# A Breakthrough in HCV Elimination:
# How HCV Point-of-Care RNA Testing Came to the United States

Hosted by the Centers for Disease Control and Prevention | NIH | Coalition for Global Hepatitis Elimination

Moving from Hepatitis Discovery to Elimination:
NIH Research Advancing Hepatitis Elimination webinar series
October 24, 2024

## Executive Summary

Hosted by the US Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Coalition for Global Hepatitis Elimination, the latest webinar in the NIH "Moving from Hepatitis Discovery to Elimination" series provided a detailed account of how HCV point-of-care RNA testing came to the United States: the new test received authorization on June 24, 2024, by the Food and Drug Administration (FDA).

Though point-of-care HCV RNA tests have been available internationally for several years, the story of their approval for use in the US begins and ends with partnerships—across government, academia, industry, and more. The newly approved fingerstick test could improve HCV testing and treatment rates nationwide, particularly among hard-to-reach populations.

Traditional two-step processes for diagnosing and treating HCV can take substantial time and multiple visits, from the initial screening to follow-up testing and provision of medication. Along the way, multiple challenges confront care providers—incomplete testing, loss to follow up, or the potential to miss early HCV infection, among other obstacles. Now, having a rapid RNA diagnostic test makes same day "test-and-treat" possible. It means that a patient can learn her infection status in one visit and, if infected, receive medication and/or linkage to care moving forward. With the June 24, 2024, authorization of the rapid HCV RNA test by the FDA, a significant step toward eliminating HCV has been achieved.

Dr. Nate Furukawa (CDC) served as host and moderator of the webinar. Dr. Francis Collins (NIH) provided welcome remarks by video recording. Currently serving as lead for the United States National Hepatitis C Elimination Initiative, Collins noted that HCV is estimated to affect 4 million Americans nationwide, though many individuals do not know they are infected until they present with serious symptoms such as liver damage. Curative therapies are available, but access to these medications remains a challenge. Only 1 in 3 adults diagnosed with the disease in the US has been cured.

With the White House proposing a National HCV Elimination Plan in 2023-2034, proponents have mobilized to urge Congress to allocate funds for the program. Collins provided a legislative update, noting that the program is currently the subject of bipartisan legislation and under review by the Congressional Budget Office.

Following Collins's welcome, five presenters who played key roles in bringing point-of-care HCV RNA testing to the US shared their perspectives and lessons learned.

**Key takeaways: What made this success story possible?**

- Strong partnerships across government, academia, and industry that enabled rapid forward progress.

- Commitment to a dramatically compressed timeline without compromising scientific rigor or quality: “There is no July” became the mantra (the project deadline was the last day of June).

- Regular communication with the FDA and other governmental agencies: the team’s communications strategy included regular (minimum twice weekly) calls with FDA, along with routine inputs and feedback obtained from other partners.

- Fluid regulatory submission and review process, together with intervention and support from government agencies when needed.

- Advanced support from academic and healthcare experts to develop the testing approvals needed (a major partner was Emory University, with clinical trial host Grady Memorial Hospital).

- Partnership with a commercial sponsor who brought experience in global HCV testing and adapted testing technology and materials for a US approval process.

**Looking ahead: Next steps for HCV elimination in the United States**

- Simplify treatment implementation, especially in nontraditional settings: simplification of the test-and-treat process remains key to HCV elimination.

- Continue to confront other barriers to patients receiving care, including the cost of treatment medication, ongoing HCV stigma, systemic health inequities, and more.

- Provide public health guidance for implementation of the new diagnostic test: this work is well underway and will need to be disseminated as widely as possible.

- Prioritize bringing point-of-care HCV RNA testing and same-encounter treatment to high-impact settings, including syringe service programs, large jails, opioid treatment programs, and mobile clinics. Scale up new testing strategies in these areas.

- Consumers at home and point-of-care diagnostic tests are the new diagnostic market across multiple disease areas, including but not limited to HCV. There is an ongoing opportunity to leverage technology advances, partnerships, and healthcare needs to create sustainable, “pandemic-ready” diagnostics and digital health infrastructure across the US.

- Ongoing investment in the RADx/ITAP program will be needed. More work also needs to be done to integrate over-the-counter/point-of-care tests into healthcare (incorporating test results into electronic health records, managing reimbursements from insurance, etc). How can policymakers and providers connect testing to sustainable economic systems? This area that needs additional support and operational research.

- Pursue point-of-care hepatitis B antigen (HBsAg) diagnostic testing, so that patients can be screened for HCV/HBV co-infection in a single visit. This work has already begun: the

FDA has signaled that HBV down-classification to Class II on the federal register is imminent. The Rapid Acceleration of Diagnostics Technologies initiative (RADx) ITAP initiative has released a solicitation for point-of-care HBsAg tests.

