Report

Re-Evaluation of HCV Ab Detection Kits Approved for Marketing in Japan

Committee for Evaluation of In Vitro Diagnostic Devices, National Institute of Infectious Diseases

INTRODUCTION

As of 2001, the Japanese Ministry of Health and Welfare (Ministry of Health, Labour and Welfare at present; MHLW) has approved approximately 30 diagnostic kits for detection of antibodies against various epitopes of HCV (Hepatitis C virus) in clinical settings. All of them are commercially available in Japan. In order to provide medical personnel with up-to-date information on each kit’s characteristics, such as its sensitivity and specificity, in order to enable them to choose appropriate HCV Ab (antibody) detection kits, National Institute of Infectious Diseases (NIID), according to the guidance of the MHLW, has re-evaluated the diagnostic kits provided by manufacturers/distributors. The present reports are the results of the re-evaluation of HCV Ab detection kits.

METHODS

HCV Ab detection kits evaluated in this study (Table 1)

In this study, we categorized HCV Ab detection kits into the following four groups according to principle/procedure used; (A) IRMA (Immunoradiometric assay), (B) Immunochromatography, (C) Agglutination/aggregation (including Passive Hemagglutination Test, Particle Agglutination Test, Latex Photometric Immunoassay, and Particle Agglutination Mediated Immunoassay, designated as PHA, PA, LPIA, and PAMIA, respectively), (D) EIA (Enzyme Immunoassay), (E) Mediated Immunoassay, designated as PHA, PA, LPIA, and PAMIA, respectively), (F) EV-FIA (Evanescent wavefluoro immunoassay), and (G) Latex Photometric immunoassay, and Particle Agglutination Test, Passive Hemagglutination Test, Particle Agglutination Test, Particle Agglutination Mediated Immunoassay, designated as PHA, PA, LPIA, and PAMIA, respectively), (D) EIA (Enzyme Immunoassay), (E) Latex Photometric immunoassay, and Particle Agglutination Test, Passive Hemagglutination Test, Particle Agglutination Test, Particle Agglutination Mediated Immunoassay, designated as PHA, PA, LPIA, and PAMIA, respectively), (F) EV-FIA (Evanescent wavefluoro immunoassay), and (G) RIBA (Immunoblot). These kits were also categorized into four groups according to another criterion, i.e., the HCV antigens utilized for detection of anti-HCV Ab, namely, Core Ab detection kit, 1st generation kit (NS3-NS4 protein), 2nd generation kit (NS3-NS4 protein + Core protein), and 3rd generation kit (NS3-NS4 protein + Core protein + NS5 protein). Listed in Table 1 are the product names, manufacturers/distributors, and assay objects.

Test Procedure

Test samples utilized in the present re-evaluation tests were as follows:

1. Negative samples: Eighteen HCV Ab-negative sera, which have been utilized at NIID for in-house qualification tests, and one HCV Ab-negative sample (Accurum I multi-marker negative control serum) purchased from Boston Biomedica Inc. (BBI), West Bridgewater, Mass., USA.

*Members of the Committee for Evaluation of In Vitro Diagnostic Devices are listed in the Appendix.

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RESULTS AND DISCUSSION

Results of each of the 25 kits, including three core Ab-detection kits (Nos. 1, 2, and 3), one 1st generation kit (No. 4), and one RIBA3 kit (No. 25), are shown in Table 2. As a whole, there are no noticeable differences in sensitivities as well as specificities between the 2nd and 3rd generation kits. In other words, we could not obtain any evidence indicating that the 3rd generation kits are more sensitive than the 2nd generation kits. These results support the previous suggestion that the inclusion of the NS5 antigen in the 3rd generation kits does not improve the specificities/sensitivities of the kits. Vervelen, K. et al. [1994]: Lancet, 343, 853-854. There are substantial differences in the sensitivities among kits within the same generation. It is likely that variation of some HCV antigens, other than the NS5 in the 3rd generation kits, might be responsible for such differences. For example, when the seroconversion panel PHV-906 was tested, the kit No.13 judged all the samples negative, although the same samples were judged positive by the kits No.10 and No.11, which belong to the same category as the kit No.13 (Table 2). On the other hand, when the PHV-907 panel was tested, the kit No. 13 seemed to be more sensitive than the kits No. 10 and No.11 (Table 2). These
Table 1.

