

CASE STUDY

Laboratory core capacities to be improved in two countries of Central Asia through addressing national sample referral mechanisms

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ABSTRACT

The International Health Regulations (IHR) (2005) require countries to strengthen national laboratory core capacities for surveillance and the detection of emerging pathogens and outbreaks, requiring sample referral between laboratories at different levels of tiered systems.

An overview of the existing laboratory systems in both Kyrgyzstan and Tajikistan was prepared and laboratory sample referrals were assessed. Key gaps and opportunities for improvement in existing sample referral mechanisms are addressed here, thus identifying measures to strengthen laboratory systems.

In both countries, three laboratory systems (the State Sanitary and Epidemiology Surveillance, HIV and tuberculosis laboratories) have three-tiered laboratory systems, while the clinical diagnostic laboratories have two-tiered systems. The tuberculosis and HIV laboratory networks have well established testing and referral algorithms, in line with the levels of the laboratories. Private laboratories have also set up well established mechanisms for sample referral.

However, in the clinical diagnostic laboratories the sample referral rates are the lowest across both countries.

In order to improve these sample referral mechanisms, clear roles and responsibilities and the tests/methods at the different levels of the laboratory systems must be clearly defined. Once the systems are well defined, comprehensive sample referral mechanisms can be designed and implemented.

Through the Better Labs for Better Health initiative, national guidelines for the transport of all types of laboratory samples are being finalized and standard operating procedures and training material for all staff involved will soon be developed.

Countries can benefit from the pilot studies that are being carried out by the HIV and tuberculosis laboratory systems and from private systems' experiences. Ideally, national laboratory working groups should reinforce coordination of all laboratory activities and advocate for integration of sample collections and transport from all laboratory systems, where possible.

Keywords: LABORATORY, SAMPLE REFERRAL, LABORATORY SYSTEMS, CENTRAL ASIA, INTERNATIONAL HEALTH REGULATIONS (IHR) (2005)

BACKGROUND

The International Health Regulations (IHR) (2005) (1) require countries to strengthen national core capacities to detect, assess, notify and report events, and to respond to acute public health events, including public health emergencies of international concern. Laboratories are an essential component of any country's early warning capacity, by supporting both surveillance and detection of emerging pathogens and outbreaks. This front-line role has been emphasized in the detection and control of recent epidemics and pandemics, including severe acute respiratory syndrome (SARS) (2), the 2009 H1N1 influenza pandemic (3), Ebola (4), and Zika virus (5).

In 2008, the Maputo Declaration called for the strengthening of laboratory systems in order to create one unified integrated tiered national laboratory network with defined tests at each level (6). In the same year the joint World Health Organization (WHO) and Centers for Disease Control (CDC), Atlanta conference on laboratory quality systems recommended the development of a national organization within the national health plan that should be responsive to the needs of patients and all users of the service. Emphasis was also placed on the need for laboratory quality management systems (7).

A laboratory system is a set of laboratories united by laboratory disciplines and organized through tiered levels, operating in a connected and dependent way according to their level. One of the main uses of a national laboratory system is to obtain more precise laboratory tests, which implies that district (rayon) laboratories refer samples to regional (oblast) or national reference laboratories for confirmatory and/or specialized testing. Consequently, a key indicator of a functional laboratory system is whether both sample referral within the system and sample transport are effective. This capacity to refer samples to perform correct testing is also essential to evaluate a country's capacity to detect and respond to emergencies.

CONTEXT

In several countries in the WHO European Region, laboratory services lack national coordination, oversight and standards. As a result, services are often fragmented, functions are duplicated, many laboratories operate under insufficient quality and safety levels, and staff are often trained using outdated curricula (8). For these reasons, in 2012 the WHO Regional Office for Europe launched the Better Labs for Better Health initiative in four countries to help them strengthen their national laboratory systems. The first step was to support countries in the

development of their national laboratory policies and strategic plans by establishing formally recognized national laboratory working groups (NLWG) (9).

