Evaluation of Contamination Risk During Processing by the cobas® e 602 Serology Module Prior to HIV/HCV Viral Load Testing on the cobas® 6800 System

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Medical and Scientific Affairs

Roche Diagnostics

Disclosures

- **Pedro Rodriguez is an employee of Roche Diagnostics Incorporation**

CDC HCV Diagnostic Algorithm

Centers for Disease Control and Prevention
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Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians

In the United States, an estimated 4.1 million persons have been infected with hepatitis C virus (HCV), of whom an estimated 3.2 (95% confidence interval [CI] = 2.7–3.9) million are living with the infection (*1*). New infections continue to be reported particularly among persons who inject drugs and persons exposed to HCV-contaminated blood in health-care settings with inadequate infection control (*2*).

Since 1998, CDC has recommended HCV testing for persons with risks for HCV infection (*3*). In 2003, CDC published guidelines for the laboratory testing and result reporting of antibody to HCV (*4*). In 2012, CDC amended testing recommendations to include one-time HCV testing for all persons born during 1945–1965 regardless of other risk factors (*1*).

CDC is issuing this update in guidance because of 1) changes in the availability of certain commercial HCV antibody tests, 2) evidence that many persons who are identified as reactive by an HCV antibody test might not subsequently be evaluated to determine if they have current HCV infection (*5*), and 3) significant advances in the development of antiviral agents with improved efficacy against HCV (*6*). Although previous guidance has focused on strategies to detect and confirm HCV antibody (*3,4*), reactive results from HCV antibody testing cannot distinguish between persons whose past HCV infection has resolved and those who are currently HCV infected. Persons with current infection who are not identified as currently infected will not receive appropriate preventive services, clinical evaluation, and medical treatment. Testing strategies must ensure the identification of those persons with current HCV infection.

This guidance was written by a workgroup convened by CDC and the Association of Public Health Laboratories (APHL), comprising experts from CDC, APHL, state and local public health departments, and academic and independent diagnostic testing laboratories, in consultation with experts from the Veterans Health Administration and the Food and Drug Administration (FDA). The workgroup reviewed laboratory capacities and practices relating to HCV testing, data presented at the CDC 2011 symposium on identification, screening and surveillance of HCV infection (*7*), and data from published scientific literature on HCV testing. Unpublished data from the American Red Cross on validation of HCV antibody testing also were reviewed.

Changes in HCV Testing Technologies

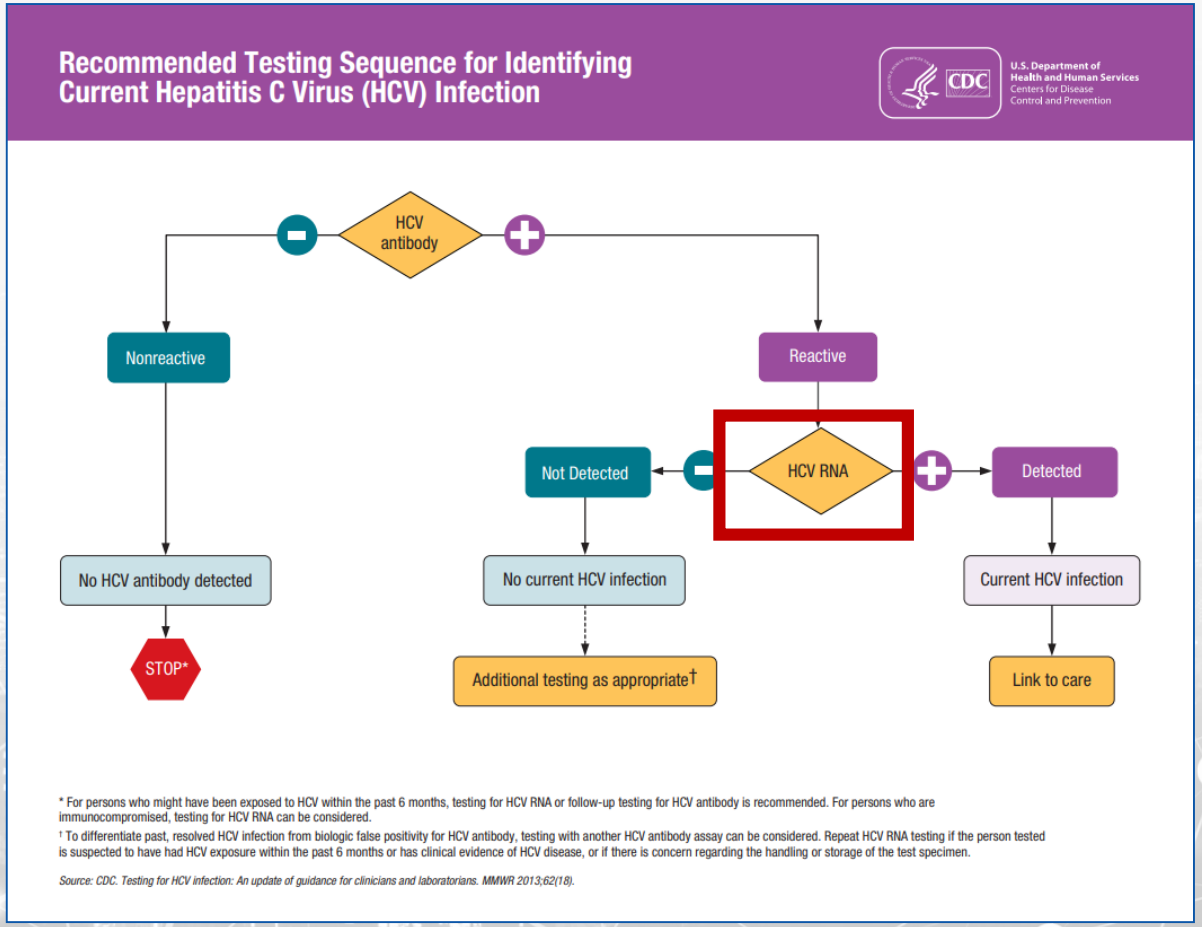
Since the 2003 guidance was published (*4*), there have been two developments with important implications for HCV testing:

