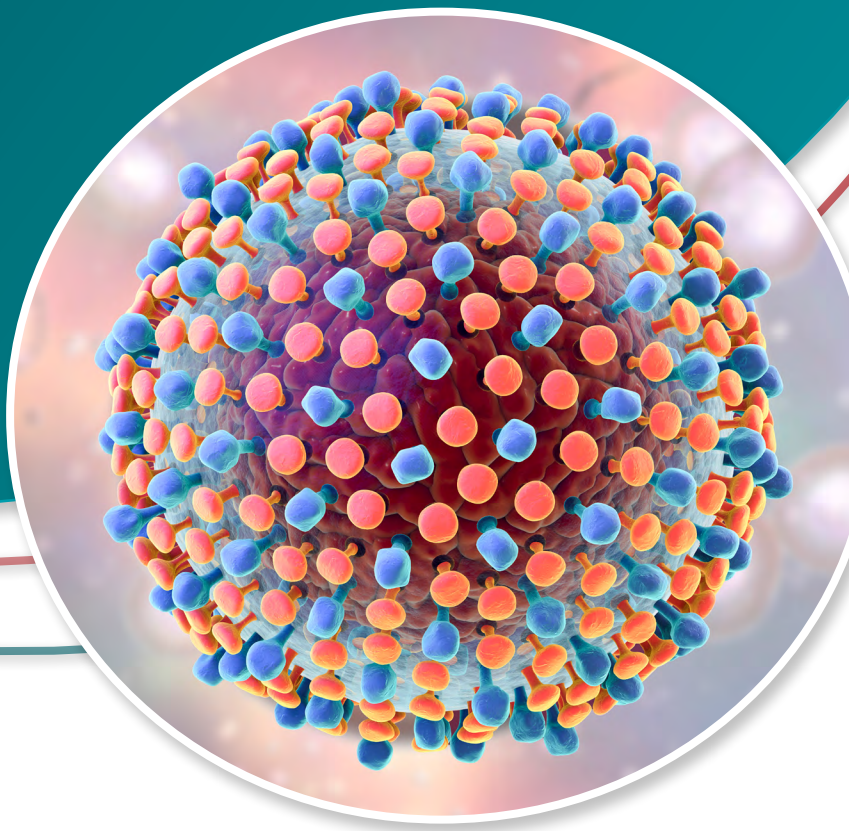
Meeting Report

Establishing a Road Map for Accelerated Diagnosis and Treatment of Hepatitis C Infection in the United States

September 16-17, 2025
Virtual Meeting



May 2026

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Glossary

Abbreviations

AASLD-IDSA ..American Association for the Study of Liver Diseases and the Infectious Diseases Society of America

Ab ..... Antibody

Ag..... Antigen

ALT ..... Alanine aminotransferase

APHL... Association of Public Health Laboratories

AST..... Aspartate aminotransferase

cAg..... Core antigen

CBC .... Complete blood cell count

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

CLIA .... Clinical Laboratory Improvement Amendments

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

CPT ..... Current Procedural Terminology

DBS..... Dried blood spot

DDA .... Direct acting antiviral

DVH .... Division of Viral Hepatitis

EHR..... Electronic health record

FDA ..... US Food and Drug Administration

HBsAg . Hepatitis B surface antigen

HBV..... Hepatitis B virus

HCV .... Hepatitis C virus

HIV..... Human immunodeficiency virus

KQ ..... Key question

LIMS.... Laboratory information management system

POC .... Point-of-care

POCT... Point-of-care test

QALYs.. Quality-adjusted life years

STD ..... Sexually transmitted disease

SME..... Subject matter expert

SSPs.... Syringe service programs

SVR ..... Sustained virologic response

TAT ..... Turnaround time

US ..... United States of America

Nomenclature

FDA FDA-authorized: We have used the term "FDA-authorized" as a simplification in the document rather than using a more specific term that indicates the type of review/approval/authorization pathway that a test method has undergone at FDA, such as "FDA-approved," "FDA-cleared," etc., because we mention different test methods that may go through different pathways. For reference we have included the definitions for the different pathways below.

- **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 authorization:** Term used to indicate that marketing authorization was granted via a De Novo classification request which provides a marketing pathway to classify novel medical devices when there is no legally marketed predicate. Once classified into class I or class II through a De Novo request, these devices can serve as predicates for future premarket notification submissions.
- **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: We have used the term capillary blood 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.

Two-step Testing Sequence for Identifying Current HCV infection: CDC's currently recommended testing sequence, updated most recently in 2023, consists of an initial antibody (Ab) test which, when reactive, is automatically followed by a nucleic acid test (NAT) for detection of HCV RNA.[1,2]

Complete Testing: We have used the term "complete testing" to describe situations where all recommended tests have been performed as part of a multi-step testing algorithm. For diagnosis of current HCV, when the initial test is reactive, an

FDA-approved nucleic acid test (NAT) intended for the detection of HCV RNA[2] is recommended and must be performed in order to ensure complete testing. The outcome of the NAT for HCV RNA is usually reported as detected or not detected or reported in IU/mL for quantitative NATs.

Incomplete Testing: We have used the term "incomplete testing" to describe the scenario where only the initial Ab test was performed even though an HCV RNA test was indicated. When the initial Ab test is reactive and no NAT for the detection of HCV RNA[2] is performed, this constitutes incomplete testing.

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 guidelines for more details.[2]

Viral-first Testing: This term is used to indicate that a test or method detects a viral component, either nucleic acid (RNA/DNA) or a protein (antigen)—rather than an indirect marker—immune response to the viral infection (antibody). Nucleic acid tests (NAT), which can detect either viral RNA or DNA, and tests that detect viral proteins, such as antigen tests are examples of viral-first test methods. For this report, tests that would fall under this category include NATs for HCV RNA and HCV core antigen (HCV cAg) tests.

Executive Summary

Hepatitis C virus (HCV) remains a significant public health challenge in the United States (US). Despite the availability of curative, direct-acting antiviral (DAA) therapies, over 2.4 million Americans are estimated to be living with current HCV infection.[3] The Viral Hepatitis National Strategic Plan for the US provides a framework for viral hepatitis elimination[4] by 2030 and measurable progress towards elimination has been made. The US is on track to meet the 2030 goal of reducing hepatitis C-related deaths by 65%[5] and HCV case rates have stabilized since 2021.[6] However, the pace of identifying and treating infections is insufficient to meet the HCV elimination goal of reducing new infections by 90%.[5]

About 70,000 new HCV infections still occur each year in the US;[6] almost twice the annual target established by the US Centers for Disease Control and Prevention's (CDC) Division of Viral Hepatitis (DVH).[5] Data shows that many diagnosed individuals do not access therapy in a timely manner, with only 34% of diagnosed patients cured of HCV.[7,8] Moreover, about 32% of HCV infections remain undetected altogether.[3]

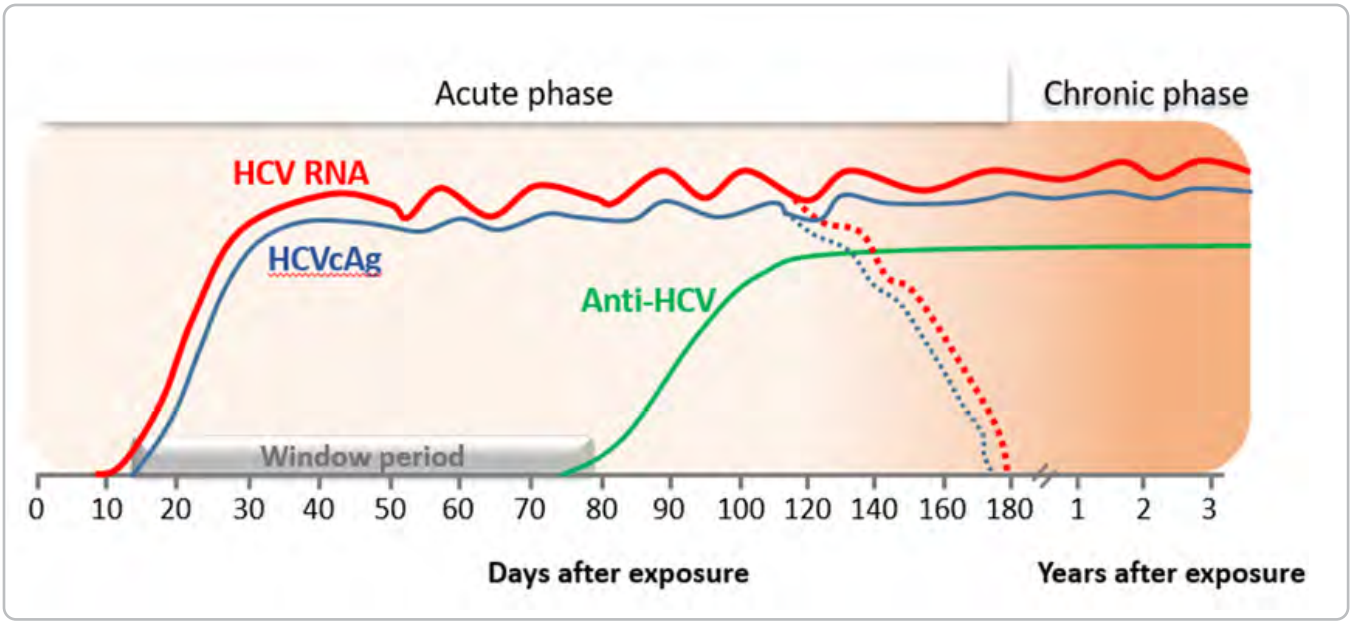
The recommended testing sequence for identifying current HCV infection begins with an HCV antibody (Ab) test followed, when reactive, by an automatic NAT for HCV RNA.[2] As shown in **Figure 1 (page 5)**, HCV antibodies typically become detectable six to twelve weeks after infection, meaning this testing sequence can delay diagnosis, miss acute infections, and reduce opportunities for early treatment.[9] Additionally, when an HCV Ab reactive specimen is not automatically reflexed to the NAT for HCV RNA, patients can be lost to follow up, resulting in incomplete diagnosis and additional missed treatment opportunities.[9,10]

In 2021 DVH partnered with the Association of Public Health Laboratories (APHL) to identify high priority diagnostic tools and strategies to advance HCV elimination goals via a virtual consultation with subject matter experts (SME). Recommendations from that meeting called for: down-classification of HCV tests by the US Food and Drug Administration (FDA) to help bring new tests to market; development of FDA-authorized, point-of-care (POC) diagnostic tools to expand access to testing; and for CDC to review the recommended testing sequence. Since the meeting, the FDA reclassified HCV diagnostic tests from class III to class II and authorized the first Clinical

Laboratory Improvement Amendments (CLIA)-waived, POC NAT for HCV RNA that enables single step HCV diagnosis. Additionally, the CDC conducted and published a cost effectiveness analysis of testing approaches for diagnosis of HCV among US adults.[11] This analysis indicated that compared with the two-step testing sequence for identifying current HCV infection, viral-first HCV testing approaches are potentially cost-effective strategies that resulted in gains in diagnoses and health outcomes.[11] In 2025, CDC began a systematic review of HCV testing guidance with consideration of strategies that include viral marker testing as the first and possibly only step.

To build on this momentum, DVH again partnered with APHL to convene a two-day consultation of HCV SMEs on September 16-17, 2025. The proceedings were guided by key questions whose answers and implications are documented in this meeting report. The purpose of the meeting was to gather the opinions of individual SMEs on accelerating the diagnosis of current HCV infection through same-day diagnosis and treatment and viral-first testing.

Figure 1. Temporal Profile Markers of HCV Infection



Overall Recommendations for Action

Efforts to eliminate HCV in the US require a coordinated national strategy that enables access to simple diagnostic pathways, expands treatment access, and supports sustainable implementation across healthcare, public health and community-based systems. Discussions across our five key questions highlighted that progress depends on addressing systemic barriers, strengthening the diagnostic toolkit, and supporting scalable implementation models that ensure testing leads directly to treatment. The recommendations below synthesize these cross-cutting priorities.

National Testing Recommendations

Flexible and modern testing guidelines are needed to advance viral-first testing and POC-supported test and treat programs. Participants emphasized the importance of modernizing HCV testing guidelines to explicitly allow viral-first testing as an alternative to two-step testing.

1. Data driven recommendations can be developed prior to FDA authorization of specific (particularly lab-based) tests.
2. Flexible recommendations that allow for implementation of setting-specific strategies are desired.
3. Both HCV RNA and HCV cAg-based testing approaches have merit. While viral-first testing based on NAT for HCV RNA detection is more supported by the literature and diagnostic toolkit in the US, experience with HIV testing algorithm development can be leveraged to move recommendations for viral-first testing based on concurrent HCV cAg-Ab testing.
4. Ensure that, as applicable, guidelines address testing sequences appropriate for diagnosis and monitoring for sustained virologic response (SVR).
5. Consider including language in future guidance clarifying that HCV screening and testing should be provided as part of routine care using an opt-out approach.
6. Ensure that testing recommendations include options for perinatally exposed infants.

