“CONTROL OF TUBERCULOSIS AND GLANDERS” SATREPS PROJECT

Progress report of NCCD
Period: Dec. 2022-Dec. 2023

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behalf of NCCD research team of the project

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1. Strengthening of Laboratory capacity building including supply equipment and reagents and training
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Strengthening of Laboratory capacity building including supply equipment and reagents and training

Strengthening of Laboratory capacity building: Supply equipment and reagents in 2023

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Total in 2021-2023
1018.3 mln ₮

Name of equipment, reagent, and kits	Quanti ty	Total amount /mln tugrug/
Biosafety centrifuge set	1	36.6
ELISA reader and washer	1/1	37.9
GridiON and kits	1	40.3
GridiON kits	1	252.8
Nanodrop	1	34.4
Laptop	1	4.7
PC and monitor	1/2	10.6
Deep freezer -20	1	6.9
Deep freezer -80	1	72.0
Autoclave	1	27.4
Tools(comptips, PCR tube, Тог баригч APC)	1	8.4 сая
Genotype MTBC and CM and AS	47	39.5
Capilia TB neo	2130	21.95
DMSO	2	3.960
MGIT suplement kits	18	32.16
Total		**612.1 mln₮**

Strengthening of Laboratory capacity building: Overseas trainings of NCCD staff

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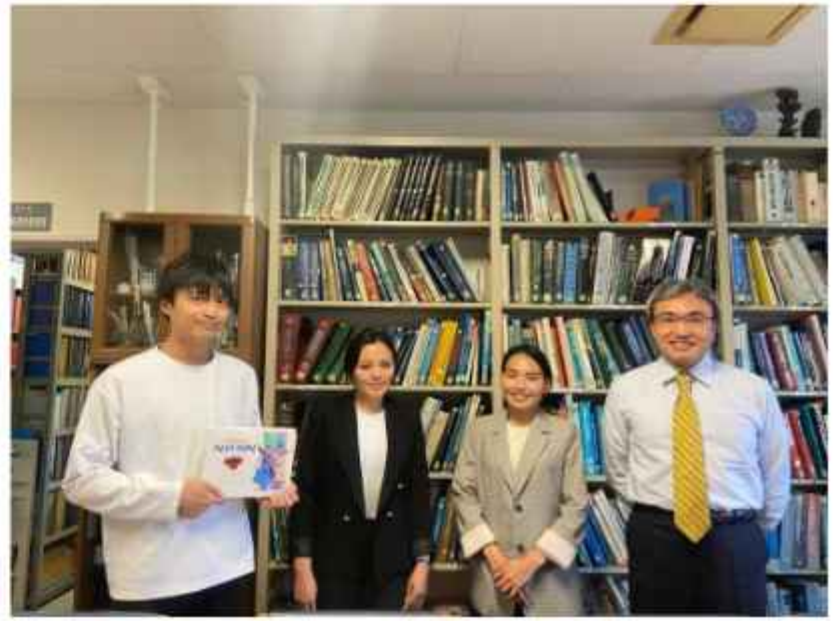
Training	Num of person	Place	When
NGS training for 1 month	2	RIT, Japan	Aug.2022 June.2023
Bioinformatics training for a month	2	RIT,Japan	Oct . 2023
IGRA training for 2 weeks	2	RIT, Japan	Aug 5-17 2023
LAMP training	2	Hokaido university, Japan	Nov 2023



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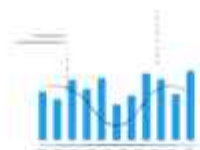
Introduction of new technologies and progress of research activities



Introduction new technologies of the SATREPS project

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National Reference TB Laboratory of NCCD introduced:

1. LAMP method for *M.tuberculosis* and *M.bovis* detection
2. Solid culture with pyruvate medium for *M.bovis* detection
3. Next generation sequencing (NGS)
4. IGRA test (QIAreach QFT and QFT plus)
5. Determination on novel anti-tuberculosis drugs resistances using MGIT DST (Bdq, Dlm, Lzd, Mfx)