## Presentation Highlights

**The NIH RADx Program** | Dr. Bruce Tromberg, National Institute of Biomedical Engineering and Bioimaging (NIBIB)

Dr. Tromberg summarized the development and implementation of the Rapid Acceleration of Diagnostics Technologies initiative (RADx), launched during the COVID19 pandemic and subsequently deployed to develop and test the new point-of-care HCV RNA test.

**Background:**

- The RADx initiative emerged in 2020 in response to the need for rapid advances in COVID19 diagnostic testing. NIH scientists proposed the creation of a competitive innovation funnel, akin to television's "shark tank" approach, that would rapidly accelerate science in priority areas.

- In April 2020, Congress allocated $1.58 billion to advance the RADx testing platforms, with the goal of expanding point-of-care and over-the-counter testing. The diagnostic advances made during the COVID19 pandemic created an infrastructure and technology platform for other advanced diagnostics and testing—including the project to bring a point-of-care HCV RNA fingerstick test to the US.

**Why RADx succeeded:**

- The initiative built on a well-established network, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) Point of Care Tech Research Network (POCTRN), and added new structures over time, including a validation core, a clinical studies core, and a deployment core.

- The POCTRN consortium quickly grew to nearly 1,000 participants from government, industry, and academia. Over 3 years, it helped drive a paradigm shift beyond COVID19 itself: the program and its structures have since been deployed to address other infectious diseases and chronic disease prevention.

  *Show slide #3: RADx Tech: Structure*

- The Independent Test Assessment Program (ITAP), launched in November 2021 to meet the Omicron variant surge during COVID19, compressed the timeline for FDA approval through the economization of multiple steps, including or especially providing the FDA with large-scale quantitative data acquired independently.

- The ITAP HCV collaboration led to approval by the FDA of the new point-of-care HCV RNA test on 6.27.2024.

Looking ahead, the RADx collaboration is taking on HBV diagnostics and other STIs, well as partnerships to advance scientific progress in other infectious and chronic diseases.

**The ITAP Process** | Eric Lai, NIH

The Independent Test Assessment Program (ITAP) collaboration, part of the RADx initiative, worked to obtain FDA clearance of a fingerstick molecular test for HCV that would enable single-visit test-and-treat programs to support the US National HCV Elimination Initiative. Collaboration partners included AASLD, CDC, Emory, FDA, NIH, and Cepheid.

**Major accomplishments:**

- ITAP's actions included setup, identification of manufacturers, a sponsor kickoff, technology derisking and analytical studies, clinical preparation and clinical trials, and closure and submission to the FDA for De Novo market authorization with a clinical laboratory improvement amendments waiver.

- The technology de-risking phase was undertaken by Emory University at Grady Memorial Hospital in Atlanta. The Grady team performed a clinical study in one month, enrolling over 100 subjects. The Emory team provided fingerstick analytical data for the FDA submission, as well, marking the first time ITAP managed this part of the process.

- The project was completed under budget and one day ahead of schedule. From the first FDA meeting to FDA marketing allocation took just 13 months, including four months for a 15-site nationwide clinical trial.

- From submission of the De Novo (April 15) to obtaining of the FDA market authorization (June 29) took just 73 days. It usually takes a minimum of 6 months.

*Show slide #2: Goals and Timeline*

*Show slide #11: ITAP: Timeline of EUAs*

**Why the ITAP HCV partnership worked:**

- Strong visionary leadership from the outset, with a project team empowered to accomplish goals set by leadership.

- A highly skilled Emory team that engaged in critical derisking activities. The partnership with Emory and Grady proved critical to planning and success.

- Clear lines of decision making and authority, together with a shared sense of urgency across broad group of stakeholders (AASLD, CDC, FDA, NIH, more).

- ITAP's communications strategy divided actions into distinct buckets (technology, leadership, execution), with tasks assigned to specific individuals, not groups, for more efficient handoffs and follow-up.

- Commitment to a people-centric approach ("People make it work, not the technology").

- Communications strategy included regular (minimum twice weekly) calls with FDA, along with routine inputs and feedback obtained from the extended team.

- Fluid regulatory submission and review process, together with intervention and support from government agencies when needed, helped the ITAP collaboration achieve its goals on time.

**Lessons learned:**

- Vigorously control scope creep ("Wouldn't it be nice to have….?" was closely managed).

- Significant adaptation and de-risking is required for CE-marked products (those that have been verified by the manufacturer to meet the European Union's health, safety, and environmental protection requirements).

