2nd Hepatitis Technical Advisory Group (TAG) Recommendations for the Georgia Hepatitis C Elimination Program

On October 24-25, 2016, the Georgian Ministry of Labour, Health, and Social Affairs (MoLHSA), together with experts from the U.S. Centers for Disease Control and Prevention's (CDC's) Division of Viral Hepatitis (DVH), the World Health Organization (WHO), and other international partners, convened Georgia's second external Hepatitis Technical Advisory Group (TAG) meeting. A total of nine experts in the field of viral hepatitis prevention and control served as TAG members. The two-day meeting began with opening remarks from the Health Minister followed by presentations from Georgian MoLHSA and National Centers for Disease Control and Public Health (NCDC) representatives, who provided TAG members with information about the progress of the HCV Elimination Program in Georgia since its launch in April 2015. The presentations covered proposed hepatitis C virus (HCV) elimination targets to be reached by 2020, health economic models of HCV elimination and the latest draft of the national HCV Elimination Plan to reach the 2020 goals. Aspects of the Elimination Plan presented included advocacy/education, and strategies to expand access to HCV screening, care and treatment, assure quality laboratory diagnostics, implement public health surveillance for HCV, and improve prevention of blood borne transmission of HCV particularly among persons who inject drugs (PWID), and through transfusion of blood and blood products, and among persons receiving care services in health care settings and other community settings with inadequate infection prevention and control

Following each of these presentations, a discussion was led by a TAG member and included other TAG members, representatives of MoLHSA and NCDC and members of the audience. The goals of the discussion was to improve the drafted elimination plan and help the government of Georgia to reach the goals for HCV elimination. Taken together, the presentations and discussions informed TAG recommendations.

The TAG applauds the Georgian government for overall progress since the last meeting of the TAG in 2015 and the national commitment to improving the overall hepatitis C Elimination Program. TAG recognizes the ambitious targets for HCV elimination outlined in the country's HCV Elimination Plan. The TAG recognizes the work that has already been accomplished. The analysis of the first national HCV serologic survey is completed and been prepared for publication. The initial phase of the elimination program that focused on providing HCV treatment to infected persons with advanced liver disease is also completed. Since June 2016, the second phase, to treat all HCV infected individuals regardless of their disease severity, is in progress. By September, 2016, a total of 30,053 HCV infected persons registered for the program, of this number, a total of 19,338 (64.3%) started treatment, and 9,668 patients (50.0%) completed HCV treatment; 4,064 of those treated received polymerase chain reaction (PCR) testing for HCV at least 12 weeks after completion of treatment, of which 3,250 (80.0%) had no detectable virus, indicative of a sustained virologic response[1], i.e., cure. Further, the TAG commends planning efforts, reflected in the draft HCV Elimination Plan, to provide Georgians with comprehensive HCV prevention services. As was discussed at the TAG meeting, a comprehensive set of clinic based and community based interventions are needed for the country to reach goals for the elimination of HCV transmission and disease. Expansion of harm reduction services, HCV testing and treatment for PWID is essential. In addition, as revealed in health models presented at the meeting, poor infection control in healthcare and other settings are also a major mode of HCV transmission of HCV. Interventions to improve infection control in these settings are also necessary. To assist the country of Georgia in meeting the country's HCV elimination goals, the TAG provides the following guidance for development of the 2020 HCV elimination plan.

[1] Sustained virologic response is defined as undetectable (or below the lower limit of quantification) HCV RNA at 12–24 weeks after cessation of treatment (Wedemeyer H et al., 2012)

1. ***Promote Advocacy, Awareness, and Education and Partnerships for HCV-Associated Resource Mobilization***
   - ***1.1.*** Revise the public-awareness campaigns to reflect changes in screening recommendations and locations of treatment facilities
   - ***1.2.*** Campaign should incorporate messages recognizing the synergistic effect of alcohol and hepatitis C infection to cause liver damage.
   - ***1.3.*** To incorporate messages that help PWID recognize their risk or HCV and come forward to accept harm reduction, testing and treatment services. The social stigma and threat of incarceration associated with injection drug must be eliminated. Mass media campaign should incorporate messages to improve public understanding of injection drug use and addiction. Drug addiction should be addressed as a health issue and not as a crime.
   - ***1.4.*** TAG strongly encourages government agencies to collaborate and find a path toward the removal of legislation that penalizes drug use.
   - ***1.5.*** Healthcare providers and other professionals should continue receiving training to reduce or eliminate the stigma related to drug use and HCV infection.