1. Availability of a rapid test for HCV antibody. The OraQuick HCV Rapid Antibody Test (OraSure Technologies) is a rapid assay for the presumptive detection of HCV antibody in fingerstick capillary blood and venipuncture whole blood. Its sensitivity and specificity are similar to those of FDA–approved, laboratory-conducted HCV antibody assays (*8*). In 2011, a Clinical Laboratory Improvements Amendments waiver was granted to the test by FDA. The waiver provides wider testing access to persons at risk for HCV infection, permitting use of the assay in nontraditional settings such as physician offices, hospital emergency departments, health department clinics, and other freestanding counseling and testing sites.
2. Discontinuation of RIBA HCV. The Chiron RIBA HCV 3.0 Strip Immunoblot Assay (Novartis Vaccines and Diagnostics) that was recommended (*4*) for supplemental testing of blood samples after initial HCV antibody testing is no longer available. As a result, the only other FDA-approved supplemental tests for HCV infection are those that detect HCV viremia.

Identifying Current HCV Infections

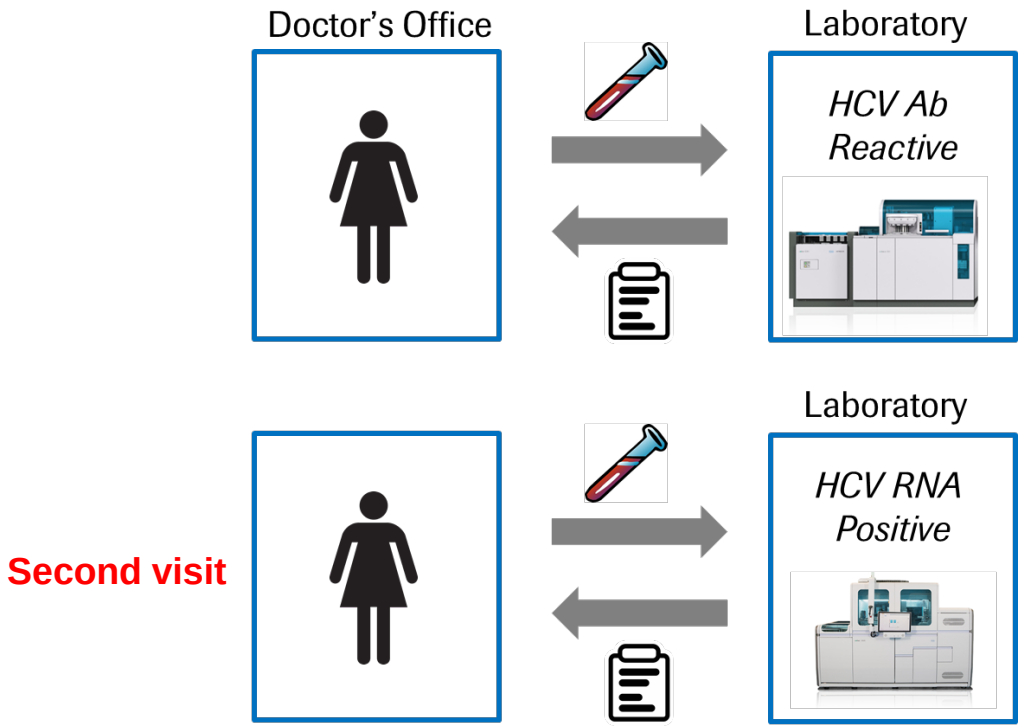
In 2011, FDA approved boceprevir (Victrelis, Merck & Co.) and telaprevir (Incivek, Vertex Pharmaceuticals) for treatment of chronic hepatitis C genotype 1 infection, in combination with pegylated interferon and ribavirin, in adult patients

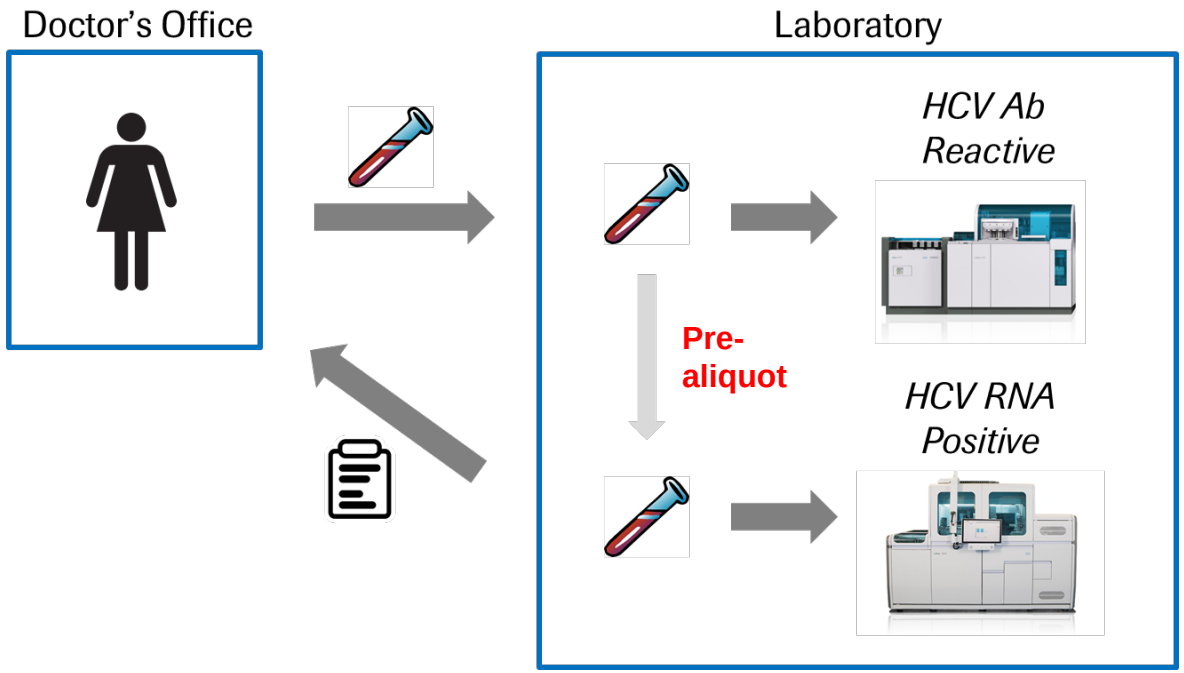
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention



