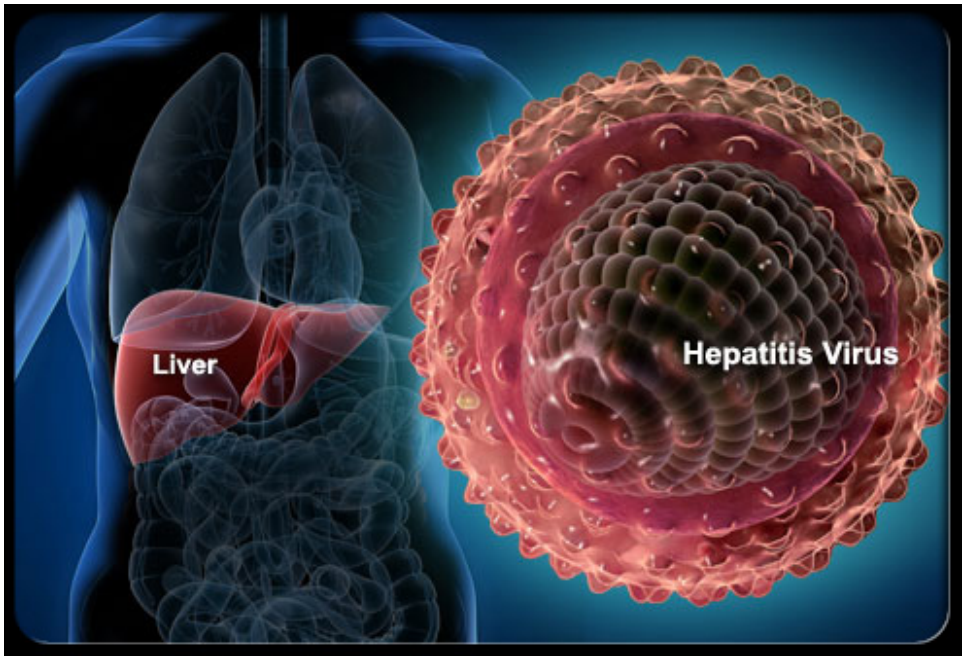
# OraQuick® HCV Product Training

U.S. Only

- Fingerstick Whole Blood
- Venous Whole Blood

# Background on Viral Hepatitis

- Hepatitis—a disorder in which a virus or other mechanisms produce inflammation or swelling of the hepatocytes (liver cells), resulting in their injury or destruction
- There are 5 distinct types of viral hepatitis known today
  - Hepatitis A virus (HAV)
  - Hepatitis B virus (HBV)
  - Hepatitis C virus (HCV)
  - Hepatitis D virus (HDV)
  - Hepatitis E virus (HEV)




**Reference:** Hepatitis C, Family Doctor, American Academy of Family Physicians, http://familydoctor.org/online/famdocen/home/common/infections/hepatitis/071.html, accessed 07/21/10.

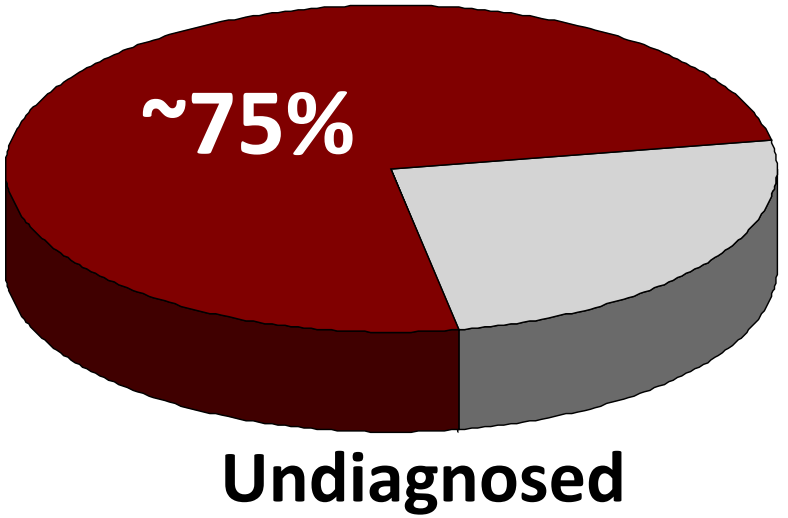
# Global HCV Surveillance


**Globally an estimated 180 million are infected with HCV—approximately 3% of the world population.**

**Reference**: WHO http://who.int/vaccine_research/diseases/viral_cancers/en/index2.html, assessed 7/22/10; Hepatitis C Global Infection Rates, Reviewed 2006, PKIDs' PHR, www.pkids.org, assessed 7/22/10.

# HCV Infection in the United States

- ~4 million in the U.S. are infected with chronic hepatitis C virus (HCV) - **3 out of 4 people don't know they are infected.**
- ~17,000 new infections occur each year.
- Hepatitis C virus is the leading cause of liver disease and cancer in the U.S.
- In the next 10 years, estimated health care burden direct and indirect cost will exceed $80 billion.




**Reference:** WebMD Health News, Interview CDC Director, Feb. 2011; CDC, The ABCs of Viral Hepatitis; McHutchison, MD J, Chronic Hepatitis C: An age Wave of Disease Burden, The American Journal of Managed Care, Oct. 2005.

