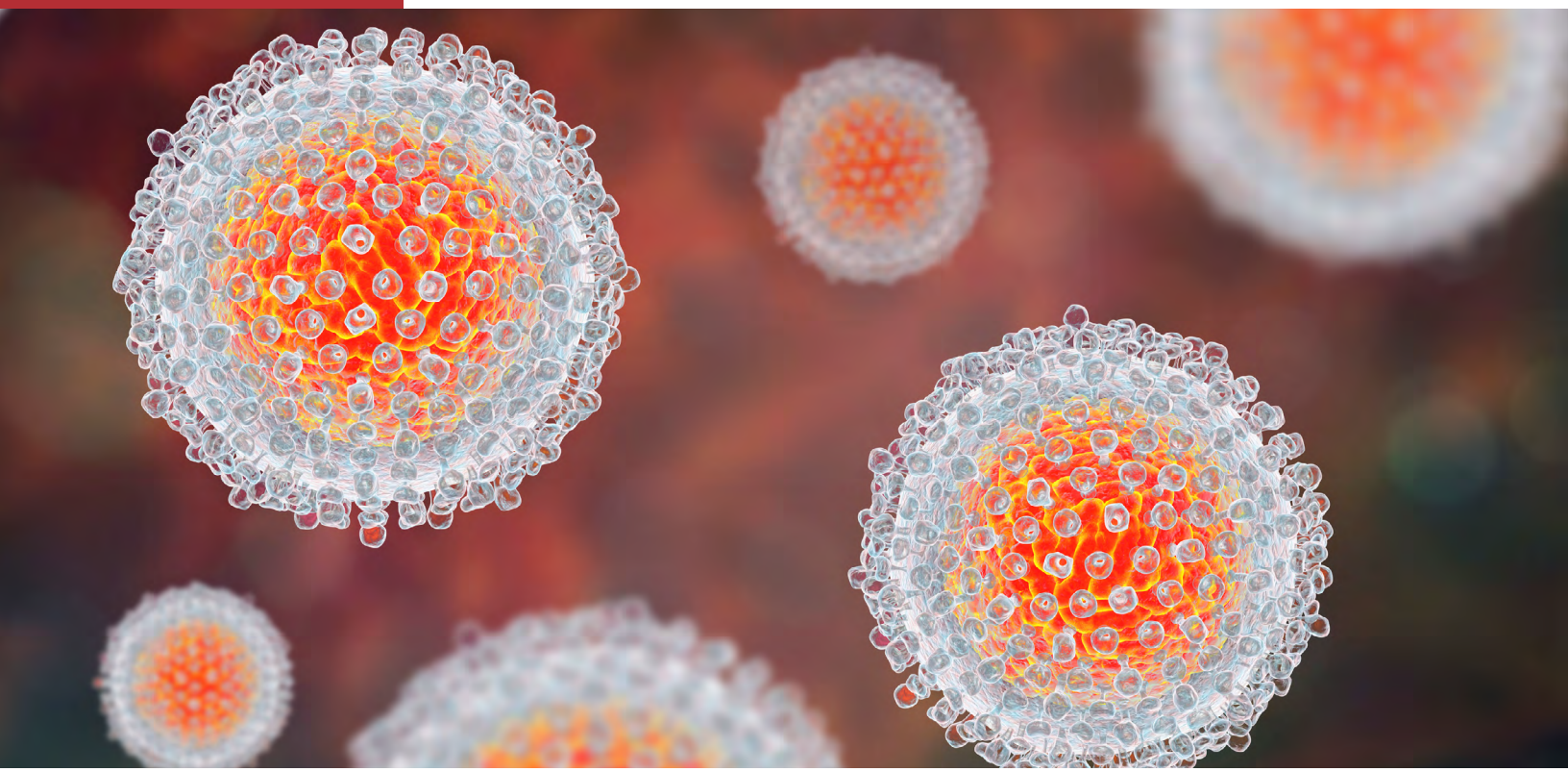
Identifying High-priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US

Final Meeting Report



NOVEMBER 2022

APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

CONTENTS

GLOSSARY

Ab ..... Antibody

Ag ..... Antigen

APHL .... Association of Public Health Laboratories

cAg ..... Core antigen

CDC ..... US Centers for Disease Control and Prevention

CLIA..... Clinical Laboratory Improvement Amendments

CMS..... US Centers for Medicaid and Medicare Services

EHR ..... Electronic health record

FDA..... US Food and Drug Administration

HBV ..... Hepatitis B virus

HCV ..... Hepatitis C virus

HIV..... Human immunodeficiency virus

POC ..... Point-of-care

PWID.... Persons who inject drugs

QC..... Quality control

STD..... Sexually transmitted disease

SME..... Subject matter expert

SVR..... Sustained virologic response

US..... United States of America

FDA-Approved/FDA Approval: The terms "FDA-approved" or "FDA approval" are used in this document as a simplification in place of a more specific term indicating the type of review/approval/authorization pathway a test method has undergone at FDA, such as "FDA-approved," "FDA-cleared," "FDA-authorized," etc., because we mention different test methods that may go through different processes. For reference, we have included the definitions for FDA approval vs. FDA clearance as it relates to the down-classification of devices discussed later in this report:

- **FDA approval:** Term used to indicate that a device has been approved through the premarket approval process (PMA), which is required for Class III devices.
- **FDA clearance:** Term used to indicate a device that has been cleared as a substantially equivalent device through Section 510(k) of the Food, Drug, and Cosmetic Act, which is required for Class II devices.

Capillary Blood: Used here to indicate whole blood collected by a fingerstick or heel stick. The blood can then be collected into a variety of different collection devices/tubes/microtainers.

Recommended Testing Sequence for Identifying Current HCV infection: Updated in 2013 by the CDC, this is a two-step testing algorithm to identify current HCV infection that consists of an initial test and a supplemental test.[1]

- **Initial Test:** The first test used in a two-step testing algorithm or sequence, regardless of whether the test is performed for screening or diagnostic use, also referred to as asymptomatic or symptomatic testing. Per the recommended testing sequence for identifying current HCV infection, the initial test should be an FDA-approved HCV Antibody (Ab) test and the outcome should be reported as either reactive or nonreactive.[1]
- **Supplemental Test:** These are additional tests, usually the subsequent (second or third) test in multi-step testing algorithms and are also referred to as "confirmatory tests." However, we have used the term supplemental test in this document as it more accurately reflects that the subsequent test in the testing algorithm isn't confirming the presence of the same type of biological marker as the initial test (i.e., antibody) but is contributing to an overall testing algorithm and diagnosis. The second test in the recommended testing sequence for diagnosis of current HCV infection is an FDA-approved nucleic acid test (NAT) intended for the detection of HCV RNA; it does not confirm the presence or absence of antibodies that are detected in the first step.[1] The outcome of the HCV NAT or RNA test is usually reported as detected or not detected.
- **Results/Interpretation:** The combination of results from the testing algorithm is used to determine the status of HCV infection in the person being tested. The potential interpretations are as follows:
  - No HCV Ab detected (HCV Ab nonreactive, HCV RNA test not performed),
  - Current HCV Infection (HCV Ab reactive, HCV RNA detected), or
  - No current HCV Infection (HCV Ab reactive, HCV RNA not detected).

  Depending on the interpretation or outcome of the testing algorithm, additional interventions are required. Please refer to the original recommendations document for more details.

Viral Detection: This term is used to indicate that a test or test method detects the virus itself, rather than an indirect marker of the virus. Examples of test methods would be nucleic acid tests (NAT), which can detect either viral RNA or DNA, and tests that detect viral proteins, such as antigen tests. For this report, tests that would fall under this category include HCV NAT or HCV RNA test methods as well as HCV core antigen (HCV cAg) tests.

EXECUTIVE SUMMARY

Hepatitis C virus (HCV) infection is the most common bloodborne infection in the United States of America (US) with more than 2.4 million persons living with HCV. Of those, approximately 40% are unaware of their infection status; and without knowing their status, they cannot benefit from curative treatment which could prevent disease progression, hepatocellular carcinoma and disease transmission—"a preventable strategy and a public health travesty."[2]

HCV infection can be cured and there are national and international hepatitis C elimination targets, yet at current incidence and treatment rates, the US is projected to reach these targets after 2050. The US Centers for Disease Control and Prevention's (CDC) Division of Viral Hepatitis (DVH) published their 2025 Strategic Plan outlining their goals for the US which were aligned with global goals to eliminate viral hepatitis as a public health threat by 2030. Specifically, 2030 goals are to reduce new HCV infections by 90% and to reduce hepatitis B- and hepatitis C-related deaths by 65%.[3,4,5] These goals are ambitious and require unfettered access to viral diagnostic, prevention and treatment services among the appropriate populations as well as coordination amongst a multitude of stakeholders.

Accurate and efficient testing to identify current HCV infection is the first step in the HCV Care Cascade (**Figure 1**) and is foundational to reach our national elimination goals.[6,7] The US currently recommends a two-step testing sequence for identifying current HCV infection; initial testing for HCV antibody (Ab) and if reactive (detectable antibody levels), supplemental testing for the detection of HCV RNA.[1] This testing algorithm was updated in 2013 to address the available diagnostic testing methods, and to recognize that individuals with detectable HCV Ab may not have current HCV infection and that significant advances have been made to the development of antiviral medications that could cure HCV. One of the largest barriers to completion of the HCV Care Cascade is that persons with detectable HCV Ab levels are not receiving the necessary supplemental testing (HCV RNA) to identify whether they have a current HCV infection and need to be linked to care (**Figure 1**).

With this as the backdrop, DVH partnered with the Association of Public Health Laboratories (APHL) to convene a two-day consultation of HCV subject matter experts (SMEs) on October 19-20, 2021, to identify high priority diagnostic tools and strategies that will have the greatest impact on advancing the elimination of HCV in the US within the next five years. The proceedings were guided by key questions whose answers and implications are documented in this meeting report. While this meeting was focused on HCV elimination, it is imperative that we also consider these recommendations and findings in the context of a holistic and coordinated response. There are ongoing and overlapping epidemics of rising STIs, substance use, HIV and HCV—addressing this syndemic, as well as the social and economic conditions contributing to their ongoing nature will be required to reach our targets and improve health at the individual and population level.

DVH 2025 STRATEGIC PLAN: HCV-RELATED GOALS[3]

- **Reduce Infections**
  Reduce new HCV infections from 44,700 in 2017 to ≤ 35,000 in 2023 and ≤ 4,400 in 2028.

- **Reduce Mortality Rate***
  Reduce HCV-related mortality rate from 4.13 in 2017 to ≤ 3 in 2023 and ≤ 1.44 in 2028.

- **Reduce Disparities**
  Reduce rate* of new HCV infections among PWID from 2.3 in 2017 to < 1.7 in 2023 and < 0.2 in 2028.