Implementation of Operational plan (OP) of the SATREPS project

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*OP 1.2. **Establishment of the LAMP-based gene detection method for M.tuberculosis complex in NCCD.***

Inputs	Year / Month	2023 Jan-Mar	2023 Apr-Jun	2023 Jul-Sep	2023 Oct-Dec	2024 Jan-Mar	2024 Apr-Jun	2024 Jul-Sep	2024 Oct-Dec
1.2.1. To introduce the LAMP-based gene detection method for tuberculosis complex into NCCD.	Plan								
	Revised plan								
	Actual								
1.2.2. To evaluate the sensitivity and specificity of the gene detection method by comparing the test results obtained from conventional methods.	Plan								
	Revised plan								
	Actual								

OP 1.2.1 Detection of MTB complex and *M.bovis* by LAMP method (1)

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OP 1.2.1. To introduce the LAMP-based gene detection method for tuberculosis complex into NCCD.

№	Samples/ isolated strains	n	*M.Tuberculosis*	*M.bovis*
1	Isolations on solid and MGIT culture	20	20	0
2	LJ with pyrubate (+), LJ gl (-)	13	13	0
3	Xpert MTB positive and negative samples	16	2	0
	Total	49	35 /100%	0 (0%)

All strains were *M. tuberculosis* Among 49 clinical samples, 33 were successfully cultured on solid media (20 LJ with glycerol and MGIT however 13 LJ with pyruvate), and they were all positive for *M. tuberculosis* by *M.tuberculosis* kit of LAMP. **No detected *M.bovis*** by *M. bovis* kit of LAMP

M.tuberculosis detected

Implementation of Operational plan (OP) of the SATREPS project

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OP 1.2.1. 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.

Inputs	Year	2023				2024			
	Month	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec
1.6.1.To introduce the methods for isolating tuberculosis complex from human sputum specimens by culturing them with liquid medium (MGIT) as well as solid (L-J) media for M. tuberculosis and M. bovis in NCCD, in conformity to the WHO-recommended methods.	Plan								
	Revised plan								
	Actual								
1.6.2. To introduce the MGIT-based drug susceptibility test mehod for secondline and new anti-tuberculosis drugs, according to the WHO recommendation.	Plan								
	Revised plan								
	Actual								
1.6.3. To introduce the techniques of whole genome sequencing of tuberculosis complex using the next-generation sequencer into NCCD.	Plan								
	Revised plan								
	Actual								

OP 1.6.1 Solid culture with pyruvate medium (2)

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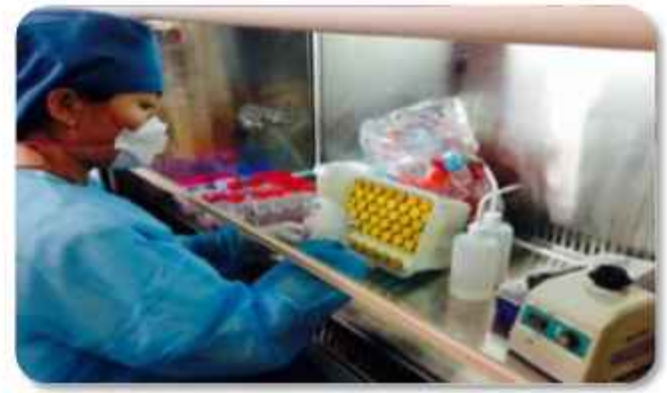
OP 1.6.1.To introduce the methods for isolating tuberculosis complex from human sputum specimens by culturing them with liquid medium (MGIT) as well as solid (L-J) media for M. tuberculosis and M. bovis in NCCD, in conformity to the WHO-recommended methods.