MMWR: Testing for HCV infection: An update of guidance for clinicians and laboratorians. (https://www.cdc.gov/mmwr/pdf/wk/mm62e0507a2.pdf) Accessed on 03/18/2019.

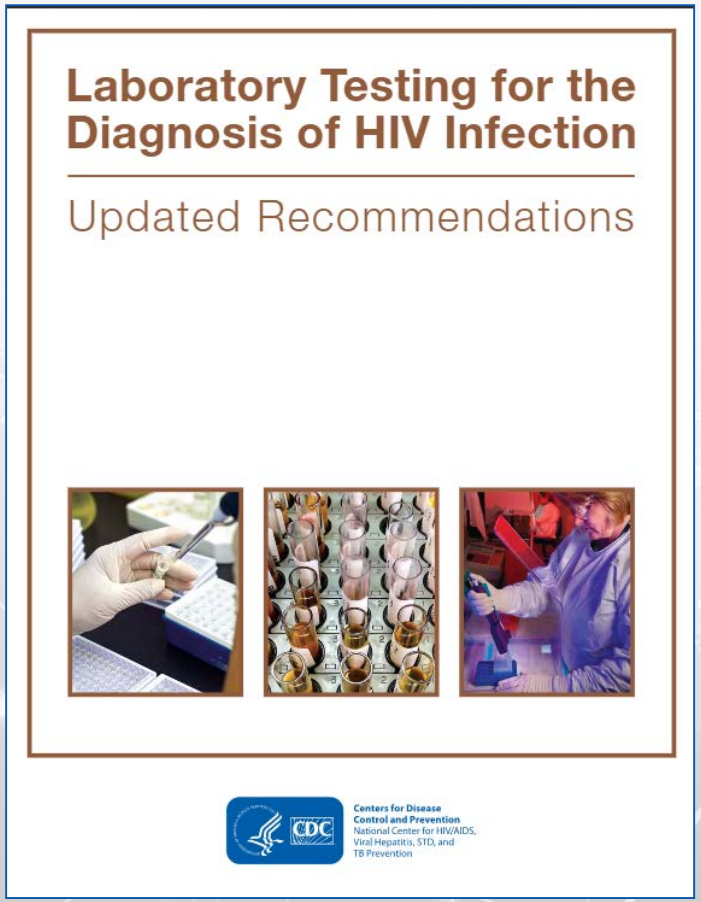
NAT Specimen Workflow Challenges: HCV

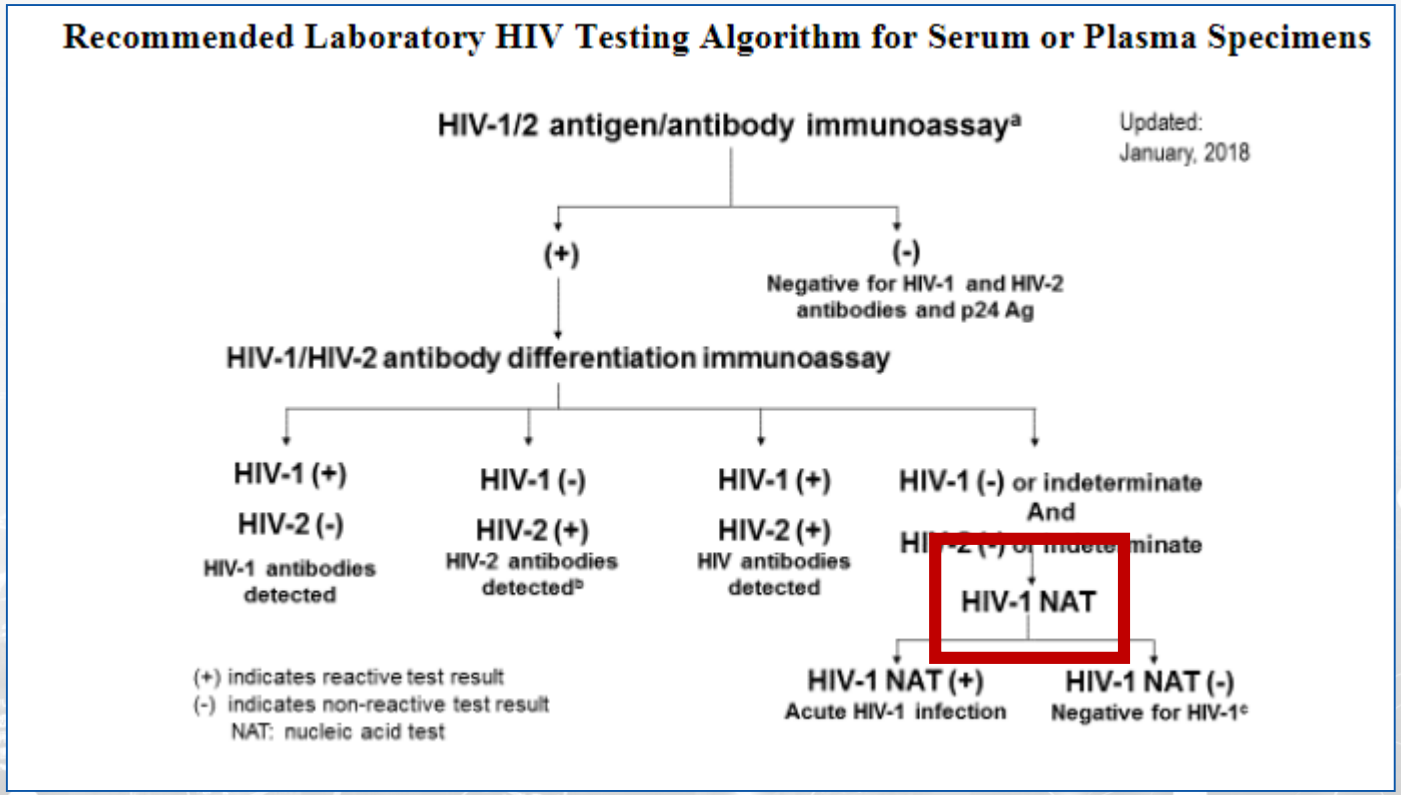




- ***Jeopardizes patient follow-up rates***
