published online 2020 Jun 23. Prepublished online 2020 Apr 20. doi: 10.1128/AAC.00537-20 PMID: 32312782

Genetic Mutations Associated with Isoniazid Resistance in *Mycobacterium tuberculosis* in Mongolia

Erdenegerel Narmandakh,[a] Oyuntuya Tumenbayar,[a] Tsetsegtuya Borolzoi,[a] Baasansuren Erkhembayar,[a] Tsolmon Boldoo,[a] Naranzul Dambaa,[a] Buyankhishig Burneebaatar,[a] Naranbat Nymadawa,[b] Satoshi Mitarai,[c] Sarantuya Jav,[d] and Chen-Yuan Chiang[5e,f,g]

Antimicrob Agents Chemother

Achievements of Output

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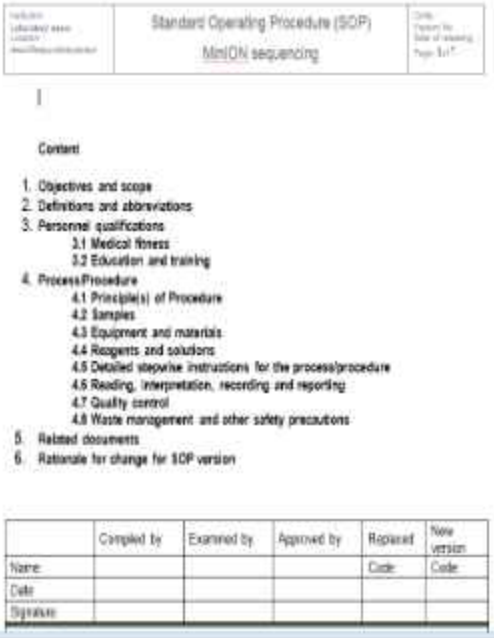
Output 2.

2. Other products (i.e. SOP, protocol, and guideline)
   - SOP for whole genome sequence has been prepared by English and Mongolian.

NGS SOP (English)



Standard Operating Procedure (SOP)

MinION sequencing

Content

1. Objectives and scope
2. Definitions and abbreviations
3. Personnel qualifications
   - 3.1 Medical fitness
   - 3.2 Education and training
4. Process/Procedure
   - 4.1 Principle(s) of Procedure
   - 4.2 Samples
   - 4.3 Equipment and materials
   - 4.4 Reagents and solutions
   - 4.5 Detailed stepwise instructions for the process/procedure
   - 4.6 Reading, interpretation, recording and reporting
   - 4.7 Quality control
   - 4.8 Waste management and other safety precautions
5. Related documents
6. Rationale for change for SOP version

	Compiled by	Examined by	Approved by	Replaced	New version
Name:				Code:	Code:
Date:					
Signature:					

NGS SOP (Mongolian)

Агуулга

1. Зорилго, хамрах хүрээ
2. Тодорхойлолт болон товчилсон үг
3. Боловсон хүчний чадвар
   - 3.1 Эрүүл мэндийн байдал
   - 3.2 Боловсрол, сургалт
4. Арга/журам
   - 4.1 Шинжилгээний явцын үндсэн зарчим
   - 4.2 Сорьц
   - 4.3 Шаардлагатай тоног төхөөрөмж, материал
   - 4.4 Шаардлагатай урвалж бодис
   - 4.5 Шинжилгээний аргын нарийвчилсан зааварчилгаа
   - 4.6 Үр дүнг унших, тайлбарлах, бүртгэх, мэдээлэх
   - 4.7 Чанарын хяналт
   - 4.8 Орчны болон аюулгүй байдлын хяналт
5. Холбогдох бичиг баримт
6. Стандарт өөрчлөлтийн үндэслэл өөрчлөлт оруулах үндэслэл

	Боловсруулсан	Шалгасан	Батлагсан	Өөрчлөлт оруулсан	Шинэ хувилбар
Нэр				Код	Код
Огноо					
Гарын үсэг					

Delay of Work schedules

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Detail	Cause and Problems (Due to the influence of COVID 19)
Expert (Project coordinator, Consultants)	**Logistics between country and intercountry** Delays: • Project coordinator appointment and placement • External expert visit • Laboratory supplies and placement • Training coverage of researchers **Human resource mobilization and overwork**
Equipment supply	
All training	
Project some activities are not implemented on planned time ***(1.5)***	

Delay of Work schedules

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Detail	Action to be taken
Expert (Project coordinator, Consultants)	**Placement of appointed project coordinator**
Equipment supply	**Procurement lab. supplies**
All training	**Conduct training** (Bacteriology, Immunology, Epidemiology, Pathology, Molecular Biology, Bioinformatics and other necessary specialized area)
Project some activities are not implemented on planned time ***(1.5)***	**Replaning of the Project operation plan**

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Thank you for your attention