

*Strengthening of STI surveillance in
the Republic of Moldova*

Report on a mission
11-15 March 2013



**World Health
Organization**

REGIONAL OFFICE FOR **Europe**

Strengthening of STI surveillance in the Republic of Moldova

**Report on a mission
11-15 March 2013**

Keywords

SEXUALLY TRANSMITTED DISEASES -
EPIDEMIOLOGY
SEXUALLY TRANSMITTED DISEASES - DIAGNOSIS
SYPHILIS - EPIDEMIOLOGY
SYPHILIS - DIAGNOSIS
GONORRHEA - EPIDEMIOLOGY
GONORRHEA - DIAGNOSIS
HIV INFECTIONS - EPIDEMIOLOGY
HIV INFECTIONS - DIAGNOSIS
SENTINEL SURVEILLANCE
REPUBLIC OF MOLDOVA

Address requests about publications of the WHO Regional Office for Europe to:

Publications
WHO Regional Office for Europe
UN City, Marmorvej 51
DK-2100 Copenhagen Ø, Denmark

Alternatively, complete an online request form for documentation, health information, or for permission to quote or translate, on the Regional Office web site (<http://www.euro.who.int/pubrequest>).

© **World Health Organization 2013**

All rights reserved. The Regional Office for Europe of the World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either express or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use. The views expressed by authors, editors, or expert groups do not necessarily represent the decisions or the stated policy of the World Health Organization.

Table of contents

Acknowledgements.....	1
Abbreviations.....	2
Executive summary.....	3
Introduction.....	6
Objectives.....	7
Methods.....	8
Findings.....	8
STI surveillance system.....	9
1. STI case reporting.....	9
2. Syphilis prevalence from routine screening programmes.....	14
3. STI prevalence assessment from integrated HIV/STI bio-behavioural surveys (IBBSS).....	15
4. Data management and analysis.....	17
5. Data dissemination.....	18
Laboratory capacities to diagnose STIs.....	18
<i>Opportunities and Ways Forward</i>	20
Recommendations.....	21
1. Recommendations for strengthening STI surveillance system.....	21
STI case reporting.....	21
STI prevalence assessment surveys.....	22
Syphilis prevalence data from routine screening programmes.....	23
Data analysis, use and dissemination.....	23
Capacity development.....	23
2. Priorities for operational research.....	24
3. Recommendations for optimization of laboratory diagnosis of STIs.....	24

4. Recommendations for validation of elimination of congenital syphilis	26
5. Optimizing STI policies, case management, promoting collaboration, partnership.....	26
Appendix 1 List of people met	28
Appendix 2 Mission schedule.....	29
References:	33

Acknowledgements

This report is the product of observations and discussions during a mission to the Republic of Moldova that took place from 11 to 15 March 2013. It was also influenced by national documents, briefing notes and other national materials that were made available prior to and during the mission by national colleagues.

All institutions and individuals visited were extremely supportive and helpful. Particular thanks to the Ministry of Health - Dr Octavian Grama, Deputy Minister of Health, Dr Mircea Betiu, Member of MOH Advisory group on Dermatovenereology, Dr Iulian Oltu, Director of the Hospital for Dermatology and Communicable Diseases (HDCD), Dr Viorel Calistru, Deputy Director HDCD; and other relevant stakeholders.

Special thanks are due to the Moldovan WHO Country Office (CO) colleagues, Dr Jarno Habicht, WHO Representative, and Dr Silviu Ciobanu, communicable diseases programme officer, for the useful insights into the country's background and context underpinning the health system reforms in Moldova, as well as for the excellent support during planning for and the implementation and follow-up to the mission.

Abbreviations

AIDS	acquired immunodeficiency syndrome
FSW	female sex workers
GASP	Global Gonococcal Antimicrobial Surveillance Programme
HIV	human immunodeficiency virus
IBBSS	integrated bio-behavioural surveillance surveys
MSM	men who have sex with men
NGO	nongovernmental organization
PWID	people who inject drugs
RDS	respondent-driven sampling
STI	sexually transmitted infections
SW	sex workers
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund

Executive summary

The World Health Organization Regional Office for Europe conducted a review of surveillance of sexually transmitted infections (STIs) in the Republic of Moldova with the aim to better characterize the components and performance of the STI surveillance system and provide recommendations to improve the effectiveness of the system.

A mission with four members visited the Republic of Moldova from 11-15 March 2013. The visit was facilitated, externally, by WHO Regional Office for Europe and, locally, by the Ministry of Health and the WHO country office in the Republic of Moldova. The mission visited institutions in different settings such as STI clinics, HIV/AIDS clinics, public health centres, obstetrics/gynecology units, primary health care centres, reproductive health centres, and laboratories representing the central secondary and primary care levels of health care delivery in the capital city of Chisinau and selected regions. Part of the team also visited city of Anenii Noi for discussions with local authorities and respective technical experts and staff. Along with the above, the mission met with colleagues representing the Medicine and Pharmacy State University and with nongovernmental organizations (NGO) colleagues. The mission also had a working meeting with United Nations colleagues including UNAIDS, UNFPA and UNICEF.

National documents relating to STI surveillance, management, control, and prevention were made available for review.

The STI surveillance system in Moldova consists of disaggregated reporting of cases of syphilis and gonorrhoea by dermatovenereology (DV) services, monitoring of syphilis prevalence in pregnant women and STI prevalence data from small integrated bio-behavioural surveillance surveys (IBBSS) in high-risk groups (female sex workers [FSW], people who inject drugs [PWID], men who have sex with men [MSM]), prisoners).

According to the data provided by the Ministry of Health, in 2012 64.6/100,000 cases of syphilis and 31.9/100,000 cases of gonorrhoea were reported in Republic of Moldova.

Electronic and paper-based case reporting of syphilis and gonorrhoea from DV services is the mainstay of STI surveillance in Republic of Moldova. This system has better representativeness for syphilis reporting since syphilis is largely treated and therefore reported by dermatovenereologists. Cases of gonorrhoea can be diagnosed outside DV settings (by gynecologists, urologists, primary health care physicians, private clinics, etc), and this, due to lower standards of reporting, results in underreporting of gonorrhoea. In addition, the current laboratory diagnostics for gonorrhoea (largely based on gram stain) have limited sensitivity (particularly for women and asymptomatic infections) and specificity. Thus, syphilis case reporting in Moldova might be considered as universal, while that of gonorrhoea functions more like sentinel surveillance from DV clinics.

Timeliness of STI case reporting from DV clinics is adequate since reporting and analysis is done on a monthly basis at the National Centre for STIs based at the Hospital for Dermatology and Communicable Diseases (HDCCD) in charge of STI reporting in Republic of Moldova.

Sensitivity of any surveillance system for detecting STI cases is affected by the screening practices. In Republic of Moldova, syphilis screening focused primarily on the general population. Contact tracing is done as part of the routine STI care and functions better for

syphilis (0.8 contacts examined per 1 case, 2012 data) than gonorrhoea (0.5 contacts per 1 case, 2012 data).

As reported by the HDCD, three cases of congenital syphilis were reported in 2010 and five in 2011 and 2012 each. Available data suggest good progress achieved by country in elimination of congenital syphilis. It appeared at almost every meeting that national colleagues feel very proud of that achievement. In-country interest was expressed during the mission in validation of elimination of congenital syphilis and in getting technical assistance for validation. If Republic of Moldova can identify a national source of data for routine monitoring of syphilis testing coverage, Republic of Moldova appears to otherwise have the pre-requisites in place to be eligible for validation of elimination of congenital syphilis once global and regional structures are in place. Global validation criteria have been elaborated and can be shared with country.

Monitoring of syphilis prevalence in pregnant women and small IBBSS surveys that assessed syphilis prevalence in FSW, PWID, MSM and prisoners provide useful information on the distribution of this infection in the general population and groups at higher risk. In 2011, syphilis prevalence in pregnant women was 0.37%. The data from the most recent IBBSS indicates the following prevalence of syphilis (measured by TPHA): PWID, 1.3%-4.2% per site (2009 data); FSW, 5.3%-5.7% per site (2010 data); MSM, 6.5% (2007 data); prisoners, 13.4% (2010 data). Analysis of syphilis and gonorrhoea case reports enables assessment of district-level distribution of the reported cases, which is important for the geographical prioritization of STI interventions.

During meetings with the representatives of various institutions it was often mentioned that the majority of syphilis cases are in Moldovan nationals who come back to Republic of Moldova from work in other eastern European countries. However, this was not confirmed by the analysis of the case reports, where only a small fraction of cases of syphilis and gonorrhoea reported being abroad two years before a diagnosis.

It was noted by the mission that it is crucial to review and revise case definitions and STI management guidelines, and improve and quality-assure the STI diagnostics used in Republic of Moldova in line with international evidence-based standards and guidelines. The first priority is to improve gonorrhoea diagnostics, but it will also be important to implement appropriate diagnostics for chlamydial infections as currently little exists. Appropriate diagnostics and case definitions are the basis for quality surveillance. It is also suggested that at least 2 specific laboratories be included as sentinel sites for Republic of Moldova in the WHO Global Gonococcal Antimicrobial Surveillance Programme (GASP), which can be supported by the WHO initially through training, supervision, centralized testing of antimicrobial resistance in gonococcal isolates, etc.

It is also suggested that Republic of Moldova no longer continue the extensive periodic STI screening of certain occupations and population groups as such screening of low risk groups does not have a public health basis. In addition, testing for *Mycoplasma hominis* and *Ureaplasma* species should be discontinued, which are mainly of importance only for bacterial vaginosis and sometimes male urethritis. It is advisable to use the resources saved by stopping these screening practices to enhance diagnostics for substantially more important STIs (syphilis and gonorrhoea, and later on urogenital chlamydial infections) and strengthen the focus on high-risk STI populations.