- ***Places additional workflow burden on the laboratory***

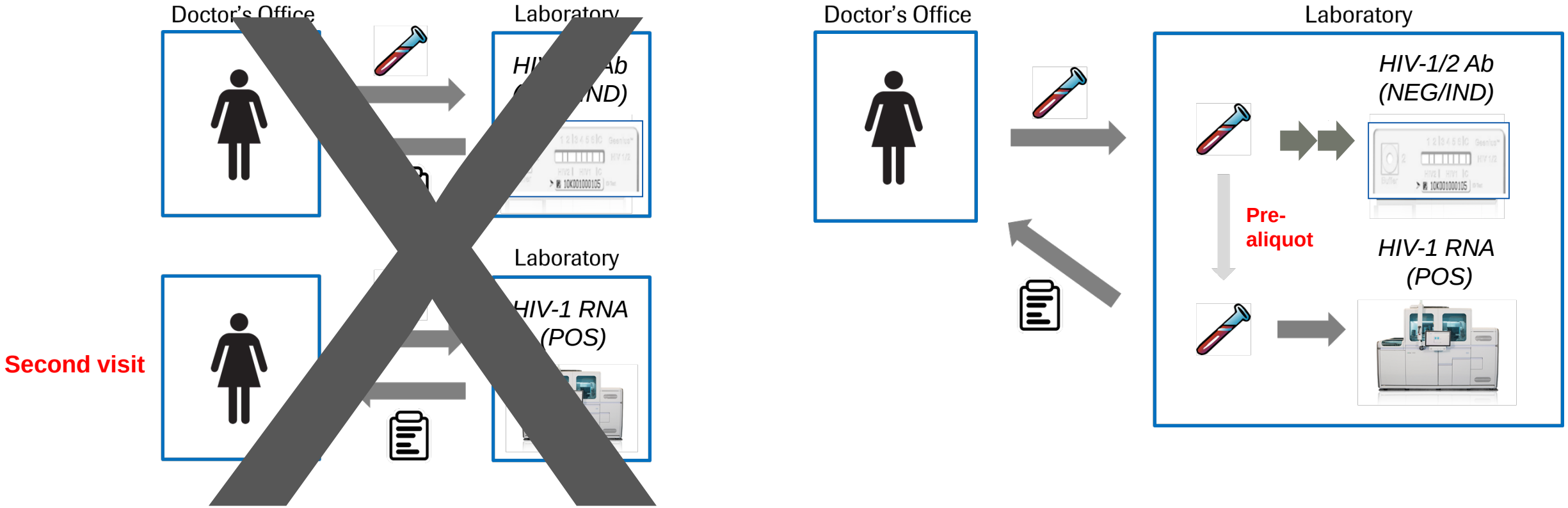
CDC HIV Diagnostic Algorithm





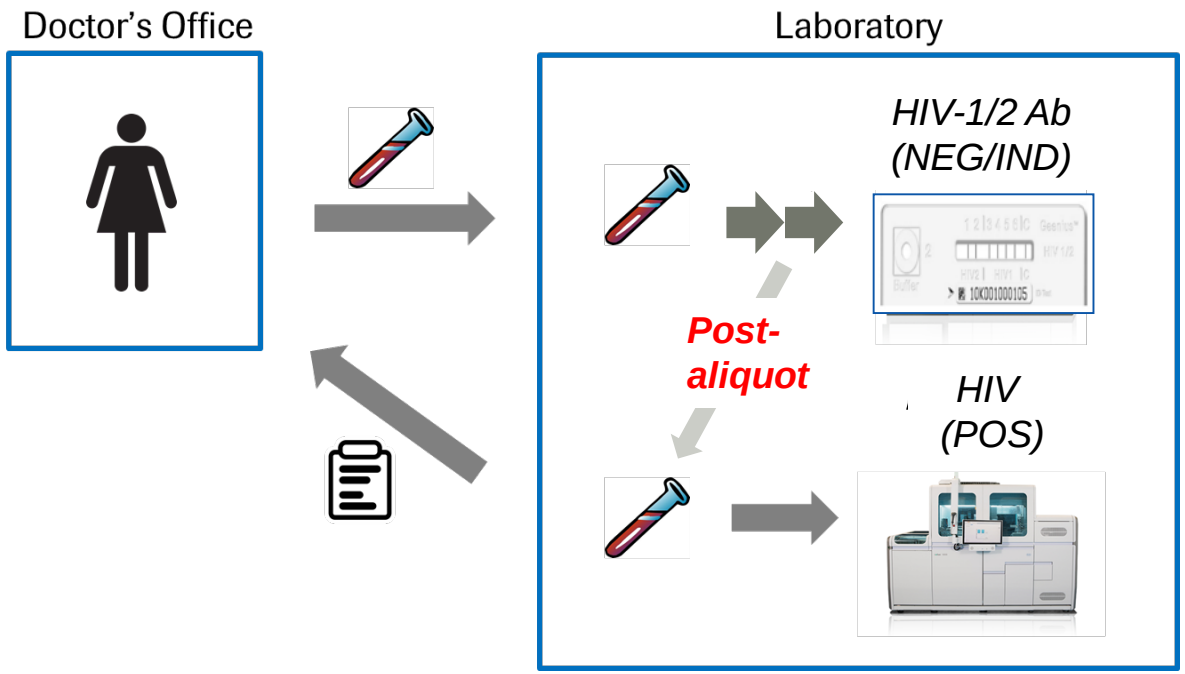
CDC Updated Recommendations: Laboratory Testing for the Diagnosis of HIV Infection. (https://stacks.cdc.gov/view/cdc/23447) Accessed on 02/26/2019.