Timeline	Number of clinical samples (by person)	Positivity rate of MTBC
Jul-Dec 2022	787	76(9.7%)
Jan-Oct 2023	3197	435(13.6%)
Total	3984	511(12.8%)



OP 1.6.1 Identification test results of Genotype MTBC

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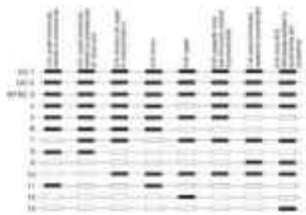
OP 1.6.1.To introduce the methods for isolating tuberculosis complex from human sputum specimens by culturing them with liquid medium (MGIT) as well as solid (L-J) media for M. tuberculosis and M. bovis in NCCD, in conformity to the WHO-recommended methods.

Total ***201*** isolated strains in 2022-2023 We tested by Genotype MTBC kit in Oct.2023

Results:

- *M.tuberculosis* was 99% (199/201) and 1% (2/201) MTBC negative
- This 2 strains we tested by Genotype Mycobacterium CM than determined NTM (*M.intracellulare*)
- ***M.bovis* not detected**

MTBC results	Isolations in2022		Isolations in 2023		Total	
	#	%	#	%	#	%
M.tuberculosis	70	100	129	98.5	**199**	99.0
Negative	0	0	2	1.5	**2**	1.0
Total	70	100	131	100	**201**	100



Previously, we tested 200 isolated strains by Genotype MTBC in March of 2022

No detected M.bovis

Total 401 isolations tested by Genotype MTBC in 2022-2023

OP.1.6.2 Determination of new anti- TB drugs (Bdq, Dlm, Lzd, Mfx) **by MGIT DST (4)**

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- A total of 90 patients were included in the study. Of these, 60.0% (54/90) were men, 40.0% (36/90) were women

- Based on the results of resistance to the new drug among the study participants: 86.7**%** (78/90) were found to be **Sensitive, 13.3%** (12/90) were identified as **Resistant.**“

- Of the 12 MFX resistant isolate culture, 100% were found to be resistant to the fluoroquinoline by Genotype MTBDR*sl* assay.

OP.1.6.3 and 1.6.4 NGS study (3)

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- *NGS for genome DNA (**n=372**)*
- *Data analysis for Tbprofilier and MTBseq*
- *M.tuberculosis (**99.7%**) and BCG La.1.2 (**0.3%**)*
- *Beijing genotype (Lineage 2) is widely distributed in all regions of Mongolia.* The isolates were mainly composed of lineage 2 (289, 77.7%), especially East-Asian Beijing
- *75* (20.2%) of lineage 4 (Euro-American LAM and
- Others 2.1% including 1 La1.2.BCG
- There were no mutations or resistance identified in novel anti-tuberculosis drugs, such as Bdq, Dlm, Lzd, Mfx.

QFT study of the results by QIAReach and ELISA (5)

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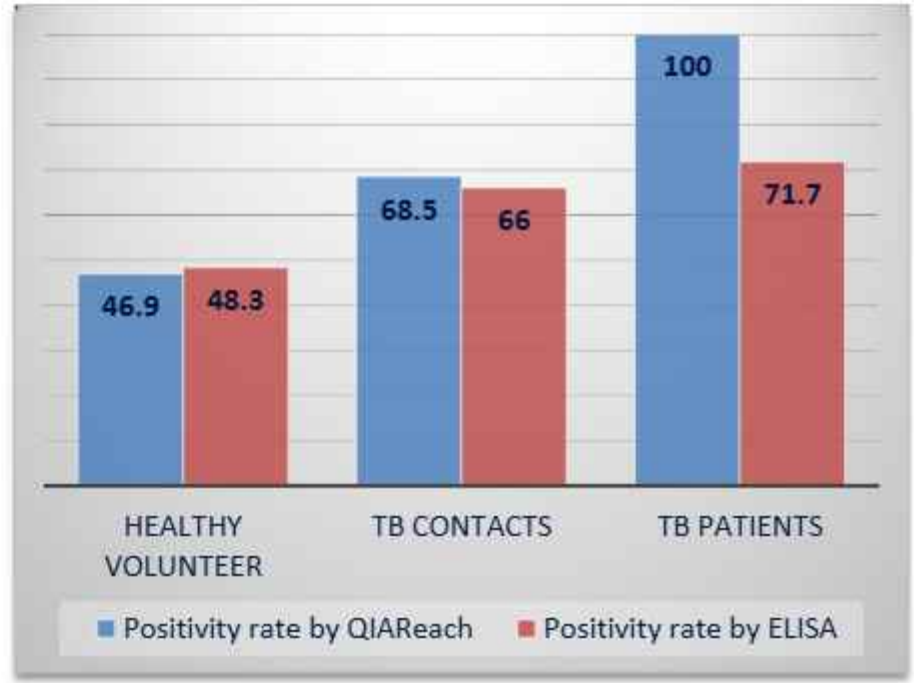
Preliminary results of the study