Antimicrobial resistance testing of *N. gonorrhoeae*, using internationally validated, approved and quality assured methods, ought also to be introduced. At a minimum, possibilities to preserve gonococcal isolates (in -70-80°C freezers or in liquid nitrogen) need to be available. If so, Republic of Moldova can be included in the WHO Global GASP. Two sentinel sites for possible inclusion in the WHO Global GASP were identified during the mission. Training of 2 national colleagues in WHO Collaborating Centre, Orebro, Sweden, will be supported.

In general, an enhanced quality assurance and control system should be implemented in all laboratories. This should include not only optimized diagnostic methods but also standard operating procedures (SOPs), internal and external quality assessment controls and calibration of all equipment used for the STI diagnostics. A first step for external quality assessment (EQA) control could be that the National Centre for STIs join the WHO global proficiency testing programme for syphilis serology.

In conclusion, STI surveillance system in Republic of Moldova is well structured. Minor revisions of the STI electronic case reporting would improve the amount and quality of information necessary for development of better targeted STI interventions. The sensitivity of the system for detecting the true population burden of STIs should be enhanced by setting up screening for syphilis, gonorrhoea and ideally also other STIs such as trichomoniasis and chlamydial infections (provided that appropriate tests are used) in groups being at higher risk of STI including, FSW, MSM, PWID, prisoners and migrants. However, in general the STI case definitions need to be reviewed and revised, and the diagnosis of gonorrhoea substantially improved and quality assured in accordance with international evidence-based guidelines. Behavioural data and data on coverage with interventions need to be more utilized by the National Program for STI/HIV/AIDS Prevention and Control Programme 2010-2015 for development of targeted interventions.

The above joint STI/HIV program and management, which is very positive feature of the country, gives an opportunity to promote integration and mutual reinforcement of HIV and STI control, prevention, treatment and care. More emphasis on data analysis is also required, which could be achieved by promotion of close collaboration with national public health settings and enhanced capacities of the surveillance personnel in data analysis and interpretation. It is of vital importance to attract young medical staff to work in public STI settings, and the creation of an attractive career path would be an important initial step to ensure their retention there. Although there is a decline in reported cases of syphilis in the last decade, the epidemic is still at unacceptably high levels. National experts suggested high prevalence of other STIs and frequent treatment challenges, especially due to *Trichomonas vaginalis*. This indicates a need to better understand the factors underlying the transmission of syphilis and other STIs and, based on this, develop targeted interventions, including voluntary screening and treatment of those most at risk. Available data also suggest an increase in sexual transmission of HIV over the last 5 years. In 2011 the number of reported HIV cases attributed to sexual transmission (both heterosexual and MSM) was 10 times higher compared to those infected via injecting drug use. This suggests the strong necessity to further strengthen STI control and prevention in Republic of Moldova not just because of high public health importance of STIs on its own but also to contribute to the prevention of sexual transmission of HIV.

There is a strong MOH commitment, dedicated stewardship and leadership, excellent technical expertise, and a well-structured STI surveillance system in Republic of Moldova. The qualified professional staff is enthusiastic, keen to acquire modern information and eager to improve their programme. This combination provides a strong foundation for the country, and means that Republic of Moldova has the potential to have highly effective STI surveillance system and STI

control and prevention program which could serve as a model for other countries of eastern Europe.

It is hoped that the recommendations discussed in this report will be of assistance in identifying how Republic of Moldova can further strengthen the national STI surveillance system, laboratory diagnosis and STI control and prevention program.

Introduction

Diagnosis and surveillance of sexually transmitted infections (STIs) is generally weak across the WHO European Region. A targeted and effective response to STIs epidemics should be guided by strategic and reliable information about the distribution of infection and the underlying factors that drive STI transmission. Available data show considerable geographical variation in the distribution of STIs across the WHO European Region. However, interpretation of STI data should be guided by understanding algorithms for use and performance characteristics of STI diagnostics, screening practices, and surveillance systems, which vary significantly across the region.

As part of a global and regional effort to improve STI surveillance, WHO initiated a review of the STI surveillance system in the Republic of Moldova with the aim to support STI surveillance strengthening in a country with a high burden of STIs and develop a more detailed understanding of the availability of data sources and performance of STI surveillance systems. According to the data provided by the Ministry of Health there were 64.6 cases of early syphilis per 100,000 in 2012 in Republic of Moldova (Figure 1).¹

Figure 1. Reported cases of early syphilis per 100,000 population, 2000-2012

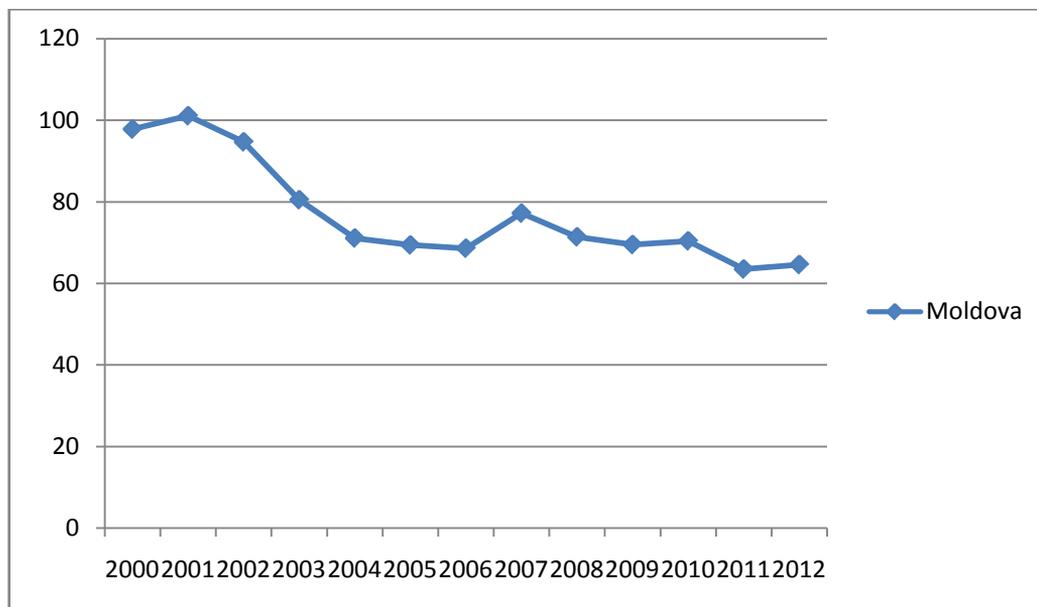
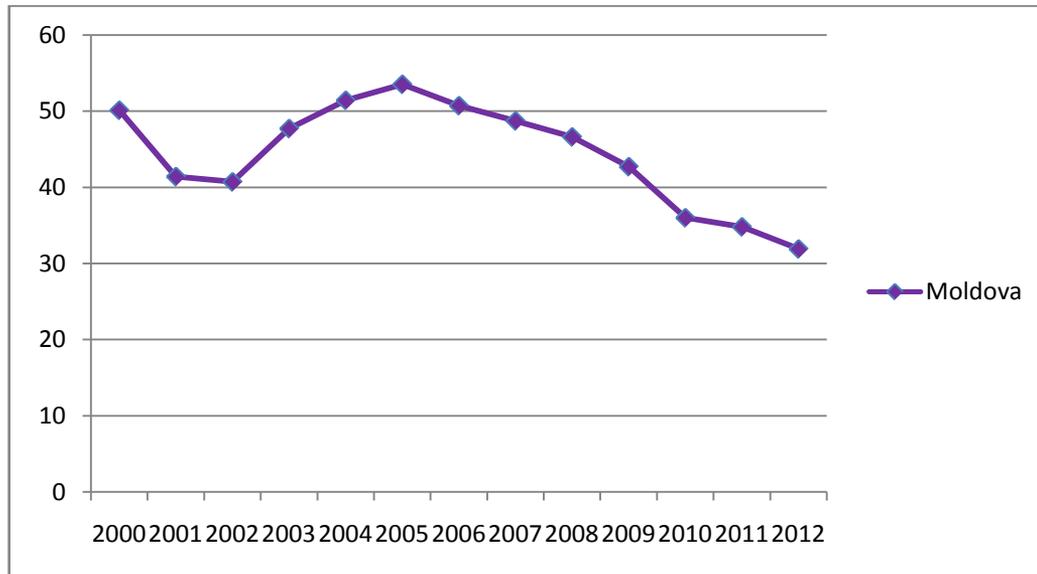


Figure 2 shows that in 2012, 31.9 cases of gonorrhoea were reported in Republic of Moldova per 100,000 population.

Figure 2. Reported cases of gonorrhoea per 100,000 population



Objectives

The objectives of the mission were:

1. to review the structure and performance of STI surveillance in Republic of Moldova and laboratory tests used to diagnose STIs
2. to support improvement of gonococcal antimicrobial resistance (AMR) monitoring through Gonococcal Antimicrobial Surveillance Programme (GASP) expansion into the eastern part of the WHO European Region
3. to develop recommendations for STI surveillance strengthening

The members of the team who participated in the mission to Republic of Moldova from 11-15 March 2013 were Dr Lali Khotenashvili (WHO Regional Office for Europe), Dr Lori Newman (WHO headquarters), Dr Magnus Unemo (WHO Collaborating Centre for STIs, Örebro University, Sweden) and Dr Ivana Bozicevic (WHO Collaborating Centre for HIV Surveillance, University of Zagreb, Croatia).

Methods

Methods for the assessment included a review of STI surveillance structure, data collection forms (including case notification forms), data flow, reports (including those on results of surveillance activities), policy documents related to surveillance activities, and other documents. In addition, the mission conducted discussions, direct observations of activities, and interviews with policy-makers, public health authorities, National STI and HIV programme manager and STI focal point, technical experts and staff who work on various surveillance-related activities (clinicians, lab managers, microbiologists, data managers), civil society colleagues, United Nations and other major partners.