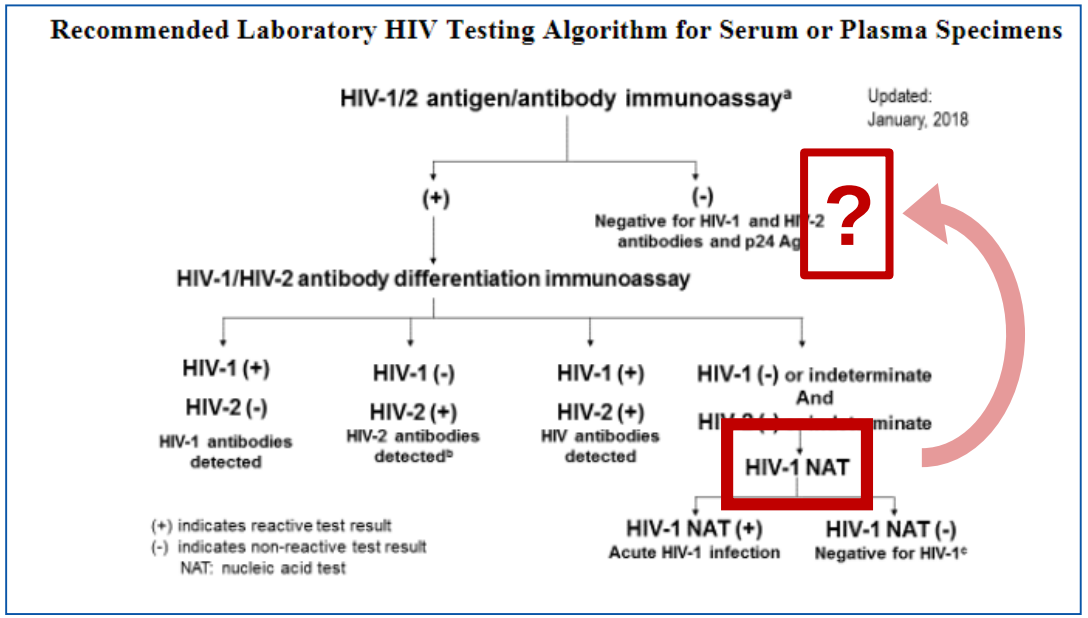
NAT Specimen Workflow Challenges: HIV



- ***Jeopardizes patient follow-up rates and time-to-treatment***
- ***Places additional workflow burden on the laboratory***

NAT After Serology Processing: HIV

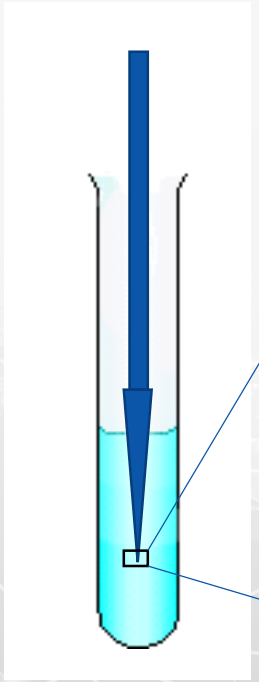


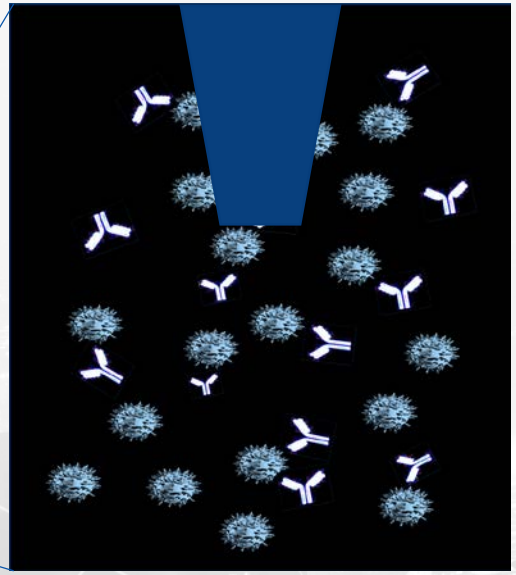


- ***What if the HIV algorithm changes?***
- ***Could this model be applied to HCV algorithm testing?***

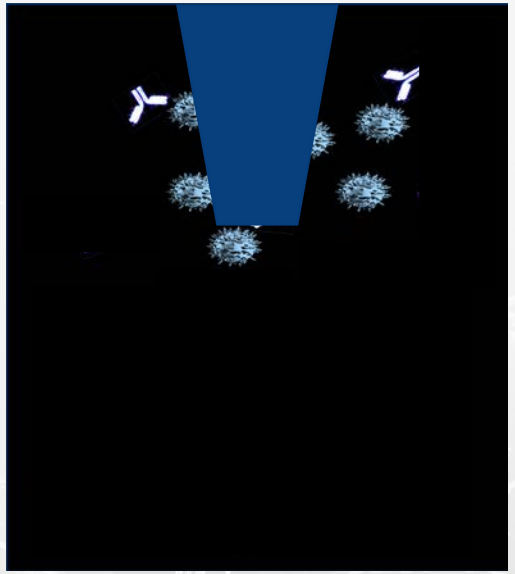
What is the risk of molecular testing (HIV/HCV) after serology processing using the same specimen?