System-Level Barriers and Structural Needs

Achieving meaningful progress towards HCV elimination requires addressing barriers that limit implementation of POCT and laboratory-based viral-first testing strategies in a sustainable way. Participants highlighted that:

1. Outdated reimbursement and coverage pathways require reform.
    a. Prior authorization requirements for viral load determination or genotyping prior to treatment must not dictate coverages.
    b. Factors such as frequency of testing or test type should not dictate coverages.
    c. Test and treat models require testing sites to dispense medication, therefore mechanisms to allow behavioral and community health programs to dispense antivirals are needed. Use of “starter packs” may help.
    d. Use of Section 1115 waivers, to allow Medicaid coverage for HCV treatment prior to discharge from carceral settings, may be a mechanism to address cost related barriers.
    e. Current reimbursement rates do not accurately account for costs of specimen collection and processing in addition to test costs. Reimbursement for HCV testing should be reassessed and Current Procedural Terminology (CPT) codes better aligned with the true cost of testing should be developed.
2. Lack of universal healthcare coverage continues to impede timely diagnosis and treatment.

3. Workforce capacity development is required. POC coordinators, community navigators, laboratory staff and non-specialist providers trained in HCV treatment must be supported.
4. Investment in informatics infrastructure is necessary. Enhanced interoperability and standardized reporting pathways will allow for leveraging of existing results and support clinical decision-making.
5. Assess barriers to bringing tests to the US market. FDA performance expectations, especially for HCV cAg and POCT, should be aligned with appropriate comparators. HCV cAg performance characteristics should not be expected to match HCV RNA NAT performance for example.

Diagnostic Tools/Approaches Needed

Viral-first testing provides earlier detection, reduces loss to follow-up, and supports same-day treatment, but broader adoption is limited by gaps in test availability, regulatory approvals, and performance considerations. Several priority areas were consistently identified:

1. Tests that should be prioritized for development and /or FDA authorization include:
    a. POC and laboratory-based NATs for HCV RNA with intended use claims independent of the requirement for Ab testing.
    b. Faster POC HCV Ab (< 5 min) and POC HCV RNA (< 30 min) tests
    c. HCV cAg or HCV cAg-Ab tests with ability to differentiate cAg-Ab results
        I. If supported by performance (sensitivity), a standalone POC HCV cAg would represent a major advancement
        II. HCV cAg performance should be evaluated in infants
    d. POC HBsAg test
    e. POC alanine aminotransferase (ALT) and aspartate aminotransferase (AST) tests
    f. POC complete blood cell count (CBC)
    g. Multiplexed POCTs for HCV Ab (or HCV Ab/Ag), HIV Ab/Ag, HBsAg, and treponemal antibodies.
2. Manufacturers should work to update indications for use on currently FDA-authorized test methods (HCV Ab and HCV RNA):
    a. For additional specimen types including:
        I. Capillary blood (including dried blood spot [DBS])
        II. Specimens self-collected outside of a clinical setting (home-collection)
        III. Plasma separation cards
        IV. Smaller specimen volumes such as those collected from infants
    b. To allow for primary diagnosis, SVR monitoring and reinfection assessment
    c. With evaluations that include special populations like infants and pregnant women.
3. Diagnostic manufacturers with commercially available tests outside the US should seek FDA authorization to enable testing in the US market.
4. Consideration should be given to development of CLIA-waived instrument-free viremic POCT.
5. CDC-led validation studies could help generate data for FDA submissions.

Performance and Evidence Gaps

More data are required across a variety of areas to inform and refine decision making. Gaps that should be addressed include:

1. US based comparisons of HCV RNA and HCV cAg-based screening with HCV Ab testing in varied prevalence settings. These studies:
    a. Will help determine whether discrepant HCV cAg and HCV Ab results require reflex NAT for HCV RNA
    b. Could help determine the role of HCV cAg testing in early infection and SVR monitoring.
2. Participants encouraged modeling studies, evaluation of existing pilots and further cost-effectiveness evaluations, especially those that factor in the cost-savings associated with decreased transmission.
3. Further evaluation and ultimately FDA authorization of capillary specimens for use with HCV RNA, cAg and Ab tests.
4. Efficacy of HCV cAg-Ab testing of exposed infants.
5. Assay performance (HCV RNA, cAg and Ab) in special populations such as pregnant women, pediatrics and individuals in early seroconversion.
6. Development of mechanisms for collaborative data generation, particularly to assess assay performance during acute infection and across diverse populations (including pediatrics and pregnant women).

Opportunities for High-impact Deployment

Viral-first testing will have the most impact in high prevalence settings, particularly where patients are unlikely to seek follow up care.

1. Short stay correctional facilities (jails) were identified as high-yield environments for piloting test and treat models due to the feasibility of same-day diagnosis and treatment.
2. Places where people who inject drugs seek care, mobile or community-based programs were also identified as critical access points.
3. Integration of telehealth, mobile health models, peer navigation, and co-located testing for comorbid infections (HIV, HBV, syphilis) can further strengthen the reach and efficiency of these settings.

Operational and Implementation Considerations

To ensure operational feasibility, clear implementation frameworks, streamlined workflows, standardized training tools, and mechanisms to share lessons learned across programs are needed. Many participants noted that the current landscape consists largely of isolated pilot projects that fail to translate across networks due to limited technical assistance, absence of institutional incentives, and insufficient planning for long-term funding.

1. A national "implementation playbook" could be developed to help standardize adoption of appropriate and recommended testing sequences. The playbook could include:
    a. Standardized needs assessment forms developed to help to identify sites where viral-first laboratory or POCT would have the greatest potential impact and assess readiness to operationalize various testing strategies
    b. Suggestions for streamlined pre- and post-analytical workflows to help ensure timely specimen processing, result delivery and streamlined linkage to care
    c. Standardized protocols for training, testing and competency evaluation of staff
    d. Standardized test reporting language
    e. Resources related to electronic health record (EHR) integration
    f. Resources for patient and provider education related to test ordering and result interpretation

g. Clinical decision tools to guide treatment initiation, especially in cases where a full workup is not yet complete
h. Reimbursement tables containing codes for various tests.

2. Peer-based and telehealth models could be used for linkage to treatment and initiation.
3. Training and technical assistance networks should be leveraged or developed (communities of practice).
4. Existing networks such as federally qualified health centers (FQHCs), correctional systems, and public health departments should be leveraged to scale successful models beyond individual pilots.
5. Bulk purchasing and negotiated pricing of diagnostic tests and DAAs would help support sustainability, particularly in public health settings.
6. The US cannot test its way to HCV elimination. Linkage to care is an essential component of any testing program.

Process Summary

Background

Beginning in May 2024, APHL and CDC worked together to plan the Establishing a Road Map for Accelerated Diagnosis and Treatment of HCV Infection in the United States meeting. Key questions (KQs) were defined (**Appendix A, page 32**) and a meeting agenda was outlined to include introductory presentations and structured discussions. For each KQ, SMEs were chosen to participate either as a moderator, presenter or panelist. Participants with diverse backgrounds were chosen to ensure the different perspectives were represented. The meeting was initially scheduled for February 2025, but was postponed and held on September 16-17, 2025.

Meeting

The objective of the meeting was to convene SME representing a range of disciplines and practice settings to evaluate KQ and provide opinions on how to advance diagnosis of HCV infection through same day diagnosis and treatment and viral-first testing. Two introductory presentations laid the framework for understanding the critical role of diagnostic testing in achieving HCV elimination and provided an overview of the current and emerging HCV diagnostic landscape (Agenda; **Appendix B, page 33**). KQ segments then followed with each including a three-minute introduction (moderator), a 10-15 minutes presentation (presenter), three minutes of commentary per panelist (n=3-5 per KQ) and a 30-40 minute facilitated question and answer session involving all invited participants. Each presentation provided relevant background information, and expert perspective to inform discussion of the assigned KQ. Panelists were invited to share insights based on their respective roles within the diagnostic and public health systems, while moderators guided the overall discussion.

Participants contributed input throughout the meeting either by speaking directly or by using the chat and Q&A features of Zoom. Central to these discussions was the goal of determining how to best implement existing diagnostics to meet the needs of patients across diverse, high-impact settings and to identify new technologies required to strengthen the HCV diagnostic toolkit.

The meeting was held virtually using Zoom, with a livestream broadcast to Vimeo and recorded. SMEs representing a range of disciplines and practice settings were invited to promote a broad and balanced discussion. 12 speakers, 5 moderators, 15 panelists and 42 invited participants attended the live meeting in the Zoom room. Participants included representatives from public health laboratories, clinical laboratories, large commercial laboratories, clinical providers, academic researchers, public health agencies, diagnostic manufacturers, staff from US Health and Human

Services including: CDC National Center for HIV, Viral Hepatitis, STD, and Tuberculosis Prevention (NCHHSTP), and DVH, FDA, Substance Abuse and Mental Health Services, Indian Health Services, National Institute of Diabetes, Digestive and Kidney Diseases, National Institute on Drug Abuse, and other partner public health organizations. For a complete list of participants see **Appendix C (page 35)**, and for financial disclosures for moderators, presenters and panelists see **Appendix D (page 39)**. Public comments were accepted via the federal register, with some comments coming by email to the meeting facilitators.

Report

This document summarizes the collective input and major discussion points organized by KQ. It reflects the perspectives of all meeting participants, as well as comments submitted through the federal register and direct correspondence to meeting facilitators during the public comment period. For each KQ, background information provided by the presenter is followed by a synthesis of panelist remarks, main discussion points and identified needs. 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 CDC.

This is the final meeting report which was developed following a structured review process. APHL distributed a draft report to participants and sought comment for six weeks. All submitted comments were reviewed, and those relevant to the accuracy or clarity of the summary were addressed and incorporated as appropriate. Additional feedback pertaining to the findings or implications of the report will be collected and shared with our partners at CDC.

Meeting Summary

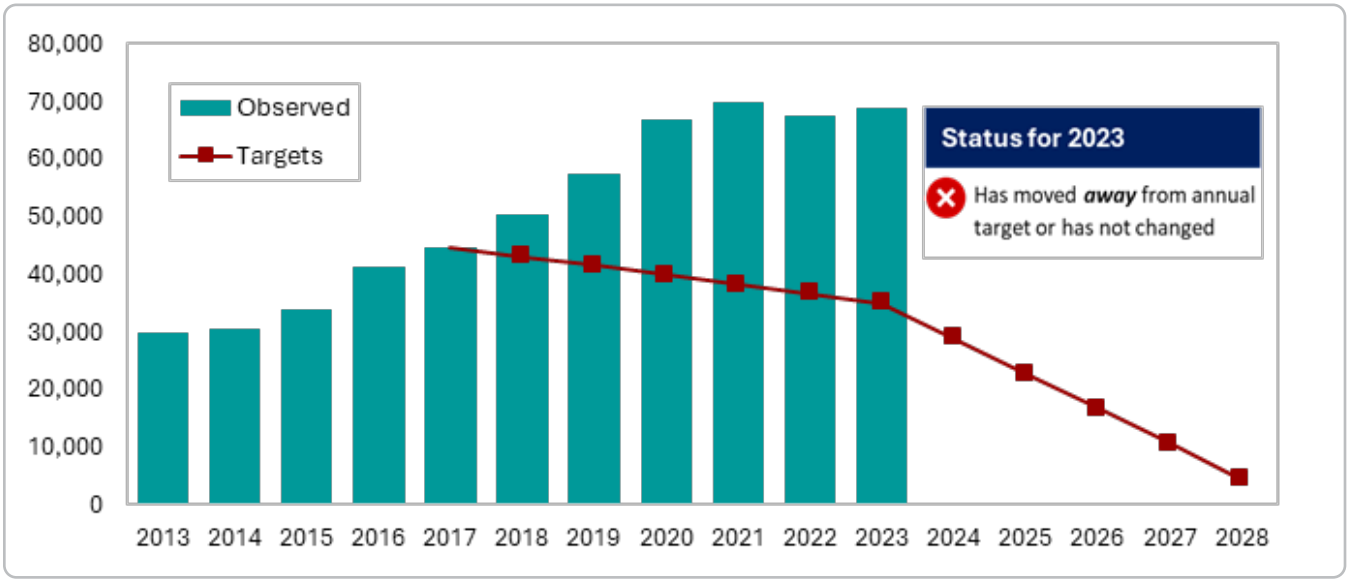
Opening Session

The opening session did not have a question and answer period or facilitated discussion. Below is a summary.