Findings

The creation of a joint National Programme for STI/HIV/AIDS prevention and control 2010-2015 (NAP) is a very positive achievement for the country. It gives an opportunity to promote integration and mutual reinforcement of HIV and STI control, prevention, treatment and care.

In Republic of Moldova, STI screening, diagnostic testing, treatment and prevention services are provided at various clinical sites, but primarily by dermatovenereology (DV) services. DV services are most often part of the general (district) hospitals, and there are 34 such district-level DV services. In the capital Chisinau, there is a special Municipal Dermatovenereology Centre. In Chisinau the National Centre for STIs is based at the Hospital for Dermatology and Communicable Diseases. The Municipal Clinical Hospital in Balti has a DV department.

General practitioners, gynaecologists, urologists, and health care providers at family planning clinics and youth clinics also diagnose and treat STI cases (with exception of syphilis). The role of private sector in STI case management and reporting was not assessed in this review.

There are National Guidelines for STI case management developed in 2004-2005 with WHO support. There are ongoing efforts to revise these guidelines in 2013. This planned update of national case management guidelines is an important initiative of the National STI Programme. Based on the findings of this mission, it is crucial to promptly review and appropriately revise those guidelines (case definitions as well as recommendations of diagnostics and treatment) and ensure that the updated guidelines strictly adhere to the WHO, International Union against Sexually Transmitted Infections (IUSTI) and other international evidence-based guidelines and recommendations. The idea of having newly updated guidelines endorsed by the MOH order should be encouraged. It will allow making the new guidelines national standards or protocols that are to be followed across the country. As soon as the new guidelines become available they should be widely disseminated and implemented, and respective staff should undergo training to ensure that new standards are well-followed in practice.

The assessment of STI surveillance focused on surveillance for syphilis and gonorrhoea, since basically no valid diagnostics of *Chlamydia trachomatis* infection was performed outside the National Centre for STIs. In other settings, chlamydial infections were syndromically diagnosed or by use of serological tests, which cannot be recommended for diagnosis of any uncomplicated urogenital chlamydial infection, due to the poor sensitivity as well as specificity.

STI surveillance system

The STI surveillance system in Republic of Moldova consists primarily of case reporting, monitoring of syphilis prevalence from routine screening programmes and STI prevalence assessment from integrated HIV/STI bio-behavioural surveys (IBBSS).

1. STI case reporting

STI case definitions

Case definitions of gonorrhoea and syphilis were provided by Dr Mircea Betiu, based on the MOH order nr. 385 from 12.10.2007, supplement no. 2 (ad litteram):

Gonorrhoea

Suspected case: falling ill with clinical expression of urethritis, cervicitis or pelvic inflammatory disease (PID).

For gonorrhoea surveillance purposes, only confirmed cases will be taken into account.

Confirmed case: a suspected case confirmed through identification of *Neisseria gonorrhoeae* culture in biological substrates or through detection of Gram-negative intracellular diplococci in a urethral and/or cervical smear.

Syphilis

- Suspected case: for primary syphilis: ulcerations on external genitalia and local adenopathy; for secondary and tertiary syphilis: skin and systemic lesions
Only confirmed cases of syphilis shall be used for syphilis surveillance purposes.
- Confirmed case: a clinical case confirmed by identifying *T. pallidum* in biologic samples through dark-field microscopy with immunofluorescent antibodies

and/or

positive result of nontreponemal and treponemal serology test:

- Syphilis microprecipitation test (MRS) or complement fixation test (WR) – tests used for triage, confirmed through a treponemal (specific) test:

- *T. pallidum* hemagglutination test (TPHA), or
- ELISA

- **Case Classification**

Congenital case: child with a positive serology test born to a mother with either a positive or a negative serology test during pregnancy.

Acquired case: all other cases

- **Primary syphilis**

Suspected (clinical) case: the stage of infection with *T. pallidum* presenting with one or several primary syphiloma (chancre, ulceration) on external genitalia and local adenopathy.

Confirmed case: clinical case confirmed by identifying specific IgM antibodies and/or identifying *T. pallidum* in biological samples through dark field microscopy with fluorescent antibodies

- **Secondary syphilis**

Suspected case (clinical case): stage of *T. pallidum* infection presenting with mucous-cutaneous diffuse lesions, often associated with generalized lymphadenopathy. Primary chancre may persist.

Confirmed case: a clinical case confirmed by identifying *T. pallidum* in biological samples through dark field microscopy with fluorescent antibodies,

and/or

positive serology test (nontreponemal Venereal Disease Research Laboratory, VDRL)

or

microhemagglutination test for *T. pallidum* antibodies (MHA-TP)

- **Latent syphilis**

Suspected case (clinical case): stage of *T. pallidum* infection characterized by persistent *T. pallidum* in human body and no clinical signs.

Confirmed case: positive test for specific EIA, but negative for contagious syphilis lab tests (see primary and secondary syphilis tests)

Only confirmed cases of syphilis shall be accounted for the syphilis surveillance purposes.

- **Case Classification**

Congenital case: child with positive serology test born to a mother with either a positive or a negative serology test during pregnancy.

Acquired case: all other cases

STI case definitions are currently being updated and revised, which is very important and timely initiative. It should be ensured that the revised case definitions are in line with WHO and ECDC case definitions.² For example, currently the case definition for gonorrhoea does not include asymptomatic infection, extragenital samples, or nucleic acid amplification tests (NAATs). And, the congenital syphilis case definition should clearly include both live and stillborn infants. Furthermore, mission noticed that despite having strong reporting system for congenital syphilis, it is not listed in the public health regulation as notifiable in the country. It is suggested to add

congenital syphilis to the list of notifiable diseases and respective case definition is included in the respective public health regulations.

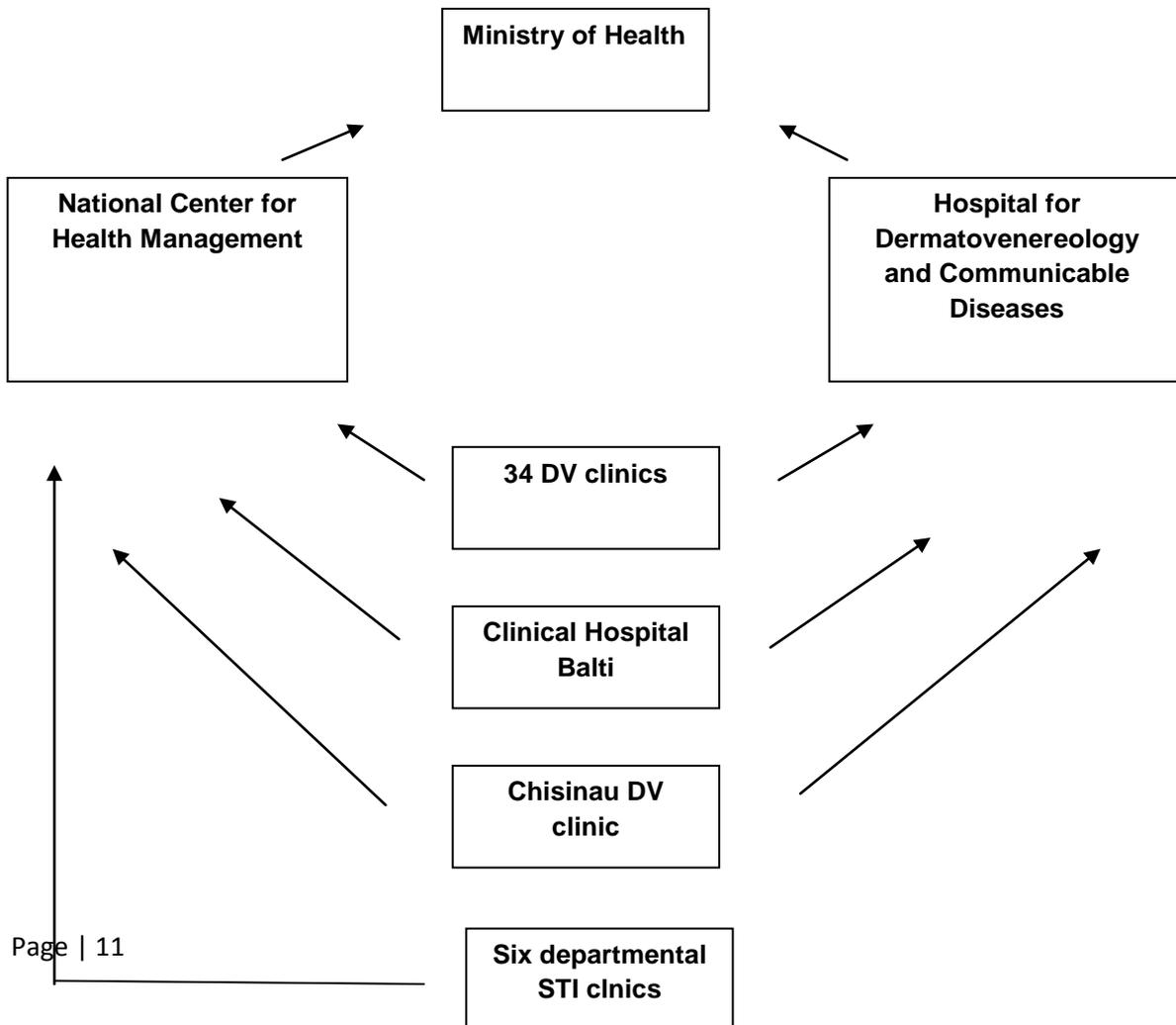
Sources of STI case report data

Flow of patient-level STI electronic case reporting is shown in Figure 3.