- Sample collection is challenging for persons who inject drugs, and a venous blood draw is more difficult than a finger stick—data that reconfirms the importance of the point-of-care fingerstick test, especially for key populations.

- Need to strike a balance between clinician support and maintaining Clinical Laboratory Improvement Amendment (CLIA)-waived submission status.

- The NIH's human-subjects approval process is not designed for rapid deployment. In addition, some institutional contracts can be nonstarters. Be prepared to find alternatives.

- Long lead-time items required a continuous push from multiple agencies.

**Industry perspective** | Jennifer Rakeman, Cepheid

In March 2023, the Federal Task Force to Eliminate HCV contacted commercial manufacturer Cepheid with interest in bringing the company's HCV RNA fingerstick test to the US. Cepheid had experience launching the Xpert HCV viral load fingerstick test globally, and its test has been available outside the US since 2018, with commercialization in Europe, Africa, and Australia.

After Cepheid's selection as the industry partner for the RADx HCV initiative, work commenced with government and academic partners. Cepheid's mission is to deliver a better way to improve patient outcomes by enabling access to PCR testing everywhere.

*Show slide #3: NYT slide on pandemic era tests speeding HCV detection*

**Lessons learned from Cepheid's global work to promote testing access and use:**

- The site of care delivery should ideally have the instrument, the test, and the ability to prescribe treatment seamlessly in a single visit.

- A pan-genotypic drug should be made available onsite to minimize loss to follow up.

- Phlebotomy is challenging: a capillary blood test is best for non-clinical sites and for ease of specimen collection.

**Highlights from US project:**

- Multi-partner collaboration was crucial to project success, across governmental agencies and others. While Cepheid's job was to make the test, the company needed collaboration to make sure the tool could be used. The ITAP team was central to the project.

- Cepheid also worked with the Centers for Medicare & Medicaid Services (CMS) to make sure the test would be eligible for coverage, coding, and reimbursement.

- A key reason for success was the team's commitment to shrink the timeline. One month = one week; one week = one day. Everyone pulled together to expedite multiple steps in the process.

- The test itself is simple, with testing workflow involving just three simple steps. HCV RNA results are available in as early as 41 minutes for RNA detected and 60 minutes for not detected results—both directly from fingerstick-collected whole blood.

  *See Slide #8: Xpert HCV Workflow*

**HCV POC Implementation Strategies** | Nate Furukawa, CDC

With the FDA's approval of the first point-of-care HCV RNA test, a major milestone has been achieved—but questions remain to be addressed. The CDC has released a new HCV testing considerations document to support public health decisions around testing implementation.

*Show slide #15: CDC just released an HCV POC testing considerations document*

**What does existing CDC guidance say about point-of-care HCV RNA testing?**

- HCV RNA testing is currently recommended by the CDC (from 2013 guidance) for the diagnosis of HCV infection among persons who might have been exposed to HCV within the last six months, even if they tested negative earlier.

- This guidance, while it does not explicitly mention point-of-care testing, provides a way forward to guide the new single-step HCV RNA testing for 2024 and beyond.

**When can providers use single-step versus two-step testing?**

- CDC has developed a new framework for determining when to use lab-based testing and when to use point-of-care testing:

  *Show slide #9: Selecting a testing sequence*

**Who will benefit most from point-of-care testing, and where can that testing be set up?**

- A high prevalence setting favors single-step HCV RNA testing strategy.
- Brief encounters favor point-of-care testing.
- Lack of access to labs and/or phlebotomy services also favor point-of-care testing.
- Client volume remains a challenge: point-of-care testing can become difficult to carry out during high-intensity testing campaigns. At the same time, extremely low-volume testing settings could find the cost of the new technology not worth the investment.

**What are potential testing strategies in high, moderate, and low prevalence settings?**

- High prevalence settings—syringe service programs, opioid treatment programs, large jails, and prisons—should consider the single-step point-of-care HCV RNA test as a strong option for use.
- Low to moderate prevalence settings—mobile units, emergency departments, primary care, rural clinics, and pharmacies—should consider a range of testing options, with decisions partly depending on the availability of phlebotomists and lab access. In some of these settings, two-step testing may be the preferred option.

**How should providers pair point-of-care HCV RNA testing with treatment?**

- Multiple models are available, including co-located treatment, telehealth, mobile units, and patient navigation systems.
- Each model has considerations that should be carefully addressed, including barriers to billing, possible loss to follow up, and the need for key infrastructure to be in place to support patients along the care continuum.