Achieving HCV Elimination and Exploring the Role of Viral-first Testing Strategies in Diagnosing HCV Infection in the US, Carolyn Wester

An estimated 2.4 million Americans are living with HCV and about one-third of them are unaware of their infection status, pointing to a need for improved uptake of diagnostic testing.[3] The US established ambitious HCV elimination goals in the National Viral Hepatitis Strategic Plan, aiming to reduce new infections by 90% and related deaths by 65% by 2030.[4] While progress has been made, particularly towards reducing mortality, the country remains far offtrack the infection reduction target (**Figure 2**).[5] Infection rates have plateaued since 2021 alongside a plateau in overdose deaths,[12] but an estimated 70,000 new cases still occur annually.[6]

Figure 2. Estimated new HCV infections per year in the US and annual targets by year



DAAs are curative, short-course, cost-saving medications recommended for essentially everyone with HCV. However, treatment uptake is insufficient. From 2014 through 2020, approximately one million people received DAA therapy, yet treatment rates have since stabilized at about 70,000 per year, far below what is needed to meet elimination targets.[13] Only one in three individuals with diagnosed HCV initiate treatment within a year, and rates are even lower among Medicaid beneficiaries and uninsured populations.[7] Similarly, only 34% of people with diagnosed HCV have evidence of viral clearance, and in those aged 20-29 years old, the percentage is only 16%.[8] These gaps underscore the need for a coordinated approach to expand testing and treatment access nationwide.

A proposed federal HCV elimination initiative, introduced in 2024 with bipartisan support, is focused on expanding diagnostic access, implementing a federal drug procurement strategy, and strengthening public health infrastructure.[14] Modeling data suggest that this initiative could prevent tens of thousands of deaths and save billions in healthcare costs over a decade. To fully expand diagnostic access, the HCV diagnostic toolkit must be refined and fully

built. The current two-step, antibody-first testing algorithm, developed in 2013,[2] has limitations, including delayed detection of acute infection, loss to follow-up, and missed diagnoses.[15,16] Antibody tests typically become reactive six to twelve weeks post-infection, whereas RNA tests can detect infection within one to two weeks.[17] Shifting to viral-first testing strategies, such as HCV RNA or cAg detection, could shorten the time to diagnosis by over a month and reduce loss to follow-up.

Recently, the first POC HCV RNA test was authorized by FDA. The test delivers a diagnosis within an hour, without the need to first screen a sample for HCV Ab. While this test marks a moment of forward progress in terms of viral-first detection of HCV, gaps remain in the diagnostic toolkit. Assays that target detection of HCV cAg are available outside of the US, but none have received FDA authorization. Moreover, there is no FDA-authorized HCV self-test, or laboratory-based viral first test available in the US. Modeling studies conducted by CDC indicate that viral-first testing strategies improve case detection and treatment initiation, yielding gains in quality-adjusted life years (QALYs) at modest incremental costs.[11] While HCV cAg testing could be cost-effective if priced under $25, RNA-based viral-first testing offers a simpler, one-step approach with clear interpretability.

To achieve HCV elimination, the US must optimize existing diagnostic tools while advancing new technologies to simplify the process of diagnosis. Strengthening diagnostic capacity across both laboratory and POC settings will be essential to ensuring all individuals with HCV infection are promptly diagnosed, linked to care, and cured, ultimately advancing the nation toward its 2030 elimination goals. The goals of this meeting are to describe how to best implement existing diagnostics to meet the needs of patients across a variety of settings and describe what technologies are needed to fully build out the HCV diagnostic toolkit by exploring POC and viral-first testing options.

Landscape Analysis of the HCV Diagnostic Toolkit, Jordan Feld

Current HCV diagnostic strategies in the US are effective but inefficient, resulting in loss of patients along the care cascade.[8] The requirement for repeated office visits for screening, confirmation, and treatment initiation remain major barriers to HCV elimination. Accelerating diagnosis and linkage to care requires diagnostic tools that deliver rapid, accurate results and ideally, also allow clinicians to assess for advanced liver disease, Hepatitis B and HIV.

Existing tools include both laboratory-based assays and POCT, each with distinct advantages and limitations and each amenable to specimens that may include serum, plasma, whole blood, DBS and/or saliva. Laboratory assays provide high throughput, automation, and relatively low cost per test but can lead to loss to follow up because they are hindered by delayed turnaround times (TATs) and dependent on two-step testing. POC assays, by contrast, offer same-day results and reduced loss to follow-up, though they may involve higher costs, limited throughput, and more operator training than expected.

HCV assays target analytes including HCV cAg, Ab and/or RNA. HCV cAg testing provides a shorter window period than HCV Ab testing (**Figure 1**), but there are no FDA-authorized HCV cAg tests available, which limits access in the US market. Core Ag testing can be performed on the same sample used for Ab testing and could reduce reliance on expensive molecular platforms. However, current cAg assays lack the sensitivity required to detect all chronic infections (i.e., only able to detect infection with HCV RNA levels of ≥~3000 IU/mL), particularly in individuals with low viral loads, genotype 3 infection, HIV coinfection, or cirrhosis.[18] Current cAg tests are also difficult to translate into POCT, which would be of greatest benefit, due to the requirement for a technically challenging Ag/Ab dissociation process. With current assay performance characteristics, a combination cAg-Ab test could help achieve viral-first testing and streamline diagnosis. However, if the sensitivity of cAg tests was increased, adaptation to a standalone HCV cAg test that could be used at the POC would be possible and would represent a major advancement.

DBS testing provides a minimally invasive option for HCV screening and diagnosis, supporting viral-first strategies by enabling Ab and RNA testing from a single specimen. DBS collection avoids venipuncture, allows peer or self-collection, and permits easy storage and mailing to a laboratory. The method offers strong sensitivity and specificity and supports multi-pathogen testing, useful in syndemic settings. However, it is limited by small sample volume, minor RNA loss affecting acute or post-treatment detection, and the lack of rapid results. Importantly, DBSs are not currently approved in the US for HCV specimen collection.

Laboratory based Ab assays are commonplace in the US, but do not facilitate test and treat models or viral-first testing. However, POC Ab assays provide rapid, accurate results without laboratory infrastructure or reliance upon instrumentation. While several are used globally, only one is FDA-authorized. These tests show high specificity and good sensitivity, though saliva-based versions perform slightly less well and are not FDA-authorized in the US.[19] Newer models, such as the one-minute INSTI test, could further reduce TAT and patient loss to follow-up, but remain unavailable in the US.[20] Expanding access to faster POC antibody tests could improve same-day testing and strengthen HCV detection efforts.

POC HCV RNA testing is a critical advancement. The first FDA-authorized, CLIA-waived qualitative assay is now available in the US, and a quantitative version of the test is available in other countries. These molecular tests provide diagnosis within about one hour and their performance characteristics align closely with laboratory-based RNA assays.[21] Evidence from international programs, including those in Australia and Canada, demonstrates that POC RNA testing shortens the time from diagnosis to treatment initiation and improves treatment uptake, particularly in high-prevalence or hard-to-reach populations such as correctional facilities and syringe service programs (SSPs).[22,23,24] Interestingly, patients without a history of HCV have a reported preference for prescreening with a POC Ab test prior to reflex POC RNA testing, and this approach may offer TAT advantages and cost savings in lower prevalence settings (< 74%).[25,26] Remaining challenges with POC RNA testing include higher implementation costs, potential challenges with reimbursement, limited instrument portability, slower TATs (1 hour vs. minutes), useability (requiring operator training), and potential test errors early in deployment.

Emerging molecular technologies, including loop-mediated isothermal amplification (LAMP) and CRISPR-based detection, offer promising avenues for RNA detection with reduced dependence on complex instrumentation. While these approaches show strong analytical performance, they remain limited by the need for blood sample extraction and yield modest reductions in sensitivity, particularly for genotype 3 infections.[27,28]

Selection of diagnostic tools should be guided by the setting and the situation. Factors such as population needs, disease prevalence, available infrastructure, and care delivery models help determine the targeted specimen type, TAT, test cost and finally the correct test for the population. In low-barrier, community-based or resource-limited settings, rapid POC testing paired with same-day treatment initiation may be the most effective strategy to prevent patient loss to follow-up. Regardless, our current paradigm involving repeated visits and two-step testing is not ideal. Better access to POC HCV Ab and RNA tests, faster tests, a POC HBsAg test, POC ALT/AST and POC CBC are needed. In order to eliminate the barriers that providers face with provision of same day treatment, policy and reimbursement frameworks that support these approaches will be essential.

Key Question 1: What are the optimal settings to utilize POC HCV testing for same-day diagnosis of current HCV infection?

Introduction and Presentation

Selecting the most appropriate diagnostic approach for HCV infection requires ensuring the right test, for the right patient, in the right setting.[29] This depends on the characteristics of the test, the target population and the testing environment; the availability of support resources; and cost-effectiveness. Established care pathways can be leveraged to help ensure timely access to treatment, but logistical barriers such as prior authorization requirements can limit the feasibility of same-visit testing and treatment models. Regardless, an improved diagnostic approach for HCV is a worthy endeavor and optimization of POC HCV testing requires attention to the setting.

Characteristics of candidate settings for POC HCV testing can be grouped into five domains by: 1) population access and reach, 2) operational feasibility, 3) integration with care pathways, 4) acceptability and patient experience and 5) sustainability and system support (**Figure 3**). In terms of population access and reach, POC testing provides greater value in high-prevalence settings that serve populations with limited healthcare access, who are also less likely to engage in follow-up care. Ideally, these POC testing sites would be convenient and familiar to the targeted population and provide a low barrier to entry (i.e., drop-in, no registration, no insurance required, etc.).

Figure 3. Five characteristic domains to help assess potential HCV POCT settings

Operational feasibility for POC testing relies upon workforce capacity and training, quality assurance procedures, the availability of reliable supply chains and data systems for timely result reporting. If two-step POC antibody to RNA testing is utilized, immediate follow-up for HCV AB reactive specimens, with automatic POC RNA testing ensures complete HCV testing and can facilitate rapid or even same-encounter treatment initiation. For both two-step and viral-first HCV POCT, the ability to link to treatment (in-person or via telehealth); integrate with existing care pathways (e.g., HIV and HBV testing), addiction treatment and / or primary care; and refer for more advanced services (e.g.: for complicated cases with decompensated cirrhosis or HBV infection) enhances efficiency and reach. Acceptability and patient experience are also critical to the success of the setting; the use of streamlined logistics and community-based, non-stigmatizing approaches that provide minimal wait times and confidential and discreet results are viewed as ideal for increasing participation and earning trust. Peer support and community navigators can also be utilized to educate the community about the value and processes related to testing, to increase service uptake.

Sustainability requires ongoing investment in infrastructure (including informatics for reporting to the EHR) and workforce development, along with alignment between public health agencies, payers, and community partners. Adaptability is also important as the needs of the population change. Importantly, cost effectiveness data helps to convince payors of the value of POC testing and more data would be beneficial. POC HCV RNA testing can be used for post-treatment monitoring for reinfection and possibly determination of SVR if the manufacturer expanded

their intended use claim. Evidence from large-scale international programs, including Australia's national rollout of POC HCV RNA testing, demonstrates that when adequately supported by infrastructure and policy, rapid testing approaches can expand access, increase same-visit diagnosis, and improve linkage to treatment.[22]

Overall, data indicate that expanding access to POC diagnostics, particularly in high-prevalence, underserved settings like SSPs and opioid treatment programs, carceral settings, and mobile units (including mobile retail pharmacy[30]), will be essential to accelerating HCV elimination.[31] However, data also shows that in some high prevalence settings treatment uptake can be low, highlighting the need for integrated treatment options. Success will depend on coordinated policy, resource allocation, and system-level support to ensure that the right test, given to the right patient, in the right setting leads to individual-level treatment uptake, SVR and ultimately population-level HCV elimination.

Panelists Remarks

The panel discussion highlighted that regardless of setting, POC testing is most impactful when treatment can be initiated during the same visit, via test and treat programs. Participants reiterated that high prevalence settings, where patients are at risk for loss to follow up represent the highest priority target for POC HCV testing. Multiple panelists mentioned that integrating HCV testing and treatment into existing infrastructure is a practical way to reach target populations. Commonly mentioned priority settings included mobile and community-based models, carceral settings and places where people who inject drugs seek care.

Experience from mobile and pop-up health programs demonstrates that test and treat strategies are feasible and effective in reaching populations with limited healthcare access, particularly in rural or underserved regions.[32] Healthcare system-based mobile units, operating in partnership with community organizations, food banks, and local agencies have successfully provided integrated HCV testing and treatment, identifying previously undiagnosed infections and initiating care in the field. These programs have achieved meaningful treatment initiation rates despite operational challenges such as staff training, limited funding, and logistical barriers related to equipment transport, reporting and integration with the EHR. Sustaining such programs requires dedicated funding streams, streamlined regulatory processes, and trained personnel to ensure quality assurance and scalability.