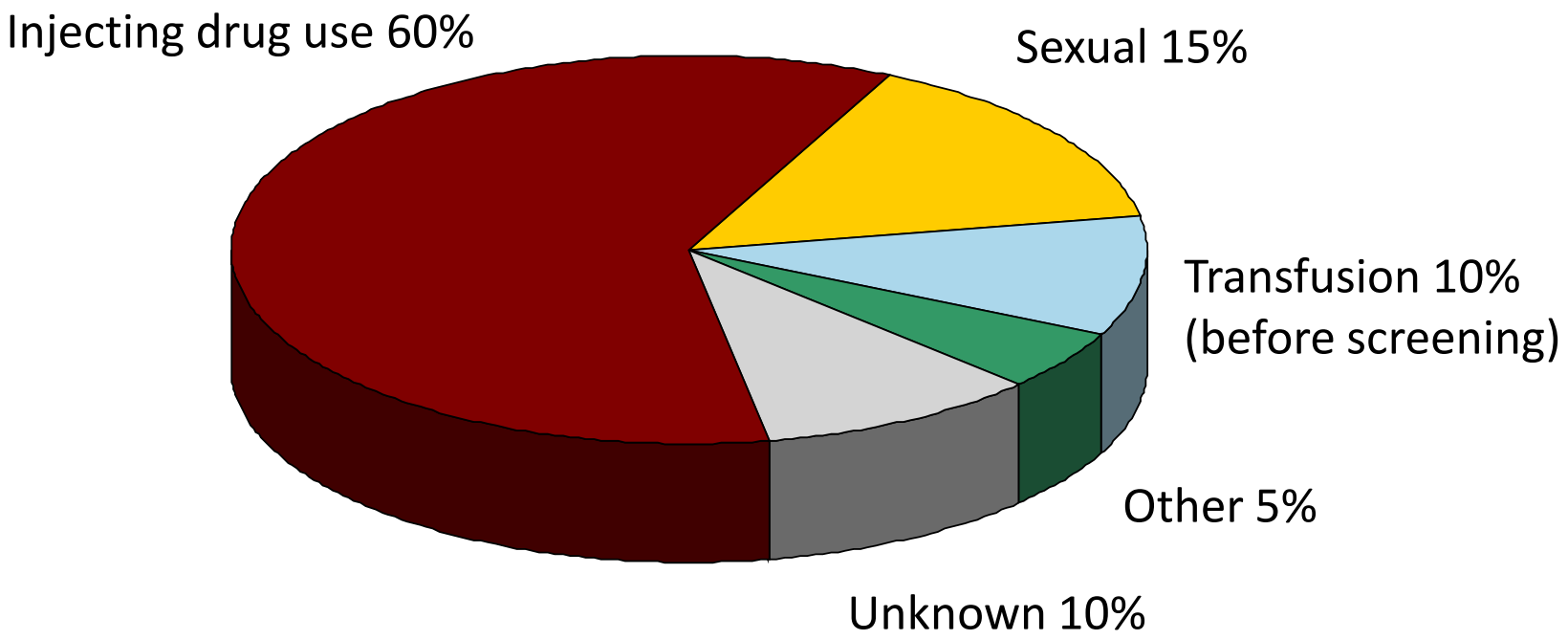
# Background on Hepatitis C

- Causative agent of hepatitis C was determined in 1989

| Hepatitis C (HCV) | Facts |
|---|---|
| U.S. prevalence statistics | 1-2% of the U.S. population infected; ~4.1 million |
| Source of virus | Blood/blood-derived body fluids |
| Route of transmission | Percutaneous, permucosal |
| Incubation period | 14-180 days (avg. 45 days) |
| Serologic tests | Anti-HCV |
| Chronic infection | yes |
| Prevention | Blood donor screening; risk behavior modification |
| Mortality rate | 1.5-2.5% |

**Resource:** World Health Organization. Hepatitis C, 2001-2003; Chou P. Hepatitis C Epidemiology, Diagnosis and Patient Management, HepC Conference 2008.; World Health Organization, Viral Hepatitis Report by the Secretariat, Sixty-Second World Assembly, 16 April 2009; Lavanchy D. *Liver Int*. 2009;29(s1):74-81.

# Sources of HCV Infection (2006)




**Reference:** CDC,Hepatitis C FAQs for Health Professionals, http://www.cdc.gov/hepatitis/hcv/HCVfaq.htm#section2

# Signs and Symptoms

- Because the liver has so many metabolic functions, individuals exposed to hepatitis tend to have generalized symptoms similar to flu. These include:
  - Fatigue
  - Joint and muscle pain
  - Loss of appetite
  - Nausea
  - Diarrhea
  - Constipation
  - Fever
  - Jaundice
- As the disease progresses, the liver becomes enlarged and tender resulting in other symptoms.
  - Chills
  - Weight loss
  - Distaste for food and cigarettes
  - Darker urine and lighter colored feces

**Reference:** Learning Guide-Hepatitis, Abbott Diagnostics, 2008.

# Acute Versus Chronic Hepatitis

- The distinction between acute and chronic viral hepatitis C is very important.
  - **Acute** illness is defined as the presence of hepatitis for less than 6 months.
  - **Chronic** illness is defined as the presence of hepatitis for greater than 6 months.
- Influencers for chronic illness may include:
  - Genotype
  - Age
  - Gender
  - Co-morbidity
  - Pregnancy