Subject	Tested samples	QFT by QIAReach	Positive % / n	QFT by ELISA	Positive % / n
Total (sample size 600)	**416 (69.3%)**	**363**	**57.3% (208/363)**	**190**	**59.5% (113/190)**
Healthy volunteer	196	196	**46.9%** (92/196)	87	**48.3%** (42/87)
TB contacts	162	162	**68.5** (111/163)	50	**66.0%** (33/50)
Tb patients	58	5	100% (5/5)	53	71.7% (38/55)



Implementation of Operational plan of the SATREPS project

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OP 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.

Inputs	Year	2023				2024			
	Month	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec
1.6.4. To establish a test method for comprehensively detecting drug-resistance-related genetic mutations for anti-microbial resistance (AMR) predictions using the next-generation sequencer (e.g., MinION) in NCCD.	Plan								
	Revised plan								
	Actual								
1.6.5. To revise or newly develop SOPs of the diagnostic flow for tuberculosis in human including the detection of *M. bovis* as well as for the detection of drug-resistant *M. tuberculosis*.	Plan								
	Revised plan								
	Actual								

OP. 1.6.5 Approved new guideline of TB care services

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МОНГОЛ УЛСЫН
ЭРҮҮЛ МЭНДИЙН САЙДЫН
ТУШААЛ

2024 оны 01 сарын 29 өдөр Дугаар А/38 Улаанбаатар хот

"Сүрьеэгийн тусламж үйлчилгээ үзүүлэх журам, заавар батлах тухай"

Монгол Улсын Засгийн газрын тухай хуулийн 24 дүгээр зүйлийн 2 дахь хэсэг, Эрүүл мэндийн тухай хуулийн 8 дугаар зүйлийн 8.1.1, 8.1.3, 8.1.4, 8.1.5, 8.1.24 дэх заалт, 35 дугаар зүйлийн 35.1 дэх хэсгийг тус тус үндэслэн ТУШААХ НЬ:

1. "Сүрьеэгийн тусламж, үйлчилгээг зохион байгуулах журам"-ыг нэгдүгээр, "Сүрьеэгийн халдвараас сэргийлэх, хянах журам"-ыг хоёрдугаар, "Сүрьеэгийн идэвхтэй илрүүлэлтийг зохион байгуулах журам"-ыг гуравдугаар, "Сүрьеэгийн тусламж, үйлчилгээний бүртгэл мэдээлэл, хяналт-шинжилгээ, үнэлгээний журам"-ыг дөрөвдүгээр, "Сүрьеэгийн дэгдэлтийг тандах, хянах, хариу арга хэмжээг зохион байгуулах журам"-ыг тавдугаар, "Сүрьеэтэй өвчтөний эмнилгээний асуудлыг шийдвэрлэх эмч нарын зөвлөгөөний журам"-ыг зургаадугаар, "Сүрьеэгийн эм бэлдмэл, урвалж бодис, халдварын сэргийлэлт, хяналтын хэрэглэлийн хангах нийлүүлэлтийн журам"-ыг долоодугаар, "Сүрьеэгийн илрүүлэлт, оношилгоо, эмчилгээний эмнэлзүйн заавар"-ыг наймдугаар, "Бүртгэлийн маягтууд"-ыг есдүгээр хавсралтаар тус тус батлалсугай.