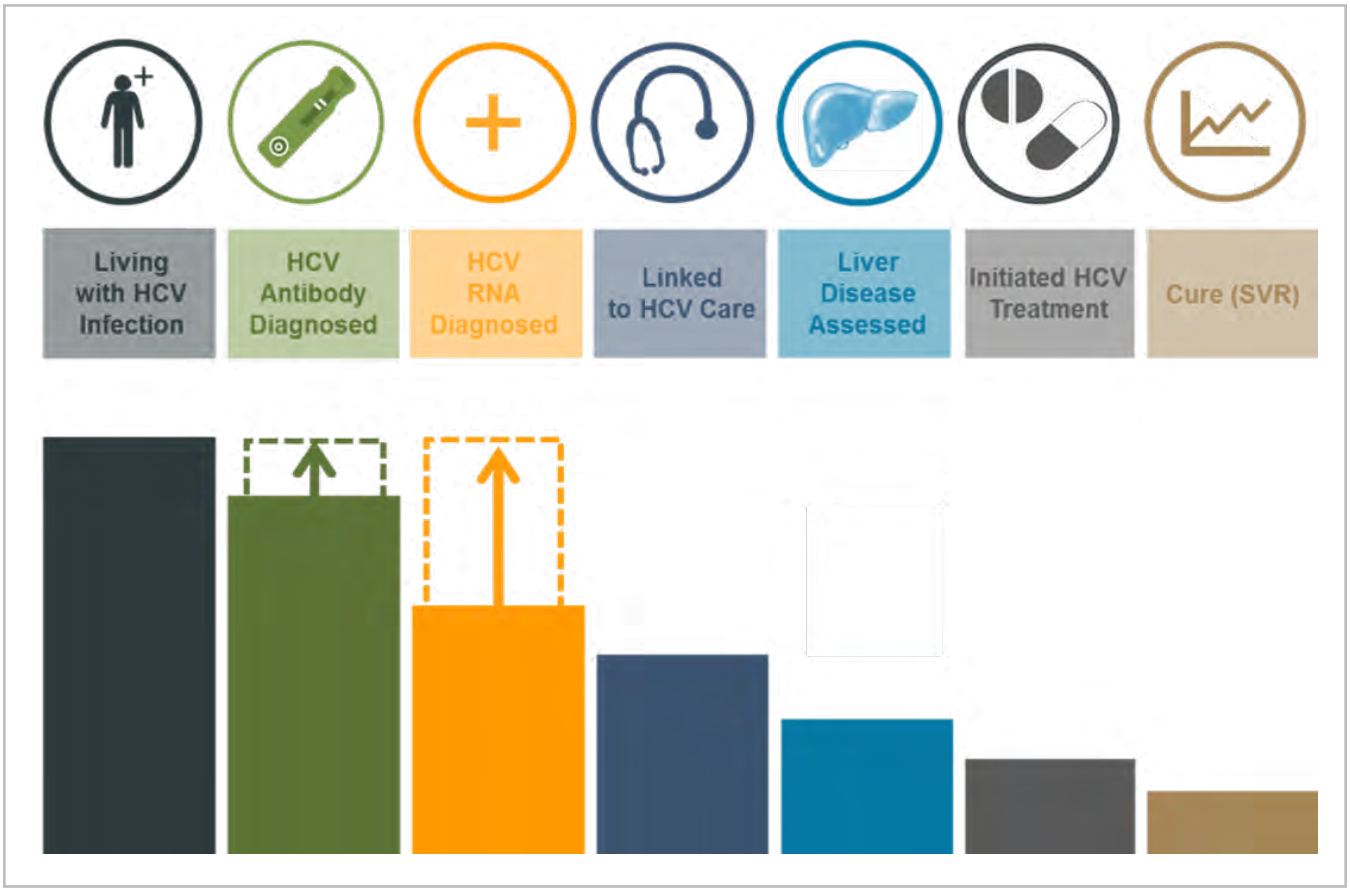
  Reduce rate* of HCV-related deaths among American Indian and Alaska Native persons from 10.24 in 2017 to < 7.17 in 2023 and < 3.58 in 2028.

  Reduce rate* of HCV-related deaths among non-Hispanic Black persons from 7.03 in 2017 to < 4.92 in 2023 and < 2.46 in 2028.

- **Establish Comprehensive Surveillance**
  Establish comprehensive national viral hepatitis surveillance for public health action.

* Rates are per 100,000 population

Figure 1: Two Step Diagnostic Process: Bottleneck in HCV Cure Cascade[6,7,8]
Credit for Image: Lynn Taylor and CDC/HRSA Advisory Committee, April 2021; graphics adapted from Grebely J Int J Drug Policy, 2015.



OVERALL RECOMMENDATIONS FOR ACTION

1. **Down-classification of HCV tests [FDA]**
2. **Address barriers to ensure appropriate reimbursement of HCV diagnostic testing [CMS and CDC]**
3. **Review and update recommendations for testing to identify current HCV infection [CDC]**
4. **Clear Messaging and Reporting of HCV Diagnostic Testing and Results**
5. **Need an FDA-approved rapid (<30 min) CLIA-waived point-of-care HCV viral detection test; ideally HCV RNA but could also be an HCV cAg or HCV cAg/Ab test**
6. **Improvements/changes to HCV tests that are already FDA-approved to optimize their use**
7. **Additional tools to facilitate testing associated with rapid treatment initiation**

There are three sub-sections below: the recommendations listed in "Foundational Changes Required" are cross-cutting issues that must be addressed to ensure the greatest impact of any other efforts identified in the "Diagnostic Tools/ Approaches Needed" sub-section. The last sub-section includes "Additional Considerations" which are other cross-cutting ideas that arose during the discussion at the meeting.

Note: *Square brackets are used to identify groups or agencies that would need to take on the primary responsibility for implementing the recommendation. They are only used in this section of the document.*

Foundational Changes Required

1. **Reclassify HCV antibody and nucleic acid tests from Class III Devices (PMA) to Class II Devices with special controls (510k) to decrease barriers to modifying currently approved methods and to bring new methods to the US Food and Drug Administration (FDA) for review [FDA].**
   Note: *On November 19, 2021 the FDA issued the final order re-classifying certain HCV Diagnostic Tests from Class III to Class II.*[9,10]

2. **Assess reimbursement challenges for HCV diagnostic testing to improve reimbursement rates and/or remove barriers to appropriate HCV Testing [Cross-cutting, US Centers for Medicaid and Medicare Services (CMS)].**
   a. Challenges were raised regarding both rates of reimbursement and ability to successfully claim with public and private health insurance plans for HCV testing under various scenarios (i.e., who and where testing is performed, frequency/interval of testing, reasons for testing, types of tests performed (bundled tests)).
   b. Assess whether the current reimbursement rates accurately account for costs of specimen collection and processing in addition to test costs. This may require multiple federal agencies working together to include the US Health Resources and Services Administration (HRSA) Bureau of Primary Health Care and Indian Health Services in addition to CMS, other agencies and private payers.
   c. Stakeholders were concerned that not all healthcare facilities/entities have re-moved requirements for specific/written informed consent following creation of additional barriers to obtain testing. Consider reviewing/ reminding and/or re-issuing guidance broadly to emphasize that HCV testing should be considered "opt-out" rather than requiring written consent.

3. **Review and update guidance for diagnostic testing for HCV [CDC].**
    a. Consider creating additional algorithms to fit the populations or settings where persons are seeking care/testing is being ordered or performed.
        I. Consider need to maintain one-time screening of all adults with HCV Ab (with automatic reflex to HCV RNA for HCV Ab reactive specimens) for persons seeking care in healthcare settings and creating updated algorithms focused solely on viral detection (see 3b) for risk-based/high-prevalence settings.
        II. Consider stakeholders' tolerance for different levels of sensitivity/specificity for a test and/or setting.
        III. Examine other situations, such as HIV testing algorithms, which have been adapted to meet the needs of different populations and settings (laboratory based, non-clinical, etc.).
        IV. Explore the role for self-collection and self-testing and how it may address unmet needs and gaps in testing.
    b. Consider single-step testing focused on viral detection as the only step or an updated two-step testing sequence with viral detection as the first step.
        I. In both cases, HCV RNA was the preferred target but either HCV RNA or HCV cAg could meet the definition for viral detection.
        II. Examples of settings where this algorithm might be most appropriate include correctional facilities, emergency departments, substance use treatment settings, opioid treatment programs, federally qualified health centers (FQHCs), other community-based testing sites and mobile/outreach settings.
        III. CDC would need to work with HCV surveillance programs to review the impacts on surveillance methods and their ability to assess movement towards elimination both locally and nationally.
        IV. CDC and other organizations would need to evaluate and recommend testing algorithms with consideration for populations where this would make the most sense for diagnosis while being mindful of cost-effectiveness and reimbursement.
        V. Diagnostic manufacturers and FDA need to collectively identify data needs to update FDA-approved HCV RNA assays to include an intended use claim that allows for the use HCV RNA methods (or potentially HCV cAg when available) in the absence of HCV Ab results for detection of current HCV infection.
    c. Consider eliminating ability to order/receive results from HCV antibody (Ab) tests in isolation.
        I. Having results only from an HCV Ab test causes confusion for patients and creates unnecessary stigma and delays in diagnosis.
        II. Implementation of this approach would likely require policy and regulatory/statue to execute.
        III. It would require laboratories performing HCV Ab tests to ensure reflexing to HCV RNA following a reactive HCV Ab result.
        IV. There is precedence for a regulatory requirement for this in New York City.
        V. Identify the role of HCV cAg in the diagnosis of current infection, treatment initiation and sustained virologic response (SVR). This will require input from numerous partners, including determining appropriate reimbursement rates.
    d. Ensure clear messaging and reporting of HCV diagnostic testing and results [Diagnostic Manufacturers, FDA, Laboratories, Partner Organizations].
        I. As testing/treatment occurs in more diverse healthcare settings, it is imperative that there are clear instructions and messaging on proper test ordering and resulting to ensure results are used appropriately prior to treatment initiation as well as for monitoring and for confirmation of SVR.
        II. If there are changes to testing recommendations/algorithms, patient and provider education and clear reporting will continue to be essential for proper interpretation and implementation of test results.

Diagnostic Tools/Approaches Needed

1. **Development and FDA approval of rapid (<30 minutes from sample collection to result), Clinical Laboratory Improvement Amendments (CLIA)-waived point-of-care (POC) HCV RNA test [Diagnostic Manufacturers, FDA].**
    a. Diagnostic Manufacturers with commercially available tests (outside the US) should take necessary steps to bring tests to market (FDA approval) and/or develop HCV diagnostic tests to fit this goal.
    b. Supplemental testing may still be required depending on recommended testing algorithms, the population being tested as well as the sensitivity, specificity and positive predictive value of the method.
    c. Considerations for development and implementation of test method should include:
        I. Test performance (e.g., sensitivity, specificity, positive predictive value, negative predictive value, etc.)
        II. Test cost and scenarios under which reimbursement will be possible
        III. Indication for use should include diagnosis and treatment monitoring (i.e., to ensure ability to use result for rapid treatment initiation and SVR)
        IV. Ensuring test results are reported to public health authorities and connected with health information systems.
    d. Coordination of stakeholders to ensure rapid and widespread implementation of new testing and test algorithms [CDC, AASLD, USPSTF] and ensuring appropriate mechanisms for reimbursement [CMS].

2. **Development and FDA approval of a rapid (<30 minutes from sample collection to result), CLIA-waived point-of-care HCV cAg or HCV cAg/Ab (with ability to differentiate cAg/Ab) to identify current infection [Diagnostic Manufacturers, FDA].**
    Same considerations as #1 above.

3. **Improvements to laboratory-based testing methods.**
    a. Increase laboratory implementation of auto-reflexing HCV Ab-reactive samples directly to HCV RNA testing [CDC, Clinical Laboratories, Public Health Agencies, State/Local Governments, Health Systems, Partner Organizations]. Provide education, training and technical assistance to all laboratories to ensure best practices are shared and implemented.
    b. Create different kit sizes and extended storage time for test reagents, controls and calibrators enabling smaller-volume laboratories to use high throughput/random access instruments more cost-effectively [Diagnostic Manufacturers, FDA].
    c. Seek and obtain updated indications for use on already FDA-approved test methods (HCV Ab and HCV RNA) for additional specimen types, such as dried blood spot (DBS), capillary blood and plasma separation cards [Diagnostic Manufacturers, FDA].
    d. Obtain updated intended use claims on previously FDA-approved HCV RNA methods to be used as first or only test for diagnosis of current HCV infection (remove requirement for HCV Ab result) so that they could be used for screening or diagnosis of current HCV infection [Diagnostic Manufacturers, FDA].

