Clinical and Procedure

Clinical Utility
The Hepatitis C Virus (HCV) NS5A Drug Resistance for Genotype 2 assay detects NS5 (nonstructural protein 5A) mutations and polymorphisms in HCV genotype 2 that are associated with resistance to direct-acting antivirals: pibrentasvir and velpatasvir found in antiviral combination therapies. The assay is intended to be used for patients with HCV viral loads who are being screened prior to treatment with the direct-acting HCV antivirals, or during treatment with these antivirals when drug resistance is suspected.

About HCV
HCV infection is the most common chronic bloodborne infection in the U.S., with approximately 3.2 million people chronically infected and an additional 17,000 (approx.) new infections acquired annually. Multiple drugs approved to treat HCV target the NS5A protein. Specific mutations in these genes have been implicated in resistance to various HCV antiviral drugs including: daclatasvir (Daklinza®), elbasvir (in Zepatier®), ledipasvir (in Harvoni®), ombitasvir (in Viekira Pak®, Viekira XR® and Technivie®), pibrentasvir (in Mavyret®), and velpatasvir (in Epclusa® and Vosevi®). Multiple mutations causing resistance to these FDA-approved HCV inhibitors have been defined, and the levels of increased resistance for each mutation have been calculated using HCV replicons or reporter constructs. Some of the mutations cause resistance to multiple NS5A inhibitors. Knowledge of these mutations is important in patients since an incomplete suppression of viral replication by an ineffective drug combination could prevent a sustained viral response (“cure”), and could readily support the development of antiviral drug resistance.

Procedure
The HCV NS5A Drug Resistance assay utilizes RT-PCR amplification with primers in highly conserved viral genomic regions to amplify HCV genotype 2. The fragments are purified and sequenced using sequencing primers from conserved regions of the fragments. The sequence is compared to a database of mutations associated with antiviral resistance. This test has not been cleared or approved for diagnostic use by the U.S. Food and Drug Administration.

Turnaround Time
4-11 business days from receipt of specimen.

Specimen Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Order Code</th>
<th>CPT Code</th>
<th>NY Approved</th>
<th>Volume</th>
<th>Assay Range</th>
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</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>30702</td>
<td>87902</td>
<td>No</td>
<td>3 mL (min. 1 mL/viral load of 1000 IU/mL)</td>
<td>Resistant/Not Detected</td>
</tr>
<tr>
<td>Serum</td>
<td>30702</td>
<td>87902</td>
<td>No</td>
<td>3 mL (min. 1 mL/viral load of 1000 IU/mL)</td>
<td>Resistant/Not Detected</td>
</tr>
</tbody>
</table>

Special Instructions
- Collect 4-5 mL whole blood in EDTA, ACD or PPT.
- Centrifuge and transfer 3 mL plasma to a sterile, screw top tube.
- Ship frozen on dry ice Monday through Friday.
Mutations in the NS5A gene will be reported as Resistant/None Detected. Interpretation of gene mutations and association with antiviral resistance of the relevant antivirals will be listed.

Shipping
Ship Monday through Friday. Friday shipments must be labeled for Saturday delivery. All specimens must be labeled with patient's name and collection date. A Viracor Eurofins test requisition form must accompany each specimen. Multiple tests can be run on one specimen. Ship specimens FedEx Priority Overnight® to: Viracor Eurofins, 1001 NW Technology Dr., Lee's Summit, MO 64086.

Causes for Rejection
HCV RNA concentrations too low to allow antiviral resistance testing (see above for minimum volume and viral load), subtypes other than those indicated, whole blood frozen, specimens beyond their acceptable length of time from collection as listed in the specimen handling, or specimen types other than those listed.

Disclaimer
Specimens are approved for testing in New York only when indicated in the Specimen Information field above. The CPT codes provided are based on Viracor Eurofins interpretation of the American Medical Association's Current Procedural Terminology (CPT) codes and are provided for informational purposes only. CPT coding is the sole responsibility of the billing party. Questions regarding coding should be addressed to your local Medicare carrier. Viracor Eurofins assumes no responsibility for billing errors due to reliance on the CPT codes illustrated in this material.

References