2. Тушаалын хэрэгжилтийг улсын хэмжээнд зохион байгуулж, мэргэжил арга зүйн дэмжлэгээр хангаж, сүрьеэгийн тусламж үйлчилгээг сайжруулахыг Халдварт өвчин судлалын үндэсний төв (Ж.Байгалмаа)-д, харьяа эрүүл мэндийн байгууллагуудыг нэгдсэн удирдлагаар хангаж, хяналт тавьж ажиллахыг аймаг, нийслэлийн Эрүүл мэндийн газрын даргад нэрт, батлагдсан журам, зааврыг хэрэгжүүлж ажиллахыг бүх шатны эрүүл мэндийн байгууллагын даргад, зөвлөмж нэрт тус тус даалгасугай.

3. Тушаалын хэрэгжилтэд хяналт тавьж ажиллахыг Нийтийн эрүүл мэндийн газар (Д.Баярболд)-т үүрэг болгосугай.

4. Энэхүү тушаал батлагдсантай холбогдуулан Эрүүл мэндийн сайдын 2021 оны А/30 дугаар тушаалыг хүчингүй болсонд тооцсугай.

САЙД Ч.ЭНХЗОРИГ

- Attachment 8: Case finding and diagnosis and treatment guidelines
- 1.7.8 In laboratory examination included:
- LAMP
- IGRA test
- MGIT DST of novel drugs

OP. 4.2 Risk assessment progress for bovine tuberculosis (Mycobacterium bovis) infection

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In the framework of Objective 1:

- An assessment was made of the policy and legal framework for the control and surveillance of livestock infectious diseases, including bovine tuberculosis, in our country.
- The evaluation included **26 legal documents** related to animal infectious diseases.

In the framework of Objective 3

- In order to assess the risk of *M.bovis* transmission of tuberculosis to the at risk population, a questionnaire was collected from a total of **238 herdsman** in 9 provinces and 5 districts of Ulaanbaatar city.

Problems and action

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Problem

- **A delay in the information regarding human contact with B. mallei in horses.**
- **Lack of Specimen referral**

(To collect the biological samples (sputum and/or throat swab) obtained from patients with human infectious pneumonitis for whom no causative agent has been identified in the NCCD, followed by transferring them to IVM.)

- **PDM implementation**

Although the first results of these implementations are available, it is not yet possible to report them .Despite extended changes to the operational plan, the performance of the matrix remains the same as the previous one.

- **Lack of budget for research and assessment from government** (onsite visit for surveillance)

Action response

- ✓ Actively engaging with the legal framework surrounding data transmission, the GAVs can transmit information to the NCCD.
- ✓ Taking prompt action and following established protocols for disease surveillance and control.
- ✓ To collect blood from the herdsmen and their related persons who raise B. mallei-infected horses by providing information on the herdsmen who raise B. mallei-infected horses owned by organizations such as GAVS to NCCD.
- ✓ To Make some changes to the PDM due to the covid situation and the revised operational plan of the project
- ✓ Request to delay extension 6 months in the execution of PDM
- ✓ Provide the opportunity to conduct surveillance in rural areas in cooperation with the IVM by meeting the expenses of the research

Example of problem: Information sharing between IVM and NCCD related to *B.mallei* infection