The main source of STI case report data are outpatient DV services which operate at 34 districts mainly as parts of the district hospitals, and in Chisinau as a part of the Municipal DV Centre. DV services are in charge of reporting cases of syphilis and gonorrhoea using individual-level electronic and paper-based forms. Submission of electronic case reporting forms is done on a monthly basis to both the National Centre for Health Management and the Hospital of Dermatology and Communicable Diseases. Electronic case reporting exists since 2009. STI cases are also reported from six departments that operate outside of the health care sector (such as the Ministry of Interior, Justice, Defence, civil aviation etc) and they report on an annual basis to the National Centre for Health Management.

Cases of syphilis are largely treated by dermato-venereologists. Patients diagnosed with gonococcal infection can be treated outside of the DV services, predominantly by gynaecologists and urologists. Case notification forms for patients with gonococcal infection should be sent to DV specialists who report them further to the National Centre for STIs and National Centre for Health Management.

Figure 3. Flow of individual-level electronic case reporting data



However, informal discussions with staff suggest that a large number of gonorrhoea cases are diagnosed and treated in primary care settings by providers other than DVs. Under-diagnosis and underreporting of gonorrhoea is more likely than that for syphilis, since syphilis should be, and is generally thought to be diagnosed, treated and reported by dermato-venereologists. Thus, syphilis reporting in Republic of Moldova is structured as universal, while that for gonorrhoea functions more like a sentinel surveillance from DV clinics. Accordingly, the sensitivity and representativeness of the system is better for syphilis than for gonorrhoea. In line with that, the higher number of reported cases of syphilis compared to the number of the reported cases of gonorrhoea (shown in Figures 1 and 2) is certainly affected by the better coverage of surveillance system for syphilis and low sensitivity of diagnostic tests for gonorrhoea used in Republic of Moldova.

Reporting is mainly name-based, though it can also be done anonymously using a system of unified codes. It was reported during a visit to the Municipal Centre for Dermatovenereology in Chisinau that approximately 80% of their STI case report forms are assigned such codes instead of names. It was reported that the same code is used for a patient who might present with two episodes of STIs in a given year, which implies that a certain number of STI cases might be underreported. Additionally, the extent to which the codes are unique to individual patients was not assessed during this mission but should be further explored in order to understand whether duplicate reporting may occur. Case reporting forms collect socio-demographic and some clinical data, but no behavioural data. Data are collected on whether a person was tested for HIV, but results of this testing are not recorded. It is advisable to record this data as it will allow getting information regarding co-infection and inform prevention actions.

As reported during the mission, DV specialists at the district level have access to the electronic database and can use it to calculate the number of reported cases of syphilis and gonorrhoea per 100,000 population in their districts and compare these with other districts and the country as a whole. However, no routine reports were noted at the national and district level.

The National Centre for STIs conducts approximately 20 monitoring and supervisory visits annually to district-level DV units with the aim to assess reporting practices and conduct the assessment of treatment and laboratory services and provide assistance to timely and efficiently address the challenges identified. It was reported that the completeness of case reports from DV units is checked against the number of cases of syphilis and gonorrhoea diagnosed by the laboratories.

Table 1 shows the number of reported cases of syphilis and gonorrhoea in 2010-2012, according to the data provided by the National Centre for Health Management. There is a high male to female ratio in the reported cases of primary syphilis and gonorrhoea.

Table 1. Reported cases of syphilis and gonorrhoea by sex, 2010-2012

	2010		2011		2012	
	Male	Female	Male	Female	Male	Female
Syphilis						
Primary	335	115	294	91	331	70
Secondary	370	370	319	298	299	291
Early latent	614	693	610	609	602	632
Late latent	5	0	14	12	6	3
Total syphilis ^a	1326	1183	1238	1016	1240	999
Gonorrhoea	1120	263	1109	194	934	201

Source: National Center for Health Management.

a= for all years, a total is somewhat greater than a sum of cases reported by a stage of syphilis

Contact tracing is obligatory for syphilis and gonorrhoea. It has better effectiveness for syphilis cases (0.8 contacts examined per 1 case, 2012 data) than gonorrhoea (0.5 contacts per 1 case, 2012 data).

As can be seen in Tables 2 and 3, according to the data of the National Centre for Health Management between 7.3%-8.9% of the reported cases of syphilis and 4.3%-6.2% of reported cases of gonorrhoea during 2010-2012 reported to have been outside of Republic of Moldova during the two years preceding the diagnosis, and the country most frequently visited was the Russian Federation. This data does not support the commonly prevailing opinion that syphilis epidemic is brought by migrants (Moldovan residents) who work in other countries of eastern Europe since their proportion in the total number of cases is relatively small. It rather indicates the presence of a domestic epidemic that, despite the efforts, is not well controlled. However, these data have limitations since they only indicate that someone was outside of the country and not whether a sexual contact occurred in another country.

Table 2. Number and proportion of reported cases of syphilis who reported being outside of the country during the two years preceding the diagnosis and the countries that they reported being to, 2010-2012 data

	Total number of reported cases of syphilis	Number of cases who were outside of Republic of Moldova two years before the diagnosis	Countries visited
2010	2521	184 (7.3%)	Russian Federation, 132; Ukraine, 22; Italy, 6; Turkey, 5; elsewhere, 19
2011	2266	179 (7.9%)	Russian Federation, 151; Ukraine, 12; Italy, 9; elsewhere, 7
2012	2236	199 (8.9%)	Russian Federation, 165; Ukraine, 11; Italy, 6; Turkey, 5; elsewhere, 12

Table 3. Number and proportion of reported cases of gonorrhoea who reported being outside of the country during the two years preceding the diagnosis and the countries that they reported being to, 2010-2012 data

	Total number of reported cases of gonorrhoea	Number of cases who were outside of Republic of Moldova two years before the diagnosis	Countries visited
2010	1395	60 (4.3%)	Russian Federation, 46; Ukraine, 4; Italy, 4; elsewhere, 6
2011	1315	71 (5.4%)	Russian Federation, 54; Ukraine, 4; Italy, 5; elsewhere, 8
2012	1129	70 (6.2%)	Russian Federation, 59; Ukraine, 4; Italy, 3; Turkey, 2; elsewhere, 2

There also exists another system of aggregate reporting of cases of *Chlamydia trachomatis*, trichomoniasis and genital HSV infection monthly from DV services to the National Centre for Public Health and annually to the National Centre for Health Management. While data on numbers of *Chlamydia trachomatis*, trichomoniasis and genital HSV infection are also collected for instance by the antenatal clinics, they are reported as totals of reported genitourinary tract infections without specifying infections.

As reported by the HDCD, three cases of congenital syphilis were reported in 2010 and five each in 2011 and 2012.

In the majority of districts, laboratory diagnosis of STIs is done at the public health laboratories (former sanitary-epidemiological service). The HDCD in Chisinau, Municipal Centre for Dermatovenereology in Chisinau and a District Hospital of Anenii-Noi that were visited during the mission had their own laboratories for STI diagnosis.

2. Syphilis prevalence from routine screening programmes

Screening for syphilis is carried out among pregnant women and several occupational and other groups.

All pregnant women should be tested for syphilis two times during pregnancy: at the first ANC visit (before 12-14 weeks of pregnancy) and at 28-30 week of pregnancy. As reported during the mission, >99% of pregnant women are screened for syphilis. This is a great achievement and an important prerequisite for congenital syphilis elimination and the country should be congratulated for that. However, the data on screening coverage in pregnant women are currently estimated as only the numerator is currently collected (number of pregnant women screened). It will be important for the country to identify a source of data where both the numerator and denominator of syphilis screening coverage can be routinely monitored. For

example, it was discussed that the national insurance plan may be able to provide actual data on this indicator.

Table 4 shows data on syphilis prevalence among pregnant women screened in 2009-2011.

Table 4. Syphilis prevalence data in pregnant women screened for syphilis, 2009-2011

	2009	2010	2011
Syphilis prevalence (%)	0.29	0.44	0.37
Number of women screened	38 189	37 408	36 833

In most laboratories, the algorithm for diagnosis of syphilis included screening with the non-treponemal Microprecipitation reaction test (MPR or MRS). If positive MPR, two treponemal tests (TPHA and an ELISA) were used. Some laboratories also had dark-field microscopy available for definitive diagnosis of primary syphilis.

By the current screening guidelines, all patients registered with general practitioners should be screened for syphilis. Syphilis screening is obligatory in a number of occupational groups (such as truckers, those working in food industry, etc) and in students attending some universities.

It is strongly recommended to carefully review and eliminate any form of mandatory, compulsory STI screening policies and practices. STI screening programmes should always be voluntary. In addition, screening policies should be based on a review of evidence, which includes a clear rationale for the screening programme, the yield of screening in that population, the potential to disrupt transmission or otherwise have a public health impact, as well as consideration of cost and cost-effectiveness of the programme.

3. STI prevalence assessment from integrated HIV/STI bio-behavioural surveys (IBSS)

IBSS started to be implemented in 2004. The National Centre for Health Management was in charge of the most recent IBSS carried out in 2009-2010, while the previous ones were conducted by the National Centre for Public Health. The National STI Centre (HDCD) was not involved in conducting IBSS in high-risk groups which should be given serious consideration and addressed in the future. It is highly recommended to involve HDCD in IBSS activities as well as include STIs in planned HIV surveys.

Respondent-driven sampling (RDS) was used as a sampling method in surveys in IDUs and FSWs, while two-stage cluster-based sample was used to sample prisoners. However, only survey data in PWID were analysed using RDS Analysis Tool (RDSAT), which implies that population estimates of the prevalence of infections are available only for PWID.

There seem to be no questions in the survey questionnaires on whether respondents were screened for syphilis 12 months prior to the survey, while such questions exist for HIV testing.