Correctional facilities, particularly jails, represent high-prevalence and high-turnover environments where POC testing can have substantial impact. With over seven million jail admissions annually in the US and an average stay of only 15 days, rapid diagnostic tools could help identify HCV infections before release. Integrating HCV testing into existing intake workflows was identified as a pragmatic strategy, that would require faster (e.g., the INSTI HCV Test, Abbott Bioline HCV Test or < 5 minute test) POC tests. Effective implementation also requires linkage to treatment either onsite or via early discharge planning and data systems that support continuity of care upon release. Several panelists did mention that jails have been hesitant to test, due to lack of funding for any subsequent treatment. Regardless, consideration of the community corrections population which includes millions of people on probation and parole, is warranted as these represent additional opportunities for engagement.

Places where people who inject drugs seek care provide essential touchpoints for diagnosing and treating HCV in the group most at risk for infection. Most often, people who inject drugs have fragmented healthcare experiences and inconsistent follow-up, underscoring the need for viral-first and rapid testing options in this population. Immediately actionable diagnostic approaches, paired with onsite or near-site treatment initiation and supported by reimbursement structures that recognize both qualitative and quantitative viral load testing would be most beneficial. Barriers such as prior authorization requirements, prescription delays, and pharmacy access continue to limit effectiveness.

Additional locations that were mentioned as potential targets for POC testing, or at least feasibility studies using POC tests, included emergency departments (ED) and pharmacies. While the ED is an ideal location to implement a test

and treat strategy, it would be most effective if the result is obtained while the patient is still in the ED which can be a challenge with currently available testing options. The ability of pharmacies to offer HCV testing and treatment and to be reimbursed for offering such services varies by state.[33] While the relative abundance and geographic spread of pharmacies makes them convenient and practical locations for provision of test and treat programs, the regulatory landscape presents a complicated reality.

Key Discussion Points and Takeaways

- **POC testing is not a standalone solution:** Participants emphasized that while POC testing increases access and engagement, it must be supported by systems that ensure linkage to confirmatory testing (if necessary), integrated treatment initiation, existing care pathways and follow-up care.
- **Prioritize high prevalence settings for POC implementation:** High HCV prevalence settings were consistently identified as high priority, particularly when patients have limited healthcare access and are unlikely to seek follow up care. Correctional facilities were identified as high-yield environments, with estimates suggesting that scaling test and treat programs in jails could cure up to 10% of US HCV cases annually. Participants also underscored the need for parallel expansion in places where people who inject drugs seek care, and use of mobile or community-based models, particularly to reach rural populations.
- **Important role for telehealth and mobile health models:** Mobile models were praised for their flexibility and ability to reach entire networks of people. Expanding telehealth-supported models was identified as a key enabler for reaching underserved and rural areas. Combining mobile testing using peer or community outreach workers with tele-prescribing and "starter packs" of medication was viewed as an innovative approach to accelerate treatment initiation and overcome logistical barriers**,** particularly when additional testing (i.e., HIV, HBV, liver function) was available at the POC.
- **Strategies should be tailored to population needs:** Speakers differentiated between long-term infected individuals at risk of liver disease and those with more recent infections that drive transmission. Tailored testing and treatment approaches were viewed as essential for maximizing both individual and public health benefits.
- **Integrate peer and lived experience expertise:** Involvement of community navigators was described as critical for building trust, improving acceptance and engagement, and facilitating linkage to care.
- **Implementation barriers and enablers:**
  - Beyond funding, participants cited major barriers as limited setting-specific training, logistical complexity, lack of standardized protocols and difficulties with EHR integration. Participants stressed the need for shared toolkits, operator training materials, and national "communities of practice" to support program scale-up and foster knowledge exchange.
  - Utilizing existing infrastructure and learning operational lessons from similar programs (e.g.: drug testing, HIV) and the experience of others was repeatedly cited as a means towards POCT and treat program implementation and optimization.
- **Financial considerations:**
  - Participants noted the absence of incentives for testing within correctional systems and the need for policy changes, such as Section 1115 waivers, to allow Medicaid coverage for HCV treatment prior to discharge. Institutional incentives and positive publicity (treatment improves quality of life, even in a carceral setting) were identified as potential motivators for adoption within custodial leadership.
  - Programmatic sustainability was also cited as a concern, with participants discussing the use of grant funding for launch of innovative test and treat programs with an eventual transition to more sustainable funding. Poor reimbursement rates for POC testing, combined with the expense of such tests (particularly in the US where market competition is currently lacking) hamper the sustainability of POC testing programs.

Identified Needs

1. **Data:** Further US-based data are needed to guide prioritization of testing sites and to assess cost-effectiveness. Participants encouraged modeling studies, evaluation of existing pilots, and adaptation of successful international models to the US context and stressed that further cost-effectiveness evaluation could help generate buy in from payors and those in charge of resource allocation.
2. **Faster POCT:** Truly rapid (<5min) POC HCV tests are available outside of the US and are needed in the US to fully capitalize on POC test and treat models. More rapid POC HCV RNA tests would also be a helpful innovation.
3. **POCT that support both diagnosis and monitoring:** Ideally a POCT could be used to diagnose HCV and monitor for SVR and reinfection.
4. **Development of standardized implementation tools:** Creation of national training resources, operational toolkits, and technical assistance networks (communities of practice) to facilitate consistent deployment of POC testing was encouraged.
5. **Policy solutions:** It is necessary to explore mechanisms such as Medicaid waivers and elimination-focused legislation to support sustainability and incentivize testing and treatment across systems. We should work to ensure that outdated prior approval requirements (e.g.: for viral load determination or genotyping prior to treatment) do not dictate coverage.

Key Question 2: What are the optimal POC HCV testing sequences and linkage to treatment strategies by setting?

Introduction and Presentation

There is not a universal model for implementation of POCT for HCV diagnosis. The optimal approach depends on the setting, available infrastructure and resources, population characteristics, and treatment capacity. Regardless, two primary POC testing sequences exist: the currently recommended two-step, antibody-first diagnostic algorithm and the single-step, viral-first strategy, which at this point relies upon HCV RNA testing.[31] The antibody-first strategy offers several advantages, including use of finger-stick sampling without phlebotomy, rapid TAT (when HCV Ab non-reactive), lower cost, and high throughput. While it may enable same-day testing and treatment in many settings, Ab-first testing misses early infections and relies on follow-up RNA confirmation, which may not always occur, leading to incomplete testing.

In contrast, the viral-first approach based on POC detection of HCV RNA diagnoses acute infections and allows for immediate treatment initiation from a single finger-stick. However, testing capacity is dependent on an instrument with limited throughput, and POC RNA testing currently involves higher cost and greater technical requirements than POC Ab testing. Current cost-effectiveness analyses suggest that POC RNA-first testing becomes more favorable in high-prevalence settings,[26] while antibody-first testing remains more practical in low-prevalence contexts, but this has only been studied outside of the US.

Several operational factors were identified as critical in determining which approach to adopt. These include: (1) access to phlebotomy and laboratory testing; (2) the type and duration of patient encounters; (3) HCV prevalence within the target population; and (4) the expected testing volume. When phlebotomy services and laboratory access already exist and the patient can be expected to seek longitudinal follow-up, laboratory testing is more favorable,

especially if integrated testing programs (for multiple pathogens) exist. Conversely, in low-infrastructure settings where brief encounters are expected, POC testing is beneficial.

Taken a step further, high-prevalence and low-infrastructure settings, such as SSPs, opioid treatment programs and some correctional facilities, may benefit most from single-step POC RNA testing due to the potential for immediate diagnosis and linkage to care. Whereas settings with moderate to low prevalence or existing phlebotomy and laboratory access, such as emergency departments, STI clinics, and primary care sites, may find the two-step antibody-first POC approach or laboratory testing more efficient and cost-effective. Testing volume, especially extremely high or extremely low, may also dictate the testing strategy with high volume testing favoring two-step POC or laboratory-based algorithms and low volume sites facing challenges with implementation of POC HCV RNA testing.

Linkage to treatment remains a key challenge across all settings. Strategies to strengthen this component include co-locating treatment services, which is ideal but not always feasible, expanding use of facilitated telehealth models, or deploying mobile health units to reach underserved populations. Partnerships between healthcare entities and non-clinical settings can help enable these linkages, as there can be insurmountable barriers related to billing and reimbursement for non-clinical settings. For settings without integrated care capacity, robust patient navigation programs can provide effective linkage to therapy,[34] though outcomes are generally stronger with directly linked treatment models.

Overall, adaptable, setting-specific models that combine accurate diagnostic tools with reliable mechanisms for treatment initiation could be established using either two-step/Ab-first or viral-first testing, depending on the previously described factors. Future work focused on refining cost-effectiveness estimates specific to the US and identifying practical pathways to integrate POC testing with scalable treatment delivery systems is needed.

Panelists Remarks

The panel explored current approaches to POC HCV testing and linkage-to-treatment strategies, focusing on improving early diagnosis, public health response, and overall care delivery. Panelists emphasized that integrating single-step, POC HCV RNA testing into SSPs offers both clinical and public health benefits. RNA testing enables the identification of acute infections missed by Ab-based testing. This allows early detection during the most infectious phase and prevents onward transmission within high-risk populations who are likely to have experienced recent infection. Moreover, POC HCV RNA testing can assist outbreak investigations by quickly detecting clusters of HCV infection within a community and providing the opportunity for rapid response. POC RNA testing transforms SSPs into active centers for diagnosis, prevention, and outbreak response, facilitating linkage to care and strengthening community-based models of care.

The importance of same-visit test and treat strategies was also highlighted as a means to reduce loss to follow-up and accelerate access to curative DAA therapy. In some settings, such as Veteran's Affairs, panelists reported that robust EHR data can be leveraged to enable clinicians to identify individuals with existing HCV diagnoses and initiate treatment when they next seek care. Given that loss to follow up has been cited as a major barrier in the HCV care continuum, especially in high-risk populations, if a national EHR systems existed to enable preexisting data to be accessed, same visit treatment could likely be initiated, and prior authorizations met more easily for many people, without requiring repeated testing.

To ensure maximum benefit, public health programs must carefully assess where to implement POC HCV RNA tests and ensure that patients can be not only linked to care but also accept the care. Provider capacity to treat in primary care, patient mistrust of the healthcare system and administrative hurdles such as prior authorization requirements are all obstacles that need to be overcome to effectively make use of POCT strategies and facilitate patient engagement in treatment.

Key Discussion Points / Takeaways

- **Prioritized implementation:** Given resource constraints, a focus on POCT implementation in high volume, high prevalence settings that serve people who inject drugs is most efficient and impactful.
- **Implement same encounter test and treat models:** Strong support was expressed for implementing HCV test and treat models that include same-day POC RNA testing (with or without a POC HCV Ab test depending on prevalence and likelihood of prior disease) and immediate access to antiviral therapy. Such approaches could improve linkage to care, reduce transmission, and advance elimination goals, particularly in high-prevalence populations. Multiple participants felt that stocking DAA "starter packs" at POC testing sites would enable provision of medication and buy time to work through prescription prior authorization requirements and denials.
- **Opt-out testing to increase uptake:** Participants emphasized the effectiveness of opt-out testing policies within SSPs and hospitals, which significantly increase testing uptake for HCV and HIV by normalizing screening as routine care while preserving individual autonomy with the right to opt-out.
- **Multiple models to suit varied needs:** Setting capacity and resources are diverse from robust, co-located clinical programs to small, mobile units, necessitating adaptable testing and treatment strategies. While POC RNA (and the required CLIA certificate of waiver and 35-lb instrument) are feasible in well-resourced settings, POC HCV Ab testing may be more attainable for others.
- **Varied models of provider access:** Co-location of providers is ideal, but often infeasible; peer-delivered and telehealth-based models can bridge this gap.
- **Data may help to reduce provider hesitancy:** The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD-IDSA) HCV Test and Treat Guidelines support same encounter testing and treatment initiation for patients without decompensated cirrhosis determined through history and physical exam. However, providers may be reluctant to prescribe treatment without knowing the patient's HBV status, especially if they are concerned about being able to contact the patient. Data driven clinical decision tools and protocols may help alleviate these concerns, although access to existing patient data (via national EHRs) could also help. Panelists pointed out that in settings like SSPs, patients were typically younger with less risk of decompensated cirrhosis.
- **Public health and healthcare integration:** Collaboration between public health, community, and clinical sectors is critical. Non-clinical, community-based programs serve as trusted anchors that can support engagement, medication adherence, treatment completion and possibly encourage patients to seek longitudinal care via their clinical or public health partners.
- **Structural barriers:** Beyond diagnostics, lack of universal healthcare and coverage limitations remain major structural barriers to widespread implementation of test and treat models.