4. **Additional tools to facilitate testing associated with Rapid Treatment Initiation.**
    a. Development and FDA approval of a rapid (<30 minutes from sample collection to result), CLIA-waived POC hepatitis B virus surface antigen (HBsAg) test [Diagnostic Manufacturers, FDA].
    b. Development and FDA approval of laboratory-based, and or CLIA-waived POC multiplex for HCV, HIV and HBV NAT test [Diagnostic Manufacturers, FDA].

Additional Considerations

These are broad additional considerations that were raised during the meeting and either fit in more than one place in the document or were not specific to any one key question.

1. **Broad and reinforced endorsement and education about opt-out testing for HCV [CDC, Stakeholders].**
   Due to issues with entities, facilities or providers requiring consent prior to testing due to actual policies or misunderstanding policies related to informed consent for HCV testing.

2. **Further assess barriers to bringing tests to market in the US [CDC, APHL, FDA, Stakeholders].**
   The assessment should include those tests approved for use outside the US.

3. **Consider mechanisms to ensure samples are available to manufacturers to conduct needed evaluations and data collection [CDC, APHL, FDA, Stakeholders].**
   This will be especially important for alternative specimen types, such as capillary blood or DBS, and access to paired specimens to establish clinical performance.

4. **Further assess current HCV Care Cascade [Meeting Stakeholders].**
   Determine if there are other aspects of testing that can be addressed (i.e., determination of SVR) to streamline and simplify HCV care pathways.

5. **Develop testing algorithms or recommendations for perinatally-exposed infants like those developed for detection of HIV [CDC, APHL, Stakeholders].**
   Testing for this population poses additional complications that must be addressed for a comprehensive HCV elimination strategy and will require FDA-approval of non-venipuncture specimens, such as capillary blood and/or smaller volume collections.

6. **Suggestion to consider possibility of HHS declaration of a public health emergency for HCV infection thereby opening the door for EUA for HCV diagnostics needed to combat it [CDC, FDA, Stakeholders].**
   This would be a temporary solution and any diagnostic tools approved under an EUA would need to still be cleared through the 510K process to be used once the emergency ended.

PROCESS SUMMARY

Background

Beginning in June 2021, APHL began planning this meeting, Identifying High-priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US, in collaboration with CDC's Division of Viral Hepatitis to convene key experts to discuss the high-priority diagnostic approaches needed for advancing hepatitis C elimination in the US over the next five years. APHL and CDC worked together to define the key questions (**Appendix A**). For each key question, SMEs were chosen to participate in a panel to present and discuss the topic. The panel included representation from different perspectives, including a clinical provider, a clinical laboratory scientist and a representative from a state or local public health agency.

Meeting

Invited participants represented SMEs and stakeholders from a variety of settings and roles to ensure comprehensive discussion and input. Participants included representatives from public health laboratories; clinical laboratories; large commercial laboratories; clinical providers; academic researchers; public health agencies; diagnostic manufacturers; CDC National Center for HIV, Viral Hepatitis, STD, and Tuberculosis Prevention (NCHHSTP) Office of the Director, and Division of Viral Hepatitis (DVH); US Centers for Medicare and Medicaid Services (CMS); US Food and Drug Administration (FDA); US Health and Human Services Office of the Assistant Secretary for Health (OASH) and Office of Infectious Disease and HIV/AIDS Policy (OIDP); US National Institutes of Health's National Institute of Allergy and Infectious Diseases (NIAID); Foundation for Innovative New Diagnostics (FIND); World Health Organization (WHO); and other partner public health organizations. For a complete list of participants see **Appendix B**, and find their financial disclosures in **Appendix D**.

The goal of the meeting was for all invited participants to listen to each panel present their input and perspective on their assigned key question. Participants were also expected to provide feedback on all the key questions to generate high priority needs and recommendations for each key question. To ensure each key question was evaluated appropriately, each panel had 75 minutes total, including a 15 minute presentation, 9 minutes for input from 3 panelists, up to 10 minutes for invited comments from FDA, CMS and/or Diagnostic Manufacturers , followed by 30-40 minutes for a facilitated discussion and input from all the participants (Agenda; **Appendix C**). The presentation was focused on the background and information necessary for consideration of the key question as well as the expert opinion of the presenter. Panelists were asked to provide their expertise on the key question from their role within the system. Moderators were asked to facilitate the discussion with three ideas in mind: 1) identifying and prioritizing diagnostic needs, 2) identifying and prioritizing research questions/data needs and 3) identifying and prioritizing the barriers that must be addressed to achieve the outlined goals. Additionally, participants were able to use the chat feature at any point during the meeting. During the second day, the panelists each had five minutes to give updated/summarized priorities and another five minutes to get feedback from the participants. At the end of the meeting a list of overall recommendations was compiled.

Report

This document summarizes the overall recommendations and then the major discussion points by key question, representing input from all participants, including those that presented slides or perspectives during the panels. For each key question that was discussed, background information is provided followed by the collective recommendations, any identified research/diagnostic development needs to fully address the question and barriers. The recommendations contained within this document represent those of the speakers, panelists and attendees at the meeting. Recommendations contained within this document do not represent recommendations from CDC.

This is the final meeting report which was developed following a process where APHL published a draft meeting report and sought public comment for six weeks. All submitted comments were reviewed. Comments relevant to the accuracy of the summary meeting report were addressed by APHL and incorporated into the final meeting report as needed. Comments about findings in the report will be collected and shared with our partners at CDC.

MEETING SUMMARY

Opening Session

As the opening session did not have any discussion or formal question and answer we have provided here a summary from each of the four invited speakers.

The Role of Diagnostics in Advancing Hepatitis C In the US,[6] Carolyn Wester

The rate of reported acute hepatitis C cases increased 333% during 2010-2019 (1.3 cases per 100,000 in 2019) with rates highest among 20–39-year-olds (2.9 cases per 100,000). There are also an estimated 2.4 million Americans living with hepatitis C, but only about 60% of people with hepatitis C are aware of their status. The US 2025 goals for hepatitis C are to reduce new infections by ≥ 20% and to reduce related deaths by ≥ 25%. In 2020, CDC updated their HCV screening recommendations to include testing for all adults (at least once), every pregnant person (every pregnancy) and everyone with risk factors (regularly).[8] Despite the new recommendations, there are challenges to increasing HCV testing in the US, including the fact that the populations affected by the recommendations (**Table 1**) and the service delivery settings vary widely. Additionally, diagnosis of HCV requires a two-step testing algorithm which poses two challenges: the first is a missed opportunity to detect early HCV infection and the second is that it is one of several known bottlenecks in the "HCV Cure Cascade" (**Figure 1**).[6,7]

Table 1: Populations affected by recommendations vary widely[6]

Population	Estimated Population Size	Estimated HCV Positivity
Adults (≥ 18 years old)	255,000,000 (2019)	1.7%
Pregnant Persons	3,790,000 births (2018)	3.8 per 1,000 live births
Persons who Inject Drugs	6,612,488 (2011)	54.2%

Dr. Wester also laid out some priorities for advancing HCV diagnostics in the US and highlighted some potential algorithms. Amongst the priorities she identified was the need to increase access to accurate, simple, rapid, affordable testing that detects current HCV infection and ideally in a single-step algorithm. Testing should be available in clinical settings as well as non-clinical settings such as community-based and home settings. Allowable specimens for testing could vary by testing setting but should ideally include venipuncture blood, capillary blood, DBS and oral fluid.

Down-classification of Hepatitis C Virus Diagnostics,[11] Maria "Ines" Garcia

The FDA follows a risk-based review of in vitro diagnostics (IVD) or medical devices which includes the reagents, instruments and systems used in the diagnosis of disease or other conditions to cure, mitigate, treat and prevent disease. The FDA is assessing the balance of the benefit and the risk to the individual. Class I devices are those that have a low likelihood of harm and risk can be mitigated using general controls. Class II devices have a moderate likelihood of harm or risk but that can be mitigated using special controls which are designed for the intended use of the device. All devices with the same intended use would comply with the same special controls. Hepatitis A virus IVDs are currently Class II, and this was the proposed Class for down-classification of HCV devices (which was approved after the meeting). Class III devices are those where there is a high or unknown likelihood of harm from an incorrect result and/or there is significant risk. Class III devices go through a review process called PMA. Dr. Garcia outlined the differences between Class III and Class II devices, the proposed down-classification for HCV diagnostic tests and discussed the proposed special controls for HCV Ab tests and HCV RNA assays. The goal of the HCV reclassification is to continue to ensure safe and effective tests enter the US market, maintain high performing tests and remove some potential perceived barriers to entry into the US market.

HCV Diagnostic Tools-in the Development Pipeline,[12] Sonjelle Shilton

The focus of FIND is on quality and cost of diagnostics for the global south with a specific interest in low- and middle-income countries. In terms of ensuring high-quality testing, Dr. Shilton described the stringent regulatory authority (SRA) that was developed by WHO and other entities to guide medicine procurement but is now widely recognized by the international regulatory and procurement community which also feeds into the WHO pre-qualification process. Globally between 2018-2020, three assays were made available: Cepheid® Xpert HCV Fingerstick cartridge, GeneDrive® HCV ID Kit and DBS HCV RNA on the Abbott m2000. In 2021, the following items were either launched or planned to launch: Fujirebio's INNOTEST HCV Ab DBS, OraSure Oraquick® HCV Ab self-test (oral fluid), Premier Medical Corp First Response HCV Ab Self-test (blood-based), DBS HCV RNA on Roche CAP/CTM and TrueNAT™ HCV (Molbio Dx). For 2022, two additional assays are expected: HCV test on BlinkOne and the HCV Assay on SAMBA II. The WHO recently recommended that HCV self-testing should be offered to accelerate progress toward achieving global elimination goals.[13]

There are four near POC HCV RNA assays currently available globally, including the Xpert HCV VL Assay (plasma), Xpert HCV Fingerstick VL Assay (capillary blood), GeneDrive HCV ID Assay (plasma) and TrueNAT™ HCV Assay (plasma, serum, capillary blood) with high sensitivity (91-99%) and high specificity (98-100%) and time-to-result in 60-110 minutes. However, while there is improving technology, it is only as good as the system that it exists within. A POC or near-POC test doesn't always equal patient impact; we also need to simplify the overall patient journey from testing to cure.

Using currently available technology, the Country of Georgia conducted a study that showed either using a POC HCV RNA assay or ensuring that HCV RNA testing is performed using direct specimen referral to a central laboratory resulted in 99.8-100% of patients getting HCV RNA testing completed compared to a patient being referred to a collection site for blood draw to obtain the HCV RNA testing (standard of care) in which case only 91% of patients obtained HCV RNA testing.

What is Needed to Move Toward Single-step Diagnosis of Current HCV Infection?[14] Jordan Feld

HCV diagnosis and treatment needs to be simplified. As was discussed previously, there are many bottlenecks or places to "get lost" in the process, especially if HCV isn't a priority (either to the patient or healthcare provider). A preferred approach would be immediate diagnosis (current infection) followed by same day treatment initiation, at least for key populations. However, the preferred approach would require a change from a two-step to a single-step testing algorithm and there are many questions that would need to be addressed for this change. Dr. Feld reviewed the following questions, providing published data to address each question:

- Is there value in knowing about past HCV infection?
- Does it have to be an HCV RNA test?
- Does it have to be POC and what do we mean by that?
- What sensitivity is acceptable?
- Do we need a one-size-fits-all solution?
- What are the cost considerations?