Why the hesitation?



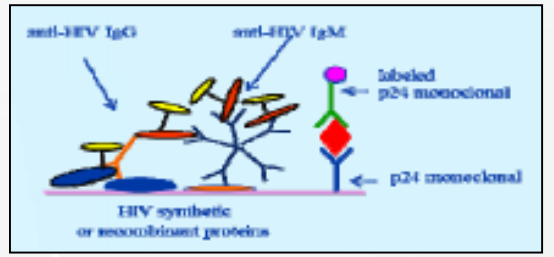


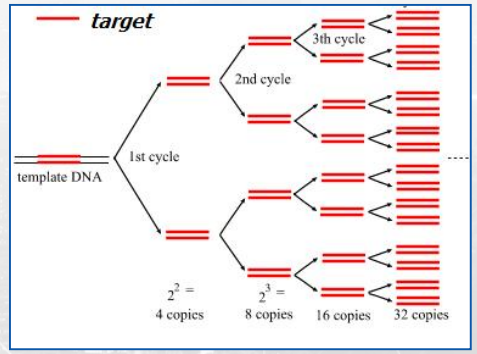
Patient 1



Patient 2
(carryover event)

IA= Non-Amplification





NAT = Amplification

Serology devices are not designed for very sensitive molecular applications, which require strict attention to contamination prevention measures

Could pipetting dynamics make a difference?

Ortho VITROS

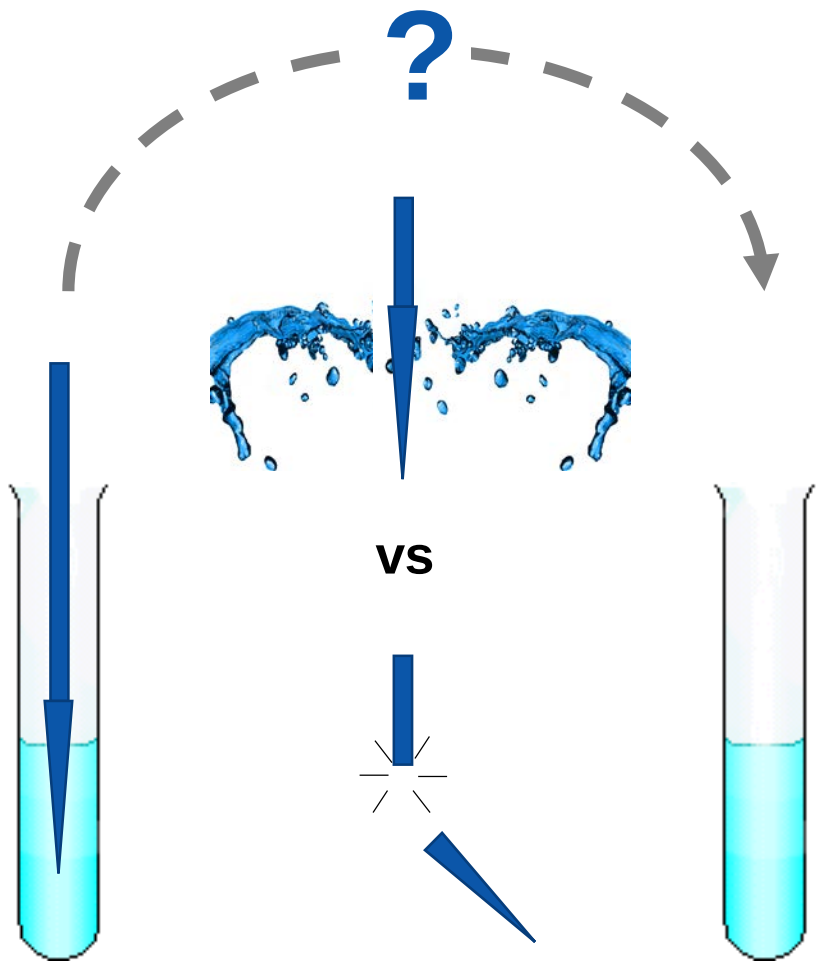
Advia Centaur

FDA Approved Systems

Roche cobas e 602

Abbott Architect

BioRad Bioplex



The literature

The risk of HCV RNA contamination in serology screening instruments with a fixed needle for sample transfer

Elin Rondahl[a], Maria Gruber[a], Sandra Joelsson[a], Martin Sundqvist[b], Britt Åkerlind[a,c], Kristina Cardell[d], Magnus Lindh[e], Lena Serrander[a,d,*]

Journal of Clinical Virology 60(2014)172–173

Previously frozen HCV clinical samples (n=298)

POSITIVE: 1E2-1E7 IU/mL (mean = 1E6 IU/mL, n=149)

NEGATIVE (n=149)

"Checkerboard" loading onto fixed needle serology instrument.