The most recent data on prevalence of infections available from IBBSS are shown in Table 5. The highest prevalence of syphilis was found in prisoners (13.4%), followed by MSM (6.5%). Since data on prevalence of infections in MSM was not available in the report on the IBBSS carried out in 2009-2010, the most recent data available from the IBBSS report for the year 2007 are presented. It is not clear what kind of sampling was used to recruit MSM in the IBBSS done in 2007.

In 2007 and 2009-2010 IBBSS, the following tests were used:

- Syphilis: TPHA tests, Bio-Rad, France
- HIV: Genscreen Ultra HIV Ag-Ab, Bio-Rad, France, Vironostika HIV Uni-Form II Ag/Ab, Holland, Biomerieux, France
- HBV: Monolisa HBs Ag ULTRA, Bio-Rad, France
- HCV: Ortho HCV 3.0 ELISA Test System, Ortho-Clinical Diagnostics, USA

The data shown in Table 5 suggests a high STI prevalence in key populations at higher risk. At the same time the reasons for that are not quite clear. NAP should put major efforts to well understand the ongoing transmission dynamics to inform the prevention efforts. It should clarify the STI needs of key populations at higher risk and possible barriers preventing them from accessing STI services. The efforts of the NAP should be directed to respond to the needs identified and remove the barriers that might exist, clarify the role of access to STI services in sexual transmission of HIV that shows a high proportion and increasing trends in Republic of Moldova. There is a need to encourage and support the NAP to offer opportunities for early STI testing and care. Potential option could be adding STI testing to the services offered by the existing network of VCT centres that currently includes 67 sites across the country.

The integration of STI and HIV under one NAP provides an excellent opportunity to share experiences and address needs in a coherent, joint manner. However, it is also necessary to promote integration of the STI issues with civil society and other HIV partners as it seems to be lacking, in order to promote a better understanding of existing needs and elaborate ways to address these needs.

Table 5. Prevalence of sexually and parenterally transmitted infections from IBBSS conducted in 2007 and 2009-2010

	Syphilis (%)	Hepatitis B (%)	Hepatitis C (%)	HIV (%)	Sample size
Persons who inject drugs (2009)					
Chisinau	4.2	10.3	77.9	16.4	301
Balti	2.7	14.2	70.2	39.8	352-362
Tiraspol	1.3	7.7	20.8	12.1	281
Female sex workers (2009-2010)					
Chisinau	5.7	9.3	19.0	6.0	300
Balti	5.3	9.5	25.8	23.8	300
Men who have sex with men (2007)					
Chisinau (2007 data)	6.5	NA	3.6	4.8	182

Prisoners (2010)					
18 prisons across the country*	13.4	16.3	15.5	3.4	523

*All selected prisons were on the right bank of the Dniester River

4. Data management and analysis

Listed below are the key STI indicators to be considered for the Republic of Moldova:

- a. number of new cases of syphilis and rate per 100,000 population
- b. number of new cases of gonorrhoea and rate per 100,000 population
- c. prevalence of syphilis, HIV and hepatitis B virus (HBV) infection in PWID, FSW, MSM and prisoners from IBBSS or sentinel surveillance programmes
- d. prevalence of syphilis from routine screening of pregnant women
- e. number of children born with congenital syphilis and rate per 100,000 population

HDCD receives on a monthly basis both individual-level electronic and paper-based forms from 34 district-level DV services, Municipal Clinical Hospital in Balti and the Municipal Centre for Dermatovenereology in Chisinau. Validity of data is somewhat ensured by pre-determined data entry checks for certain variables. A data manager at the HDCD cross-checks the electronic reports with those paper-based and also assesses the completeness of forms. Data analysis is done monthly by calculating the absolute number and the number of cases of syphilis and gonorrhoea reported per 100,000 population for each district and for the whole country. The number of cases for the reporting month is compared to the number of cases reported for the same month in the previous year.

The Monitoring and Evaluation unit under the Department for Medical Statistics of the National Centre for Health Management also receives electronic STI case reports from DV clinics. This institution is in charge of STI data analysis, which is done annually.

There is no narrative description of STI case reporting data and apparently there are no reports that describe the STI epidemiology in Republic of Moldova.

Reports on IBBSS surveys are generally well written and provide a comprehensive description of the indicators, but there are gaps. For example, they lack the comparison of results with the previous survey data and the relevance of the results for planning of interventions. Analysis of the most recent RDS data was done using RDSAT only in surveys in PWID. RDSAT was not used to analyse RDS data collected in FSW and MSM, which means that the indicators calculated cannot be extrapolated to the populations sampled.

An existing electronic STI case reporting statistical database builds a strong and important platform for the NAP. The ongoing efforts of the NAP to strengthen M&E including efforts to establish a dedicated unit at the HDCD should be supported. There is a need to promote interaction and collaboration of M&E of the NAP. NAP manager is the deputy director of the HDCD. The ongoing efforts to finalize establishment of the HIV electronic database, a.k.a. SIME-HIV (Integrated System for the M&E) should be strongly supported. The mission was informed that data entry of the previous paper-based database has been already finalized and there are ongoing efforts to optimize the software in order to allow development of data exchange platform with other major databases such as STI and Public Health. The link to the

National Public Health database should be ensured. The optimal platform for data exchange among STI, SIME-HIV and National Public health databases should be elaborated and implemented. Data should be routinely shared with public health settings for epidemiological surveillance to ensure data analysis and use of data to inform decision-making. There currently appears to be limited epidemiological analysis of STI data and this challenge should be addressed by the NAP. It is advisable that the reports and other analytical documents being published by the public health institutions also include address and discuss STI data and programmatic implications of the data.

STI capacity-building should be given serious consideration as the majority of DV doctors appeared to be nearing retirement. There appears to be limited interest by younger medical doctors to work in STI public settings. Many of them may be leaving for private settings. There is a strong need to attract young medical staff to the specialty. The issues such as creating an attractive career path for young colleagues should be given serious attention. STI continuous education should be further strengthened. Republic of Moldova is encouraged to cover STI surveillance in the curricula for medical school and postgraduate students. Developing national capacity on STI prevention education is another important issue to consider. The existing electronic curricula/courses on HIV/AIDS of the School of Public health give an excellent opportunity to add STI issues there.

5. Data dissemination

HDCD organizes meetings with DV specialists three times per year, which is an opportunity to present STI case reporting data and the results of the quality assurance programme conducted by the HDCD Reference Laboratory. The meetings are attended by approximately 80 dermatologists.

These important efforts of the NAP including regular national meetings discussing epidemiological trends and data analysis should involve on a regular basis also HIV epidemiologists and public health epidemiologists and surveillance staff and outcomes of these meetings should be widely documented, disseminated and available to a broader audience. Along with that, the National Centre for Health Management is encouraged to improve the availability in a public domain of STI data other than syphilis case reporting statistics. STI analytical reports should be widely shared and made publicly available on a regular basis.

Laboratory capacities to diagnose STIs

The staff was competent in the performance of the diagnostic methods used. However, with exception of testing for syphilis, symptomatic male gonococcal urethritis and culture of *Trichomonas vaginalis*, the methods in use, were generally not in adherence to international norms and guidelines. International modern, highly sensitive, validated and quality assured and controlled methodologies for diagnosis of STIs were mainly not available.

In details regarding diagnosis of syphilis, the majority of samples were initially screened using MPR (most frequently using cardiolipin antigen from Ekolab, Russian Federation, on large plates that were automatically rotated). This method is relatively adequate. However, compared to the internationally recommended rapid plasma reagin test (RPR), the MPR has been shown to have a lower, suboptimal sensitivity.^{3 4} It was positively noted by the Mission that in most

laboratories visited in the Republic of Moldova, all MPR positive samples were then subsequently tested with *T. pallidum* haemagglutination assay (TPHA) and an ELISA, i.e. to confirm the diagnosis. Some laboratories also had dark-field microscopy available for definitive diagnosis of primary syphilis. A quantitative MPR was used to follow the disease progression and effectiveness of treatment. No PCR was available for syphilis (i.e., for ulcer samples for detection of early infection).

In detail regarding diagnosis of gonorrhoea, most samples were diagnosed with microscopy after Methylene Blue and/or Gram staining of smears. However, at the HDCD, the Municipal DV Centre and some additional laboratories, culture was available. PCR diagnostics were not observed in any laboratory. All samples analysed were urethral and cervical samples, and no extragenital samples (e.g. pharyngeal and rectal samples) were examined (mostly because the clinicians did not take and submit these for testing). The staff performed adequate maintenance of the microscopes and were skilful in reading and interpreting the microscopic slides. Nevertheless, according to international norms and guidelines, identification of intracellular (not only extracellular) Gram-negative diplococci in microscopy of Gram-stained smears has sufficient sensitivity and thus can only provide a definitive diagnosis of gonorrhoea in symptomatic males with urethritis. Accordingly, in order to provide a definitive, sensitive and specific diagnosis of gonorrhoea in other patients such as asymptomatic patients of either sex, symptomatic women, children, and extragenital samples, culture or nucleic acid amplification tests should be performed. The culture methods used in the few laboratories culturing gonococci were also suboptimal and not in accordance with international evidence-based guidelines. Culture was performed in tubes (slant agar with 2-3 mL agar), instead of Petri dishes, and the agar was non-selective or only contained lincomycin, instead of appropriate selective agents such as vancomycin, colistin, nystatin (and ideally also trimethoprim). Oxidase was used in some (but not all laboratories) for confirmation; however, no appropriate species confirmatory test was available in any laboratory.

Antimicrobial resistance in *N. gonorrhoeae* is a major public health concern worldwide. In fact, due to the recent emergence of resistance to extended-spectrum cephalosporins such as cefixime and ceftriaxone, it is feared that gonorrhoea may become untreatable in certain circumstances and settings. Despite this grave threat, there are no internationally published studies regarding gonococcal antimicrobial resistance in Republic of Moldova, and no valid antimicrobial resistance testing or resistance data for *N. gonorrhoeae* was available during the mission.