In summary, a single test HCV diagnosis is possible, but it is critical to match the testing paradigm to the clinical situation—time to diagnosis is not always the biggest challenge or item to be addressed. HCV cAg testing could be useful (cheaper than HCV RNA testing) but is not yet available or good enough as a stand-alone diagnostic and would be better as an HCV cAg/Ab differentiating test. True POC testing needs to be faster (< 5 minutes) and utilize specimens that don't require phlebotomy.

Key Question 1:
What HCV diagnostic tools are needed to optimize diagnosis of current HCV infection in moderate to high-volume laboratories performing moderate or high complexity testing?

Laboratories performing moderate or high complexity testing perform the majority of HCV diagnostic testing in the US currently. They can utilize large/multi-access, high-throughput instruments which can test hundreds of samples a day. They are also able to perform testing for HCV Ab, HCV RNA as well as genotyping in addition to testing needed to initiate HCV treatment and/or screening for co-morbid conditions. The tools that currently exist are highly sensitive and specific and functionally meet the needs of HCV diagnosis. However, there are still challenges that must be addressed. Since a large majority of testing is happening in these laboratories, if they do not require that submitters order testing that is sufficient for diagnosis, there are missed opportunities (i.e., ability to order HCV Ab only as compared to requiring an automatic reflex for all HCV Ab-reactive samples to be tested for HCV RNA) for improving HCV diagnosis. Additionally, laboratories must follow rules and regulations set forth by the FDA as well as their accrediting agency (e.g., CLIA, CAP, etc.) which means that tests can only be used for their intended purpose, or the laboratory must establish the performance characteristics to use the test in ways that are not included in the FDA approval, also known as validating the test as a laboratory developed test). This means that an HCV RNA test, which is not currently approved for use in the absence of an HCV Ab test, should not be ordered as a stand-alone test unless the laboratory has established the performance characteristics for using the method in this way. This is also true for specimen types that are not FDA-approved, such as DBS, plasma separation cards, microtainers or specimen types that are self-collected (in a clinical or non-clinical setting).

New Diagnostic Approaches Needed

1. **Laboratory-Based HCV cAg/Ab Differentiation Combination Assays**
    a. The ideal assay design would include multiple targets for both HCV cAg and Ab to ensure high specificity and must differentiate between the two targets and would include the following specimen types: serum, plasma, capillary blood and DBS
    b. Guidelines and recommendations should be aligned to ensure that that the detection of HCV cAg (especially if HCV Ab nonreactive) would be sufficient to indicate current HCV infection.
    c. Clear reporting language and interpretations would be available, and education would be necessary.

2. **Low-throughput/Cost-effective Testing Platforms**
    Testing platforms (both serology and molecular) that have lower throughput and would be more cost effective in a small-to-medium volume laboratory.

3. **Integrated Multianalyte Serologic Assays**
    HCV with HIV, HBV, syphilis.

Opportunities for Improvement of Current Diagnostic Methods or Approaches

1. **Modifications to intended use of currently FDA-approved HCV RNA assays to allow for use in the absence of HCV Ab results or if HCV Ab-nonreactive for suspected current/acute infection.**
    a. Important for detecting acute infections and for early infant diagnosis.
    b. Instructions for use would need to be developed that allowed for appropriate test result interpretations depending on whether an HCV Ab result exists or not.

2. **Modifications to specimen types on currently FDA-approved HCV Ab and HCV RNA tests to include capillary blood, DBS, plasma separation cards and/or other alternative specimen types.**
    This would allow for a diversity of options and facilitate flexible implementation of test methods and approaches to align with the capacity and resources of the programs/laboratories/providers. Ultimately, this also promotes access and acceptability of testing among individuals who seek or would benefit from testing. Specifically, it allows for specimens to be collected in the absence of phlebotomy or when phlebotomy is not preferred.

a. Develop accompanying best practices for collection of these alternative specimen types and processing of them in the laboratory to maximize sample recovery.

b. Considerations for additional measures around handling DBS given the potential for very high HCV RNA levels in persons with HCV infection and the highly sensitive methods used for detection. Laboratories must be cautious about processing these specimens. Perforated DBS cards would be helpful. Additionally, testing of DBS would likely be most appropriate for small-to-medium volume laboratories due to the significant hands-on time necessary for processing the specimens (in the absence of any major change).

3. **Modifications to currently FDA-approved HCV RNA assays, including offering smaller kit sizes and/or extending the storage time allowable for test reagents, calibrators and controls.**
Currently some instruments require that the calibrators/controls be used within 24 hours after opening. A small-to-medium volume laboratory may not be able to use the full volume within that timeframe without batching. To optimize turnaround times and not waste resources, a smaller volume of calibrators/controls and/or a longer storage time (increasing to 72 hours) would enable laboratories to decrease or eliminate batching.

4. **Increased implementation of automatic reflexing of HCV Ab reactive specimens to HCV RNA Testing (following the current recommended algorithm).**
Based on US CAP Survey June 2021: 2,242 laboratories perform HCV Ab testing but only 452 perform HCV RNA testing (may not all be US laboratories). To decrease barriers to implementation, the following items should be considered:

   a. Policy/Regulatory Items:
      I. National organizations (federal and non-governmental) to recommend automatic reflexing of HCV Ab reactive specimens to HCV RNA testing and provide support for implementation, including methods to minimize, reduce or remove concerns about cross-contamination of samples.
      II. CDC and other funding agencies could incentivize laboratories to implement automatic reflex testing by making it an essential including component of future funding opportunities targeting laboratories.
      III. Work with Accountable Care Organizations (ACO) to make automatic re-flex testing a quality metric.
      IV. Work with laboratory regulatory/accreditation agencies to require reflexing as a practice whether performed in-house or through referral. An example of one potential option is to work with CAP (laboratory regulatory agency) to add automatic reflexing of HCV Ab reactive specimens to HCV RNA testing as part of the checklist used for reviewing/inspecting laboratories. If a laboratory does not complete something on the check-list there are different level of deficiencies that can be assigned. If this item was a Phase II deficiency it must be corrected before accreditation is granted since they seriously affect the quality of patient care. Alternatively, a Phase I error requires correction and a written response and could be a good place to start to require a change in testing practices.
      V. Assessing the regulatory landscape to determine who has the regulatory authority to require laboratories to perform HCV RNA testing on all HCV Ab-reactive specimens.

   b. Implementation Items:
      I. Create standardized laboratory workflows or best practices (to cover specimen collection, minimizing cross-contamination and extra specimen handling) to be shared broadly with all laboratories performing HCV testing
      II. Laboratory to implement mechanisms to ensure that all HCV Ab-reactive samples receive HCV RNA testing (i.e., programming of LIMS or other alerts/reminders).
      III. Laboratory to remove option for ordering HCV Ab only.

   c. Education/Awareness:
      I. Work with clinical providers, health systems and laboratories to deter-mine barriers to implementation and identify alternative methods to help address identified barriers.
      II. Ensure all stakeholders understand the purpose for the automatic re-flex, ordering of the test and receiving results.

Barriers to be Addressed

1. **Billing and Reimbursement for HCV Testing**
   a. Billing and reimbursement for HCV testing is complex and varies depending on who is covering the payments (i.e., Medicaid, Medicare and/or private insurance). To be reimbursed for laboratory testing the appropriate procedure codes, screening codes and/or diagnostic codes must be utilized.
   b. CMS/Medicaid reimbursement is based on USPSTF screening recommendations to determine if the preventative screening is beneficial. The coverage criteria do not specify whether testing is started with HCV Ab or HCV RNA testing. CMS reimburses testing for once in a lifetime testing and for at-risk individuals, such as perinatal, infant, person with injection drug use. However, CMS, nor other entities define the interval for repeat screening for at-risk individuals and coverage
   c. Medicare has stringent criteria regarding the type of provider and setting for which screening tests may be reimbursed.
   d. There is no standard, accepted or codified interval for repeat screening for at-risk individuals and therefore coverage of repeat screening is variable.
   e. When billing for laboratory tests for HCV there are different coding requirements for screening and diagnosis, but this is true for many disease conditions so sharing best practices for billing and reimbursement could be useful.

2. **HCV Testing Algorithms**
   Testing algorithms would need to be updated to allow for using HCV RNA as an initial testing option, including for specific situations such as early infant diagnosis, detection of acute HCV RNA infection in persons without HCV Ab or persons at high-risk that have not had an HCV Ab test performed.

3. **Consent Requirements**
   Pre-testing consent requirements should be removed. Consent requirements (or lack of) should be clearly communicated to persons/agencies offering and/or ordering testing.

4. **Regulatory Approval Process**
   In order for IVD manufacturers to obtain regulatory approval for new assays and/or modifications to currently approved methods, the cost and effort required to navigate the regulatory approval process must be reduced.

Other Considerations

1. **Public Health and Institutional Policies/Operational Decisions**
   Public health and institutional policies/operational decisions are also important for addressing the barriers in the HCV Care Cascade using already available diagnostic tools.

   One health department (HD) forced the discontinuation of rapid testing (for HIV and HCV) and required testing sites to submit to their public health laboratory (PHL). This allowed the PHL/HD to implement integrated testing (HIV, HCV, syphilis) with automatic reflexing for confirmation which has helped them achieve public health objectives, including testing for multiple pathogens, timely data for surveillance along with implementation of third-party billing (Medicaid, Medicare, commercial insurance) which has resulted in generation of revenue for the laboratory.

   Another consideration that was addressed, though not fool proof, is implementing mechanisms in electronic health records (EHRs) to facilitate appropriate testing and follow-up.

2. **Reflex to HCV Genotyping**
   There are certain situations where HCV genotyping is required to initiate treatment (i.e., typically payer requirements) and/or evaluate a potential treatment failure versus re-infection. When this is the case, it is important to ensure rapid access to HCV genotyping to minimize delays in treatment initiation. Some laboratories may be able to offer a reflex to HCV genotyping as part of their test order (if HCV RNA is detected), which would provide a more rapid turnaround than having to order a new test once the HCV RNA result is provided.

Key Question 2a:
What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in low-volume settings performing moderate complexity laboratory testing?

This key question spanned two "settings" a moderately complex laboratory with low volume (not likely to use high-throughput instrumentation as in Key Question 1) and a CLIA-waived setting where testing would be performed by trained, but non-laboratory staff. Testing in these settings would need to be relatively rapid with less than 30 minutes from sample collection to result in order to return a result within the same office visit/encounter and ideally with specimen types that don't require phlebotomy. Additionally, the testing should utilize either lower throughput instrumentation or CLIA-waived testing that can detect current HCV infection (i.e., HCV cAg, HCV RNA). These settings could be clinical settings facilitating rapid diagnosis and/or HCV test and treat strategies, such as primary care/traditional healthcare settings, medication-assisted treatment and/or substance use treatment facilities and correctional facilities. However, any CLIA-waived testing that could be used in these settings would also likely be amenable to testing in non-clinical test settings (see Key Question 3 for more focus on these settings) whereas a moderate complexity test would be required to be performed in a laboratory setting and might not be suitable for use in the settings described in **Key Question 3**.

New Diagnostic Approaches Needed

1. **Laboratory-based HCV cAg/Ab Differentiation Combination Assays**
   a. The ideal assay design would include multiple targets for both HCV cAg and Ab to ensure high specificity and must differentiate between the two targets and would include the following specimen types: serum, plasma, capillary blood and DBS.
   b. Guidelines and recommendations should be aligned to ensure that the detection of HCV cAg (especially if HCV Ab nonreactive) would be sufficient to indicate current HCV infection.
   c. Clear reporting language and interpretations would be available, and education would be necessary.