- **6/149 (4.05%) contamination rate**
- **VLs observed: <15 – 33.9 IU/mL**

The literature

A-275

Feasibility of using same serum/plasma sample tubes for HCV antibody and reflex HCV RNA testing

A. Tejada-Strop, L. McNamara, T. Mixson-Hayden, S. Kamili. *CDC, Atlanta, GA*

Abstract presented at 2018 AACC annual meeting (#A-275)

HCV clinical samples (n=20)

POSITIVE: 1E2-1E8 IU/mL (n=10)

NEGATIVE (n=10)

"Checkerboard" loading in triplicate onto 1 fixed needle and 3 disposable tip serology instruments.

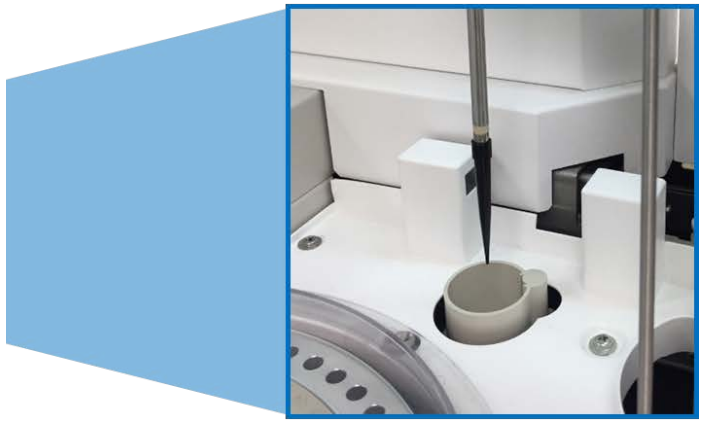
Disposable tips

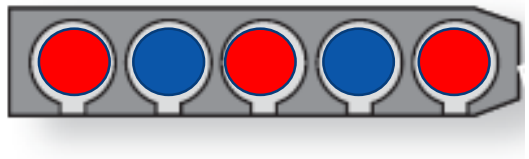
- **0/30 (0%) contamination rate**

Fixed needle

- **7/30 (23%) contamination rate**
- **VLs observed: <15 IU/mL**

Study Design: cobas e 602 (HIV and HCV)

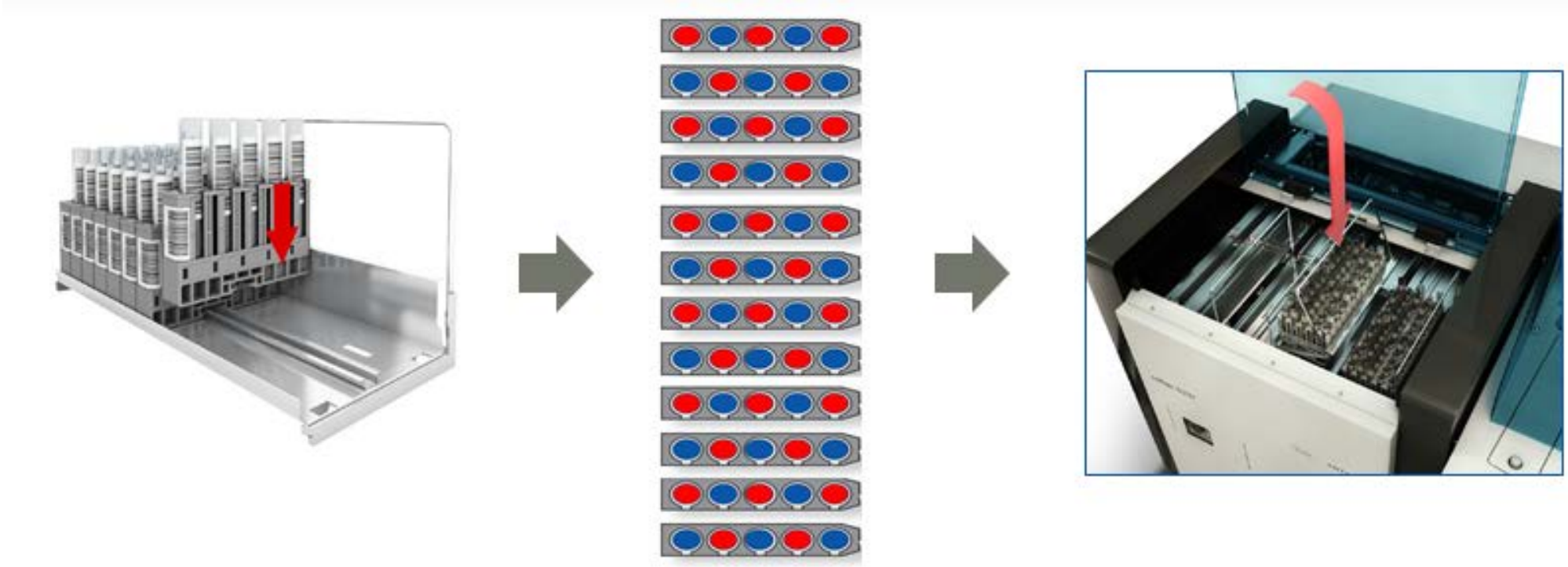




POSITIVE (n=60)

NEGATIVE (n=60)

Study Design: cobas e 602 (HIV and HCV)



Study Design: Viral load testing (HIV and HCV)

cobas HCV
LOD=8.5 IU/mL

cobas HIV
LOD=13.2
cp/mL

Results: HCV

HCV contrived samples [Armored RNA] (n=120)

POSITIVE: 1E6-1E7 IU/mL (n=60)

NEGATIVE (n=60)

“Checkerboard” loading (2x) onto e 602 serology instrument.