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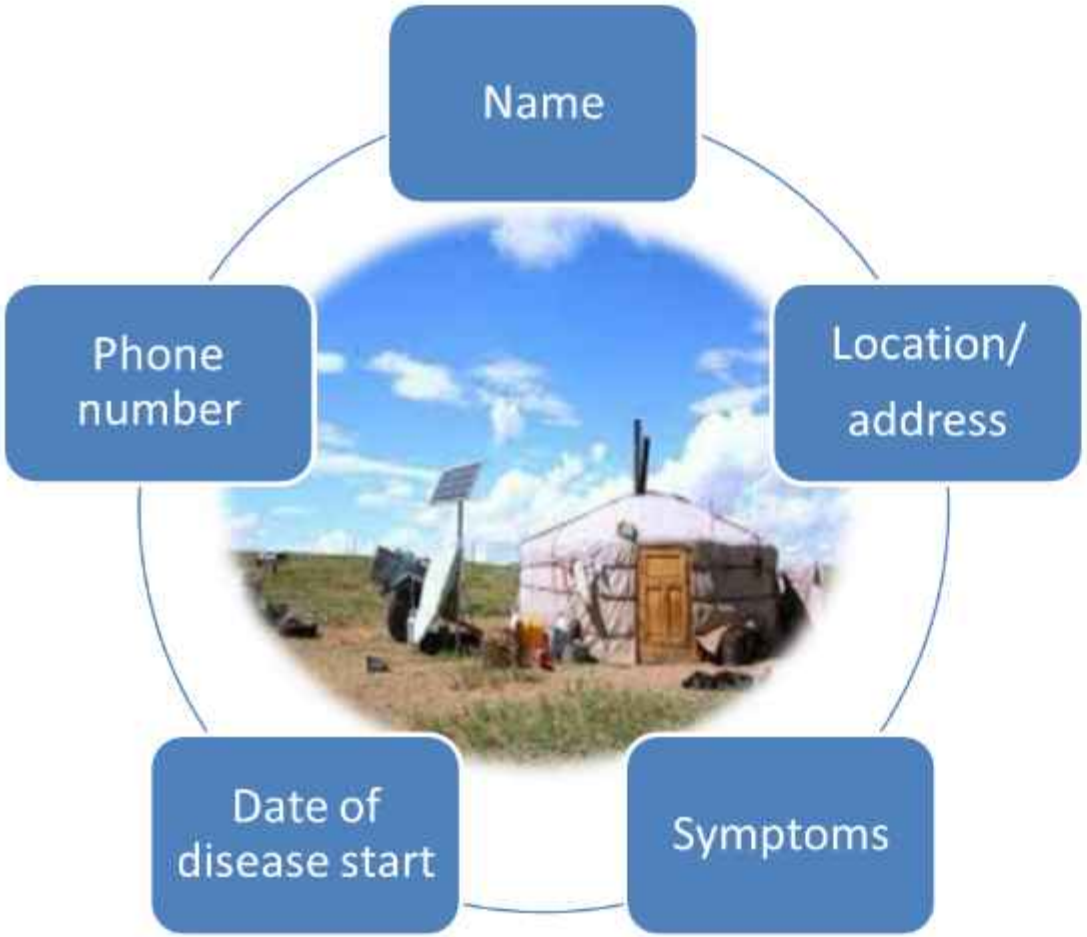

Information sheet from IVM to NCCD on 16th Jan 2024

Date of Disease start	Duration	Location / Address	Name	Phone #
May 2018	55 month	UB KHUD	O.	NA
July 2019	41 month	Khentii Bayankhutag	B	Available
March 2022	21 month	UB KHUD	No name	No
Oct. 2022	14 month	Tuv Sergelen	T.G	Available
Jan. 2023 (Nov. 2022)	12 month	UB KHUD	U.T	NA

PDM implementation

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Problem: *Although the first results of these implementations are available, it is not yet possible to report them.*

Outcome 1.The epidemics of tuberculosis and glanders as zoonotic diseases in human are evaluated using molecular epidemiological techniques.

- ☐ 2-1. By January 2024, the prevalence of *M. bovis* infection in human tuberculosis is estimated.
- ☐ 2-2. By January 2024, the evaluation work of the epidemic situation of drug-resistant (multidrug-resistant) *M. tuberculosis* in human using molecular epidemiological techniques is completed.
- ☐ 2-4. By February 2024, the presence (or absence) of a case of *B. mallei* infection in human is evaluated using molecular-epidemiological techniques.

Activities in future

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- To intensify the project implementation, evaluation of research results, and concern the project outcomes and PDM implementation
- To assess the potential presence of B. mallei, equine glanders, and bovine tuberculosis in the herder community, the IVM and NCCD should effectively conduct surveillance, sample collection, and testing
- To disseminate to domestic and foreign audiences are important for highlighting the project's impact and outcomes.