2. **Low-throughput Testing Platforms**
   Testing platforms (both serology and molecular) that have lower throughput and would be more cost effective in a small-to-medium volume laboratory.

3. **Integrated Multianalyte Serologic Assays**
   HCV with HIV, HBV, syphilis.

Opportunities for Improvement of Current Diagnostic Methods or Approaches

1. **Modifications to intended use of currently FDA-approved HCV RNA assays to allow for use in the absence of HCV Ab results or if HCV Ab-nonreactive for suspected current/acute infection.**
   a. Important for detecting acute infections and for early infant diagnosis.
   b. Instructions for use would need to be developed that allowed for appropriate test result interpretations depending on whether an HCV Ab result exists or not.

2. **Modifications to specimen types on currently FDA-approved HCV Ab and HCV RNA tests to include capillary blood, DBS, plasma separation cards and/or other alternative specimen types.**
   This would allow for a diversity of options and facilitate flexible implementation of test methods and approaches to align with the capacity and resources of the programs/laboratories/providers. Ultimately, this also promotes access and acceptability of testing among individuals who seek or would benefit from testing. Specifically, it allows for specimens to be collected in the absence of phlebotomy or when phlebotomy is not preferred.
   a. Develop accompanying best practices for collection of these alternative specimen types and processing of them in the laboratory to maximize sample recovery.

b. Considerations for additional measures around handling DBS given the potential for very high HCV RNA levels in persons with HCV infection and the highly sensitive methods used for detection. Laboratories must be cautious about processing these specimens. Perforated DBS cards would be helpful. Additionally, testing of DBS would likely be most appropriate for small-to-medium volume laboratories due to the significant hands-on time necessary for processing the specimens (in the absence of any major change).

3. **Modifications to currently FDA-approved HCV RNA assays, including offering smaller kit sizes and/or extending the storage time allowable for test reagents, calibrators and controls.**
Currently some instruments require that the calibrators/controls be used within 24 hours after opening. A small-to-medium volume laboratory may not be able to use the full volume within that timeframe with-out batching. To optimize turnaround times and not waste resources, a smaller volume of calibrators/controls and/or a longer storage time (in-creasing to 72 hours) would enable laboratories to decrease or eliminate batching.

4. **Increased implementation of automatic reflexing of HCV Ab-reactive specimens to HCV RNA testing (following the current recommended algorithm).**
Based on US CAP Survey June 2021: 2,242 laboratories perform HCV Ab testing but only 452 perform HCV RNA testing (may not all be US laboratories). To decrease barriers to implementation, consider the following items:

   a. Policy/Regulatory Items:

      I. National organizations (federal and non-governmental) to recommend automatic reflexing of HCV Ab reactive specimens to HCV RNA testing and provide support for implementation, including methods to minimize, reduce or remove concerns about cross-contamination of samples.

      II. CDC and other funding agencies could incentivize laboratories to implement automatic reflex testing by making it an essential including component of future funding opportunities targeting laboratories.

      III. Work with Accountable Care Organizations (ACO) to make automatic re-flex testing a quality metric.

      IV. Work with laboratory regulatory/accreditation agencies to require reflexing as a practice whether performed in-house or through referral. An example of one potential option is to work with CAP (laboratory regulatory agency) to add automatic reflexing of HCV Ab reactive specimens to HCV RNA testing as part of the checklist used for reviewing/inspecting laboratories. If a laboratory does not complete something on the check-list there are different level of deficiencies that can be assigned. If this item was a Phase II deficiency it must be corrected before accreditation is granted since they seriously affect the quality of patient care. Alternatively, a Phase I error requires correction and a written response and could be a good place to start to require a change in testing practices.

      V. Assessing the regulatory landscape to determine who has the regulatory authority to require laboratories to perform HCV RNA testing on all HCV Ab-reactive specimens.

   b. Implementation Items:

      I. Create standardized laboratory workflows or best practices (to cover specimen collection, minimizing cross-contamination and extra specimen handling) to be shared broadly with all laboratories performing HCV testing

      II. Laboratory to implement mechanisms to ensure that all HCV Ab-reactive samples receive HCV RNA testing (i.e., programming of LIMS or other alerts/reminders).

      III. Laboratory to remove option for ordering HCV Ab only.

   c. Education/Awareness:

      I. Work with clinical providers, health systems and laboratories to deter-mine barriers to implementation and identify alternative methods to help address identified barriers.

      II. Ensure all stakeholders understand the purpose for the automatic re-flex, ordering of the test and receiving results.

      III. Policy and Operational Considerations to support and facilitate optimal implementation of the diagnostic tools (new or current).

Barriers to be Addressed

1. **Billing and Reimbursement for HCV Testing**
   Billing and reimbursement for HCV testing is complex and varies depending on who is covering the payments (i.e., Medicaid, Medicare and/or private insurance). To be reimbursed for laboratory testing the appropriate procedure codes, screening codes and/or diagnostic codes must be utilized.

   a. CMS/Medicaid reimbursement is based on USPSTF screening recommendations to determine if the preventative screening is beneficial. The coverage criteria do not specify whether testing is started with HCV Ab or HCV RNA testing. CMS reimburses testing for once in a lifetime testing and for at-risk individuals, such as perinatal, infant, person with injection drug use. However, CMS, nor other entities define the interval for repeat screening for at-risk individuals and coverage.

   b. Medicare has stringent criteria regarding the type of provider and setting for which screening tests may be reimbursed.

   c. There is no standard, accepted or codified interval for repeat screening for at-risk individuals and therefore coverage of repeat screening is variable.

   d. When billing for laboratory tests for HCV there are different coding requirements for screening and diagnosis, but this is true for many disease conditions so sharing best practices for billing and reimbursement could be useful.

2. **HCV Testing Algorithms**
   Testing algorithms would need to be updated to allow for using HCV RNA as an initial testing option, including for specific situations such as early infant diagnosis, detection of acute HCV RNA infection in persons without HCV Ab or persons at high-risk that have not had an HCV Ab test performed.

3. **Consent Requirements**
   Pre-testing consent requirements should be removed. Consent requirements (or lack of) should be clearly communicated to persons/agencies offering and/or ordering testing.

4. **Regulatory Approval Process**
   In order for IVD manufacturers to obtain regulatory approval for new assays and/or modifications to currently approved methods, the cost and effort required to navigate the regulatory approval process must be reduced.

Other Considerations

1. **Public Health and Institutional Policies/Operational Decisions**
   Public health and institutional policies/operational decisions are also important for addressing the barriers in the HCV Care Cascade using already available diagnostic tools.

   a. One health department forced the discontinuation of rapid testing for HIV and HCV and required testing sites to submit to their public health laboratory, allowing the jurisdiction to implement integrated testing (HIV, HCV, syphilis) with automatic reflexing for confirmation. This system has helped them achieve public health objectives—including testing for multiple pathogens and timely data for surveillance—and enabled third-party billing (Medicaid, Medicare, commercial insurance), which has resulted in revenue generation for the laboratory.

   b. Another consideration that was addressed, though not fool proof, is implementing mechanisms in electronic health records (EHRs) to facilitate appropriate testing and follow-up.

2. **Situational Reflex to HCV Genotyping**
   There are certain situations where HCV genotyping is required to initiate treatment (i.e., typically payer requirements) and/or evaluate a potential treatment failure versus re-infection. When this is the case, it is important to ensure rapid access to HCV genotyping to minimize delays in treatment initiation. Some laboratories may be able to offer a reflex to HCV genotyping as part of their test order (if HCV RNA is detected), which would provide a more rapid turnaround than having to order a new test once the HCV RNA result is provided.

Key Question 2b:
What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in CLIA-waived testing in clinical settings?

This key question spanned two "settings" a moderately complex laboratory with low volume (not likely to use high-throughput instrumentation as in Key Question 1) and a CLIA-waived setting where testing would be performed by trained, but non-laboratory staff. Testing in these settings would need to be relatively rapid with less than 30 minutes from sample collection to result in order to return a result within the same office visit/encounter and ideally with specimen types that don't require phlebotomy. Additionally, the testing should utilize either lower throughput instrumentation or CLIA-waived testing that can detect current HCV infection (i.e., HCV cAg, HCV RNA). These settings could be clinical settings facilitating rapid diagnosis and/or HCV test and treat strategies, such as primary care/traditional healthcare settings, medication-assisted treatment and/or substance use treatment facilities and correctional facilities. However, any CLIA-waived testing that could be used in these settings would also likely be amenable to testing in non-clinical test settings (see **Key Question 3** for more focus on these settings) whereas a moderate complexity test would be required to be performed in a laboratory setting and might not be suitable for use in the settings described in Key Question 3.

New Diagnostic Approaches Needed

1. **CLIA-waived POC Test for Diagnosis of Current HCV Infection**
   a. Does not require venipuncture, capillary blood preferred
   b. Ideally CLIA-waived
   c. Minimal waste
   d. Result in <20 minutes, ideally 5 minutes
   e. Cost $10-15 and affordable device (if required)
   f. Ideally it could also be used for SVR assessment
   g. Ability to report to LIMS, EHR, public health authority, etc.

2. **CLIA-waived POC HCV cAg Test at Lower Cost than HCV RNA Testing**
   a. The European Association for the Study of the Liver (EASL) and WHO recognize HCV cAg as an alternate to HCV RNA when HCV RNA testing is not affordable or available.
   b. Ideally would be used for diagnosis and assessment of SVR.[15,16]
   c. Assay would need to be accompanied by CDC/USPSTF recommendations for use, CMS reimbursement and insurance provider acceptance of use case for test as well as education for providers on role of the assay per the above guide-lines/coverage policies, etc.
   d. Guidelines/recommendations should be aligned to ensure that the detection of cAg would be sufficient to indicate current HCV infection.
   e. Clear reporting language, interpretations and education would be necessary.

3. **CLIA-waived POC Confirmation of Current HCV Infection**
   HCV cAg or HCV RNA.

4. **Assess Role for CLIA-waived POC HCV Ab with Oral Fluid/Saliva Claim**
   a. This test would clearly have lower sensitivity and there are mixed opinions about whether this should be a priority or not.
   b. FDA noted that they could consider a lower performance bar depending on risk/benefit profile.

5. **Low-throughput Testing Platforms**
   See **Key Question 1**.

Opportunities for Improvement of Current Diagnostic Methods or Approaches

1. **Decrease Cost/Increase Market Competition for CLIA-waived HCV Ab Testing**

2. **Bring Internationally-available POC HCV RNA Test(s) to the US**
   a. Advocate that IVD manufacturer(s) that have products outside the US bring those to the FDA for review and approval.
   b. May require partnerships to collect or address gaps in data that would be needed for submission.

Barriers to be Addressed

1. **Test-to-treat Algorithms**
   Simplified treatment algorithms that make embedded treatment models possible if coupled with efficient testing. Testing is only one component of test and treat models and is suboptimal without access to treatment.

2. **Training/Education of Healthcare Providers**
   a. Increase number of healthcare providers that can treat HCV and ensure sufficient provider education and engagement.
   b. May need champions to help develop expertise in routine screening and treatment. Examples given of successful approaches are Extension for Community Healthcare Outcomes or ECHO or programs designed to train and support primary care providers and substance use treatment providers to screen, evaluate, treat and cure HCV, including evaluation for cirrhosis.
   c. Need to address organizational issues, including how members of interdisciplinary care teams can be involved in care management.
   d. Develop best practices for sustainably integrating HCV screening and treatment into primary care as well as Office Based Addiction Treatment (OBAT) and other modalities of increasing access to HCV screening and treatment.