The ministries of health in Kyrgyzstan and Tajikistan have endorsed a national policy and/or strategic plan for their countries, which has allowed the Better Labs for Better Health initiative to address the core cross-cutting elements of laboratory health addressed in these plans, amongst which are the organization of national laboratory systems and specimen referral mechanisms (9).

The subject of this paper addresses key gaps and opportunities for improvement in existing sample referral mechanisms, thus identifying measures to strengthen laboratory systems in order for countries to better detect, assess, notify and report events, and to respond to emergencies.

METHODOLOGY

In order to have an overview of the existing laboratory systems in each country, qualitative analyses of the laboratory system structures under the respective ministries of health were performed in 2017 through interviews with relevant staff of the Ministry and the NLWG, assisted by an international laboratory expert in Kyrgyzstan and Tajikistan. The analyses led to the drafting of the Ministry of Health's laboratory component's organigrams, which were presented in both country reports.

From April to August 2017, members of the NLWGs, supported by an international laboratory expert, developed a checklist to obtain a detailed situational analysis of existing sample referrals in tiered laboratory systems in Tajikistan and Kyrgyzstan. The heads of various laboratory networks (the HIV and tuberculosis (TB) laboratories; the Republic Center of Quarantine and Especially Dangerous Infections (RCQEDI); the State Sanitary and Epidemiology Surveillance (SSES) laboratories within SSES Stations; SSES parasitology laboratories; virology laboratories; bacteriology and hygiene laboratories; clinical diagnostic laboratories and laboratories from the private sector were interviewed by the NLWG members. RCQEDI and the SSES hygiene laboratories were only assessed in Kyrgyzstan.

Reports describing the evaluation outcomes and gaps were prepared for both countries and discussed by the NLWGs from both Tajikistan and Kyrgyzstan during a workshop. Discussions covered the need to develop national guidelines for sample referral and transport, as well as future national action plans on the subject.

So-called grey literature on national laboratory capacity assessments was also reviewed (for example reports from international conferences, WHO and other organizations' reports, national laboratory policies and strategic plans).

RESULTS

OVERVIEW OF NATIONAL LABORATORY SYSTEMS

Kyrgyzstan and Tajikistan have similar laboratory systems, as illustrated in Fig. 1.

In both countries, there are three three-tiered laboratory systems: the SSES, HIV and TB laboratories. At the national level, one or several national laboratories function as reference laboratories, at each oblast level there is a regional laboratory; and at the rayon level there are district laboratories that fall under the oblast laboratory authority.

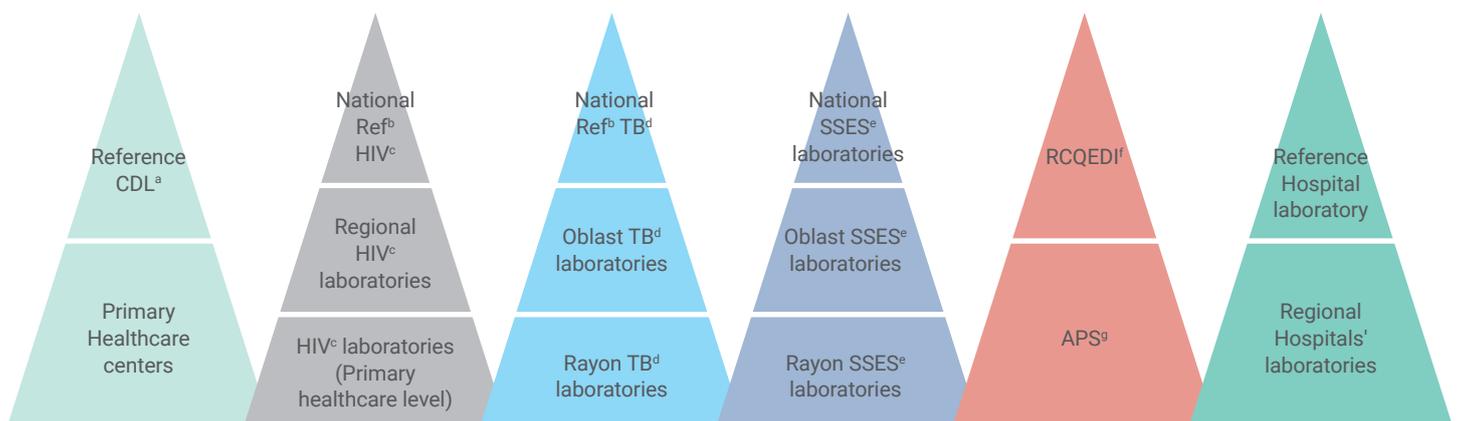
The SSES laboratory system, including all laboratory disciplines, effectively represents a network of around 200 institutions in Tajikistan and 300 in Kyrgyzstan (republican, oblast and rayon) contributing to public health management, and performing tests on human and environmental samples. The HIV laboratory