(A) Core-Ab detection kit

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Manufacturer/Distributor</th>
<th>Method</th>
<th>Detection of HCV Ab in</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ortho HCV Core-Ab IRMA test</td>
<td>Mitsubishi Kagaku Medical, Inc.</td>
<td>IRMA</td>
<td>serum/plasma</td>
</tr>
<tr>
<td>2</td>
<td>SMITEST (HCV Core Ab) ELISA</td>
<td>MEDICAL &amp; BIOLOGICAL LABORATORIES CO., LTD.</td>
<td>EIA</td>
<td>serum/plasma</td>
</tr>
<tr>
<td>3</td>
<td>Lumipulse II Ortho HCV Core-Ab</td>
<td>FUJIREBIO INC.</td>
<td>CLEIA/CLIA</td>
<td>serum/plasma</td>
</tr>
</tbody>
</table>

(B) 1st generation kit

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
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<th>Method</th>
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</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Ortho HCV IRMA test</td>
<td>Mitsubishi Kagaku Medical, Inc.</td>
<td>IRMA</td>
<td>serum/plasma</td>
</tr>
</tbody>
</table>

(C) 2nd generation kit

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Manufacturer/Distributor</th>
<th>Method</th>
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</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>ABBOTT HCV PHA 2nd Generation</td>
<td>DAINABOT CO., LTD.</td>
<td>PHA</td>
<td>serum/plasma</td>
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<tr>
<td>6</td>
<td>SERODIA-HCV</td>
<td>FUJIREBIO INC.</td>
<td>PA</td>
<td>serum/plasma</td>
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<tr>
<td>7</td>
<td>Ortho HCV Ab PA test II Auto</td>
<td>FUJIREBIO INC.</td>
<td>PA</td>
<td>serum/plasma</td>
</tr>
<tr>
<td>8</td>
<td>Lumispot “Eiken” HCV-Ab</td>
<td>EIKEN CHEMICAL CO., LTD.</td>
<td>CLEIA/CLIA</td>
<td>serum/plasma</td>
</tr>
<tr>
<td>9</td>
<td>ABBOTT HCV EIA 2nd Generation</td>
<td>DAINABOT CO., LTD.</td>
<td>EIA</td>
<td>serum/plasma</td>
</tr>
<tr>
<td>10</td>
<td>IMx Abbott HCV</td>
<td>DAINABOT CO., LTD.</td>
<td>EIA</td>
<td>serum/plasma</td>
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<td>11</td>
<td>AxSYM Abbott HCV</td>
<td>DAINABOT CO., LTD.</td>
<td>EIA</td>
<td>serum/plasma</td>
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<td>12</td>
<td>Imuccheck F-HCV C50 Ab Kokusai</td>
<td>International Reagents Corporation</td>
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<td>serum/plasma</td>
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<td>13</td>
<td>DETECT-HCV</td>
<td>AZWELL Inc.</td>
<td>EIA</td>
<td>serum/plasma</td>
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<tr>
<td>14</td>
<td>ARCHITECT Anti-HCV</td>
<td>DAINABOT CO., LTD.</td>
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</table>