**Reference:** Worman, Howard, M.D., The Hepatitis C Sourcebook, McGraw-Hill Company, 2002.

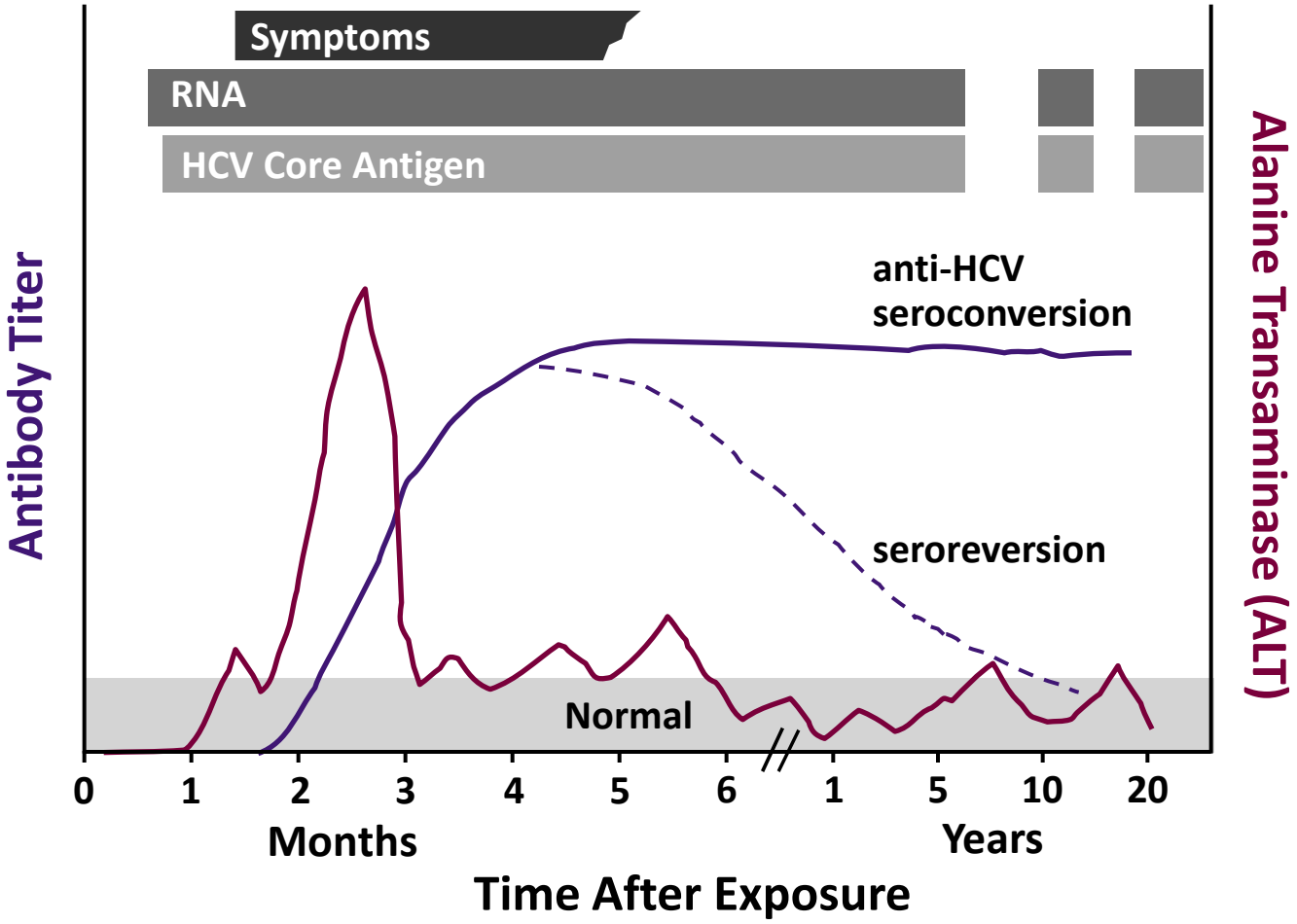
# Characteristics Associated With Chronic Infection

- Acute hepatitis C will develop into chronic infection in 75%-85% of cases[1]

| Risk Factors for Developing Chronic HCV Infection[1] |
|---|
| Age at time of infection >25 years |
| Male gender |
| No jaundice or symptoms during acute infection |
| African American race |
| HIV or HBV coinfection |
| Other immunosuppressive infections |

**Reference:** Chen SL and Morgan TR. *Int J Med Sci*. 2006;3(2):47-52.

# Diagnostic Profile of Hepatitis C Virus Infection




**Reference:** Adapted from Chen SL and Morgan TR. *Int J Med Sci*. 2006;3(2):47-52.

# Advantages of HCV Treatment

- Treatment can clear the virus
- Treatment can improve liver health by reducing inflammation
- It may also reverse fibrosis
- It will stop the risk of passing HCV to sexual and drug-using partners
- Clearing the virus removes the risk of mother-to-infant transmission
- Treating HCV before starting HIV treatment will reduce the risk of liver toxicity from HIV drugs
- The treatment period is likely to be only 12 to 18 months, not lifelong
- Potential for harm reduction
  - Alcohol intake, vaccinations, secondary transmission, treatment
- Treatment reduces long-term adverse outcomes
- Treatment benefit will improve further as Sustained Virology Rate (SVR) increases

**Reference**: http://www.thebody.com/content/art44397.html, accessed 7/26/10.

# HCV Screening Cost Effectiveness Modeling

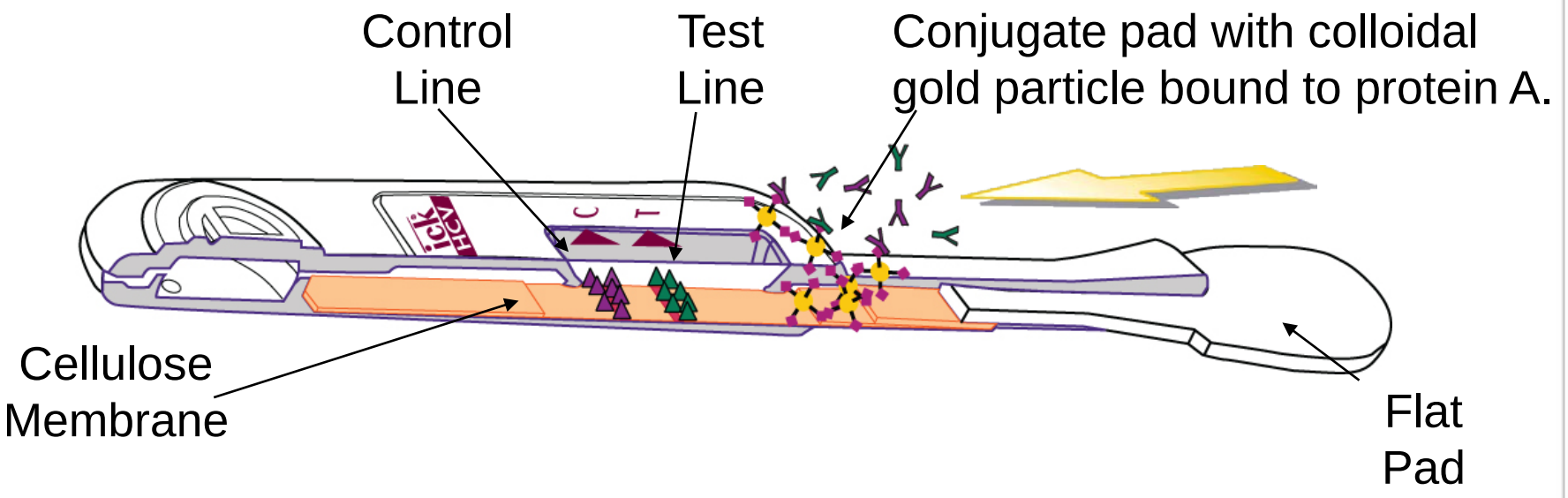
- Based on 2005 to 2006 NHANES data, an estimated 2.8 million Americans in primary care are chronically infected with HCV
- Without enhanced interventions to identify and treat, we estimate that of these 2.8 million
  - 1.47 million will develop cirrhosis (scarring of the liver)
  - 546,000 will develop decompensated cirrhosis
  - 350,000 will develop liver cancer
  - 115,000 will receive liver transplants (if sufficient donor livers are available)
  - 897,000 will die from complications of hepatitis C