system represents approximately 40 laboratories in Tajikistan and 50 in Kyrgyzstan. HIV diagnostic laboratories also perform hepatitis diagnosis in these countries. The TB laboratory system represents approximately 90 TB diagnostic laboratories in Tajikistan and 130 in Kyrgyzstan.

For the HIV and SSES laboratories, samples are regularly referred from rayon laboratories to the oblast and national laboratories for specialized analysis and confirmatory testing. Oblast laboratories send samples to national reference laboratories when testing is not available at their level and, more rarely, for confirmatory purposes. For both networks, there are no specific guidelines or schedules for referral, and referral is based on the judgement of the laboratory. For the TB network, testing and referral algorithms are well established according to the levels of the laboratories.

The clinical diagnostic laboratories' systems, represented in Fig. 1 as hospital system and primary health care system, are two-tiered laboratory systems, not three-tiered systems as described above. Clinical diagnostic laboratories are public laboratories mostly based in hospitals, clinics or primary health care centres at oblast and rayon level. Their number is estimated at approximately 565 in Tajikistan and 300 in Kyrgyzstan. This number includes very small laboratories associated with a polyclinic or family health care centre up to large polyvalent laboratories associated

FIG. 1. SCHEMATIC REPRESENTATION OF THE LABORATORY SYSTEMS IN KYRGYZSTAN AND TAJIKISTAN



- ^a CDL: Clinical Diagnostic Laboratory
- ^b Ref: Reference laboratory
- ^c HIV: Human Immunodeficiency Virus laboratories
- ^d TB: Tuberculosis laboratories
- ^e SSES: State Sanitary and Epidemiology Surveillance Laboratories
- ^f RCQEDI: Republic Center of Quarantine and Especially Dangerous Infection laboratories
- ^g APS: Anti-Plague Station

with large hospitals in the main cities. Laboratories without a bacteriology unit at the oblast and big city levels send their samples to the oblast SSES bacteriology laboratories for analysis. There are clinical diagnostic reference laboratories at national level that perform specialized analyses and confirmatory testing.

The RCQEDI is a two-tiered system with a reference laboratory and anti-plague stations referring samples.

In both countries, private laboratories have set up collection points throughout the country and the analyses are performed in a central laboratory in the capital city.

SAMPLE REFERRAL MECHANISMS

Table 1 shows the results of the responses to the checklist that were provided by the heads of the clinical diagnostic, HIV, TB, RCQEDI, SSES parasitology, virology, bacteriology and hygiene laboratory systems, and by those private laboratories that agreed to participate.

For the two countries together, six systems out of nine monitor the quality of samples upon receipt, two systems check acceptance criteria and note the temperature upon receipt of the samples, and one system does not check any criteria. Transport systems between the different laboratories in the networks exist; however, it was reported that many patients nonetheless transport samples to the laboratories by their own means. The clinical diagnostic laboratory system shows few transport mechanisms in place in both countries; consequently, many patients are reported as having to send samples through personal channels, following no biosafety precautions, or by having to travel to the laboratory.

All laboratory systems provide training for laboratory staff in charge of packaging. Three laboratory systems (TB and SSES virology laboratories, and RCQEDI in Kyrgyzstan) provide training to their drivers to raise their awareness of what they are transporting so that they can act appropriately in the event of accidents. Three (the HIV, private and clinical diagnostic laboratories) have not provided training to all drivers across their network, and three (the SSES bacteriology, SSES parasitology and Kyrgyz SSES hygiene laboratories) have not provided any training and have no documents supporting training. It should be noted that the pre-analytical phase for environmental samples does not fall under the responsibility of the SSES hygiene laboratory.