2. ***Prevent HCV Transmission: Harm Reduction***
   - ***2.1.*** Guided by health modeling, expand coverage and improve quality of Needle Syringe Program (NSP) and Opioid Substitution Therapy (OST) including measurable targets for expanding access to these services. The progress toward these target will be a topic for TAG discussions in 2017.
   - ***2.2.*** Develop a target for number of PWID who are currently using drugs to be treated and cured per year and monitor successfully treated patients to assess reinfection. TAG recommends a goal of successfully treating at least 5,000 PWID by October of 2017.
   - ***2.3.*** Include Needle Syringe Program (NSP) and Opioid Substitution Therapy (OST) sites in the screening and treatment monitoring and evaluation system. A unique identifier would be ideal for monitoring and evaluation, and linkage to care.
   - 2.4. TAG would like to highlight the importance of a realistic, orderly and achievable transition plan of the Global Fund. The continuous support for harm reduction services in Georgia is essential for HCV elimination.

3. ***Prevent HCV Transmission: Blood Safety***
   - ***3.1.*** Establish a task force consisting of local and international experts and technical advisors which will align national regulations with European directives.
   - ***3.2.*** Establish a government agency or board that will provide the required oversight to ensure the national regulations are followed to provide safe blood transfusion services in Georgia including the validation of methods used in processing blood products and testing, regular inspections and audits of blood banks
   - ***3.3.*** All blood banks need to participate in the state safe blood program, including licensure, for production of blood and blood products. Government agency will implement mandatory participation of all blood banks in Donor Database, state quality control system and Safe Blood Program.
   - ***3.4.*** Develop national, universal standard operating procedures and guidelines for manufacturing of blood products This will include standards for donor selection and blood testing for TTI with validation of all TTI screening assays and quality assurance/quality control (QAQC) of tests that are performed in the blood banks.

3.5. Consider in the future expansion of the current donor database to include more information such as hospital receiving blood, transfusion recipients, adverse reaction of recipients, assays used to screen donations and include linkage to treatment database.

3.6. Increase voluntary blood donations to reduce the demand for donations from family recruited and paid donors. Prioritize recruitment of repeat HCV seronegative, low risk, volunteer donors.

3.7. All anti-HCV negative donations should have nucleic acid testing and where not possible, HCV core antigen testing.

3.8. Guided by Europe standards, develop a centralized repository beginning with specimens from all HCV+ blood donations at the Lugar Center.

3.9. Incorporate training in transfusion medicine into the medical education and training curricula.

3.10. Consider repositories of collected aliqouts of seronegative blood donations that have been transfused that are in storage at the Lugar center can undergo virologic detecting testing for HBV,HBV and HIV to estimate the rate of false negative and window period positive donations that have been transfused.

4. Prevent HCV Transmission: Infection Control

4.1. Continue to strengthen regulations aimed at improving infection control in healthcare settings. To demonstrate how to educate providers in infection control and enforce these regulations, the TAG recommends the launch of a model infection control program in a large clinical setting by October 2017 that includes an evaluation plan to track program results.

4.2. Continue to strengthen regulations aimed at improving infection control in non-traditional healthcare and community settings where there is the potential for HCV transmission.

4.3. Assess health care settings and providers to better understand the risk of HCV transmission in community settings.

4.4. Establish collection of surveillance data including laboratory tests from large inpatient settings to better understand where HCV transmission is occurring.

4.5. TAG recommends that Georgia consider requiring every healthcare worker with direct patient contact be mandated to take a web-based course on infection-control practices. The ECHO care model can facilitate conducting such courses.

5. Identify Persons Infected With HCV

5.1. The immediate expansion of HCV testing and linkage to care and treatment is key to successful achievement of HCV elimination goals in Georgia. In 2017, guided by the results of the national serologic survey and WHO recommendations, the TAG recommends HCV testing for all males aged 30 years or older (or all persons aged 30 years or older); this strategy can identify >70% of persons living with HCV in Georgia.