# OraQuick® Rapid HCV Antibody Test

- Test with Ease and Convenience
  - The only FDA-approved rapid HCV test for use with:
    - Fingerstick whole blood
    - Venipuncture whole blood
  - Results in just 20 minutes
  - Clinical performance with >98% accuracy

# OraQuick® HCV Clinical Features
# Operating Principle

- Anti-Human Antibody
- HCV Antigen
- Colloidal Gold Conjugated to Protein A
- Human Antibodies
- HCV Antibodies




Using a lateral flow process, a sample specimen is wicked up by the flat pad of the device and transferred to the cellulose membrane. Human antibodies and HCV antibodies (if present) bind to the colloidal gold particles.

# OraQuick® HCV Clinical Features
# Operating Principle

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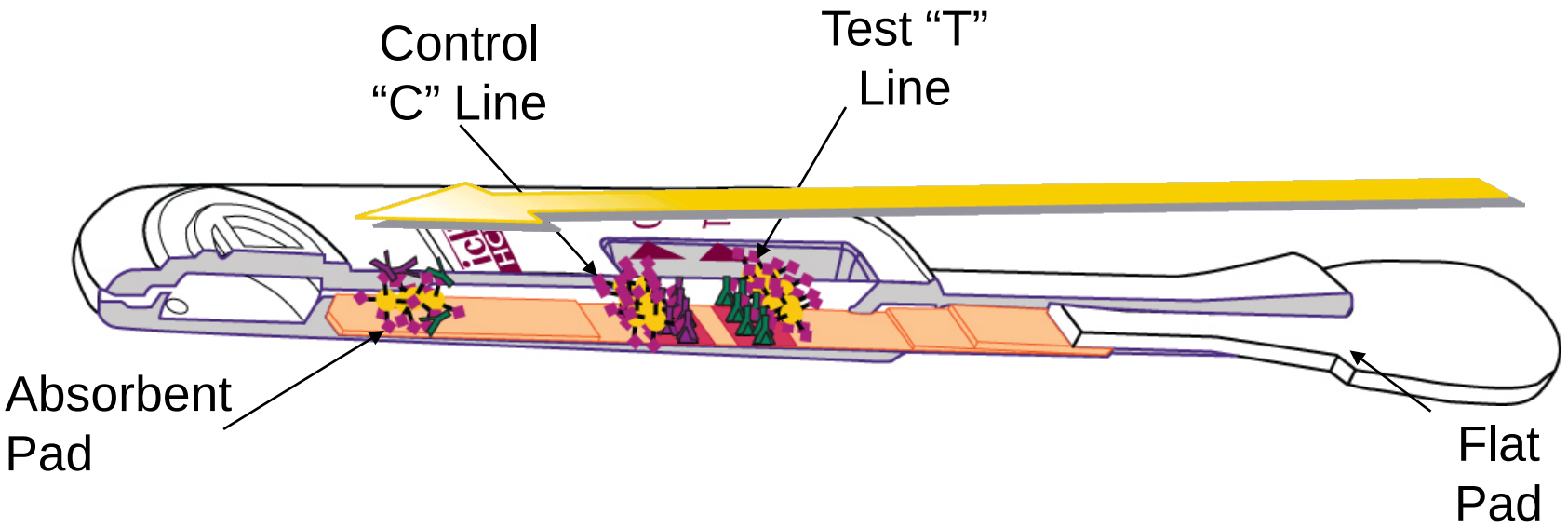
- HCV Antigen
- Colloidal Gold Conjugated to Protein A
- Human Antibodies
- HCV Antibodies




Colloidal gold particles containing HCV antibodies bind to the HCV antigen "T" line forming a visible red band. Colloidal gold particles containing Human antibodies bind to the Anti-Human Antibodies "C" line forming a visible red band. Any remaining colloidal gold particles are captured and retained by the absorbent pad.

# OraQuick® HCV Clinical Features Product Training

# Intended Use

- The OraQuick® Rapid HCV Antibody Test is a single-use, qualitative immunoassay to detect antibodies to Hepatitis C Virus (anti-HCV) in fingerstick whole blood and venipuncture whole blood specimens (EDTA, sodium heparin, lithium heparin and sodium citrate) from individuals 15 years or older.
- For *in vitro* diagnostic use.
- **Complexity**: Moderate for Fingerstick Whole Blood and Venipuncture Whole Blood.

# Clinical Performance- Positive & Negative Agreement

- In the case of HCV tests, clinical performance is defined by the terms *positive agreement* and *negative agreement.*
- These are essentially synonymous with the terms sensitivity and specificity
- They define the % of truly HCV positive subject that a test correctly identifies as anti-HCV reactive and the % of HCV negative subjects that a test correctly identifies as nonreactive for anti-HCV antibodies.
- Positive and negative agreement for both venous blood and fingerstick were assessed by prospective testing of populations at risk for HCV or with signs and symptoms of hepatitis.
- HCV serostatus of these subjects was independently determined by FDA approved laboratory tests (EIA, RIBA and PCR).

# Venipuncture Whole Blood Performance Claims

- The percent of positive agreement and negative agreement between OraQuick® HCV and the subject HCV infected status was calculated for the analysis population (n=1207).

| Percent Positive Agreement and Percent Negative Agreement According to Risk | | | | | |
|---|---|---|---|---|---|
| **Study Subjects** | **Total** | **Percent Positive Agreement** | **95% Exact Confidence Interval** | **Percent Negative Agreement** | **95% Exact Confidence Interval** |
| Overall | 1207 | 99.5%* (435 / 437) | 98.4%, 99.9% | 99.0%* (762 / 770) | 98.0%, 99.6% |

*Includes subjects with "unable to determine" status

# Venipuncture Whole Blood Performance Claims

- Of the 1207 subject specimens tested, 436 were HCV infected, 762 were negative, and 9 specimens had the status of “Unable to Determine”.

| OraQuick® HCV Rapid Antibody Test Results | Subject HCV Infected Status | | |
|---|---|---|---|
| | Positive | Negative | Unable to Determine Infected Status |
| Positive | 435 | 0 | 8 |
| Negative | 1 | 762 | 1 |
| Invalid | 0 | 0 | 0 |

# Positive Predictive Value: Venipuncture Whole Blood

The following were the supplemental test results when subjects that were reactive by OraQuick® HCV in venipuncture whole blood were tested by RIBA

| Number of OraQuick® Reactive Results | RIBA Results | | |
|---|---|---|---|
| | Positive | Indeterminate | Negative |
| 443 | 418 | 25* | 0 |

* Seventeen (17) of the RIBA indeterminate results were positive for HCV RNA when tested by PCR.