Safe and secure transport, including the use of triple packaging and the traceability of samples, are ensured for HIV and TB sample referrals, especially in pilot regions. Triple packaging is of poorer quality in the cases of RCQEDI and the SSES hygiene laboratory, because of a lack of funding.

None of the laboratory systems provide computerized tracking of samples throughout the referral process, and only some private laboratory systems return the results through electronic reporting platforms such as a laboratory information system or by SMS. In all public laboratory systems, paper-based reports are given to the drivers when new samples are delivered to the reference laboratory. In general, all the laboratories have paper forms that document referred samples, except for the SSES parasitology laboratories, which have no forms or electronic information. Only three laboratory systems (HIV, TB and private) have standard operating procedures (SOPs) in place for sample packaging and transport.

For both countries, guidelines are being prepared and progressively implemented for the referral and transport of samples within the HIV and TB laboratory systems, in which pilot studies are also being carried out. Neither country has national guidelines for the transport of all samples throughout the entire laboratory systems.

For emergency responses, the SSES laboratories and RCQEDI in Kyrgyzstan have plans to refer samples to reference laboratories within the country, but no system has been through any practical emergency exercise.

DISCUSSION

The Better Labs for Better Health initiative has been working to improve laboratory systems by addressing sample referral mechanisms. In both countries, assessments of the existing sample referral mechanisms have shown that patients still either have to find the means of transporting their samples or go to the laboratory by themselves. The referral mechanisms exist, but show many weaknesses in that they are not routine, biosafety measures are not always in place and the quality of the samples is not always monitored.

In order to improve sample referral, organization of the laboratory systems needs to be improved. Clear roles and responsibilities and the tests/methods at the different levels of the laboratory systems for public health and clinical diagnostics must be clearly defined (10). Once the systems are well defined, comprehensive sample referral mechanisms can be designed to cover transport companies, equipment, logistics, results reporting, trained personnel, data management, monitoring and evaluation, budget lines with sufficient financing, and proper governance.

In both countries, the HIV and TB sample referral processes are stronger, because these benefit from global funding against AIDS, TB and malaria. Private laboratories have also shown

TABLE 1. SUMMARY OF RESULTS OF SAMPLE REFERRAL SYSTEMS ASSESSMENTS IN TAJIKISTAN AND KYRGYZSTAN

Activity	State CDL ^a	Private ^b CDL ^a	SSES ^c Virology lab	SSES ^c Parasitology lab	SSES ^c Bacteriology lab	RCQED ^d (KGZ ^e)	SSES ^c Hygiene lab (KGZ ^e)	HIV ^f	TB ^g
Quality of samples is monitored	-/+	++	++	-	-/+	+	+	++	++
Coverage of dependent primary health care units	-/+	++	++	++	++	++	++	++	++
Transport system exists	-/+	++	+	+	+	+	+	++	++
Patients reported to transport samples/ go to lab from remote area	++	+	+	+	+	+	+	+	+
Trained laboratory personnel	+	+	+	+	+	+	+	+	+
Trained drivers	-/+	-/+	+	-	-	+	-	-/+	++
Safe and secure transport packaging	-/+	-/+	-/+	-	-/+	+	+	++	++
Documents (SOPs ^h , sample referral form, etc...)	-/+	++	+	-	-/+	+	+	++	++
Result sent by LIS ⁱ / SMS	-	-/+	-	-	-	-	-	-	-
On-line tracking of samples	-	-	-	-	-	-	-	-	-
Pilot studies	-	-	-	-	-	-	-	+	+
Sample referral guideline	-	-	-	-	-	-	-	-/+	-/+
Preparedness to emergency	-	-	-	-	-	-	-	-	-
Source of financing	State	Private	State	State	State	State	State	GF ^j	GF ^j
++ in place and functional + existing/in place, but not used in regular standard practice +/- in place in reference laboratories only or in a few laboratories - not existing/not in place ^a CDL: Clinical diagnostic laboratories ^b Private: Private laboratory system ^c SSES labs: State Sanitary and Epidemiology Surveillance Laboratories ^d RCQED: Republic Center of Quarantine and Especially Dangerous Infection laboratories ^e HIV: Human Immunodeficiency Virus laboratories ^f KGZ: Evaluated only in Kyrgyzstan ^g TB: Tuberculosis laboratories ^h SOP: Standard operating procedure ⁱ LIS: Laboratory Information System ^j GF: Global Fund against AIDS, tuberculosis and malaria									