Regarding diagnosis of trichomoniasis, in the country the majority of the diagnostics seemed to be performed using microscopy of stained smears (according to observations and discussions). Compared to microscopy of wet mount, culture or PCR of *T. vaginalis*, microscopy of stained smears, which does not detect trichomonads that are viable and have characteristic movements, has a clearly suboptimal specificity and sensitivity, and cannot be recommended for diagnosis. However, several larger laboratories were also culturing *T. vaginalis*, using relatively adequate selective culture media and methods. PCR for *T. vaginalis* was available at the HDCD, however, very few samples were tested due to the substantially higher cost of this method.

Regarding diagnosis of urogenital *C. trachomatis* infection, at the HDCD a direct fluorescent antibody (DFA) test for antigen detection was used. The test was manufactured by Ekolab, Russian Federation, and no data regarding performance characteristics or validation of the assay was available, apart from data from the manufacturer. Internationally it is believed that DFA tests have substantially lower sensitivity (and specificity) compared to PCR, which is

strongly recommended to be used for diagnosis of chlamydial infections. However, if resources are lacking for using PCR, validated and quality assured DFA tests are the second choice for diagnostics in this type of setting. Most worrying, the HDCD was the only visited laboratory that used DFA or PCR (which was available but very few samples were analysed due to the high cost of this test) and all other laboratories visited or discussed did not have any etiologic diagnosis of chlamydial infection, or used antibody detection for diagnosis of uncomplicated chlamydial infections. Unfortunately, antibody detection methods have highly suboptimal sensitivity and specificity for diagnosis of acute uncomplicated *C. trachomatis* infection. E.g., in regards to using detection of specific antibodies towards *C. trachomatis* for diagnosis, no generally agreed standards exist, some individuals have a delayed or even absent chlamydial antibody response, and in individuals having an adequate antibody response, it generally persists long after the infection has been cleared. Accordingly, measurement of chlamydial antibodies should not be used for the routine diagnosis of chlamydial genital tract infection.

A large number of samples were also screened for *M. hominis* and *Ureaplasma* species. These should only be tested if there are a strong clinical indication according to internationally approved guidelines and case definitions, which is exceedingly rare.

In general, any evidence-basis or results from adequate evaluations of the performance characteristics of the assays used compared to any internationally acknowledged and quality assured methods, or other manufacturer of similar assays in the region, was not available.

Some level of quality assurance and control system was available at all visited laboratories. However, no laboratories had any complete quality assurance system implemented. Elaboration of national standards and/or a national plan for quality assurance of STI diagnostics would be important for ensuring quality STI diagnostics.

Opportunities and Ways Forward

There is currently a strong MOH commitment, dedicated stewardship and leadership, excellent technical expertise, and a well-structured STI surveillance system in Republic of Moldova. The qualified professional staff is enthusiastic, keen to acquire modern information and are eager to improve their programme. This combination provides a strong foundation for the country, and means that Republic of Moldova has the potential to have highly effective STI surveillance system and STI control and prevention program which could serve as a model for other countries of eastern Europe.

It is hoped that the recommendations discussed in this report will be of assistance in identifying how Republic of Moldova can further strengthen the national STI surveillance system, laboratory diagnosis and STI control and prevention program.

Recommendations

1. Recommendations for strengthening STI surveillance system

STI case reporting

- Planned revision of STI case definitions to be done during the process of updating STI guidelines for diagnostics, treatment and prevention of STIs is strongly encouraged. The revised STI case definitions and STI management guidelines should adhere, as strictly as possible, to international evidence-based guidelines.
- Case reporting of *Chlamydia trachomatis* infection should be discontinued until valid and quality assured etiological diagnostics (that do not include serology) are available outside the HDCD.
- Comparison of numbers of clinical and laboratory reports for syphilis and gonorrhoea should be done annually at the district and national level to understand what proportion of laboratory diagnosed syphilis and gonorrhoea cases are reported by clinicians
- Since the system has a lower sensitivity for gonorrhoea case reporting, it is necessary to assess the extent to which other providers participate in diagnostics and treatment. The representativeness of gonorrhoea case reporting can be enhanced by encouraging these other clinical sites to report and finding the way to encourage them to do so. In case that reporting of gonorrhoea cannot be made universal as reporting of syphilis, it is important that the composition of sentinel sites reflects the distribution of STI care.
- The STI data manager should assess on a regular basis the completeness of the data elements on the case reporting, as well as the extent to which there is duplicate reporting of cases assigned codes instead of names.
- The STI case reporting form should be revised as follows, in order to collect information necessary for understanding STI epidemiology:
 - Reporting should not be name-based but done by using unified anonymous codes. There is a need to ensure that coding is unique for individuals, so that duplicate reporting can be avoided as much as possible
 - A unified coding system could provide data on results of HIV testing among newly reported STI cases. That would enhance the utility of STI surveillance and enable assessment of HIV prevalence among those recently diagnosed with STIs
 - Add divorced and widowed to the marital categories, since there are only two marital categories currently (single and married)
 - Change the questions 14.1a “Been outside of the country in the past two year” to “Had sexual partners while outside of the country in the past two years”
 - Add a question on the result of HIV test on the reporting form, and tests used to confirm the diagnosis
 - Add a question on the gender of partners in the past 3 months
 - Add a question on the number of partners in the past 3 months
 - Add a question on antibiotic treatment given for the current episode of infection
 - Add a question on whether a case attended as a contact
 - Add a question on diagnostics performed to identify a case

STI prevalence assessment surveys

- STI shall be part of all HIV surveys planned in at risk populations.
- NAP should consider having STI prevalence surveys in key populations at higher risk (FSW, MSM, PWID) on a regular basis to complement case reporting data.
- Assessment of prevalence of syphilis and gonorrhoea should continue to be a part of IBBSS in FSW, MSM, PWID and prisoners. Testing for syphilis should include non-treponemal test also (ideally RPR) to identify more recent infections.
- These surveys should use probabilistic methods among prisoners and quasi-probabilistic methods in PWID, MSM and FSW, which are primarily RDS and time-location sampling (TLS).⁵
- It needs to be ensured that data collected by RDS are analysed by RDSAT in order to obtain population estimates of STIs and other indicators. If RDS data are not analysed by RDSAT, estimates calculated should be interpreted as obtained by non-probabilistic sampling.
- There is a need to improve the eligibility criteria for inclusion in IBBSS. For example, exclusion criteria for an PWID cannot be enrolment in a methadone treatment programme. For MSM, eligibility criteria should include having anal sex with another man in the past 6 months, and not “homosexual contact in the past 6 months”. Also, all respondents should be asked to give a consent for both behavioural and biological data collection, and not only behavioural as it was in the 2009-2010 surveys.
- There is a need to add a question on whether respondents (in all groups surveyed) got a test for syphilis in the past 12 months, and whether they know syphilis test result. This should be added in the next survey round.
- IBBSS should report on the proportion of respondents that were given back the test results and what linkages with treatment services were provided to those with reactive/ positive test results.
- Reports on IBBSS should contain an executive summary that describes the key findings and identifies the priorities for HIV and STI prevention. Executive summary should also compare the bio-behavioural indicators with those collected in the previous survey rounds and interpret the changes in the epidemic in the context of the services provided. That is particularly important in case no annual HIV/STI surveillance reports are available in Republic of Moldova .
- The reports on IBBSS should contain recommendations for HIV and STI interventions based on the survey results, for each group separately.
- Tables showing key indicators for all groups surveyed should be at the end of reports on IBBSS.
- Since there is either limited or no reporting of chlamydial infection, trichomoniasis, HPV and genital HSV infection, surveys done periodically in groups at higher risk, including young people, should include testing for these infections using tests which have high validity. Molecular diagnostics (such as PCR) should be used to test for chlamydial infection and trichomoniasis, and PCR or immunofluorescence assays for genital HSV in surveys in order to determine more accurately their prevalence, if resources permit.

Syphilis prevalence data from routine screening programmes

- Data on syphilis (and gonorrhoea) prevalence from routine screening should be available for those groups that have epidemiological significance (truckers, military, police, etc).
- Data on syphilis prevalence in blood donors should be available and analysed.
- It is necessary to set up STI screening programmes in groups at higher risk of STIs (FSW, MSM, PWID, prisoners, migrants, people living with HIV+) and collect data on the number of people tested and number of those testing positive for infections.
- Prevalence data from screening programmes should be presented by age groups (15-24; >25).

Data analysis, use and dissemination

- Surveys that require analysis of weighted data should be analysed with the appropriate survey functions (in STATA or SPSS) or software such as RDSAT. Otherwise, the primary intention of the survey design to obtain indicators generalisable at the population-level is not achieved.
- STI case reports and other data should be analysed by age groups by the internationally accepted standard classification, which is:
 - 15-24 years of age and >25;
 - 15–19 years, 20–24 years, 25–29 years, etc if data are presented by five-years age groups
- It is necessary to prepare an annual STI surveillance report that would present the data collected and analysed for the previous year, provide interpretation of the results of all STI data sources and their implications for planning STI prevention and treatment interventions under the NAP.
- In order to be able to prepare such report, at least two epidemiologists should be trained in STI and HIV data analysis and report writing.
- NAP should develop and implement a plan to effectively communicate STI surveillance data. Annual STI surveillance report should be disseminated at a joint meeting of epidemiologists, clinicians, microbiologists and to staff that plan and provide STI services to high-risk groups.
- An annual surveillance report or a summary of a report should be disseminated to health care providers who participate in STI case management, and should be available at the web site of the National Centre for Health Management and HDCD.
- Behavioural data and data on the coverage with interventions collected as part of IBBSS should be used by the NAP for planning and monitoring STI and HIV intervention strategies.