These data indicate that the positive predictive value of OraQuick® HCV in this high prevalence (36%) population was 98% (435/443)

# Fingerstick Whole Blood Performance Claims

- The percent of positive agreement and negative agreement between OraQuick® HCV and the subject HCV infected status was calculated for the analysis population (n=1660).

| Percent Positive Agreement and Percent Negative Agreement According to Risk | | | | | |
|---|---|---|---|---|---|
| **Study Subjects** | **Total** | **Percent Positive Agreement** | **95% Exact Confidence Interval** | **Percent Negative Agreement** | **95% Exact Confidence Interval** |
| Overall | 1660 | 97.9%* (708 / 723) | 96.6%, 98.8% | 98.5%* (923 / 937) | 97.5%, 99.2% |

*Includes subjects with "unable to determine" status

# Fingerstick Whole Blood Performance Claims

- Of the 1690 subject specimens tested, 719 were HCV infected, 926 were negative, and 15 specimens had the status of “Unable to Determine”.

| OraQuick® HCV Rapid Antibody Test Results | Subject HCV Infected Status | | |
|---|---|---|---|
| | Positive | Negative | Unable to Determine Infected Status |
| Positive | 708 | 3 | 11 |
| Negative | 11* | 923 | 4 |
| Invalid | 0 | 0 | 0 |

*6 of the 11 were negative for HCV RNA by PCR.

# Positive Predictive Value: Fingerstick Whole Blood

The following were the supplemental test results when subjects that were reactive by OraQuick® HCV in fingerstick whole blood were tested by RIBA

| Number of OraQuick® Reactive Results | RIBA Results | | |
|---|---|---|---|
| | Positive | Indeterminate | Negative |
| 722^ | 690 | 29* | 2 |

^ Eighteen (18) of the RIBA® indeterminate were positive for HCV RNA when tested by PCR.
* One (1) subject reactive by OraQuick® did not have RIBA® or PCR completed.

These data indicate that the positive predictive value of OraQuick® HCV in this high prevalence (43%) population was 98% (708/722)

# Seroconversion Panels

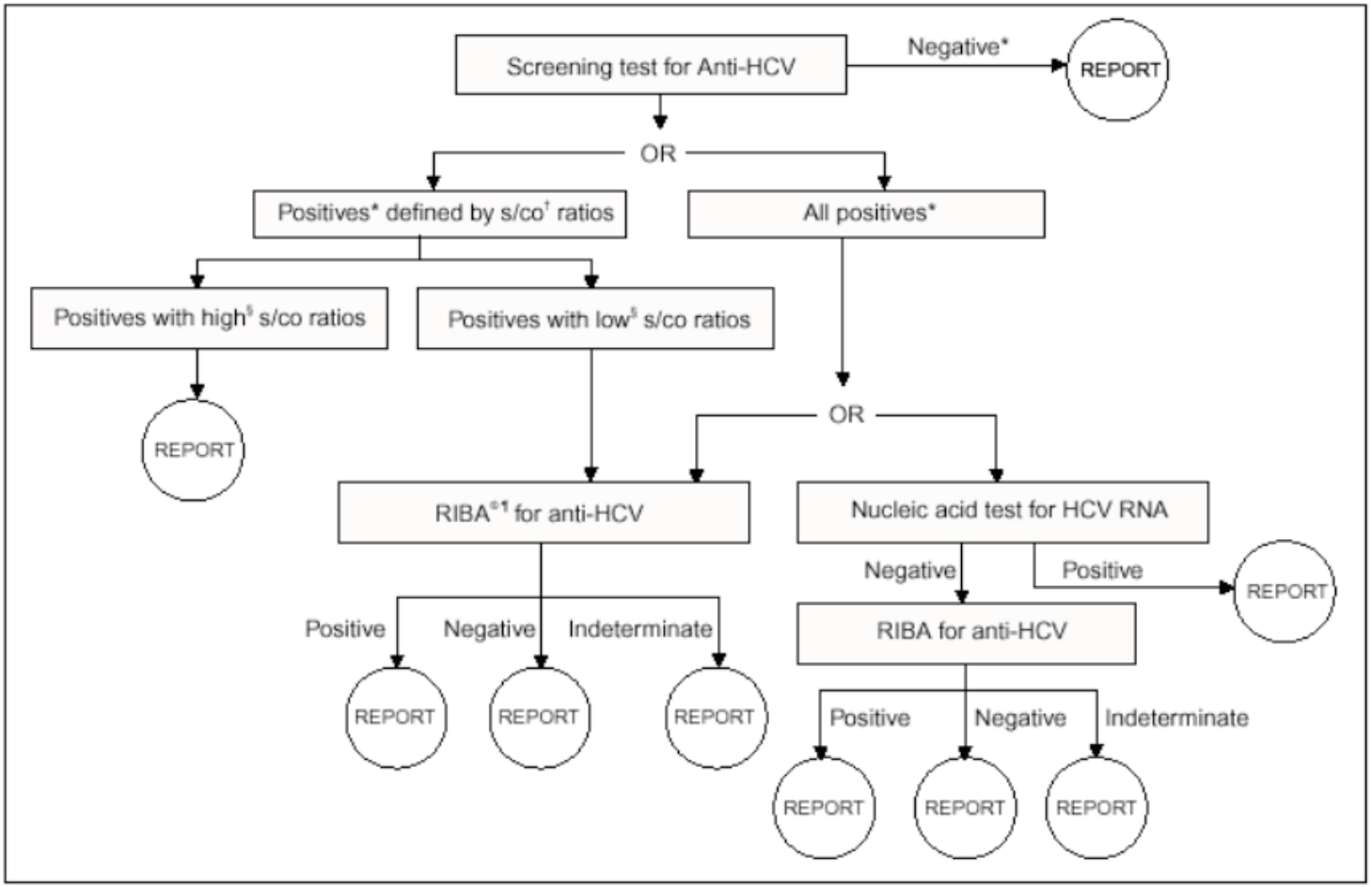
OraQuick® HCV seroconversion results compared to FDA-approved EIA were as follows:

- OraQuick® HCV was able to detect antibodies earlier than the approved

| | Days to Evidence of HCV Infection | | |
|---|---|---|---|
| | OraQuick® HCV Rapid Antibody Test | FDA-Approved anti-HCV EIA | |
| | Time to Detection | Time to Detection | Difference (OraQuick-EIA) |
| **Average** | **59.2** | **62.7** | **-3.6 (-5.9 to -1.2)** |

# Supplemental Testing Algorithms for HCV

- This illustrates the current CDC testing algorithm for HCV as recommended by CDC.



# OraQuick® Rapid HCV Antibody Test Kit

- Single-use testing device with built-in procedural control
- Single-use test developer solution vial
- Reusable test stand
- Disposable single-use specimen collection loop

# Additional Materials Required


- ☑ Timer or Watch
- ☑ Biohazard Waste Container
- ☑ Disposable, Absorbent Workspace Cover

**Additional Required Phlebotomy Materials (Whole Blood):**

- ☑ Disposable Gloves
- ☑ Sterile Lancet
- ☑ Phlebotomy materials
- ☑ Centrifuge
- ☑ Antiseptic Wipe
- ☑ Sterile Gauze Pads

# Test Kit Configurations

| Kit Size | 25 Count | 100 Count |
|---|---|---|
| **Item No.** | **1001-0181** | **1001-0180** |
| Test Devices | 25 | 100 |
| Reusable Test Stand | 5 | 10 |
| Specimen Collection Loops | 25 | 100 |
| Package Insert | 1 | 1 |

| | |
|---|---|
| Storage Requirements | 2-30°C (36-86°F) |
| Operating Requirements | 15-37°C (59-99°F) |
| Test Sample Type | Fingerstick or Venipuncture Whole Blood |
| CLIA Complexity | Moderate |
| Test Type | Qualitative Immunoassay |
| CPT Code | 86803-QW |
| Shelf-Life | 18 Months from Date of Manufacture |

# Prior to Testing

- Remember to observe “Universal Precautions” at all times.
- Read the package insert instructions *first*.
- Gather testing materials.
- Allow the test to come to operating temperature.
- Set up workspace cover and reusable Test Stand on a flat level surface.
- Put on disposable gloves if working with blood specimens.

# General Test Preparation

- Open two chambers of Divided Pouch by tearing at the notches.
- Leave the Test Device in the Pouch.
- Remove the Developer Vial. Gently rock the cap back and forth to remove.
- Slide the Vial into the top of one of the slots of the Stand. Make sure it is seated in the stand.

# Specimen and Test Performance

- Fingerstick whole blood
- Venous whole blood

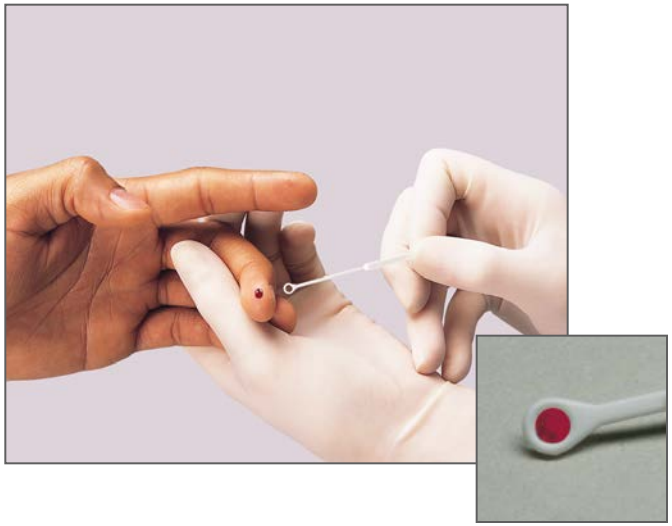
# Fingerstick—Specimen Collection



- Remove test device from Pouch. **DO NOT** touch the Flat Pad.
- Make sure an Absorbent Packet is present. If no Absorbent Packet is present, discard Device; obtain a new Pouch for testing.
- Label device with subject's ID information. **DO NOT** block holes on back of device.

**NOTE:** Test Device must be inserted into Vial within 60 minutes of sample introduction.

# Fingerstick—Specimen Collection



- Use an antiseptic wipe; clean finger of person being tested. ***Dry completely.***
- Using sterile lancet, puncture skin off center of finger pad.
- **WIPE** first droplet with gauze. Hold the hand downward for new droplet. Gently apply pressure to express if needed.
- With new Specimen Collection Loop, touch to droplet.
- *Make sure Loop is completely filled with blood.*

# Fingerstick—Mixing Specimen

- Insert blood-filled end of Loop into the vial. **Be careful not to touch the sides of the vial.**
- Use Loop to stir sample in Vial. Dispose of used Loop in biohazard waste container.
- Check Solution to make sure it appears pink in color.

# Fingerstick—Test Performance


- Insert Flat Pad of device into the bottom of Developer Vial.
- Start timing test.
- Pink fluid will travel up Result Window. Fluid disappears as test develops. **DO NOT** remove device while test is running.
- Read results after 20 minutes but ***not more*** than 40 minutes. Adequate lighting must be available.