5.2. A minimum of 30,000 patients per year will need to be treated to reach the 2020 elimination goal. Population-based testing as proposed above will be needed to achieve this goal.

- ***5.2.1.*** Older patients are more likely to have advanced liver disease and will benefit from treatment.
- ***5.2.2.*** Demographic based recommendation will help reduce stigma related to HCV testing.
- ***5.2.3.*** Older persons (>60) are more likely to use healthcare services – easier to reach.

5.3. Involve a bioethicist to better address stigma-related issues in local policy development:

- ***5.3.1.*** Among healthcare workers
- ***5.3.2.*** Among younger men due to perceived IDU-related infection risk

5.4. Additionally, TAG recommends expanding access to HCV testing for populations with high HCV prevalence and with highest risk of HCV infection, particularly former or current

injection-drug users, persons undergoing haemodialysis and persons on admission and release from prison.

6. Improve HCV Laboratory Diagnostics

6.1. Assays for testing, diagnosis, and treatment monitoring should be approved by a stringent regulatory authority (such as WHO, U.S. Food and Drug Administration (FDA), or European CE marked) or validated by an evaluation protocol with results reviewed and approved appropriate experts in the field.

6.2. All specimens positive on anti-HCV testing should be tested to detect current HCV infection either with HCV-RNA or HCV-cAg if found feasible and cost-effective.

6.3. TAG requests that data coming from monitoring evaluation indicators, particularly results of quality evaluations of laboratories, be presented to the TAG in 2017.

7. Provide HCV Care and Treatment

7.1. To reach persons where they are accustomed to receiving clinical care primary care clinicians should be trained to diagnose and treat HCV infection at these sites.

7.2. Where possible, HCV testing and treatment should occur at the same center.

7.3. By October 2017, TAG recommends the launch of demonstration projects to identify the best strategies for co-locating HCV testing, diagnosis, and treatment with addiction treatment at OST centers and a NSP site.

7.4. Ensure the completion of HCV screening, care and treatment for incarcerated persons before they are released into the community.

8. Improve HCV Surveillance

8.1. Target high-risk subjects including PWIDs, and dialysis patients for case surveillance and /or serologic surveys to identify trends in disease burden, new infections, and response to treatment.

8.2. Create uniform electronic database to include all HCV surveillance data.

8.3. Repeat national seroprevalence study in 2021.

8.4. Evaluate the quality of HCV associated deaths in national registries to determine if the data can be used for baseline mortality assessment, and for periodic monitoring to assess the impact of the Elimination Program on trends in HCV mortality. If deficits in quality are found but are feasible to correct, develop a plan to improve data quality or develop an analysis plan that takes into account the limitations of the data.

8.5. Consider collecting data on hepatocellular carcinoma and cirrhosis and association with HCV infection

9. Research and Development

9.1. HCV laboratory testing

9.1.1. Evaluate all point-of-care assays to determine their appropriateness for the Elimination Program.

9.1.2. Consider establishing a system for archiving (storing) samples for HCV infected individuals for future studies. Some potential studies include: study of current HCV anti-viral resistance levels; the transmission of anti-viral resistant strains among active PWID who may fail in treatment adherence; viral RNA sequencing of individuals re-infected to discriminate between treatment failure and reinfection.

9.2. HCV Care and treatment

9.2.1. With Introduction of SOF/VEL for use in the Elimination Program, strategies that simplify screening, care and monitoring should be piloted and evaluated. Consider prospective studies and/or modeling studies to determine whether HCV genotyping can be omitted from the program, or among some selected patients or circumstances.

9.3. Prevent transmission: Harm reduction

9.3.1. Conduct research to identify the surveillance, prevention and treatment strategies that are most effective in reducing the incidence of HCV among PWID, including incidence of primary infection or reinfection after treatment.

9.3.2. After a NSP is established by removal of laws identifying opiate injection as a crime, consider studying used needle/syringes for HCV RNA and Human DNA from more than one person to indicate sharing.

9.3.3.

9.4. Improve HCV surveillance

9.4.1. Collect data on alcohol use and HCV risk behaviors among HCV-infected individuals.