Identified Needs

1. **Regulatory:**
    - FDA-authorized tests including HCV RNA POCT, HCV cAg POCT and HBV sAg POCT need to be brought to market
    - Mechanisms to support antiviral dispensing at non-clinical sites will improve treatment initiation. The ability to dispense starter packs may improve linkage to care for full treatment
    - Streamlined prior authorization and medication procurement pathways are needed

2. **Data:**
    - Support for FDA authorization studies to bring additional HCV RNA, HCV cAg and HBsAg POCTs to market is needed
    - Data from US-based POC test and treat trials to support cost-effectiveness and modeling studies is needed. This includes studies that consider treatment as prevention and factor in the cost savings associated with decreased transmission
    - Evidence to guide optimal sequencing of Ab and RNA testing in varied prevalence settings
    - Tools and validation studies to identify decompensated cirrhosis and manage safety concerns without extensive lab work
3. **Implementation support:**
    - Guidance and technical assistance to tailor testing and treatment models to capacity and resource levels
    - Clinical decision tools to drive treatment initiation prior to completion of full workup
    - Expanded use of peer-based and telehealth delivery for linkage and treatment initiation
    - Integration of harm reduction services into broader healthcare systems
4. **Systems-level:**
    - Ability to leverage existing test results and ensure data interoperability across systems via a national EHR will increase efficiency
    - Greater investment in workforce and provider training to reduce stigma and expand HCV treatment capacity
    - Cross-sector partnerships to ensure continuity of care and address social barriers (e.g., medication storage, stable contact points)
    - Policy change to address structural inequities in healthcare access via universal healthcare
5. **Emerging and future diagnostic priorities:**
    - Faster POCTs
    - POC HBsAg tests
    - Bundled or multiplex POC testing options to include HIV/HCV/HBV/syphilis, for syndemic testing
    - FDA-authorized options for capillary blood, including dried blood spot (DBS) approaches
    - Instrument-free POC HCV diagnostics for viremia

Key Question 3: What are the benefits of various laboratory-based viral-first testing strategies for the diagnosis of HCV infection in the US?

Introduction and Presentation

Laboratory-based testing practices rely on the two-step testing sequence for identifying current HCV infection. There are no FDA-authorized laboratory-based options with an intended use for viral-first testing. While most people in the US are tested for HCV using laboratory-based testing, the approach may require multiple patient visits and lead to loss to follow up. CDC recently released updated operational guidance to recommend single-visit sample collection, meaning that when HCV testing is offered, specimen(s) that enable complete testing (i.e., HCV Ab testing and when reactive automatic HCV RNA testing) should be collected during one patient encounter.[1] However, difficulties with specimen workflow, the inability to use the same specimen on some automated Ab and RNA analyzers, issues with

the supply chain (e.g. blood tube shortages), and concerns about blood waste create challenges that lead to lack of single-visit collection. In contrast, viral-first testing strategies rely on a single test for diagnosis, so single-visit specimen collection is assured.

Moreover, viral-first testing detects recent infections and can increase the number of diagnosed individuals.[11,35] While many highly accurate and FDA-authorized options for HCV Ab testing exist, they are all subject to the seroconversion window period and will only be reactive six to twelve weeks post-HCV infection (**Figure 1**). Whereas HCV RNA can be detected at one to two weeks post-infection, with HCVcAg detectable shortly thereafter. In fact, the CDC recommends HCV RNA testing for people with recent exposures[2] as well as perinatally exposed infants.[36] Given the current lack of FDA-authorized laboratory-based viral-first testing options, these recommendations are sometimes overlooked with providers forced to retest patients later and thus require subsequent visits.

Modeling data indicates that viral-first cAg or RNA testing can improve detection rates and increase QALYs as compared to two-step testing, but this may come with increased cost ($8.60 increase for Ag and $21.48 increase for RNA based testing).[11] The cost effectiveness depends on the cost of the tests, which could decline with expanded market competition and broader adoption. There are currently no FDA-authorized HCV cAg tests in the US and laboratory-based HCV RNA tests all require reactive HCV Ab according to their intended use. Although HCV RNA tests could be validated as standalone diagnostic laboratory developed tests (LDTs), the cost of these studies is likely prohibitive to most laboratories. The US needs more flexible laboratory-based tests to come into the market and then, additional US specific studies to determine cost effectiveness.

As compared to POCT, lab-based testing tends to have better performance characteristics (specificity and sensitivity) and reduced analytical error. This enhanced performance may be particularly important in low prevalence settings where the positive predictive value of a test can be negatively impacted by the low prevalence. In terms of quality management, laboratorians are specifically trained and accustomed to rigorous requirements for quality assurance, quality control, operator competency and proficiency testing. In contrast, POCT may be more difficult than imagined to effectively perform and come with a steep learning curve, especially due to lack of environmental control, operator variability and reduced regulatory oversight. Additionally, laboratory-based tests have been rigorously tested with the diverse genotypes that are present in the US, but most studies with the RNA POCT have been limited, so more work is needed to evaluate diagnostic performance across diverse HCV genotypes to ensure reliability and generalizability.

From a public health systems perspective laboratory-based testing remains a cornerstone of population-level detection and surveillance and can be used with a syndemic approach, making efficient use of limited resources. There are many testing platforms available to run FDA-authorized laboratory-based RNA tests and these platforms tend to have large testing menus, which enables integrated testing of HCV, HBV, HIV, syphilis and more. These laboratory-based platforms are often high-throughput and highly automated. Currently available FDA-authorized molecular platforms can test anywhere from 144 to 960 specimens for HCV RNA on a single instrument during an eight-hour shift as opposed to the eight samples per test bay per eight-hour shift that the only available POC RNA test can offer. Currently available HCV RNA tests can generate results in roughly two to three hours depending on the instrument. While this is longer than the POC RNA TAT by about 60 minutes, it is still relatively fast considering the throughput.

Laboratory-based viral-first testing offers a streamlined workflow for patients, providers and laboratorians, which would reduce loss to follow up, detect early infections and improve patient and public health outcomes. Laboratory-based testing is sensitive, specific, and scalable, and it enables bundled syndemic testing, high throughput and relatively rapid turnaround. Broader adoption of viral-first testing in a laboratory will depend on FDA authorization of HCV RNA and cAg assays intended for use without prior Ab screening, and cost considerations in US populations.

Panelists Remarks

Panelists expanded on findings from CDC cost-effectiveness analyses comparing viral-first approaches, including HCV cAg and RNA testing, with traditional two-step testing algorithms.[11] These studies demonstrated that while viral-first strategies increase cost, they also facilitate earlier detection of infection, increase the number of diagnosed and treated cases, increase QALYs and reduce HCV-related deaths. In the study, 41% of the specimens used were in the window period of infection with both RNA and cAg detected with 100% concordance. Two-step testing would have missed all of these infections. Panelists also advocated for either RNA or cAg-based viral-first testing as less anxiety provoking than two-step testing because patients do not have to wait for a second test result. Although viral-first approaches may be associated with higher per-test costs, the overall gains provide a favorable public health trade-off.

FDA authorization of laboratory-based viral-first assays as standalone diagnostic tools, outside the context of Ab testing, are needed. CDC is evaluating commonly used HCV RNA platforms in the context of the window period to help with these expanded FDA claims. CDC already recommends viral-first testing for perinatally exposed infants because maternal Ab transfer renders serologic testing unreliable. However, many pediatric primary care settings lack phlebotomy services and rely on capillary blood (heel stick) sampling. If a pediatric primary care facility cannot access a laboratory that accepts capillary blood for HCV testing, babies are referred to another facility that offers phlebotomy, which can lead to loss to follow up. Research validating capillary blood, including DBS and other alternative sample types for RNA or antigen testing is needed to facilitate access and improve testing rates among exposed infants, which remain suboptimal. Additionally, research examining the efficacy of Ag-Ab testing in exposed infants should be conducted.

The ability to validate LDTs is a benefit of laboratory-based assays, however laboratories cannot validate specimen collection devices as LDTs, as those are considered standalone medical devices requiring their own FDA authorizations. Some laboratories do make use of LDTs for HCV testing and evaluate the use of reduced specimen volumes and in-house protocols for nucleic acid extraction. As nucleic acid extraction from blood poses a unique challenge, there is an opportunity for technical innovation to improve this process with respect to yield, performance, consistency and TAT. Dissociation of Ag-Ab complexes in blood is also technically challenging and required for all HCV cAg tests with a direct impact on assay sensitivity, so this is also an area that requires improvement.

Panelists suggested that as laboratories look to operationalize viral-first testing, a differentiating combination cAg-Ab test, reflexed to an HCV RNA test when discordant, may be advantageous due to parallels with established HIV cAg-Ab testing workflows. The combination test could shorten the diagnostic window by 50–60 days compared with Ab-only testing, would benefit laboratories serving diverse populations and may be cost-effective. Patients and providers already understand the HIV testing algorithm and laboratories have already established the workflow and laboratory information systems (LIS) result decision tables for this type of testing sequence. There is a drawback when the HCV RNA reflex test is needed however, as laboratories tend to batch samples and run them less frequently due to decreased RNA testing volume when the two-step testing sequence is used.

In general, panelists expressed support for viral-first testing sequences and agreed that earlier detection, simplified workflows, and integration into high-throughput laboratory systems would strengthen the national response to HCV. The ability to bundle tests for multiple pathogens and integrate viral-first testing into routine care for pregnancy, addiction treatment and primary care was viewed as a benefit. Remaining priorities include addressing regulatory barriers, FDA authorizations for alternative specimen types, and improving laboratory and data infrastructure to support large-scale implementation. Support for additional improvements including faster TAT via shorter overall workflows, especially related to the pre- and post-analytical processing steps of sample collection, shipment and reporting was also expressed.

Key Discussion Points / Takeaways

- **Viral-first testing sequences have advantages:**
  - Viral-first testing enables detection of acute infections. HCV RNA and cAg can be detected one to two weeks post-infection, whereas Ab seroconversion takes six to twelve weeks.
  - Viral-first testing streamlines diagnosis for patients, providers and laboratorians. When all specimens required for diagnosis can be collected at a single visit, fewer patients are lost to follow up.
  - Viral-first testing increases QALYs and decreases HCV-related deaths.
  - Viral-first testing may allow for earlier detection of ongoing transmission.
- **Viral-first testing is already recommended:** Viral-first (RNA-based) testing is already used in cases of suspected acute HCV infection, recent exposure, reinfection, and testing among perinatally exposed infants. These applications reflect recognition of the limitations of Ab testing including inability to detect early or recurrent infection.
- **Viral-first testing may be cost effective:** Compared with the two-step testing approach, viral-first HCV testing approaches are potentially cost-effective strategies resulting in gains in diagnoses and health outcomes. Further, higher testing volumes could reduce per-test costs through economies of scale. Pooled testing strategies, while difficult to implement, were also discussed as a potential cost-saving measure in low-prevalence settings. Moreover, market competition could drive prices down as tests come to market.
- **Laboratory based testing platforms have advantages:**
  - Instruments for laboratory-based HCV testing are scalable, high throughput, highly automated, run in well controlled environments using rigorous quality standards and often allow for testing using a syndemic approach with options available for integrated testing of HCV, HIV, HBV and syphilis.
  - Laboratory based RNA tests offer quantitative results, which are not yet available at the POC in the US.
- **Viral-first testing method of choice may depend on setting or provider preference:**
  - When available, whether to use a RNA or cAg first testing may depend on factors such as laboratory volume, setting prevalence, and cost. While cAg assays show good agreement with RNA in most cases, lower analytical sensitivity may miss infections with very low viral loads.
  - Some participants expressed a preference for RNA testing due to increased sensitivity over cAg testing, the ability to provide a baseline viral load and use an RNA test to monitor for SVR. Others argued that the majority of patients have sufficient cAg levels to ensure detection with methodologies available outside of the US and cited studies that show cAg can be used to monitor response to therapy as effectively as RNA.[37,38,39]
- **Laboratory infrastructure and workflows exist:**
  - Many laboratories have sufficient equipment and staffing to handle increased RNA testing volume that would come with viral-first, RNA-based testing.
  - For tests that combine HCV cAg and Ab testing existing laboratory workflows and laboratory infomration management system (LIMS) schematics used for HIV testing can be leveraged.