3. **Testing Education, Training, Financing, Quality Management and Equitable Access**
   a. Education, training, financing, quality management and equitable access are required to ensure not only that the test is useful but that all the other aspects of using the test and the test result are considered within a system.
   b. Amongst others, laboratory scientists, particularly public health laboratory staff, play a key role in helping to educate submitters and train staff in CLIA-waived settings to ensure regulatory compliance and an understanding of basic quality control and assurance activities that they should be performing.

4. **Test Cost and Cost-effectiveness**
   a. Cost-effectiveness of potential/proposed new strategies and approaches (i.e., single test for current HCV infection (HCV RNA), alternative testing algorithms) must be evaluated to guide decision making about implementation, including in certain settings/venues and/or with certain populations.
      I. There is an overall focus on minimizing cost per test. However, for a solitary case of HCV infection, the cost of testing is still quite low com-pared to the cost of treatment. If the goal is HCV elimination, we may need to consider overall cost to cure for a solitary case.
      II. Include assessments of how a higher cost per test (i.e., for a CLIA-waived POC HCV RNA test) could be absorbed into the public health/healthcare system to obviate downstream costs of additional cases due to unmitigated transmission.
   b. Determining how the cost sharing between more expensive tests but cheaper overall care should and could occur and how costs are shared in a system is a significant barrier that if addressed would be a paradigm shift for many diseases.
   c. Decisions about reasonable/acceptable costs for testing reagents, instrumentation and overall test cost will be required.

5. **Stakeholders Coordination**
   Coordination between federal partners, such as CDC and FDA, and diagnostic manufacturers is needed to determine how they could incorporate high-quality international data and approvals from other stringent regulatory authorities to expedite the FDA approval process. This must be addressed to help create a process for review/approval rather than a determination for each IVD/diagnostic manufacturer.

Other Considerations

1. **Prioritizing Better, Faster or Cheaper Tests**
   All stakeholders want better, faster and cheaper tests than are currently available. However, achieving all three is difficult and stakeholders will need to prioritize potential solutions that address one or two of these features rather than all three.

2. **Community Education**
   Educate and discuss any new tests with community organizers, patients, etc. to ensure better uptake and implementation.

Key Question 3:
What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in outreach settings and self-collection/self-testing in non-clinical settings?

Testing in these settings, like those in **Key Question 2**, would need to be relatively rapid with less than 30 minutes from sample collection to result to return a result within an office visit/encounter and ideally with specimen types that don't require phlebotomy. CLIA-waived testing may help to facilitate testing in outreach or other settings where traditional testing is not possible. However, other approaches that include phlebotomy and laboratory testing are also possible in these settings when the appropriate coordination and workflows have been established. Self-collection of specimens either in these settings above or in a home or other non-clinical setting will also be important to improve overall access to testing. These self-collected specimens could then be either mailed or dropped off for laboratory-based testing (see **Key Question 1**), or if the CLIA-waived test allowed for it, they could be brought to a non-clinical site for testing. For self-collection, the type of testing available will depend on what test (and where) it will be performed though the same considerations will exist for ensuring a high-quality specimen is obtained.

Overall, the goal of this question was to determine what is needed to take testing to the patient (rather than the other way around) and how to be adaptable and responsive to advance HCV elimination.

New Diagnostic Approaches Needed

1. **CLIA-waived POC HCV Viral Detection Test Available for Wide-scale Use in Non-clinical Settings**
   a. Ideally HCV RNA, though HCV cAg is also possible.
   b. Results in 60 minutes or less, ideally less than 15-30 minutes.
   c. Cost: Affordable to public health and community-based organizations; ideally less than $30/test.
   d. Same or better sensitivity/specificity to FDA-approved HCV RNA methods.
   e. Minimally invasive samples, including capillary blood.

2. **Collection of specimens without venous draw/outside of a clinical setting, including self-collection**
   DBS may be more acceptable and less invasive to patients, can be collected at the time of a reactive HCV Ab test and requires less training as compared to phlebotomy to collect. DBS can also be done in outreach/mobile settings (doesn't require processing like venipuncture blood) and has good stability for shipment to a central laboratory. Other capillary blood collection systems have similar utility. Additionally, these specimen types could also be self-collected in these non-clinical settings, allowing for diagnosis of current HCV infection. There are other collection devices (i.e., Tasso collection device or neotreryx MITRA devices) which collect capillary blood, which could also be explored. However, despite the advantages of DBS, it is important to recognize that testing of DBS will have lower sensitivity compared to other specimen types.

3. **Need for testing for multiple pathogens at point-of-contact to rapidly initiate treatment**
   Many healthcare providers will be reluctant to initiate treatment without knowing infection status for HIV and HBV (HBV sAg) as well as cirrhosis status. To advance elimination of HCV and rapidly initiate treatment there is a need to have point-of-contact testing to confirm and/or rule out infection with HIV and HBV.

Opportunities for Improvement of Current Diagnostic Methods or Approaches

1. **Decrease Cost/Increase Market Competition for CLIA-waived HCV Ab testing**

2. **Shorten Time-to-result on CLIA-waived HCV Ab Tests**
   There are CLIA-waived HIV Ab tests with results in 2-5 minutes; need to shorten the time for HCV Ab test, ideally to about 5 minutes.

3. **Improve Provider Understanding of HCV Screening, Diagnosis and Treatment**

4. **HCV Ab Positivity as Marker for HCV Viremia**
   A study looked at time to HCV Ab positivity as a surrogate marker for HCV viremia. Could this approach be more widely implemented? If so, there would be major challenges with convincing third-party payers to supply treatment without an HCV RNA result, which is not aligned with current recommendations for initiating HCV treatment.

Barriers to be Addressed

1. **Improve/Expand Providers that can Prescribe Treatment for HCV**
   a. This currently varies by state but should include the following: physicians, nurse practitioners (NP), PAs and PharmDs.
   b. May also need to address the setting in which these professionals operate (i.e., primary care healthcare provider vs. board-certified, etc.)

2. **Collective Determination of Acceptable Test Sensitivity and Specificity in CLIA-waived Settings**
   This requires FDA to work with relevant stakeholders.

3. **Identification of "Must be Assessed" Initiation Items**
   Items that must be assessed are those that influence whether, when and how to treat versus "assess as possible/after initiation" items, which are relevant to overall patient care but are not required to initiate treatment.
   a. Need to define a minimal assessment for patients who would benefit from immediate or near-immediate treatment initiation. The minimal assessment would be analogous to minimal monitoring.
   b. To offer simplified HCV treatment (and other treatment approaches) the pre-treatment laboratory testing that is required includes testing for the following viral markers: quantitative HCV RNA testing, HIV Ag/Ab and HBsAg.
   c. If HCV cAg became an alternative method for viral detection, American Association for the Study of Liver Diseases guidelines would need to be re-viewed and updated and significant education would also likely need to be provided to ensure effective implementation of the test method.

4. **Must Address Prevention of Cases to Meet Elimination Goals**
   This requires identifying acute HCV infection and interrupting transmission.

5. **Lack of Sufficient Funding to Meet Elimination Goals**

Other Considerations

1. **Ensure that appropriate training, QC, competency and oversight of CLIA-waived POC testing is occurring to maintain high-quality testing.**

2. **Effective Waste Management/Disposal**
   Effective waste management and disposal should be part of the action plan/goals for widespread delivery of rapid POC HCV RNA testing. Ameliorating the health sec-tor's environmental effects and reducing greenhouse gas emissions can improve health and reduce costs of care from the start. This must include avoiding, reducing and safely managing healthcare waste, especially at POC, given the scale of the plan.[17]

   a. Include language/requirements on environmental impact in funding related to development. For example, SBIR announcements from federal agencies.

   b. Diagnostic manufacturers should be developing test systems with minimal impact on the environment and addressing medical waste management. May re-quire guidance and requirements from regulatory bodies to enforce.

   c. Certain sites performing POC testing may still need to establish partnerships with hospitals, public health programs and/or public health laboratories to help manage medical waste if they lack the capacity and/or capability to handle it in-dependently.

3. **Ensuring we maintain necessary HCV surveillance with CLIA-waived POC testing solutions.**
   There are reasonable mechanisms that could be used to allow for continued HCV surveillance with POC testing.

4. **Incentivizing Return Visits**
   Consideration for incentivizing return visits (or testing) to complete HCV diagnosis as a short-term solution in certain settings.

5. **Multisite-collaborative effort to better monitor and detect acute infection and build linkage to care.**
   There is data to support that there are currently hundreds of thousands of people who inject drugs. Those persons may inject up to 8 times a day and it is estimated that 10-20% of those injections involve syringe sharing. Collectively we are under ascertaining acute infections and need to develop and share best practices to pick up the most acute infections as quickly as possible. Examples include evaluating the role of HCV cAg, use of DBS for HCV Ab and HCV RNA testing (increase access to testing for populations not otherwise seeking or receiving testing), using reduced read time for rapid Ab testing[14,18] and embedding care/one-stop shopping where populations are already seeking other services.

Key Question 4:
What other tools are needed to support same-day diagnosis and treatment of current HCV infection?

Treatment of newly diagnosed HCV infection is guided by AASLD/Infectious Diseases Society of America (IDSA) guidelines and requires diagnostic testing beyond HCV. The goal of treatment is to reduce all-cause mortality and liver-related adverse health consequences through the achievement of virologic cure as evidenced by SVR. Furthermore, treatment is recommended for all persons with acute or chronic HCV infection regardless of symptoms or acuity/chronicity, except for those with a short life expectancy that cannot be remedied by HCV treatment. When evaluating persons for treatment, it is recommended that individuals be evaluated for the presence of liver disease, specifically liver fibrosis, to stratify patients for appropriate liver disease care, not for treatment selection. This evaluation can be done in non-invasive ways through physical exam, serum tests (i.e., FIB-4, APRI, Fibrosure and ELF), elastography (ideal tool but limited availability in point-of-contact testing/treatment) and imaging (limited availability in point-of-contact testing/treatment). Persons with cirrhosis need to be provided with medical care to ensure management of liver disease as they remain at risk of hepatocellular carcinoma and complications of cirrhosis despite successful HCV treatment.

The ideal model for streamlined HCV diagnosis and treatment would begin with a single, ideally rapid, CLIA-waived test sufficient for HCV diagnosis that does not require venipuncture followed by on-site/same-day treatment initiation with minimal post-treatment monitoring.11 While ideal, we are many steps away from truly achieving this ideal model though we will focus on the improvements needed for diagnostic testing.

New Diagnostic Approaches Needed

Affordable Rapid, CLIA-waived POC Testing with Rapid Results (<30 minutes)

This would allow for patient evaluation and interpretation of test results in one visit with priority for:

a. Detection of HCV viral markers: HCV RNA (or HCV cAg)

b. Detection of HBsAg (one test available outside the US that has been submitted for prequalification to WHO with results in 15 minutes)

c. Multiplex assays to detect HIV, HBV and HCV concurrently (there are laboratory-based molecular platforms with approved multiplex assays for organ/transfusion screening, but not diagnosis)

d. Need to determine what would be sufficient/acceptable as far as performance, turnaround time and cost from multiple perspectives, including FDA (performance), patients, providers (turnaround time and cost) as well as insurance carriers (cost).