that it is possible to establish functional country-wide sample referral. Countries can benefit from the pilot studies that are being carried out by the HIV and TB laboratory systems and from private systems' experiences. Ideally, countries should try and integrate sample collections from all systems and centralize transport to improve cost effectiveness. This comes back to implementing better coordination within and between the laboratory systems within the Ministry of Health.

Developing a national guideline for sample referral of all regular samples was identified as a key improvement. The Better Labs for Better Health initiative therefore organized a joint workshop for Kyrgyzstan and Tajikistan in August 2017 to draft both action plans and guidelines. Nonetheless, numerous documents are still needed including SOPs and work instructions (including policies and procedures for specimen collection, packaging, sample transport, temperature control or cold chain maintenance in transit, specimen and shipment tracking, spill containment and clean-up) as suggested in the best practice for sample management (11). Forms such as referral forms and registers, tracking slips and chain of custody forms, transport logs, and data collection forms for monitoring and evaluation purposes also need to be available.

Plans of action were drafted by both countries to take into account training to reinforce the skills of laboratory staff and drivers, for further work on defining laboratory systems' activities (with tests/methods to be defined for each level of the system), and for implementing a pilot test with full transport logistics for all samples.

The Better Labs for Better Health initiative also plans to develop and implement programmes for the regular training of staff involved in the preparation, transportation and reception of laboratory samples, in order to understand and implement best practices. These programmes should be incorporated into the curriculum and into service training, and certification for sample transport should be introduced.

To prepare their systems for an emergency, countries should perform actual test exercises that involve all relevant staff, including those involved in sample referral.

CONCLUSION

For countries to be able to detect and respond to any potential emergency, they need to have a well-designed and well-managed comprehensive public health specimen referral process in place for any type of specimen at any level of the health system. Such

systems can be substantially strengthened through clarifying the roles, responsibilities and activities of the laboratory systems, elaborating national guidelines, preparing SOPs and providing training for sample referrals.

Since 2012, the WHO Regional Office for Europe has worked with its Member States through the Better Labs for Better Health initiative to establish intersectoral NLWGs, in order to develop national laboratory policies and strategies. The endorsed national strategic plans set the basis for focusing on identified critical components in an intersectoral manner across all laboratory systems, for example the organization of tiered national laboratory systems and sample referral.

National guidelines for the transport of all types of laboratory samples are being finalized and SOPs and training material for all staff involved in sample referral will be developed in the coming year. The two countries have recognized that strengthening laboratory sample referral also requires work to optimize laboratory systems.

Disease-specific programs and private laboratory systems have shown that, with funding, sample referral can be implemented and coordinated. Their inclusion in the further development of national sample referral mechanisms will be beneficial, because it will make their experience and expertise available.

NLWGs have been approved by the respective ministries of health and have a coordinating role. These entities should reinforce coordination of all laboratory activities, as called for by the Maputo declaration (6). The NLWGs should encourage the health ministries to discuss the possibilities of integration of the different laboratory systems.

Acknowledgements: We thank the members of the NLWGs of Kyrgyzstan and Tajikistan for their contribution to this analysis.

Sources of funding: European Commission Directorate General for International Cooperation and Development; United States of America Centers for Disease Control and Prevention; and Deutsche Gesellschaft für Internationale Zusammenarbeit.

Conflicts of interest: None declared.

Disclaimer: The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the World Health Organization.

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