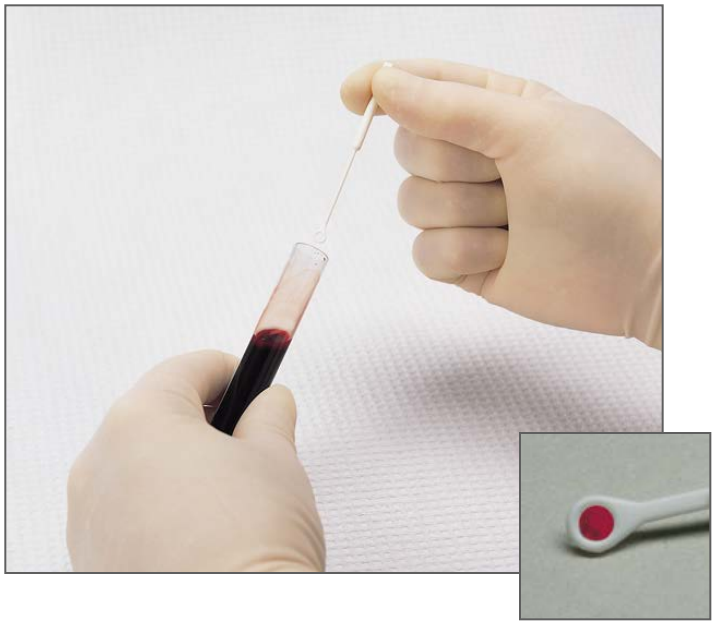
# Whole Blood—Specimen Collection



- Remove test device from Pouch. **DO NOT** touch the Flat Pad.
- Make sure an Absorbent Packet is present. If no Absorbent Packet is present, discard Device; obtain a new Pouch for testing.
- Label device with subject's ID information. **DO NOT** block holes on back of device.

**NOTE:** Test Device must be inserted into Vial within 60 minutes of sample introduction.

# Whole Blood—Specimen Collection



- Using standard phlebotomy procedures, collect whole blood sample with an EDTA, sodium heparin, lithium heparin, or sodium citrate test tube.
- Mix blood tube by inversion.
- With new Specimen Collection Loop, dip Loop into test tube.
- Visually inspect the Loop to make sure that it is completely filled with a specimen.

# Whole Blood—Mixing Specimen

- Insert blood-filled end of Loop into the Vial. **Be careful not to touch the sides of the Vial.**
- Use Loop to stir sample in Vial. Dispose of used Loop in biohazard waste container.
- Check Solution to make sure it appears pink in color if using whole blood.

# Whole Blood—Test Performance


- Insert Flat Pad of device into the bottom of Developer Vial.
- Start timing test.
- Pink fluid will travel up Result Window. Fluid disappears as test develops. **DO NOT** remove device while test is running.
- Read results after 20 minutes but ***not more*** than 40 minutes. Adequate lighting must be available.

# Test Reading & Interpretation

- Non-reactive result
- Reactive result
- Invalid

# Reading a **Non-Reactive** Test


## A test is NON-REACTIVE if:

- A line appears in the “C” zone and no line appears in the “T” zone.

# Interpreting a **Non-Reactive** Test


A **Non-Reactive** test result means that HCV antibodies were not detected in the specimen.

Patient is presumed not to be infected with HCV**.**

# Reading a **Reactive** Test


## A test is REACTIVE if:

- A line appears in the “C” zone **and** a line appears in the “T” zone. Lines may vary in intensity

**NOTE:** The test is reactive if any line appears in the “T” zone **and** in the “C” zone, no matter how faint.

# Interpreting a **Reactive** Test


A **Reactive** test result means that HCV antibodies have been detected in the specimen.

The patient is presumed to be infected with HCV.

Individuals with a reactive result should undergo appropriate clinical follow-up according to CDC recommendations for supplemental testing.

# Reading an **Invalid** Test


**A test is INVALID if:**

- No line appears in the “C” zone, **or**
- A pink background in the result window makes it difficult to read the result during the 20 to 40 minute read times, **or**
- If any of the lines are **partially developed** on one side of the “C” or “T” zones

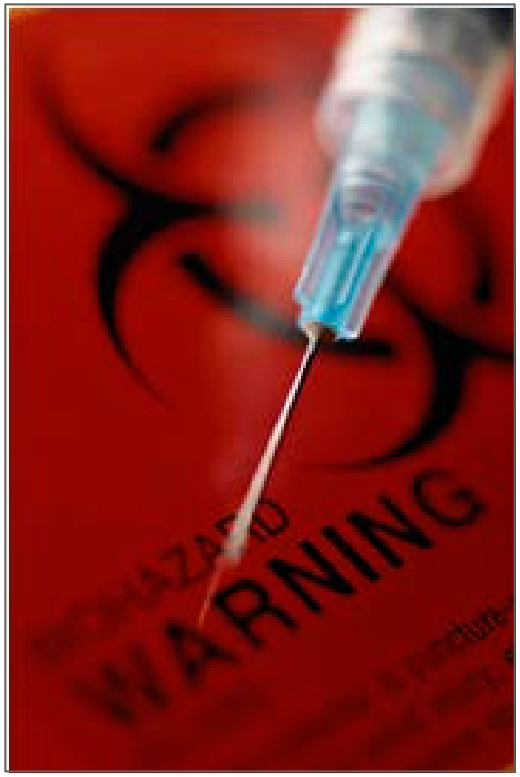
# Interpreting an **Invalid** Test


An **Invalid** test result means that there was a problem running the test, either related to the specimen or to the Device.

**IT CANNOT BE INTERPRETED.**

Repeat test with a new Pouch and a fingerstick or venipuncture whole blood, sample.

# General Test Clean-Up




- Dispose of the used test materials in a biohazard waste container.
- When using gloves, change your gloves between each test to prevent contamination. Throw away the used gloves in a biohazard waste container.
- Use a freshly prepared 10% solution of bleach to clean-up any spills.

# Quality Control

- Positive and Negative Kit Controls provide:
  - Quality Control to:
    - Assure test performance
    - Provide for user proficiency
- Positive Controls
  - Are calibrated specifically to a very low assay reactivity level (challenge line)
    - Low assay performance reaffirms assay functionality (assay chemistry)
    - Provide better training tool for user proficiency

# OraQuick® Rapid HCV Antibody Test Kit Controls

## Positive Controls

- Purple-capped vial—inactivated human plasma positive for antibodies to HCV.

## Negative Control

- White-capped vial—human plasma negative for antibodies to HCV.

Sufficient volume for a minimum of 25 tests.