Identified Needs

1. **Regulatory authorizations of lab-based viral-first testing options:** FDA authorizations of laboratory-based HCV cAg assays (differentiating and in combination with HCV-Ab or as a standalone alone target) and standalone HCV RNA tests that are not dependent on Ab reactivity are needed.
2. **Intended uses that support use of alternative specimen types:**
    - FDA authorization of assays intended for use with capillary blood specimens (including DBS) and more data to show that capillary specimens are generally acceptable for use with HCV tests are desired.
    - FDA-authorization of devices for self-collection of HCV specimens in clinical and non-clinical settings and tests authorized to be used with these specimen types would help expand access to laboratory-based testing methods.
3. **Data to guide optimization of testing sequence(s):**
    - More research is needed to determine if HCV cAg testing can be used to monitor for SVR
    - Research is needed to determine whether discrepant cAg and Ab results require confirmatory HCV RNA testing.
4. **Studies in infants:** Efficacy of cAg-Ab testing of exposed infants should be evaluated.
5. **Improved methods for specimen processing:**
    - Dissociation of Ab/Ag complexes in clinical specimens is critical to cAg testing and method improvement is needed.
    - Nucleic acid extraction is critical to HCV RNA testing and processes could be improved upon.
6. **Improvements in pre- and post-analytical workflows:** While TAT of laboratory-based tests is longer than POC, recommendations and guidelines for improved pre and post-analytical workflows could help shorten TATs and possibly result in generation of same day results.
7. **Cost reduction mechanisms:** Implementation of bulk purchasing, pooled testing or negotiated pricing models could help to improve affordability and sustainability.

Key Question 4: What barriers need to be overcome to implement laboratory-based viral-first HCV testing in the US?

Introduction and Presentation

The lack of FDA-authorized RNA and cAg methods for laboratory-based viral-first testing is a major barrier to implementation of viral-first HCV testing in the US. Additional barriers differ somewhat across public health, clinical, and commercial laboratory settings and include: change management, varied ability to validate LDTs, testing costs and limited reimbursement mechanisms. Education for healthcare providers and laboratory staff was also identified as essential to support appropriate test selection and interpretation. Implementation of viral-first algorithms would require new laboratory workflows, software modifications for result resolution, and ongoing staff training.

Existing FDA-authorized quantitative HCV RNA assays are indicated only for use in individuals who are HCV Ab reactive. While a qualitative, viral-first POC RNA test exists, it is not authorized for use on the company's large-scale platform. Core Ag-only and combined Ag/Ab assays are not FDA-authorized in the US, although several are in use

internationally. Efforts to gain FDA clearance have stalled due to additional data requirements requested during the review process, and there are no ongoing plans for FDA submissions in the near term.

Assay performance may be a roadblock for cAg testing. While viral-first testing detects acute infections, data indicates that cAg tests may miss low-level infections, with approximately 3–4% of RNA-positive cases testing negative for cAg.[40] Sensitivity of cAg testing decreases notably when HCV RNA levels are below 3,000 IU/mL, as demonstrated in CDC evaluations of the Abbott Architect cAg assay.[41] Studies using the Roche Duo showed that the combination cAg-Ab assay has high specificity overall and high sensitivity for Ab, but variable cAg sensitivity (approximately 70-74%) when compared to RNA testing, pointing to the need for additional testing in cases of discordance.[42,43] Early seroconversion remains a period of potential false negatives, possibly due to Ab-Ag complex formation, underscoring the need for assays with improved analytical performance and improved preanalytical disassociation steps. In contrast, the sensitivity of RNA assays is high, but data, ideally FDA authorization studies, are needed to prove efficacy in a viral-first testing sequence.

Viral-first testing must also be supported by guidelines and recommendations. Currently, AASLD-IDSA, CDC and the US Preventative Services Task Force all recommend universal HCV screening with Ab testing reflexed to HCV RNA, with caveats included for testing infants, immunosuppressed individuals and in cases of recent infection.[1,44,45,46] HCV RNA tests may be subject to false positives, especially when specimens are shared between Ab and nucleic acid analyzers, and cAg tests may be subject to false negatives. Decisions on whether cAg or qualitative RNA testing is sufficient for treatment or require viral load testing should be data driven and formalized in testing guidelines and recommendations. This is especially important, because payors use these guidelines to inform their decisions and cost was identified as a major barrier to implementation of viral-first testing.

RNA-based tests are more expensive than Ab assays, with US list prices ranging from $30–$50 per test for RNA and $5-7 per test for Ab. Meanwhile, current Medicare laboratory test reimbursement rates for qualitative and quantitative HCV RNA tests (CPT codes 87521 and 87522, HCPCS code G0567) are lower than that of HCV Ab screening (HCPCS code G0472) for high risk individuals or those born in the 1945–1965 period.[47,48] Further reductions in laboratory reimbursement are expected under the Protecting Access to Medicare Act (PAMA), which mandates 15% annual payment cuts each year through 2028, unless it is replaced by new legislation. Proposed reforms, such as the RESULTS Act, aim to stabilize rates but remain under Congressional review. There are currently no CPT codes for cAg or Ag-Ab assays and the process of obtaining a new CPT code takes time as well as national practice guidelines supporting and recommending use of such tests, complicating reimbursement for new technologies.

The absence of FDA-cleared, high-throughput RNA screening assays and any cAg assays limits the ability to deploy viral-first testing at scale. Current process of finding and collecting blood specimens from thousands of eligible individuals at various stages of early HCV infection, especially those around the time of Ab seroconversion, for medical device registration trial studies required for submission to FDA to obtain clearance or authorization for in vitro diagnostic use is quite burdensome and expensive for assay manufacturers. Such requirements often discourage manufacturers from pursuing the development and commercialization of virus-first assays. Consequently, laboratories must rely on multi-step algorithms, increasing time to diagnosis and potentially leading to loss to follow-up. Broader adoption of viral-first, laboratory-based testing for HCV will require regulatory approval of new assays, defined reimbursement pathways, clear clinical guidance, and in some instances, investment in laboratory capacity.

Panelist Remarks

The two-step testing sequence for identifying current HCV infection creates delays and gaps in diagnosis. In many healthcare settings, specimens that test reactive for HCV Ab internally must be sent to external laboratories for RNA testing, which then may be batched and tested only a few times per week. This can extend TAT to one or two weeks, hamper timely reporting and initiation of care, and contribute to loss to follow-up. Two-step testing can also fail to identify acute or recent HCV infections, as Ab may not yet be detectable for six to twelve weeks post-infection (**Figure 1**). These limitations underscore the need for more efficient testing strategies.

Implementation of viral-first testing is currently constrained by lack of US guidance for clinicians and laboratorians and regulatory limitations. No FDA-approved laboratory-based HCV RNA assay is authorized for diagnostic use independent of Ab results. Similarly, HCV cAg and combined Ag-Ab assays, which are included in World Health Organization and European Association for the Study of the Liver diagnostic recommendations, lack FDA approval for use in the US. Moreover, further evidence is needed to inform the use of these tests. The CDC is currently evaluating real-world performance of viral-first strategies, including RNA-only and combined Ag-Ab approaches, in adult clinical populations in order to generate the needed data.

Existing laboratory infrastructure in clinical, commercial and public health laboratories could support viral-first RNA testing through high-throughput molecular platforms already used for HIV, STI and COVID-19 testing. The instruments allow for automated processing of a large numbers of samples relatively quickly and with that capacity fully leveraged, linkages between public health programs and referral networks could help close the gap in diagnoses. While smaller and rural facilities may face limitations in access to equipment, staffing and workflow integration, public-private partnerships may help. Participants emphasized that viral-first testing could be feasible if current systems were optimized, with flexibility to accommodate both high-throughput and POC models depending on population needs.

A streamlined FDA approval pathway was identified as essential for enabling viral-first testing as the cost and complexity of FDA trials, paired with the relatively low prevalence of HCV in the US, deters diagnostic manufacturers from seeking additional authorizations. Participants noted that the FDA expectation for cAg assays to demonstrate performance characteristics equivalent to RNA tests introduces additional risk for manufacturers of cAg assays, further discouraging pursuit of such studies. Expanded intended-use claims for existing RNA assays were cited as a need and participants suggested that FDA could apply a least-burdensome approach by allowing manufacturers to leverage existing clinical performance data, real-world evidence, and bridging studies rather than requiring new large-scale clinical trials. Collaboration among industry, regulatory agencies, and public health entities could facilitate more efficient evaluation of new assays, for example through CDC-led validation studies that generate performance data for FDA consideration.

Similarly, expansion of FDA authorizations to include the use of alternative sample types like capillary blood and home collected specimens, would also help enable viral-first testing. The use of capillary blood would reduce the dependence on phlebotomy, which is not feasible in some settings. Linking simplified collection methods with centralized, high-throughput molecular testing could strengthen the diagnostic network and reduce logistical barriers for patients, providers and laboratorians.

Cost is still an important barrier as RNA-based tests remain more expensive than antibody screening, and inconsistent payer coverage poses a disincentive for laboratory adoption. Participants emphasized that reimbursement policies should align with HCV elimination goals, recognizing that earlier diagnosis and treatment reduce long-term healthcare costs associated with chronic liver disease. Stable reimbursement mechanisms for RNA testing as a first diagnostic step are essential for widespread implementation.

However, even with updated guidelines and expanded testing access, gaps persist in provider awareness, laboratory training, and patient understanding of HCV testing. Broad-based educational initiatives targeting healthcare professionals, laboratories and the public were identified as necessary to ensure effective uptake of new diagnostic strategies. Implementation of viral-first HCV testing in the US will require coordinated action to address regulatory approvals, infrastructure readiness, reimbursement alignment and education. Leveraging existing laboratory capacity and fostering collaboration among federal agencies, industry partners and public health programs were identified as key steps in the process.

Key Discussion Points / Takeaways

- **A Complete HCV Diagnostic Toolkit Requires Options:**
  - Ideal testing sequences vary based on the population and the setting. High-risk and routine screening populations have different needs that should be reflected in the testing sequence.
  - Patients, providers and public health would benefit from faster, viral-first testing approaches that detect more infections, reduce TAT and loss to follow-up. Viral-first testing has merit in high-risk and / or high-prevalence settings and may be more broadly useful depending on the cost of the assays.
- **Regulatory Barriers Exist:** Many laboratories have existing high-throughput platforms that could support viral-first testing, but widespread implementation requires FDA-authorization of assays for HCV RNA testing in the absence of Ab reactivity and HCV cAg or combined cAg–Ab tests. While HCV RNA could be validated as a diagnostic test, performing LDTs in the current regulatory environment poses difficulties, including comparator assay requirements, lack of international standards for cAg, and the need to obtain validation data from antibody-negative populations.
- **Challenges in Generating Early Infection Data:** Identifying patients in the acute or early infection phase remains difficult, hindering evaluation of assay performance during this critical window. For one cAg-Ab assay, regulatory bodies requested more data from patients in early infection and this was viewed as an insurmountable problem by the test manufacturer due to difficulties identifying and enrolling such patients in their studies.
- **Cost and Reimbursement:** RNA and cAg-based tests are more costly than antibody assays. Participants noted the potential for the US Center for Medicaid and Medicare Services (CMS) to crosswalk reimbursement from existing HIV Ag–Ab codes if HCV cAg-Ab tests become FDA-cleared.

Identified Needs

1. **Regulatory Advancement:**
   - Expanded intended-use claims for RNA assays as first-line diagnostics are needed.
   - FDA authorization of cAg or combined cAg–Ab assays to enable viral-first testing is needed.
   - Expansion of intended-use claims to allow for use of alternative specimen types such as capillary blood are needed.
2. **Improvements in cAg Test Performance:** Sensitivity of cAg tests may require improvement, alternatively guidance is needed to determine when follow up testing would be necessary.
3. **Data to Drive Decision-Making:** Data to compare RNA and cAg-based screening with Ab testing are needed. This will show how many infections are missed during early seroconversion and help drive decisions regarding future testing sequence recommendations.

4. **Collaborative Data Generation:**
    - Partnerships among manufacturers, public health agencies, and clinical laboratories to generate data on assay performance during acute infection and across diverse populations (including pediatrics and pregnant women) could help overcome some of the logistical barriers associated with viral-first testing.
    - CDC-led validation studies that generate performance data for FDA consideration could help hasten availability
5. **Prevalence and Study Feasibility:**
    - Clear, achievable criteria for study design and sample size to support regulatory submissions are needed, particularly with respect to the number of acute infections required in studies intended for FDA submissions. Low prevalence of early infections in most populations makes data collection resource-intensive; realistic expectations for study size and statistical power are needed. This could also aid in generating intended use claims that extend to pregnant women and infants.
    - The GeneXpert HCV Test would benefit from authorization for use on laboratory-based testing platforms. As the test is already authorized for use on the GenXpert Xpress (POC), abbreviated studies may be appropriate.
6. **Guidelines and Recommendations:** The use of HCV tests should be informed by national guidelines and recommendations. CDC should work to expand HCV testing recommendations to accommodate diverse settings and population needs and allow for viral-first testing.
7. **Reimbursement Alignment:**
    - Stable and appropriate reimbursement policies to incentivize laboratory adoption of viral-first and antigen-based testing approaches are needed.
    - CPT codes that are aligned with testing and labor costs are needed for viral-first HCV tests.
8. **Education and Awareness:** Expanding viral-first testing to diverse settings will require targeted education for providers, laboratorians, and others regarding appropriate test selection, assay/testing sequence limitations, laboratory workflows, billing, result reporting and submission of data for surveillance purposes.