*Show slide #14: There is great potential in pairing POC testing and same-encounter treatment in certain high-impact settings.*

**Simplifying Hepatitis C Treatment** | Andrew Aronsohn, AASLD

HCV guidance (www.hcvguidance.org) is a joint effort of the Infectious Disease Society of America (IDSA) and the American Association for the Study of Liver Diseases (AASLD), with additional input from CDC and community partners.

Launched in 2014 as a response to the rapidly changing landscape of HCV therapy, this website is intended to be a living document, updated every other year and with a focus on clinical HCV guidance for providers.

*Show slide #3: HCVguidelines.org – sample page*

**HCV Guidance highlights:**

- The guidelines include everyone—no group or patient population is excluded. Everyone can be treated for HCV infection, including those with transplantations, renal impairment, pregnant persons, and children.

- Simplifying treatment in nontraditional settings—and making treatment more accessible in general—is an essential step to eliminating HCV as a public health threat.

- The MINMON study, published in 2022, was a phase 4, open-label, single-arm trial conducted across 38 sites (Brazil, South Africa, Thailand, Uganda, and the US). It assessed a minimal monitoring, low-touch approach for treating HCV over a 12-week period.

    - The study conducted no pre-treatment genotyping, provided all treatment medications at trial entry, and only saw patients at entry and then at the completion of their treatment.
    - Results demonstrated that the MINMON approach with sobosbuvir-velpatasvir treatment is safe and achieved sustained virologic response rates (SVR) comparable to standard monitoring.
    - Of 399 patients treated, 95% were cured, including those co-infected with HIV, and including 11 of 12 patients with ongoing substance use disorder.
    - No patients should be excluded from these test-and-treat protocols.

- A new section in the HCV Guidance is being developed as an aid to implementing same-day test-and-treat HCV protocols. The release date for this algorithm is anticipated this fall. HCV guidance intends to offer treatment algorithms to incorporate the new point-of-care testing in support of public health implementation.

*Show slide #15: Test and Treat Algorithm for HCV guidance*

## Notes from the Field

A final segment of the webinar featured brief comments from public health practitioners who are either currently engaged with the new point-of-care HCV RNA diagnostic test or preparing to incorporate the test into their programs.

Dr. Jennifer Havens spoke as principal investigator of the Kentucky Viral Hepatitis Treatment Project, a longitudinal cohort study implemented in 2019. The study made same-day test-and-treat the model of care and has been using the Cepheid device through a research exemption (the device is used both for diagnosis and to assess HCV cure within this study). Their data has shown that same-day test-and-treat promises to be a useful testing option for rural areas, which typically experience significant barriers to transportation.

Colleen Flanigan shared the New York State Department of Health's plan for incorporating the new point of care (POC) HCV RNA fingerstick test into its 12 Drug User Health Hubs already providing rapid HCV antibody testing, as well as additional primary care and opioid treatment programs currently offering hepatitis C treatment on site. State dollars have been allocated to invest in the new test. New York currently operates a large HCV community-based rapid antibody testing program in high-impact settings, including syringe service programs. Workflow is sure to be a challenge with the new POC test and will need addressing, and the department is also working to build HCV treatment capacity at the Drug User Health Hubs. All programs using the new POC test will also address social determinants of health and other barriers, such as clients who are lost to follow-up.

Finally, Tyler Bartholomew of the University of Miami's Miller School of Medicine noted that while syringe service programs are optimal venues for reaching people who inject drugs, equitable implementation of this new technology will need to be a priority. Many programs lack funding support or access to implementation assistance—these inequities must be taken into account. In addition, integrating telehealth models into the HCV care flow will be essential to long-term success—such integration will allow programs to bring care to where people are located and need it most.

## Conclusion

Point-of-care HCV RNA testing opens the possibility of same-day test-and-treat strategies for helping eliminate hepatitis C in the United States. While multiple barriers to HCV treatment still exist, overcoming the two-step testing process represents a major success story that deserves to be widely told and celebrated. The new test promises to improve diagnosis rates, save lives, and conserve millions of dollars in healthcare costs.

In closing remarks, Dr. John Ward (Coalition for Global Hepatitis Elimination) called for new operational research to clarify and confirm where point-of-care HCV RNA testing will be most helpful and have the greatest impact. A comprehensive public health campaign for implementation of the new testing technology is also needed, as is a commitment to making treatment affordable and accessible, especially for marginalized populations.

With RadX scientists now turning to point-of-care hepatitis B antigen diagnostics, public health is moving closer to testing for HCV/HBV coinfection in a single visit. These advances, combined with the safe and simple oral medications already available for treating HCV, mark a major step forward in the effort to eliminate a lethal disease in the United States and globally.