(D) 3rd generation kit

<table>
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<tr>
<th>No.</th>
<th>Name</th>
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<th>Method</th>
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<td>15</td>
<td>Quick CHASER HCV Ab</td>
<td>MIZUHO MEDIT</td>
<td>Immunochromato.</td>
<td>serum/plasma</td>
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<td>RANREAM HCV II EX</td>
<td>SYSMEX CORPORATION</td>
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<td>17</td>
<td>Ortho HCV Ab LIPA test</td>
<td>Mitsubishi Kagaku Medical, Inc.</td>
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<td>18</td>
<td>Ortho HCV Ab IRMA test III</td>
<td>Mitsubishi Kagaku Medical, Inc.</td>
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<td>19</td>
<td>Ortho HCV 3.0 ELISA TEST SYSTEM with Enhanced SAVe</td>
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<td>EIA</td>
<td>serum/plasma</td>
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<td>20</td>
<td>ABBOTT EIA 3.0</td>
<td>DAINABOT CO., LTD.</td>
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<td>21</td>
<td>Cobas Core Anti-HCV EIA</td>
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<td>22</td>
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<td>EV-FIA</td>
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<td>ABBOTT PRISM HCV</td>
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<td>CLEIA/CLIA</td>
<td>serum/plasma</td>
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<td>24</td>
<td>Lumipulse II Ortho HCV</td>
<td>FUJIREBIO INC.</td>
<td>CLEIA/CLIA</td>
<td>serum/plasma</td>
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<td>25</td>
<td>CHIRON RIBA 3.0 Strip Immunoblot Assay (SIA)</td>
<td>Ortho Clinical Diagnostics K.K.</td>
<td>RIBA (Immunoblot)</td>
<td>serum/plasma</td>
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Results may indicate that the kit No. 13 is more sensitive in detecting anti-Core Ab but less sensitive in detecting the NS3/NS4 antigens than the kits No. 10 and No. 11. It is suggested that kits within the same category differ in their ability for detecting HCV-related Ab, depending on the qualitative as well as quantitative differences in their utilization of HCV antigens as epitopes. This kind of difference is quite apparent when the seroconversion panel PHV-906, whose donor did not elicit the anti-Core Ab, was tested. The results indicate that there are substantial differences in capabilities of detecting the NS region antigens among various kits.

**CONCLUSION**

Since the HCV Ab detection kits available in Japan have in general been developed rather recently, they appear to be indistinguishable from each other with respect to their quality, whereas several kits, such as No.15 (immunochromatography), seem to have room for improvement. As already mentioned in the report regarding the re-evaluation of HBsAg detection kits, diagnosis of HCV infection should not rely solely upon the results obtained by a single HCV detection kit. Serological confirmatory tests such as the RIBA3 and/or tests for detection of HCV virus RNA should be utilized to obtain the final judgment.

Legends to Table 2.

Numbers 1 through 25 at the top of the charts indicate the serial numbers of the kits tested, and correspond to the numbers appearing in Table 1. Symbols:

- **☐** Negative.
- **■** Positive in duplicate assays.
- **▲** Positive in one assay and negative in the other.
- **□** +/- in one assay and negative in the other.
- **□** Indeterminate.
- **X** Not done.

Principle/procedure of the kits are indicated as alphabets:

- **a**: IRMA (Immunoradiometric assay)
- **b**: Immunochromatography
- **c**: Agglutination/aggregation (PHA / PA / LPIA / PAMIA)
- **d**: EIA (Enzyme immunoassay)
- **e**: CLEIA/CLIA (Chemiluminescent [enzyme] immunoassay)
- **f**: EV-FIA (Evanescent wave fluoro immunoassay)
<table>
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APPENDIX

The members of the committee are as follows:

Toshitada Takemori (Chairperson), Hiroshi Yoshikura, Takeshi Kurata, Toshio Kishimoto, Ichiro Kurane, Nobuhiro Okabe, Katsutoshi Komuro, Masahiro Sakaguchi, Tetsuro Suzuki, Masato Tashiro, Shu-ichi Nakayama, Toshiaki Mizuochi, Tatsuo Miyamura, Namiko Yoshihara, and Haruo Watanabe.

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