Key Question 5: Is it time to move to viral-first HCV testing guidance for clinicians and laboratorians in the US?

Introduction and Presentation

Viral-first testing sequences enable earlier detection of HCV than the two-step, Ab-based approach. HCV RNA can be detected one to two weeks after infection, and HCV cAg typically appears within two to three weeks, whereas sero-conversion requires six to twelve weeks (**Figure 1**). Early detection enables faster linkage to care, reducing the likelihood of ongoing transmission and improving treatment outcomes. CDC guidance already endorses viral-first testing for individuals with recent exposure, and similar approaches have been widely adopted in HIV diagnostics through the use of Ag-Ab combination assays. Emerging data also demonstrate the effectiveness of viral-first test and treat models, in which diagnosis and treatment initiation occur during the same patient encounter, leading to markedly reduced time to cure and improved retention in care.[23]

Viral-first strategies are more expensive than the two-step testing sequence, but they result in more diagnoses, increased treatment rates and increased QALYs.[11] While the public health benefit may outweigh the increased cost when HCV prevalence is high, there may not be one size fits all model for HCV testing. Instead, the decision whether

to implement viral-first testing may depend on HCV prevalence in the population, the type of patient encounter and likelihood for long-term follow-up, the available resources (phlebotomy, laboratory, etc.) and testing volume. Moreover, as market competition increases, costs may become more favorable and the dynamic may shift.

There are real barriers to implementation of viral-first testing including the need for more FDA-authorized testing options and reimbursement models better aligned with the cost of testing. Beyond these structural issues, laboratory and provider readiness is also a challenge. This includes updating EHR systems and test order sets, establishing standardized electronic reporting from POC settings to public health agencies, training healthcare providers to interpret and act on viral-first results and ensuring that treatment can be delivered at the time of diagnosis. Broader systemic barriers, such as limited healthcare access, fragmented behavioral health services and insurance restrictions on treatment authorization, also influence the effectiveness of any testing strategy and must be addressed in parallel.

Regardless, viral-first testing aligns with the national HCV elimination agenda and recent policy efforts such as the CURE Hepatitis C Act, which proposes large-scale funding to expand access to diagnosis and treatment. Operational and financial challenges may persist but waiting for ideal conditions risks delaying progress. Building the infrastructure and policy support for viral-first testing now could accelerate the transition once regulatory and market conditions align. Readiness will follow investment. The transition toward viral-first HCV testing in the US is both inevitable and essential, and early action will be key to realizing its potential impact.

Panelist Remarks

Panelists expressed that viral-first testing represents the next logical step towards timely diagnosis and felt that viral-fist strategies could help facilitate treatment initiation and enable progress toward national HCV elimination goals. Participants emphasized that the feasibility, cost, and impact of implementation would vary by setting, and that a flexible and phased approach may be most appropriate.

POC RNA testing using fingerstick samples was cited as the most immediately accessible viral-first testing method due to the existence of the FDA-authorized Cepheid HCV Xpert assay. POC viral-first RNA testing could facilitate same-day diagnosis and linkage to treatment and would be most impactful when used in high-prevalence, brief-encounter settings where people who inject drugs seek care. While two-step testing sequences may remain appropriate for lower-prevalence or longitudinal care settings, participants noted that viral-first approaches will likely become increasingly cost-effective and faster as time goes on, which may broaden the utility of the viral-first approach. Development of HCV cAg assays with increased sensitivity[49] would help expand the utility of viral-first testing.

The discussion also highlighted the importance of leveraging pharmacies and other nontraditional care sites to expand access to testing and treatment. Pharmacies were described as highly accessible community resources that could play a key role in HCV elimination if supported by collaborative practice agreements and reimbursement structures. Expanding testing through pharmacies could be particularly beneficial for people who inject drugs, who may face stigma, or have phlebotomy-related barriers in traditional healthcare settings. Such models could enable pharmacists to perform POC RNA testing, initiate treatment under physician oversight, and provide additional preventive health services such as vaccination or counseling. These are not entirely new ideas, as such models were utilized during the COVID-19 pandemic.

From a laboratory systems perspective, panelists emphasized that updated guidance should provide flexibility to accommodate diverse settings rather than utilize a prescriptive implementation model. The goal should be to identify viral-first testing as an acceptable alternative to two-step testing within clinical guidelines, thus enabling laboratories and providers to determine the most feasible and appropriate approach for their setting. The discussion also noted that innovation often outpaces regulatory approval, with existing US guidelines that already recommend use of

non–FDA-authorized methods when supported by evidence. Such a forward-looking approach could accelerate adoption of viral-first strategies while maintaining compliance and quality standards.

Several system-level changes were identified as essential for successful implementation of viral-first testing. These include: ensuring interoperability of EHRs, standardizing reporting from decentralized testing sites, removal of prior authorization requirements and retreatment restrictions, supporting provider training on interpretation and follow-up of viral-first results and ensuring accessible treatment options exist for those that test positive. Development of a "playbook" or standardized framework for different clinical and community settings was suggested to guide testing and treatment and reduce complexity for providers unfamiliar with HCV management. Panelists felt that simplicity and system integration will be key to sustaining progress as testing expands beyond traditional laboratory environments.

Viral-first testing represents a critical evolution in the HCV diagnostic paradigm. While not a universal solution for all settings, flexible guidelines and phased implementation of viral-first testing sequences in prioritized (i.e., high-prevalence) populations could substantially accelerate diagnosis and treatment, reduce transmission, and advance national elimination efforts. Achieving these outcomes will require coordinated policy, economic investment, and updated guidance that supports modern, flexible diagnostic strategies.

Key Discussion Points / Takeaways

- **Flexibility is Key:** Viral-first testing has clear benefits, but universal viral-first testing is unlikely to be practical across all settings. Viral-first approaches may be most effective in high-prevalence environments, such as sites where people who inject drugs seek care, whereas two-step testing may remain appropriate for lower-prevalence or longitudinal care settings. This may shift as market conditions change.
- **Phased Implementation:** Phased implementation of viral-first testing in prioritized sites is more practical and attainable than widespread and universal change. Conducting needs assessments to prioritize sites for implementation and mapping steps required for effective implementation will help assure financial feasibility and linkage to care.
- **Infrastructure Improvements:** Workforce training, development of quality control processes (especially at the POC), integration with EHRs and removal of barriers with reimbursement and preauthorization will help advance viral-first testing.
- **Scale-Up Opportunities:** Correctional facilities, particularly jails with short-term stays, were identified as ideal sites for piloting test and treat models due to the feasibility of same-day diagnosis and treatment. Participants also stressed the importance of moving beyond isolated pilot programs toward coordinated national or network-based approaches (e.g., across networks of Federally Qualified Health Centers, jail systems, etc.) to achieve meaningful population-level impact.
- **Workforce Engagement and Education:** Successful implementation depends on engaging healthcare providers who are not traditionally involved in HCV care. Expanding training programs, such as through Project ECHO,[50] could help increase provider knowledge, promote adoption of new testing models, and disseminate lessons learned from early implementers.
- **Alternative Testing Models:** Participants noted that home testing could increase incomplete testing rates, with limited utility among the highest-burden groups, including those experiencing homelessness or unstable housing. A home-collection-to-lab model, rather than full at-home testing, was considered a more feasible option for broader populations.

- **Regulatory and Policy Barriers:** Progress toward viral-first testing will require close coordination with regulatory agencies. Current FDA performance expectations for cAg and POCT may discourage test developers due to high validation costs and preauthorization requirements stall treatment and increase loss to follow up. Reducing regulatory barriers and allowing flexibility for non–FDA-approved methods, when supported by evidence, were identified as essential steps to accelerate implementation.

Identified Needs

1. **Guidelines and Recommendations:** Development of flexible testing recommendations and guidelines to allow for viral-first testing sequences as an alternative to two-step testing would kick start utilization (regardless of the availability of FDA-authorized tests).

2. **HCV Playbook:** Development of a national implementation framework or "playbook" to guide stepwise adoption of viral-first and / or POCT along with integrated treatment strategies for HCV, would be beneficial, particularly for providers that don't usually treat HCV.

3. **EHR Integration:** Integration solutions for EHRs to ensure POCT results are captured and accessible within patient records are needed. EHR vendors and test manufacturers should be made aware of this emerging need and collaboration encouraged.

4. **Training Networks:** Expanded training and technical assistance to support workforce capacity, especially among non-specialist providers and community-based settings.

5. **Continued Investment in Assay Development and FDA-Authorizations:**
    - HCV cAg assays with better sensitivity and FDA authorizations are needed, alone or in combination with Ab.
    - Expanded intended-use claims for RNA assays as first-line diagnostics are needed.
    - Expansion of intended-use claims to allow for use of alternative specimen types such as capillary blood and self-collected specimens (most importantly those collected outside of a healthcare setting) will enhance accessibility of testing.
    - Intended use claims that support primary diagnosis, diagnosis of reinfection and assessment of SVR will facilitate appropriate treatment
    - Development of POCT for HBV sAg, disease staging will help complete the diagnostic toolkit.

6. **Scale-up Strategies:** To extend beyond pilot programs and reach diverse settings, existing networks, such as correctional system and FQHC networks could be leveraged.

7. **Infrastructure Investments:** Continued investment in infrastructure, quality management, staffing (including POC coordinators) and embedded models of care will ensure that diagnostic advances translate into treatment access.

8. **Regulatory Reform:** Cumbersome prior authorization requirements and coverage silos that complicate co-located physical and behavioral health care delay treatment and must be addressed.

Appendix

Appendix A. Key Question and Panelists

#	Key Question	Moderator	Presenter	Panelists
1	**What are the optimal settings to utilize POC HCV testing for same-day diagnosis of current HCV infection?**	Jason Grebely, PhD	Arthur Kim, MD	• Alain Litwin, MD • Matthew Akiyama, MD • Daniel Raymond
2	**What are the optimal POC HCV testing sequences and linkage to treatment strategies by setting?**	Andrew Seaman, PhD	Nathan Furukawa, MD	• Hansel Tookes, MD • Susanna Naggie, MD • Liisa Randall, PhD
3	**What are the benefits of various laboratory-based viral-first testing strategies for the diagnosis of HCV infection in the US?**	John Ward, MD	Michael Pentella, PhD, D(ABMM)	• Saleem Kamili, PhD • Ravi Jhaveri, MD • Berry Bennett, MPH • Kristen Marks, MD
4	**What other tools are needed to support same-day diagnosis and treatment of current HCV infection?**	Heba Mostafa, MD PHD	Joseph Yao, MD	• Emily Cartwright, MD • Randall Fowler, PhD, D(ABMM) • Karen Harrington, PhD • Denise Heaney, PhD • Alexa Bisinger, MD
5	**Is it time to move to viral-first HCV testing guidance for clinicians and laboratorians in the US?**	Marc Ghany, MD	Stacey Trooskin, MD, PhD	• Raymond Chung, MD • Lynn Taylor, MD • Elizabeth Marlowe, PhD, D(ABMM) • Andrew Aronsohn, MD

Appendix B. Meeting Agenda

Day 1 | September 16, 2025

Time	Topic	Presenter/Facilitator
2:00-2:10 pm	**Welcome**	
	Welcome from APHL CEO	**Scott Becker,** APHL
	Meeting Objectives and Logistics	**Sarah Buss,** APHL
2:10-2:50 pm	**Opening Session**	
2:10-2:15 pm	Opening Remarks	**Carolyn Wester,** CDC
2:10-2:30 pm	Achieving HCV elimination and exploring the role of viral-first testing strategies in diagnosing HCV infection in the US	**Carolyn Wester,** CDC
2:30-2:50 pm	Landscape analysis of HCV diagnostic toolkit	**Jordan Feld,** Toronto Centre for Liver Disease
	Session 1: Utility of POC Testing for Accelerating Same-day HCV Diagnosis & Rapid Treatment Initiation	
2:50-4:00 pm	**Key Question 1**: What are the optimal settings to utilize POC HCV testing for same-day diagnosis of current HCV infection?	**Jason Grebely,** Kirby Institute
	Presentation	**Arthur Kim,** MGH/Harvard
	Panelist Remarks	**Alain Litwin,** Prisma Health **Matthew Akiyama,** Albert Einstein College of Medicine **Daniel Raymond,** National Viral Hepatitis Roundtable
	Facilitated Question and Answer Session	Participants
4:00-4:15 pm	*Break*	
4:15-5:25 pm	**Key Question 2:** What are the optimal POC HCV testing sequences and linkage to treatment strategies by setting?	**Andrew Seaman,** Central City Concern / OHSU
	Presentation	**Nate Furukawa,** CDC
	Panelist Remarks	**Hansel Tookes,** UMiami School of Medicine **Susanna Naggie,** Duke School of Medicine **Liisa Randall,** Massachusetts DPH
	Facilitated Question and Answer Session	Participants
5:25-5:30 pm	**Wrap-up and Closing**	
	Close out & preview of the next day	**Sarah Buss,** APHL