Opportunities for Improvement of Current Diagnostic Methods or Approaches

1. **Revisit Guidelines to Streamline Treatment Initiation Prior to Pre-treatment Assessment**
   a. Refining/updating minimal assessment for patients who would benefit from immediate or near-immediate treatment start (i.e., significant risk of loss-to follow-up). (AASLD/IDSA)
   b. Clarify/update the “must assess” criteria. The “must assess” criteria currently include items that are required to determine whether to treat, when to treat or how to treat as opposed to items that could be categorized as “assess as possible/after initiation.” Items that fall into the latter category would be relevant to patient care but not be required to initiate treatment.

2. **Reconsider On-treatment Monitoring Requirements to Allow Minimal Monitoring/Follow-Up or Remote Monitoring**

3. **High Incidence/Remote Sites Need Pre-approved Regimens or Supply Stock-piles**
   Need pre-approved regimens or for sites to purchase supplies to stockpile and have take-home treatment at high incidence or remote sites.

4. **Use of Peer Navigators to Help With Complex Systems and Overcome Barriers of Stigma**

Barriers to be Addressed

1. **Lack of Long-acting Injectables**
   This would be especially beneficial for persons at risk for loss to follow-up.

2. **Testing Access and Affordability**
   Even if available, it is likely that a CLIA-waived or near patient HCV RNA testing will be expensive and access/affordability will need to be addressed.

3. **Treatment Access and Restrictions**
   Continue to remove/reduce barriers to treatment access, such as prior authorization, fibrosis restrictions (disease severity), substance use restrictions, prescriber restrictions as well as retreatment and other restrictions.

4. **Cost of Pan Genotypic Regimens**

5. **Updates to Clinical Guidance**
   Updating clinical guidance (e.g., AASLD/IDSA) to incorporate minimal monitor-ing/removal of SVR12 testing for certain populations/persons or situations.

6. **Systemic Issues**
   Policy and system-wide solutions are needed:

   a. Commitment to elimination—must meet need with funding
   b. Develop public-private partnerships for diagnostic development and subsidize treatment.

Other Considerations

7. **Leverage Existing Healthcare Interactions**
   Settings for implementation should include those where persons have chance/brief en-counters with healthcare, such as:

   a. Substance use disorder treatment facilities
   b. Correctional facilities
   c. Syringe service programs
   d. Mobile treatment settings
   e. Primary care settings encountering persons at high risk (i.e., FQHCs)
   f. Inpatient settings or emergency departments that deal with consequences of injection drug use or obstetrics (deferral of therapy until after delivery)

8. **Maximize Improvement with Limited Contact Tools and Technologies**
   Explore expansion of limited contact tools and technologies for maximal improvement, such as:

   a. Linkage to care
   b. Minimal monitoring
   c. One and done/test and treat models
   d. Injectable long-acting antivirals

APPENDIX A. KEY QUESTION AND PANELISTS

#	Key Question	Moderator	Presenter	Panelists
1	**What HCV diagnostic tools are needed to optimize diagnosis of current HCV infection in moderate to high volume laboratories performing moderate or high complexity testing?**	Michael Busch, MD, PhD	Joseph Yao, MD	• Lesley Miller, MD • Monica Parker, PhD • Liisa Randall, PhD
2	**What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in low volume settings performing moderate complexity laboratory testing or CLIA-waived testing in clinical settings?**	Tanya Applegate, PhD	Stacey Trooskin, MD, PhD	• William Meyer, PhD, D(ABMM) • Arthur Kim, MD • Biz McChesney
3	**What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in outreach settings and self-testing in a non-clinical setting?**	Judith Feinberg, MD	Kimberly Page, PhD	• Colleen Flanigan, RN, MS • Marty Soehnlen, PhD, PHLD(ABB) • Lynn Taylor, MD
4	**What other tools are needed to support same-day diagnosis and treatment of current HCV infection?**	John Ward, MD	Raymond Chung, MD	• Marc Ghany, MD • Jorge Mera, MD • Benjamin Pinsky, MD, PhD

APPENDIX B: INVITED PARTICIPANT LIST

Name	Title/Affiliation
Tanya Applegate, PhD	Senior Lecturer, Surveillance and Evaluation Research Program, Kirby Institute
Paige Armstrong, MD, MHS	Associate Director for Global Health, Division of Viral Hepatitis, CDC
Danae Bixler, MD, MPH	Medical Officer, Division of Viral Hepatitis, CDC
Michael P Busch, MD, PhD	Vitalant Research Institute & University of California San Francisco
Raymond T Chung, MD	Professor of Medicine, Massachusetts General Hospital & Harvard Medical School
Daniel Church, MPH	Epidemiologist, Massachusetts Department of Public Health
Gavin Cloherty, PhD	Abbott
Mona Doshani, MD, MPH	Medical Epidemiologist, Division of Viral Hepatitis, CDC
Julie Dyall, PhD	Program Officer, NIH/NIAID/DMID
Judith Feinberg, MD	Professor of Behavioral Medicine and Psychiatry & Professor of Medicine/Infectious Diseases, Dr. EB Flink Vice Chair of Medicine for Research, West Virginia University School of Medicine
Jordan Feld, MD, MPH	University Health Network, Toronto Centre for Liver Disease
Colleen Flanigan, RN, MS	Director, Bureau of Hepatitis Health Care, New York State Department of Health
Nathan Furukawa, MD, MPH	Division of Viral Hepatitis, CDC
Maria Ines Garcia, PhD	Assistant Director, Division of Microbiology Devices, Center for Devices and Radiological Health, FDA
Annette Gaudino	Director of Policy Strategy, Treatment Action Group
Marc Ghany, MD, MHSc	NIH
Laura Gillim, PhD	Labcorp
William A Glover II, PhD	Assistant Director, Infectious Diseases, North Carolina State Laboratory of Public Health
Karen Harrington, PhD	Sr. Manager Scientific Affairs, Hologic, Inc.
Tonya Hayden, PhD	Deputy Chief, Laboratory Branch, Division of Viral Hepatitis, CDC
Ravi Jhaveri, MD	Professor of Pediatrics, Ann and Robert H. Lurie Children's Hospital of Chicago & Northwestern University Feinberg School of Medicine
Saleem Kamili, PhD	Chief, Laboratory Branch, Division of Viral Hepatitis, CDC
Hema Kapoor, MD, D(ABMM), SM	Senior Medical Director, Quest Diagnostics
Arthur Yu-shin Kim, MD	Massachusetts General Hospital & Harvard Medical School

Name	Title/Affiliation
Rajen Koshy, PhD	National Institute of Allergy and Infectious Diseases, NIH
Carl Li, MD, MPH	CMS
Lily Li, MD, PhD, MBA	Medical Safety Officer; Medical Director, Ortho Clinical Diagnostics
Anna Lok, MD	University of Michigan
Niklas Luhmann, MD, MscPH	WHO - HQ
Kristen Marks, MD	Weill Cornell Medicine
Randy Mayer, MS, MPH	Chief, Bureau of HIV, STD, and Hepatitis, Iowa Department of Public Health
Jorge Mera, MD	Cherokee Nation Health Services
Biz McChesney	HIV and Hepatitis Prevention Program, Iowa Department of Public Health
Rachel McLean, MPH	Chief, Policy and Viral Hepatitis Prevention Section, STD Control Branch, California Department of Public Health
Jonathan Mermin, MD, MPH	Division of Viral Hepatitis, CDC
William A Meyer III, PhD, D(ABMM), MLS(ASCP)CM	Quest Diagnostics
Lesley Miller, MD, FACP	Emory University School of Medicine
Susanna Naggie, MD, MHS	Vice Dean of Clinical Research & Associate Professor of Medicine, Duke University School of Medicine
Michael Ninburg, MPA	National Viral Hepatitis Roundtable
Emi Okamoto, MD	Clinton Health Access Initiative
Chinedu R Okeke, MD, MPH-TM, MPA	Acting Chief Medical Officer, Office of Infectious Disease and HIV/AIDS Policy, Office of the Assistant Secretary for Health, HHS
S. Michele Owen, PhD	Associate Director for Laboratory Science, National Center for HIV, Viral Hepatitis, STD and TB, CDC
Kimberly Page, PhD, MPH, MS	Professor, University of New Mexico Health Sciences Center
Jayme Parker, PhD, MB(ASCP)	Health Program Manager IV & Chief, Alaska State Public Health Labs, Division of Public Health, DHSS
Monica Parker, PhD	Laboratory Chief, Bloodborne and Parasitic Diseases & Director, Bloodborne Viruses Laboratory, Wadsworth Center, New York State Department of Health
Sai Patibandla, PhD	Senior Director, Siemens-Healthineers
Thaddeus Pham	Viral Hepatitis Prevention Coordinator & BS, Hawai'i Department of Health
Benjamin Pinsky, MD, PhD	Stanford University School of Medicine

Name	Title/Affiliation
Jennifer Rakeman, PhD	Cepheid
Liisa M Randall, PhD	Bureau of Infectious Disease and Laboratory Sciences, Massachusetts Department of Public Health
Daniel Raymond	National Viral Hepatitis Roundtable
Pedro Rodriguez, PhD	Roche Diagnostics, Medical and Scientific Affairs
Anita Sands, MPH	WHO
Silke Schlottmann, PhD	Team Lead, General Virology and Hepatitis Branch, Division of Microbiology Devices, Center for Devices and Radiological Health, FDA
Sonjelle Shilton, MPH	Hepatitis Lead, FIND
Marty Soehnlen, PhD, MPH, PHLD(ABB)	Michigan Department of Health and Human Services
David Spindell, MD	Vice President Medical and Governmental Affairs, OraSure Technologies
Lynn E. Taylor, MD	CODAC Behavioral Health, University of Rhode Island
Norah Terrault, MD, MPH	USC
David L Thomas, MD, MPH	Johns Hopkins Medicine
Stacey Trooskin, MD, PhD	Philadelphia FIGHT Community Health Centers
Charles Walworth, MD	Associate VP, Medical Affairs and Education, Labcorp
John W Ward, MD	Coalition for Global Hepatitis Elimination, Task Force for Global Health
Carolyn Wester, MD, MPH	Director, Division of Viral Hepatitis, CDC
Kathleen (Kat) B Whitaker, PhD	Division of Microbiology Devices, Center for Devices and Radiological Health, FDA
Joseph D Yao, MD	Mayo Clinic, Mayo Clinic Laboratories

APPENDIX C: MEETING AGENDA

Day 1: October 19, 2021

Time	Topics	Presenter/Facilitator
1:00-1:20 pm	**Welcome**	
	Welcome from NCHHSTP Director	Jonathan "Jono" Mermin, CDC
	Meeting Objectives and Logistics	Anne Gaynor, APHL
1:20-2:10 pm	**Opening Session**	
	The Role of Testing in Advancing Hepatitis C Elimination	Carolyn Wester, CDC
	Down-classification of Hepatitis C Virus Diagnostics	Maria Ines Garcia, FDA
	HCV Diagnostic Tools-in the Development Pipeline	Sonjelle Shilton, FIND
	What is needed to move toward single-step diagnosis of current HCV infection?	Jordan Feld, Toronto Centre for Liver Disease
2:10-2:15 pm	**Break**	
2:15-3:30 pm	**Key Question 1: What HCV diagnostic tools are needed to optimize diagnosis of current HCV infection in moderate to high volume laboratories performing moderate or high complexity testing?**	**Michael Busch, Vitalant Research Institute**
	Presentation	Joseph Yao, Mayo Clinical Lab
	Panelist Remarks	• Monica Parker, Wadsworth Center • Liisa Randall, Massachusetts DPH • Lesley Miller, Emory University
	Invited Comments	• FDA • CMS • Diagnostic Companies
	Facilitated Discussion	Participants
3:30-3:40 pm	**Break**	