Capacity development

- Staff working on STI-surveillance related areas at the national level should receive training in STI surveillance.
- Staff should be also trained in STI data analysis and interpretation and report writing.
- Key staff from the HDCED should be trained (theoretically and practically) in quality assured diagnosis of STIs (syphilis, gonorrhoea, urogenital chlamydial infections and trichomoniasis), in accordance with international evidence-based guidelines (from WHO, IUSTI and CDC). These staff members can subsequently train additional professionals in Republic of Moldova.

- Key bacteriology specialists from the HDCD and Chisinau Municipal DV Centre should also be trained (theoretically and practically) in quality assured diagnosis, antimicrobial resistance testing, and surveillance of antimicrobial resistance in *N. gonorrhoeae*. Republic of Moldova can in this way be included in the WHO Global GASP, i.e. as one of very few countries in Eastern part of WHO European Region.

2. Priorities for operational research

Some of the priorities for the operational research include:

- Understanding of health-seeking behaviour for STIs among high-risk groups, such as FSW, MSM, migrants and PWID.
- Prevalence of gonorrhoea, chlamydial infection, trichomoniasis and genital HSV infection in the STI population and particularly the high-risk groups (using internationally recommended diagnostic methods).
- Determining the modalities for provision of STI prevention services to high-risk groups.
- Exploring why prisoners had the highest measured syphilis prevalence in IBBSS in 2012.
- Exploring a role of access to STI services for key populations in sexual transmission of HIV.
- Identifying key barriers preventing key populations from accessing STI services.
- Survey the true prevalence of gonorrhoea, antimicrobial resistance in *N. gonorrhoeae* and gonorrhoea treatment used.
- Survey the true prevalence of *C. trachomatis* and *T. vaginalis*, including trichomoniasis treatment failures.

3. Recommendations for optimization of laboratory diagnosis of STIs

- Syphilis diagnostics in Republic of Moldova are relatively adequate. However, ideally qualitative and quantitative RPR tests (always with mechanical, standardised and quality controlled rotator) should be used instead of MPR, which compared to RPR has been shown to comprise a suboptimal sensitivity.^{3 4} At a minimum, at the HDCD, RPR should be available, i.e. qualitatively for screening and quantitatively for following disease progression and/or treatment outcome. Finally, ideally TPPA should replace TPHA for ideal sensitivity and specificity.
- The capacity to perform culture for diagnosis of gonorrhoea needs to be substantially enhanced. Identification of intracellular Gram-negative diplococci in microscopy only provides a sensitive and specific definitive diagnosis for urethral specimens from males with symptomatic urethritis. For patients with only extracellular Gram-negative diplococci in microscopy, females, children, asymptomatic patients of both sexes and extragenital gonorrhoea, diagnosis based on microscopy only comprises a suboptimal sensitivity and specificity. Accordingly, these cases should be cultured and appropriate culture diagnostics is strongly recommended to be implemented in additional settings in Republic of Moldova. Furthermore, also extragenital samples should be examined when indicated by patient risk assessment.
- Culture methods for gonorrhoea are also essential to optimize in accordance with international evidence-based guidelines. Accordingly, culture should not be performed in tubes (slant agar with 2-3 mL agar) and instead ideally in Petri dishes (plates) containing

about 20 mL of selective agar, i.e. including selective antimicrobials such as vancomycin, colistin, nystatin and ideally also trimethoprim. If it is not possible to culture in plates due to limited resources, the agar used in the tubes should include the antimicrobials mentioned above (and not only lincomycin that is highly suboptimal alone to eradicate contaminating bacteria). Oxidase testing and ideally also a species confirmatory test (at least at the HDCD, a sugar utilization test, other biochemical test, or PCR) must also be available.

- Antimicrobial resistance testing of *N. gonorrhoeae*, using internationally validated, approved and quality assured methods, ought also to be introduced. At a minimum, possibilities to preserve gonococcal isolates (in -70-80°C freezers or in liquid nitrogen) need to be available. If so, Republic of Moldova can be included in the WHO Global GASP, which will be supported by WHO in regard to training, supervision and quality assurance and if required also centralized testing of the antimicrobial resistance of the frozen gonococcal isolates. Two sentinel sites for possible inclusion in the WHO Global GASP were identified during the mission. Training of 2 national colleagues at the WHO Collaborating Centre, Örebro, Sweden, will be supported. Support shall be provided locally and nationally to ensure that the gained knowledge and experience would be applicable and further put to practice in the national context for the following years.
- Diagnosis of trichomoniasis should not be performed with fixed Gram-stained smears of vaginal fluid. Instead, all samples should be diagnosed with wet-mount preparation microscopy, culture or PCR.
- Appropriate diagnosis of urogenital chlamydial infections using ideally a validated and quality assured PCR and, if not possible, at least a validated and quality assured Ag detection method, e.g. DFA, is strongly recommended. Furthermore, serology for diagnosis of acute urogenital chlamydial infections should be abandoned, due to highly suboptimal sensitivity and mostly also specificity. Subsequent to the implementation of appropriate diagnostics of urogenital chlamydial infection in Republic of Moldova, it is recommended to consider including also this infection as a mandatorily notified infection.
- Regarding PCRs and other NAATs for diagnosis of STIs, international commercially-available, validated, approved and well-recognized NAAT systems are unfortunately expensive (equipment and kits). However, there are also regionally manufactured NAATs available, e.g. Russian-manufactured PCRs, that are substantially cheaper and that also have been internationally validated to internationally acknowledged PCRs for the detection of *N. gonorrhoeae*, *C. trachomatis*, and *T. vaginalis*.⁶⁻⁸ Some of these PCRs have been proved to have an adequate sensitivity and specificity, and some can even be used in multiplex format and detect several STIs (e.g. *N. gonorrhoeae*, *C. trachomatis*, *M. genitalium* and *T. vaginalis*) at the same time.
- At the HDCD, evidence-basis or results from adequate evaluations of the performance characteristics of different STI diagnostic methods and tests used in Republic of Moldova should be available and adequate validation of new diagnostic methods should be possible to perform. The results of these evaluations need to be taking into account when selecting and procuring adequate tests for diagnosis, i.e. tests should not be selected mainly based on the lowest price.
- It is also recommended to consider to stop parts of the extensive periodic STI screening of certain occupations and population groups (i.e., those that do not evidently have a high prevalence of STIs and do not evidently represent any high-risk frequently transmitting STI population) and, in many settings, extensive testing for *Mycoplasma hominis* and *Ureaplasma* species, which are mainly of importance only for bacterial vaginosis and rarely urethritis in males, respectively. These should only be tested if there are a strong clinical indication according to internationally approved guidelines and case

definitions. This would allocate resources for enhancing the diagnostics for the substantially more common STIs mentioned above and strengthen the focus on high-risk STI populations.

- In general, an enhanced quality assurance and control system should be implemented in all laboratories. This should include not only optimised diagnostic methods but also SOPs, internal and external quality assessment controls and calibration of all equipment used for the STI diagnostics. A first step for external quality assessment (EQA) control could be that the HDCD join the WHO global proficiency testing programme for syphilis serology, which is also free of charge. In a longer perspective (after improving the diagnostics) the HDCD should consider to join EQA schemes also for *N. gonorrhoeae* (using international reference strains) and *T. vaginalis* culture as well as NAAT.

4. Recommendations for validation of elimination of congenital syphilis

- Preliminary review of data suggests that Republic of Moldova's programme to eliminate congenital syphilis is successful in elimination of congenital syphilis as a public health problem as defined by global criteria.
- Republic of Moldova should identify a routine source for monitoring syphilis testing coverage in antenatal attendees and review the national case definition for congenital syphilis to ensure that the surveillance system meets global validation standards.
- Moldova Ministry of Health could credibly request initiation of the process for validation to the WHO regional office, once regional and global systems are in place.

5. Optimizing STI policies, case management, promoting collaboration, partnership

- The ongoing efforts to revise and update national STI case management guidelines is strongly encouraged. Based on the findings of this mission, it is crucial to promptly review and appropriately revise existing national guidelines (case definitions as well as recommendations of diagnostics and treatment) and ensure that the updated guidelines strictly adhere to the WHO, International Union against Sexually Transmitted Infections (IUSTI) and other international evidence based guidelines and recommendations. The idea of having newly updated guidelines endorsed by an MOH order is encouraged. As soon as new national guidelines becomes available they should be widely disseminated, implemented and respective staff should undergo training to ensure that new standards are well followed in practice across the country. National guidelines should be updated on a regular basis.
- It is strongly recommended to carefully review and eliminate any form of mandatory, compulsory STI screening policies and practices
- It is necessary to further promote wide scale collaboration and partnership of the STI component under the NAP including that with civil society settings involving them in policy formulation, programme development, implementation and M&E
- There is a need to promote interaction, collaboration of M&E of STI, HIV and public health settings and optimize and implement data exchange platform of databases and support capacity building including trainings of staff. Data should be widely shared ensuring data analysis and use to inform a decision-making. It is advisable that the

reports and other analytical documents being published by public health institutions also include, address and discuss STI issues.

- It is advisable to attract young generation of medical doctors to work in STI public settings. The issues such as creating an attractive career path for young colleagues should be given serious attention.
- STI continuous education should be further strengthened. It is encouraged to include STI surveillance issues in the curricula for medical school and postgraduates. The existing electronic curricula/courses on HIV/AIDS of the School of Public Health might be an opportunity to consider for incorporating STI issues there.
- The important efforts of the NAP of organizing regular national meetings discussing epidemiological trends and data analysis should involve on a regular basis also HIV epidemiologists and public health epidemiologists and surveillance staff and outcomes of these meetings should be widely disseminated and become available.
- HDCD is encouraged to promote the availability in a public domain of STI data other than syphilis case reporting statistics. The STI analytical reports should be widely shared and become publicly available on a regular basis.