Day 2 | September 17, 2025

Time	Topic	Presenter/Facilitator
1:00-1:05 pm	**Welcome and Recap**	**Sarah Buss,** APHL
1:05-1:10 pm	Introduction to Day 2	**Carolyn Wester,** CDC
	Session 2: Utility of Viral-first Testing Strategies for Accelerating HCV Diagnosis and Treatment Initiation in the US	
1:10-2:15 pm	**Key Question 3:** What are the benefits of various laboratory-based viral-first testing strategies for the diagnosis of HCV infection in the US?	**John Ward,** Task Force for Global Health
	Presentation	**Michael Pentella,** U of Iowa State Hygienic Laboratory
	Panelist Remarks	**Saleem Kamili,** CDC **Ravi Jhaveri,** Ann & Robert H. Lurie Children's Hospital of Chicago Berry Bennett, FL Bureau of Public Health Laboratories **Kristen Marks,** Weill Cornell Medical School
	Facilitated Question and Answer Session	Participants
2:15-2:30 pm	*Break*	
2:30-3:35 pm	**Key Question 4:** What barriers need to be overcome to implement laboratory-based viral-first HCV testing in the US?	**Heba Mostafa,** Johns Hopkins
	Presentation	**Joseph Yao,** Mayo Clinical Lab
	Panelist Remarks	**Emily Cartwright,** CDC **Randall Fowler,** TN PHL **Karen Harrington,** Hologic **Denise Heaney,** Roche **Alexa Bisinger,** Abbott
	Facilitated Question and Answer Session	Participants
3:35-4:40 pm	**Key Question 5: I**s it time to move to viral-first HCV testing guidance for clinicians and laboratorians in the US?	**Marc Ghany,** NIH, NIDDK
	Presentation	**Stacey Trooskin,** Mazzoni Center
	Panelist Remarks	**Raymond Chung,** MA Gen Brigham **Lynn Taylor,** U. Rhode Island **Elizabeth Marlowe,** Quest Diagnostics Inc. **Andrew Aronsohn,** U of Chicago
	Facilitated Question and Answer Session	Participants
4:40-4:45 pm	**Next Steps and Closing**	**Sarah Buss,** APHL **Carolyn Wester,** CDC

Appendix C. Participant Lists

Moderators, Presenters and Panelists

Name	Position	Organization
Matthew Akiyama, MD, MSc	Associate Professor of Medicine	Albert Einstein College of Medicine
Andrew Aronsohn, MD	Associate Professor of Medicine	University of Chicago
Berry Bennett, MPH	Technical Consultant	Florida Bureau of Public Health Laboratories
Alexa Bisinger, MD, MBA	Director of Medical Affairs for the Americas	Abbott Core Diagnostics
Emily Cartwright, MD	Medical Officer	CDC
Raymond Chung, MD	Director of the Liver Center Chief of Gastroenterology	Mass General Brigham
Jordan Feld, MD, MPH	Director of Hepatology	University Health Network / Toronto Centre for Liver Disease
	Professor of Medicine	University of Toronto, Ontario, Canada
Randal Fowler, PhD, D(ABMM)	Deputy Laboratory Director	Tennessee Department of Health, Division of Laboratory Services
Nathan Furukawa, MD, MPH	Senior Advisor for Hepatitis C Elimination	CDC
Marc Ghany, MD, MHSc	Senior Investigator	NIH, NIDDK
Jason Grebely, PhD	Professor	The Kirby Institute, UNSW
Karen Harrington, PhD, HCLD (ABB)	Head of Scientific Affairs	Hologic, Inc.
Denise Heaney, PhD	Chief Medical Partner for Molecular Solutions and Infectious Diseases	Roche Diagnostics
Ravi Jhaveri, MD	Professor of Pediatrics	Ann & Robert H. Lurie Children's Hospital of Chicago
	Division of Infectious Diseases	Northwestern University Feinberg School of Medicine
Saleem Kamili, PhD	Chief, Laboratory Branch	CDC DVH
Arthur Y. Kim, MD	Associate Professor of Medicine / Harvard Medical School	Massachusetts General Hospital
Alain Litwin, MD	Chief Scientific Officer	Prisma Health
Kristen Marks, MD	Associate Professor of Medicine	Weill Cornell Medicine
Elizabeth Marlowe, PhD, D(ABMM), SM(ASCP)	Executive Scientific Director	Quest Diagnostics

Name	Position	Organization
Heba Mostafa, MD, PhD, D(ABMM)	Section Director of Medical Microbiology Director of Molecular Virology	The Johns Hopkins School of Medicine
Susanna Naggie, MD, MHS	Vice Dean for Clinical and Translational Research	Duke Clinical Research Institute
Michael Pentella, PhD, D(ABMM)	Laboratory Director and Clinical Professor	University of Iowa
Liisa Randall, PhD	Director, Healthcare Planning	Massachusetts Department of Public Health
Daniel Raymond	Director of Policy	National Viral Hepatitis Roundtable
Andrew Seaman, MD	Associate Professor	Oregon Health & Sciences University
	Medical Director	Central City Concern
	Interim National Medical Director	Better Life Partners
Lynn E. Taylor, MD	Professor	University Of Rhode Island
	Physician	HealthFirst Family Care Center (FQHC)
Hansel Tookes, MD, MPH	Professor	University of Miami
Stacey Trooskin, MD, PhD	Chief Medical Officer	Mazzoni Center
John Ward, MD	Director	CGHE/TFGH
Carolyn Wester, MD, MPH	Director	CDC DVH
Joseph Yao, MD	Director, Clinical Virology Laboratory	Mayo Clinic

Invited Participants

Name	Position	Organization
Tyler Bartholomew, PhD	Associate Professor	University of Miami
Debika Bhattacharya, MD	Professor of Medicine	UCLA
Catherine Chappell, MD MSc	Associate Professor	University of Pittsburgh
Cody Chastain, MD, FACP, FIDSA	Associate Professor	Vanderbilt University Medical Center
Daniel Church, MPH	Senior Epidemiologist	Massachusetts Department of Public Health
Wilson Compton, MD, MPE	Deputy Director	National Institute on Drug Abuse (NIDA)
Maria Corcorran, MD, MPH	Assistant Professor	University of Washington
Adrian Di Bisceglie, MD	Emeritus Professor of Internal Medicine	Saint Louis University

Name	Position	Organization
Rachel Epstein, MD, MScE	Assistant Professor of Medicine & Pediatrics	Boston University School of Medicine
Oluwaseun Falade-Nwulia, MBBS, MPH	Associate Professor	Johns Hopkins University
Judith Feinberg. MD, FIDSA	Professor	West Virginia University
Colleen Flanigan, RN, MS	Director, Bureau of Hepatitis Health Care and Epidemiology	New York State Department of Health
Neeraj Gandotra, MD	Chief Medical Officer	SAMHSA
Laura Gillim, PhD, HCLD(ABB)	Medical Science Liaison	Labcorp
Prabhu Gounder, MD	Medical Director, Viral Hepatitis Unit	LA County Public Health
Jennifer Havens, PhD, MPH	Professor	University of Kentucky
Rick Haverkate	Chief, HIV/HCV/STI Branch	Indian Health Service
Shashi Kapadia, MD	Assistant Professor	Weill Cornell
Amy Krawiec, MD	Chief Hepatitis, HIV and Renal Transplant	California Correctional Health Care Systems
Isabel Lechuga, PhD	Director, Hepatitis	NASTAD
Jake Liang, MD	Chief of Liver Diseases Branch	NIH
Katie Margulieux, PhD	Virology Section Manager	Michigan Department of Health and Human Services
Anthony Martinez, MD	Medical Director Hepatology	University at Buffalo
Rachel McLean	Chief, Policy and Viral Hepatitis Prevention	CA Department of Public Health
Jorge Mera, MD	Director, Infectious Diseases	Cherokee Nation
Lesley Miller, MD	Professor of Medicine	Emory University
	Medical Director, Grady Liver Clinic	Grady Health System
Boatemaa Ntiri-Reid, JD, MPH	Senior Director, Syndemic Ap-proaches	NASTAD
Melissa Nyendak, MD	Chief, Prevention Branch, DVH	CDC
Michele Owen, PhD	Associate Director for Laboratory Science	CDC
Jayme Parker, HCLD(ABB), PhD, MSPH, MB(ASCP)	Chief, CLIA Director	Alaska State Public Health Laboratories
Bhawna Poonia, PhD	Team Lead -Biologist	FDA
Jennifer Price, MD	Professor of Medicine	University of California, San Francisco

Name	Position	Organization
Jennifer Rakeman-Cagno, PhD	Senior Director, Scientific Affairs, Public Health Programs	Cepheid
Amy Sandul, PhD	Associate Director for Science	CDC
Ulrike Siemetzki-Kapoor, PhD	Assistant Commissioner and Laboratory Director	NYC DOHMH - Public Health Laboratory
Mark Sulkowski, MD	Medical Director, Viral Hepatitis Center	Johns Hopkins University
Andrew Talal, MD	Professor	SUNY Buffalo
Eyasu Teshale, MD	Medical Officer	CDC/DVH
David Thomas, MD	Professor of Medicine	JHU
Karla Thornton, MD	Professor, Division of Infectious Diseases	University of New Mexico Health Sciences Center
	Executive Director	Project ECHO
Rania Tohme, MD	Associate Director for Global Health	CDC
Julius Wilder, MD	Associate Professor	Duke

APHL Staff

Name	Position
Scott Becker, MS	Chief Executive Officer
Ashton Blair	Associate Specialist
Sarah Buss, PhD, D(ABMM)	Program Manager, Infectious Diseases (ID)
Erin Estes, MBA, MLS(ASCP)	Specialist, ID
Kelly Wroblewski, MPH, MT(ASCP)	Director, ID

Appendix D. Disclosures*

Name	Commercial Entity	Relationship
Matthew Akiyama	AbbVie, Gilead Sciences	Research Funding
Alexa Bisinger	Abbott Core Diagnostics	Employee
Jordan Feld	Abbott, AbbVie, Atea, Cepheid, Gilead, GSK, Janssen, Vir	Research Funding
	Arbutus, Abbvie, Gilead, GSK, Janssen, Vir	Consultant
Marc Ghany	VIR BIO	Grant funding to institution
Jason Grebely	AbbVie, bioLytical, Cepheid, Gilead Sciences	Advisory Board
	AbbVie, Abbott, Cepheid, Gilead, Roche	Research Funding
Karen Harrington	Hologic, Inc.	Employee
Denise Heaney	Roche Diagnostics Corporation	Employee
Ravi Jhaveri	AstraZeneca, Seqirus, Sanofi, Gilead Sciences	Consultant
	GSK, Royalties from UptoDate	Research Funding
	Pediatric Infectious Diseases Society	Editorial Stipend
Arthur Kim	Shionogi Inc. (DMC)	Consultant/Scientific Advisory Board
Alain Litwin	Gilead Sciences	Research grants and speaker's bureau
	AbbVie, Gilead Sciences	Advisory Board
Kristen Marks	Gilead Sciences	Grant funding to institution
	Gilead Sciences, Immorna, Novo Nordisk	Consultant
Elizabeth Marlowe	Quest Diagnostics	Employee
Heba Mostafa	Hologic Inc, Qiagen, DiaSorin	Research Funding
	Seegene	Advisory Board
	Roche Diagnostics, DiaSorin, BD Diagnostics	Honoraria
Susanna Naggie	NIH	Grant funding to institution
	Opman (Practice Point), AETC, ACTHIV	Honoraria
	BMS/PRA, IAS-USA, PHI and CID (editorial)	Advisory Board
	Vir Biotechnology	Stockholder
Daniel Raymond	Cepheid	Corporate Sponsorship
Andrew Seaman	Abvvie Pharmaceuticals, Gilead FOCUS Foundation, Merck Pharmaceuticals	Research Funding
	Abvvie Pharmaceuticals	Advisory Board
Lynn Taylor	UpToDate	Royalties
Hansel Tookes	Gilead Sciences	Research Funding
Stacey Trooskin	Gilead Sciences	Grant funding to institution
John Ward	Abbott, Dynavax, Gilead Sciences, AbbVie, Merck, Siemens, Cepheid, Roche, Pharco, Virions, Zydus-Life Sciences	Grant funding to institution
Joseph Yao	Abbott Molecular, Inc. Roche Molecular Systems, Inc.	Research Funding

* The following invited participants had nothing to disclose: Andrew Aronsohn, Berry Bennett, Emily Cartwright, Raymond Chung, Randal Fowler, Nathan Furukawa, Saleem Kamili, Michael Pentella, Liisa Randall, Carolyn Wester.

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