	% False Positive	95% CI
Run 1 (n=60)	0%	0.00 – 0.06%
Run 2 (n=60)	0%	0.00 – 0.06%
Total (n=120)	**0%**	**0.00 – 0.03%**

Results: HIV

HIV contrived samples [Inactivated Virus] (n=120)

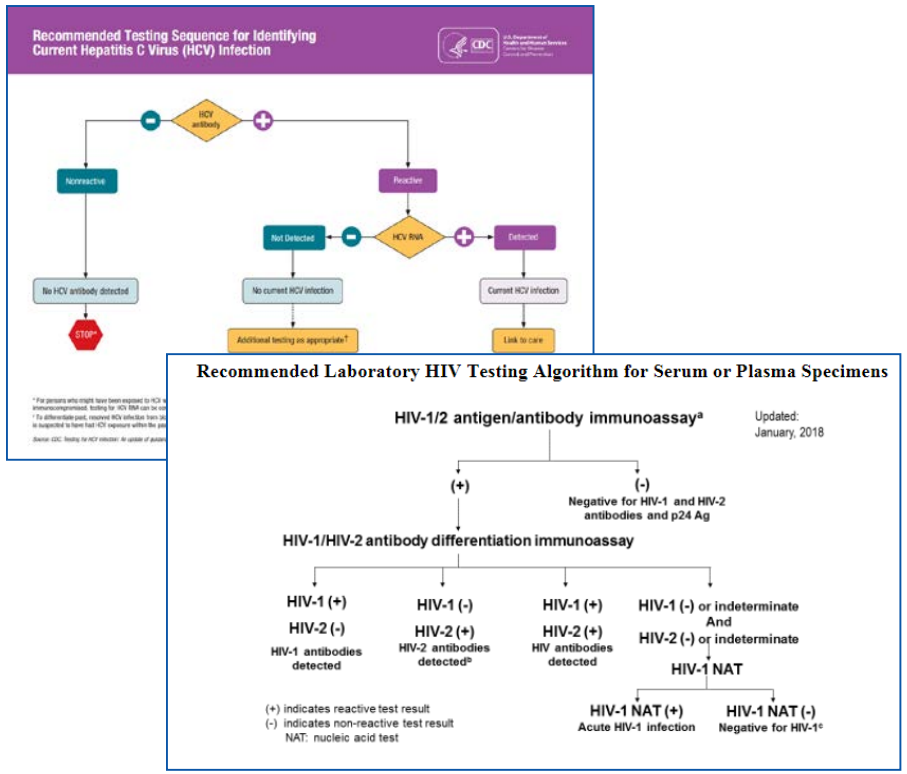
POSITIVE: 1E6 cp/mL (n=60)

NEGATIVE (n=60)

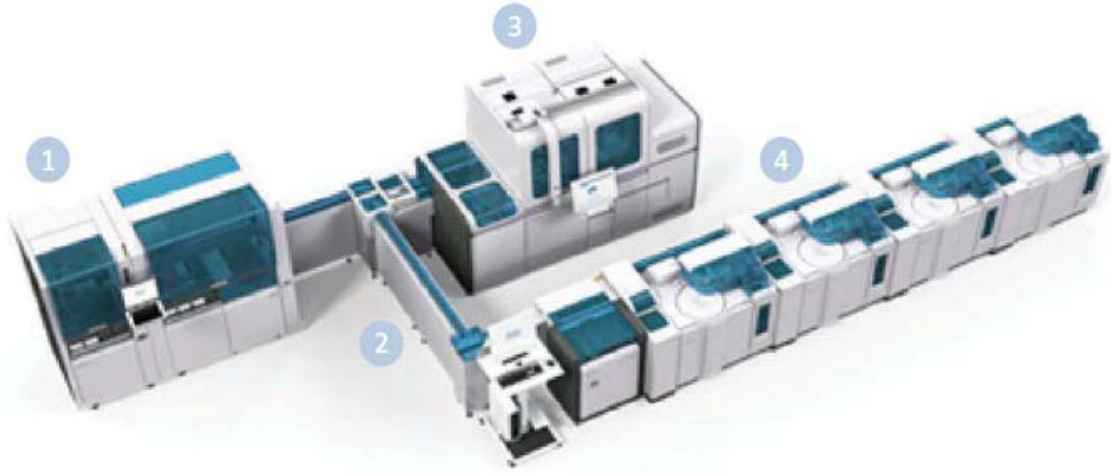
“Checkerboard” loading (3x) onto e 602 serology instrument.

	% False Positive	95% CI
Run 1 (n=60)	0%	0.00 – 0.06%
Run 2 (n=60)	0%	0.00 – 0.06%
Run 3 (n=60)	0%	0.00 – 0.06%
Total (n=180)	**0%**	**0.00 – 0.02%**

Final Thoughts



1. Aging workforce/Skilled personnel shortages
2. Demand for timely results
3. Aging population/Growing demand
4. Lower Reimbursement and Budget cuts
5. Tighter regulation of LDTs/Standardized procedures



More studies needed to assess the inherent risks with non-molecular devices handling specimens intended for molecular testing

Ledeboer NA and Dallas SD. *J Clin Microbiol*. 52(9): 3140-3146.

Conclusions

- As specimen workflow constraints associated with HIV/HCV testing algorithms might jeopardize patient follow-up rates or place additional workflow burden on the lab, the ability to streamline the process and to allow the single specimen vial use for both testing procedures is of high importance.
- One design feature that may potentially reduce or eliminate the possibility of carry-over contamination would be the use of disposable tips for the process of transferring specimens from the primary tube directly into the reaction, as suggested in previous studies.
- Specimens originally analyzed on the cobas e 602 serology module may be suitable for direct, single specimen reflex testing by a sensitive HCV RNA confirmatory test or HIV RNA test, respectively, but additional studies are warranted.
- Automated processes that minimize the need for manual intervention during the transfer of specimens, either prior to or after cobas e 602 assessment, may further reduce the chance of a contamination event.

THANK YOU