# Test Kit Control Contents

| #1001-0182 OraQuick® HCV Rapid Antibody Test Kit Controls | |
|---|---|
| Positive HCV Control Vial (Purple Cap) | (1) 0.2mL |
| Negative Control Vial (White Cap) | (1) 0.2mL |
| Package Insert | 1 |
| Storage Requirements | 2-8°C (35-46°F) |
| Shelf-Life | 1 Year from Date of Manufacture or 8 weeks after initial opening of packaging |

**Note:** Kit Controls do not have to be brought to operating temperature prior to performing quality control testing.

# Test Kit—Kit Controls

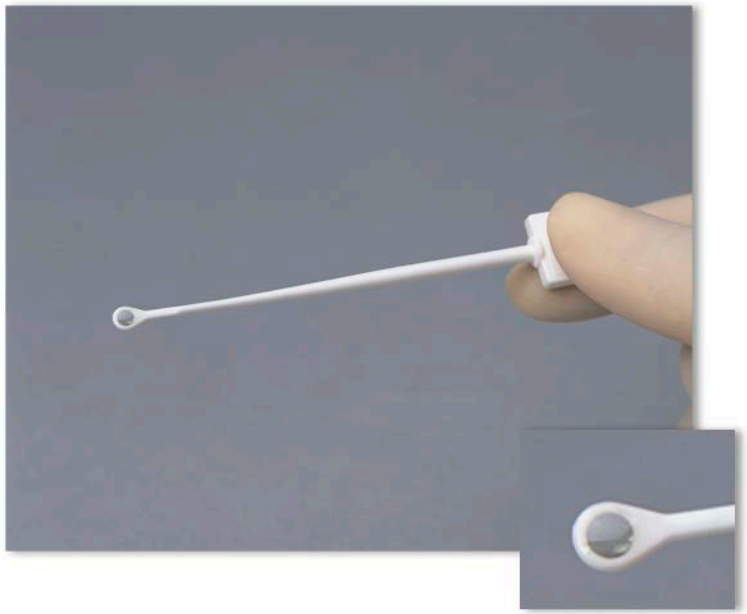
## Run one positive HCV control (+), and one negative control (-) for:

- Each new operator
- Each new lot of test kits
- Each new shipment of test kits
- Test kit storage temperature falls outside 2-30°C; 36-86°F
- Testing area temperature falls outside of 15-37°C; 59-99°F
- At periodic intervals dictated by user facility

# Performing Kit Controls

- Getting Started
  - Remember to observe “Universal Precautions” at all times.
  - Follow directions for setting up workspace.
  - Label devices for Negative and Positive Controls.
    **DO NOT** block holes on back of device.
    **DO NOT** touch Flat Pad of device.

# Performing Kit Controls



- Open a Kit Control vial.
- Insert round end of a new Specimen Collection Loop into the reagent vial.
- Remember to use separate unused Loop for each control reagent.

**NOTE: The Kit Control reagents are clear to straw-colored. Do not use if the reagent appears cloudy or discolored.**

# Performing Kit Controls

- Immerse Loop into Developer Solution Vial.
- DO NOT touch side of Vial.
- Use the Loop to stir contents.
- Discard Loop in a biohazard waste container.

# Performing Kit Controls


- Retrieve correct labeled device.
- Insert Flat Pad of device into the bottom of Developer Vial.
- Start timing test.
- Pink fluid will travel up Result Window. Fluid disappears as test develops. **DO NOT** remove device while test is running.
- Read results after 20 minutes but ***not more*** than 40 minutes. Adequate lighting must be available.

# Performing Kit Controls

**Example of a Non-Reactive Result (Negative)**

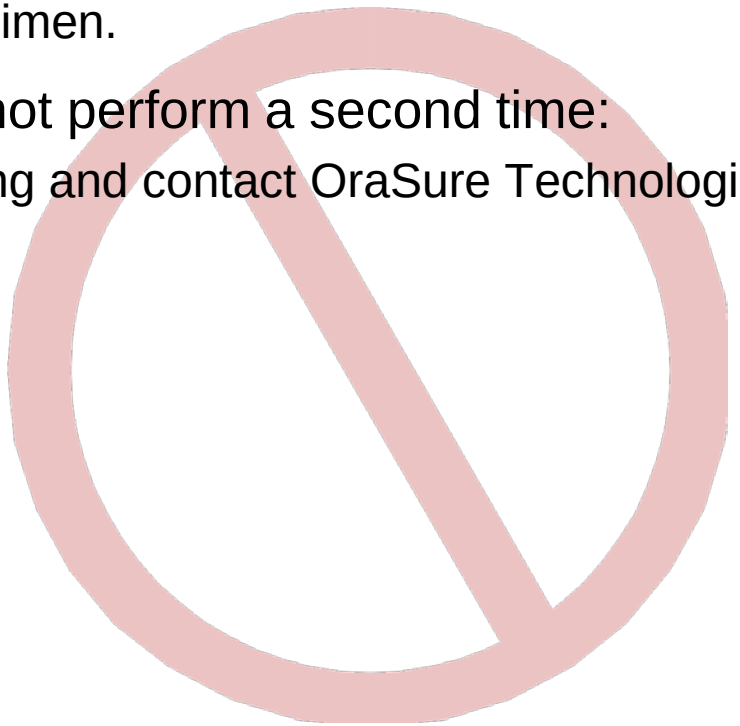

**Example of a Reactive Result (Positive)**


## Expected Results:

- Negative Control will produce a Non-Reactive test result. A line should be present at the “C” zone in result window.
- Positive Controls will produce a Reactive test result specifically manufactured to produce a faint (*Challenge Test*) “T” line. Lines should appear at “C” and “T” zones in result window.

# Kit Control Failure

- If test result does not perform as expected:
  - Repeat test using new Test Device, Developer Solution Vial, and Control Specimen.
- If test result does not perform a second time:
  - Discontinue testing and contact OraSure Technologies Customer Care.



# Universal Precautions
## Handling of Potentially Infectious Human Samples

- Before handling any specimens, please refer to your facility's procedures on universal precautions.
- Universal guidelines stress that all patients should be assumed to be infectious for blood-borne diseases such as HIV and hepatitis B.
- Barriers are used for protection against occupational exposure to blood and certain body fluids.
  - These barriers consist of:
    - Personal protective equipment (PPE)
    - Engineering controls
    - Work practice controls

# OraQuick® HCV Interpretation Quiz