Time	Topics	Presenter/Facilitator
3:40-4:55 pm	**Key Question 2: What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in low volume settings performing moderate complexity laboratory testing or CLIA-waived testing in clinical settings?**	**Tanya Applegate, Kirby Institute**
	Presentation	Stacey Trooskin, Fight.org
	Panelist Remarks	• William Meyer, Quest • Biz McChesney, Iowa DPH • Arthur Kim, Mass General Hospital/Harvard
	Invited Comments	• FDA • CMS • Diagnostic Companies
	Facilitated Discussion	Participants
4:55-5:00 pm	**Wrap-up and Closing**	**Anne Gaynor, APHL**

Day 2: October 20, 2021

Time	Topics	Presenter/Facilitator
1:00-1:05 pm	**Welcome and Recap**	**Anne Gaynor, APHL**
1:05-2:20 pm	**Key Question 3: What HCV diagnostic tools are needed to advance diagnosis of current HCV infection in outreach settings and self-collection/self-testing in non-clinical settings?**	**Judith Feinberg, WVU Medicine**
	Presentation	Kimberly Page, U. New Mexico
	Panelist Remarks	• Marty Soehnlen, Michigan PHL • Colleen Flanigan, NYSDOH • Lynn Taylor, U. Rhode Island
	Invited Comments	• FDA • CMS • Diagnostic Companies
	Facilitated Discussion	Participants
2:20-2:25 pm	**Break**	
2:25-3:35 pm	**Key Question 4: What other tools are needed to support same-day diagnosis and treatment of current HCV infection?**	**John Ward, Task Force for Global Health**
	Presentation	Ray Chung, Mass General Hospital
	Panelist Remarks	• Marc Ghany, NIDDK • Jorge Mera, Cherokee Nation HS • Benjamin Pinsky, Stanford Health
	Invited Comments	• FDA • CMS • Diagnostic Companies
	Facilitated Discussion	Participants
3:35-3:40 pm	**Break**	
3:40-4:50 pm	**Final Session: Recommendations, Prioritization, Other Considerations**	**APHL and Presenters**
	Overview of Session	Anne Gaynor, APHL
	Refinement of Key Questions	• Joseph Yao, Mayo Clinical Lab • Stacey Trooskin, Fight.org • Kimberly Page, U. New Mexico • Ray Chung, Mass General Hospital
	Overall Recommendations and Needs	Kelly Wroblewski, APHL
4:50-5:00 pm	**Next Steps and Closing**	• **Anne Gaynor, APHL** • **Carolyn Wester, CDC**

APPENDIX D: DISCLOSURES

Name	Commercial Entity	Relationship
Anna Lok	Gilead Sciences	Research Grant
Arthur Kim	Kinto Pharmaceuticals	Data Monitoring Committee, DSMB
David Thomas	Merck	Advisory, DSMB
David Thomas	Excision Bio	Advisory
Hema Kapoor	Quest	Employee and Stockholder
Jennifer Rakeman	Cepheid	Employee
Joseph Yao	Abbott Molecular, Bio-Rad Laboratories, Ortho Clinical Diagnostics, Roche	Advisory board member; research funding support
Karen Harrington	Hologic, Inc.	Employee
Lesley Miller	Gilead Sciences	Grant Funding through Emory University
Lesley Miller	AbbVie	Advisory Board
Lily Li	Ortho Clinical Diagnostics	Employee
Lynn Taylor	Up to Date	Royalties
Marty Soehnlen	Catalyst Diagnostics LCC	Contracted Laboratory Director
Michael Busch	Abbott, Bio-Rad Laboratories, Grifols, Hologic, Ortho Clinical Diagnostics, Roche	Grant Funding to Employer/Institution
Norah Terrault	Gilead Sciences, Genentech Roche, EXIGO Mgnt LLC, ENYO, PPD Pharma, Entourage	Consultant/Research
Pedro Rodriguez	Roche Diagnostics Corp.	Employee
Ravi Jhaveri	AstraZeneca (Flu vaccine), Seqirus (Flu vaccine), Dynavax (Adjuvanted Hep B vaccine)	Consultant
Ravi Jhaveri	Elsevier (Co-EiC of Journal Clinical Therapeutics	Editorial Stipend
Raymond Chung	AbbVie Pharmaceuticals, Gilead Sciences, BMS, Janssen, Boehringer, Roche	Research Grant
Stacey Trooskin	Gilead Sciences	Grant Funding to Institution, Advisory Board
Susanna Naggie	AbbVie Pharmaceuticals, BioMarin Pharmaceutical, Inc., Bristol-Myers Squibb/PRA, Gilead Sciences, Inc., IAS-USA, Theratechnologies	Consultant
Susanna Naggie	Vir Biotechnology	Interest
Tonya Applegate	Cepheid, Abbott, SpeeDx	Research Support
Tonya Applegate	FIND	Reviewer
William Meyer	Quest	Employee
John Ward	Abbott, Gilead, AbbVie, Merck, Siemens, Cepheid, Roche, Pharco, Zydus-Cadila, US Govt Agencies and Philanthropic Agencies	Funding to Employer for Coalition for Global Hepatitis Elimination efforts

Note: Disclosures for Invited Participants that did not attend are not included.

REFERENCES

1 US Centers for Disease Control and Prevention (CDC). Testing for HCV infection: an update of guidance for clinicians and laboratorians. Morbidity and Mortality Weekly Report. 2013 May 10;62(18):362–5.

2 Mermin J. Welcome from NCHHSTP Director. Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US; 2021 Oct 19; Virtual. Available from: https://www.aphl.org/programs/infectious_disease/Pages/Hepatitis-C-Virus-Diagnostic-Meeting.aspx

3 CDC. Division of Viral Hepatitis: 2025 Strategic Plan. 2020 p. 24. Available from: https://www.cdc.gov/hepatitis/pdfs/DVH-StrategicPlan2020-2025.pdf

4 World Health Organization (WHO). Interim guidance for country validation of viral hepatitis elimination. Geneva: World Health Organization; 2021 Jun. p. 96. Available from: https://www.who.int/publications-detail-redirect/9789240028395

5 WHO. Global health sector strategies on respectively, HIV, viral hepatitis and sexually transmitted infections, 2022-2030. Available from: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/strategies/global-health-sector-strategies/developing-ghss-2022-2030

6 Wester C. The Role of Testing in Advancing Hepatitis C Elimination. Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US; 2021 Oct 19; Virtual. Available from: https://www.aphl.org/programs/infectious_disease/Pages/Hepatitis-C-Virus-Diagnostic-Meeting.aspx

7 Grebely J, Bruggmann P, Treloar C, Byrne J, Rhodes T, Dore GJ, et al. Expanding access to prevention, care and treatment for hepatitis C virus infection among people who inject drugs. Int J Drug Policy. 2015 Oct;26(10):893–8.

8 CDC/HRSA Advisory Committee on HIV, Viral Hepatitis and STD Prevention and Treatment (CHACHSPT) Meeting Minutes. 2021 Apr. Available from: https://www.cdc.gov/faca/committees/pdfs/chachspt/chachspt-minutes-20210420-21-508.pdf

9 US Food and Drug Administration (FDA). Microbiology Devices; Reclassification of Certain Hepatitis C Virus Antibody Assay Devices, Renamed to Hepatitis C Virus Antibody Tests. 86 FR 66173. Sect. Docket No. FDA-2020-N-1082 Dec 22, 2021 p. 66173–7. Available from: https://www.federalregister.gov/documents/2021/11/22/2021-25374/microbiology-devices-reclassification-of-certain-hepatitis-c-virus-antibody-assay-devices-renamed-to

10 FDA. Microbiology Devices; Reclassification of Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Assay Devices, Renamed to Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Tests. 86 FR 66169. Sect. Docket No. FDA-2020-N-1088 Dec 22, 2022 p. 66169–73. Available from: https://www.federalregister.gov/documents/2021/11/22/2021-25379/microbiology-devices-reclassification-of-nucleic-acid-based-hepatitis-c-virus-ribonucleic-acid-assay

11 Garcia M. Down-classification of Hepatitis C Virus Diagnostics. Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US; 2021 Oct 19; Virtual. Available from: https://www.aphl.org/programs/infectious_disease/Pages/Hepatitis-C-Virus-Diagnostic-Meeting.aspx

12 Shilton S. HCV Diagnostic Tools-in the Development Pipeline. Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US; 2021 Oct 19; Virtual. Available from: https://www.aphl.org/programs/infectious_disease/Pages/Hepatitis-C-Virus-Diagnostic-Meeting.aspx

13 WHO. Recommendations and guidance on hepatitis C virus self-testing. 2021 July 15. Available from: https://www.who.int/publications-detail-redirect/9789240031128

14 Feld J. What is Needed to Move Toward Single-step Diagnosis of Current HCV Infection? Identifying High-Priority Diagnostic Approaches for Advancing Hepatitis C Elimination in the US; 2021 Oct 19; Virtrual. Available from: https://www.aphl.org/programs/infectious_disease/Pages/Hepatitis-C-Virus-Diagnostic-Meeting.aspx

15 Pawlotsky JM, Negro F, Aghemo A, Berenguer M, Dalgard O, Dusheiko G, et al. EASL Recommendations on Treatment of Hepatitis C 2018. J Hepatol. 2018 Aug 1; 69(2):461–511. Available from: https://www.journal-of-hepatology.eu/article/S0168-8278(18)31968-8/fulltext

16 Freiman JM, Tran TM, Schumacher SG, White LF, Ongarello S, Cohn J, et al. HCV Core Antigen Testing for Diagnosis of HCV Infection: A systematic review and meta-analysis. Ann Intern Med. 2016 Sep 6 [cited 2022 Oct 7];165(5):345–55. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5345254/

17 Dzau VJ, Levine R, Barrett G, Witty A. Decarbonizing the U.S. Health Sector - A Call to Action. N Engl J Med. 2021 Dec 2;385(23):2117–9. Available from: https://www.nejm.org/doi/full/10.1056/NEJMp2115675

18 Smookler D, Vanderhoff A, Biondi MJ, Valencia J, Ryan P, Karkada J, et al. Reducing Read Time of Point-of-Care Test Does Not Affect Detection of Hepatitis C Virus and Reduces Need for Reflex RNA. Clin Gastroenterol Hepatol. 2021 Jul 1;19(7):1451-1458.e4. Available from: https://www.sciencedirect.com/science/article/pii/S1542356520310685

ACKNOWLEDGMENTS

This document was prepared by APHL with significant contributions from the following individuals:

Anne Gaynor, PhD

This publication was 100% funded with federal funds from a federal program. This publication was supported by Cooperative Agreement #NU60OE000104-02 funded by the US Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC or the US Department of Health and Human Services. Office of Surveillance, Epidemiology and Laboratory Services (OSELS) National Center for HIV, Viral Hepatitis, STDs and TB Prevention (PS) National Center for Zoonotic, Vector-borne, and Enteric Diseases (CK) National Center for Immunization and Respiratory Diseases (IP) National Center for Environmental Health (NCEH) National Center for Birth Defects and Developmental Disabilities (NCBDD).

Funding for this meeting was made possible by the US Centers for Disease Control and Prevention. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services, nor does the mention of trade names, commercial practices, or organizations imply endorsement by the US Government.

ASSOCIATION OF PUBLIC HEALTH LABORATORIES

The Association of Public Health Laboratories (APHL) works to strengthen laboratory systems serving the public's health in the US and globally. APHL's member laboratories protect the public's health by monitoring and detecting infectious and foodborne diseases, environmental contaminants, terrorist agents, genetic disorders in newborns and other diverse health threats.

8515 Georgia Avenue, Suite 700, Silver Spring, MD 20910 | 240.485.2745 | www.aphl.org