Acknowledgements

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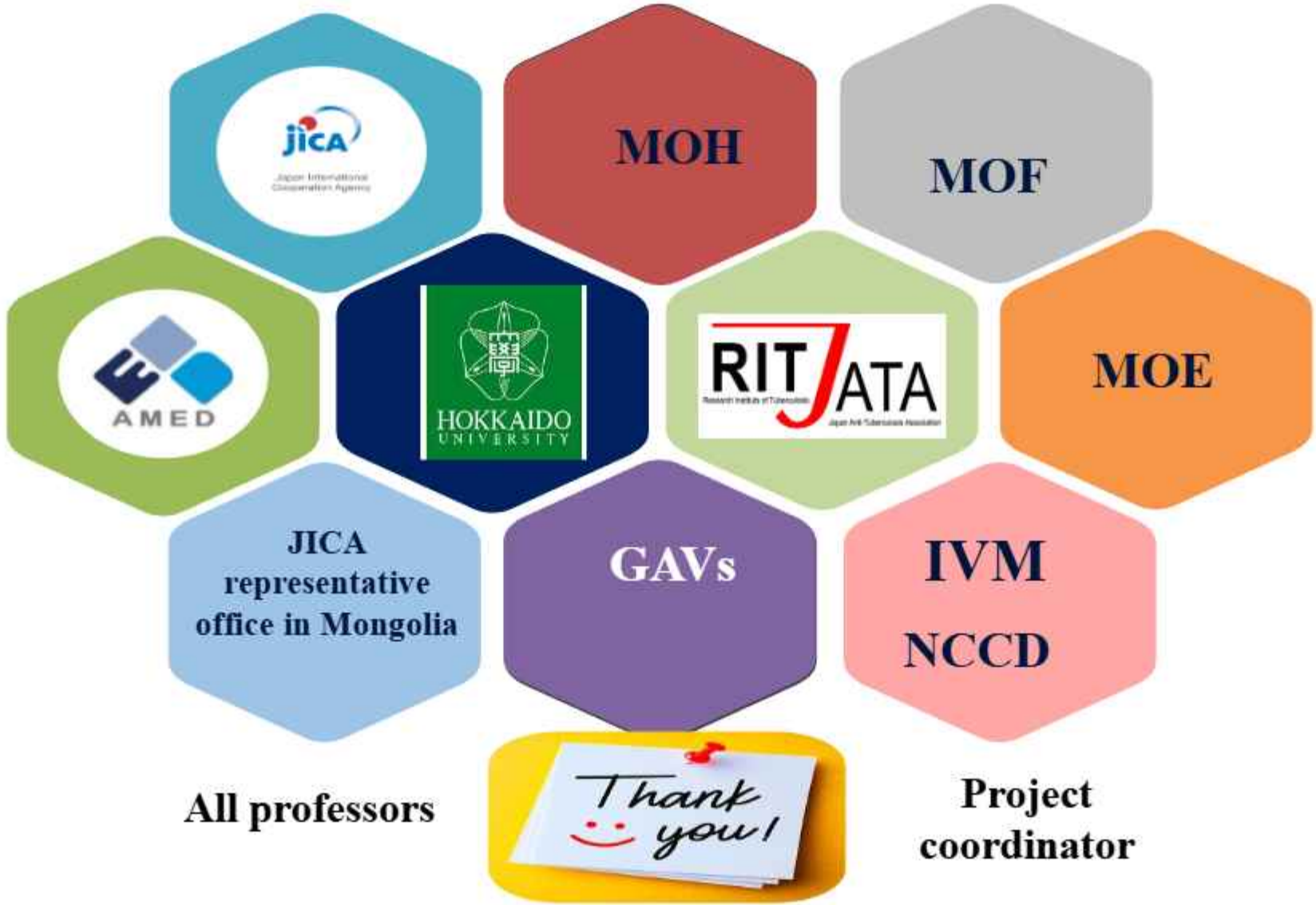

Thank you for your attention