Appendix 1 *List of people met*

Dr Octavian Grama, Deputy Minister of Health

Dr Mircea Betiu, Head of the University Department for Dermato-Venereology; Hospital for Dermatovenereology and Communicable Diseases (HDCD)

Dr Viorel Calistru, deputy director, HDCD

Dr Iulian Oltu, director, HDCD

Mr Valeriu Plesca, director, National Centre for Health Management

Dr Tatiana Cotelnic-Harea, National Centre for Health Management

Dr Petru Bulgac, director, Municipal Centre for Dermatovenereology

Dr Vasile Morcov, deputy director, Municipal Centre for Dermatovenereology, Chisinau

Dr Victor Cebotaru, director, District Hospital of Anenii-Noi

Dr Ion Rusu, dermatovenereologist, District Hospital of Anenii-Noi

Dr Stefan Gheorghita, director, National AIDS Centre, deputy director of the National Centre for Public Health

Dr Stela Georgita, deputy director, National Centre for Public Health

Mrs Gabriela Ionascu, UNAIDS Moldova

Dr Viorel Gorceag, UNFPA Moldova

Dr Cornel Riscanu, UNICEF Moldova

Dr Angela Capcelea, UNICEF Moldova

Mr Veaceslav Mulear, GenderDoc-M (NGO)

Dr Liudmila Untura, League of People living with HIV

Dr Adriana Tudor, head of the national program department a.i., MOH

Appendix 2 Mission schedule

Monday, 11.03.2013

	Venue	Scope of discussion
09.00 - 09.45		Briefing meeting
10.00 - 11.00		Briefing meeting with MOH
11.30 – 13.30	Hospital for Dermatovenereology and communicable diseases (National STI Centre)	Meeting with STI surveillance staff. It would be good if leading person could make a presentation describing general issues re national STI surveillance system including organizational structure, data flow, staffing, M&E etc. of national STI surveillance system; STI surveillance in key populations (primarily in SW, migrants, MSM, IDUs, prisoners, PLHIV), What are the main challenges re STI surveillance and how they see the ways for improvement
13.30 - 14.30	<i>Lunch</i>	
15.00 - 17.30	MOH Head of department dealing with STI surveillance and HIV surveillance	Policy and strategy re STI surveillance ; STI surveillance data collection and management, presentation and use; capacity building
15.00 - 17.30	National STI Centre	<ol style="list-style-type: none"> 1. Discuss and review national recording and reporting formats 2. review of data collection, data flow, indicators, M&E forms and mechanisms, data dissemination and use 3. review the electronic STI surveillance data base 4. discuss the actions for national STI surveillance strengthening 5. discuss the need and potential areas for operation research 6. review national STI surveillance related normative documents

Monday, 11.03.2013

	Venue	Scope of discussion
15.00 - 17.30	National STI Centre	<ol style="list-style-type: none"> 1. Review national Lab for GC diagnosis and AMR monitoring, lab diagnosis of Syphilis and C. Trachomatis 2. discuss connections with overall national STI surveillance system and develop recommendations for improvement 3. discuss and draft the outline for operation research 4. review national STI Lab diagnosis related normative documents and advise on an update 5. discuss national STI lab diagnosis capacity building and draft recommendations for improvement
17.30 - 18.30		Meeting for mission team to discuss outcomes of first day and plan for second day

Tuesday, 12.03.2013

	Venue	Description
09.00 – 11.00	National Center for Health Management	Health information system; reporting forms, database
09.00 – 11.00	Labs other than National STI Centre that offer STI lab services	
11.30 – 13.30	Municipal Centre for Dermatovenerology	STI surveillance, STI lab, data collection, management, recording, reporting
11.30 – 13.30	Maternity no. 1	STI management and surveillance, data recording, reporting; lab
11.30 – 13.30	AMT Centre (primary health care)	STI management and surveillance, data recording, reporting
14.00 - 15.00	<i>Lunch</i>	

Tuesday, 12.03.2013

	Venue	Description
15.30 – 17.30	National AIDS Center	It would be very good if staff of National AIDS Center could give a presentation on connections, collaboration, integration of national STI and AIDS programmes; how surveillance systems are connected; data sharing; reporting; prevalence of STI in PLHIV; major challenges and ways of improvement of collaboration and integration
17.30 – 18.30		Meeting for mission team to discuss outcomes of the day and plan for next day

Wednesday, 13.03.2013

10.00 - 14.00	Field trip to the District of Anenii-Noi, Diagnostic-Consultative Department of the District Hospital	District-level outpatient (urologist/andrologist, gynecologist, maternity obstetrician, dermatovenerologist, lab)
14.00 - 15.00	<i>Lunch</i>	
15.30 – 17.30	Hospital for Dermatovenereology and Communicable Diseases (National STI Centre)	To discuss preliminary findings; ask for clarifications, additional issues etc
17.30 – 18.30		Meeting for mission team to discuss outcomes of the day and plan for next day

Thursday, 14.03.2013

	Venue	Description
09.00 – 10.30	Round table with civil society organizations	Soros Foundation, Gender-Doc-M etc. (female sex workers, MSM, harm reduction, surveys)

Thursday, 14.03.2013

	Venue	Description
11.00 - 12.30	Round table with UN	UNICEF, UNODC, UNFPA, UNAIDS
12.30 - 13.30	<i>Lunch</i>	
13.30 - 14.30		Debriefing at the WHO CO
14.30 - 18.00		Team discussion and preparing for debriefing at the MOH; preparing mission report

Friday, 15.03.2013

09.00 – 10.00		Debriefing at the MOH
11.00 – 14.00		Working on the report Finalizing draft report
		Departure

References:

¹ Centralized information system for infectious diseases. Available at:

<http://data.euro.who.int/cisid/> Accessed on 24 apr 2013.

² Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection Geneva: World Health Organization, 2012.

³ Kourbatova EV, et al. Assessment of the routine, occupation-based gonorrhoea and syphilis screening program in Moscow, Russia: an analysis of sexually transmitted infection prevalence and cost-effectiveness. *Sex Transm Dis* 2008;35:453-60.

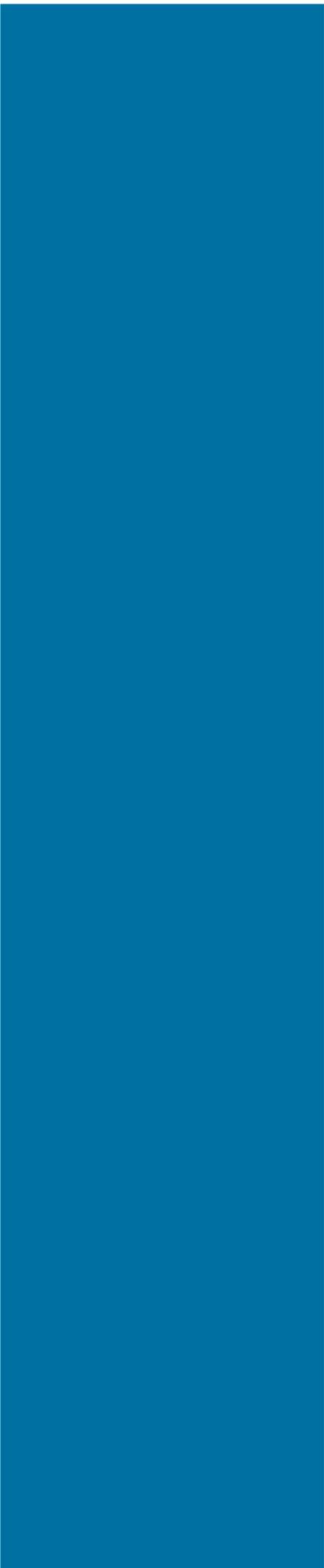
⁴ Shimanskaya I, Zhuravskaya L, Pankratov O, Unemo M, Ballard R, Domeika M. Evaluation of Three Serological Tests Manufactured in Belarus for the Diagnosis of Syphilis. *Acta Derm Venereol*. 2011;91:299-302.

⁵ Guidelines on surveillance among populations most at risk for HIV. Geneva: World Health Organization 2011.

⁶ Shipitsyna E, Zolotoverkhaya E, Agné-Stadling I, Krysanova A, Savicheva A, Sokolovsky E, Domeika M, Unemo M. First evaluation of six nucleic acid amplification tests (NAATs) widely used in the diagnosis of *Chlamydia trachomatis* in Russia. *J Eur Acad Dermatol Venereol* 2009;23:268-76.

⁷ Shipitsyna E, Zolotoverkhaya E, Hjelmevoll SO, Maximova A, Savicheva A, Sokolovsky E, Skogen V, Domeika M, Unemo M. Evaluation of six nucleic acid amplification tests used for diagnosis of *Neisseria gonorrhoeae* in Russia compared with an international strictly validated real-time *porA* pseudogene polymerase chain reaction. *J Eur Acad Dermatol Venereol* 2009;23:1246-53.

⁸ Shipitsyna E, Zolotoverkhaya E, Chen CY, Chi KH, Grigoryev A, Savicheva A, Ballard R, Domeika M, Unemo M. Evaluation of polymerase chain reaction assays for the diagnosis of *Trichomonas vaginalis* infection in Russia. *J Eur Acad Dermatol Venereol*. 2013;27:e217-23.



World Health Organization
Regional Office for Europe
UN City, Marmorvej 51
DK-2100 Copenhagen Ø
Denmark
Tel.: +45 45 33 70 00
Fax: +45 45 33 70 01
Email: aids@euro.who.int
Web site: www.euro.who.int/aids