Hepatitis is an inflammation of the liver that can be caused by viruses, chemicals, drugs, alcohol, inherited diseases, or the patient’s own immune system. This inflammation can be acute, flaring up and then resolving within a few weeks to months, or chronic, enduring over many years. Chronic hepatitis may simmer for 20 years or more before causing significant symptoms related to progressive liver damage such as cirrhosis (scarring and loss of function), liver cancer, or death.

The symptoms of hepatitis are the same, regardless of the cause, but vary from person to person and may vary over time. With acute hepatitis, many people have few or mild symptoms that may be mistaken for the flu. These may include fatigue, nausea, loss of appetite, fever, and abdominal pain. Others may experience jaundice, itching, dark colored urine, and light colored stools.

A physical examination may reveal a liver that is tender and enlarged. Chronic hepatitis usually causes no symptoms or may be noticeable as only a loss of energy and tiredness. In some people, chronic hepatitis can gradually damage the liver and, after many years, cause liver failure. The chronic form typically lasts for many years and only rarely goes away without treatment.

Hepatitis A virus (HAV)

Hepatitis A refers to liver inflammation caused by infection with hepatitis A virus (HAV). Infections occur early in life where sanitation is poor and living conditions are crowded. Unlike hepatitis B and hepatitis C, hepatitis A does not cause chronic (ongoing, long-term) disease. Although the liver does become inflamed and swollen, it heals completely in most people without any long-term damage. Once infected with Hepatitis A, our body develops immunity towards this virus and it is unlikely to be infected with it again.

The Hepatitis A infection is caused by Hepatitis A virus (HAV) which is non-enveloped and contains a single-stranded RNA packaged in a protein shell.

The infection with HAV induces strong immunological response and elevated levels first of HAV IgM and then IgG are detectable within a few days after the onset of the symptoms.
The presence of anti-HAV IgM is an important serological marker for the detection of early infection and observation of the manifestation of the disease. Increasing levels of anti-HAV IgM are detectable about three weeks after exposure with highest titer after four to six weeks later. Within six months after infection IgM concentration declines to non-detectable levels.

HAV IgG antibodies develop later and remain present for many years. For this reason, HAV IgG is used to detect previous infections of Hepatitis A virus.

<table>
<thead>
<tr>
<th>HAV IgM</th>
<th>Total HAV Antibody (IgM and IgG)</th>
<th>Results Indicate</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>Acute HAV infection</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>No active infection, but previous HAV exposure; has developed immunity to HAV</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>Has been exposed to HAV but does not rule out acute infection</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>No current or previous HAV infection; vaccine may be recommended if at risk</td>
</tr>
</tbody>
</table>

Table 1. Typical interpretation of serologic test results for hepatitis A virus infection

Hepatitis B virus (HBV)

Hepatitis B virus (HBV) is a small double stranded DNA virus composed of an outer envelope containing hepatitis B surface antigen (HBsAg) and an inner nucleocapsid consisting of hepatitis B envelope antigen (HBeAg) and hepatitis B core antigen (HBeAg).

HBV infection can cause both acute and chronic hepatitis. Approximately 90% of adults who are infected will resolve the infection without permanent organ damage, while 10% becomes carriers and 6% progress to chronic disease. On the other hand, chronic infection occurs in 90% of infants infected at birth and in 30% of children infected between ages 1 and 5 years.

In Malaysia, about 5 to 8 percent of the population is chronically infected with hepatitis B, indicating that they are positive for hepatitis B virus surface antigen. In a survey carried out by Malaysia Liver Foundation, MLF, 50% of the hepatitis B carriers are infective, and of these 30 to 40% of them have evidence of liver disease.

After exposure to HBV, the virus enters an incubation period of 45 to 180 days. During this time, the patients will not show any symptoms or positive serologic results. The most common symptoms include nausea, anorexia, malaise and jaundice.

HBsAg is the first serologic marker which develops between 6 weeks and 6 months following an infection, but prior to onset of symptoms. Presence of HBsAg in serum may indicate acute HBV infection, chronic HBV infection, or asymptomatic carrier. In acute infection, HBsAg usually disappears within 1 to 2 months after onset of symptoms but persists in patients with chronic hepatitis.

Antibody to HBsAg, known as Anti-HBs, is detectable several weeks after the disappearance of HBsAg. The interval between the disappearance of HBsAg and appearance of anti-HBs is known as window period and may last as long as 6 months. The detection of this antibody normally shows clinical recovery and subsequent immunity to HBV. Since Anti-HBs may persist after the resolution of the infection, the detection of anti-HBs does not discriminate between current or previous infection.
Other important serologic markers for HBV include HBeAg, antibody to HBeAg (Anti-HBe), total antibody to HBcAg (Total anti-HBc) and IgM anti-HBc. These serologic markers play important roles not only in the detection of HBV but also in the interpretation of the different stages of HBV infection.

Table 2 shows how the combined results of different serologic markers reveal different interpretation of the stages of the HBV infection. The proper use of the serologic markers is important as it helps to give a clearer interpretation of the infection and thus reducing the possibility of a false diagnosis.

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Anti-HBc Total</th>
<th>Anti-HBc IgM</th>
<th>HbeAg</th>
<th>Anti-HBe</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td>Early HBV infection, asymptomatic</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Acute HBV hepatitis</td>
</tr>
<tr>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>Chronic HBV infection</td>
</tr>
<tr>
<td>+</td>
<td></td>
<td>-</td>
<td>+</td>
<td>-</td>
<td></td>
<td>Chronic HBV hepatitis, replicating</td>
</tr>
<tr>
<td>+/-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HBV exposure with recovery/immunity</td>
</tr>
</tbody>
</table>

Table 2. Typical interpretation of serologic test results for hepatitis B virus infection

**Hepatitis C virus (HCV)**

Hepatitis C Virus (HCV) is an RNA virus related to Flavivirus and has been implicated to be the major cause of transfusion viral hepatitis. HCV infection is viewed as serious because 40 to 50% of all patients with HCV infection would develop chronic liver disease. This infection results in a higher morbidity and mortality compared to HBV infection.

Despite this, HCV infection is a growing problem in Malaysia as more and more people are found to have the antibodies to hepatitis C through routine screening. In year 2000, there were 500 reported cases of hepatitis C in Malaysia and in year 2004, the number increased to 741 cases.

In 2007, The World Health Organization, WHO, estimated that about 180 million people are infected with the virus and 130 million of whom are chronic HCV carriers are at risk of developing liver cirrhosis and/or liver cancer. Besides that, HCV is also responsible for 50-76% of all liver cancer cases and two thirds of all liver transplants in the developed world.

One of the common markers of HCV is HCV antibody (anti-HCV). Since the introduction of this anti-HCV screening in blood donation in 1990, the incidence of this infection in transfusion recipients have been significantly reduced. Despite this, the screening of HCV antibody does not differentiate between acute, chronic or resolved infection. It is suggested that an HCV RNA test or recombinant immunoblot assay (RIBA) be performed on positive HCV antibody results as a confirmatory test.

Reference:
1. Hepatitis C-The Malysian Story, M.Sinniah, B.G.Ooi
ACCURUN® Serology Controls- Single Analytes

Features and Benefits:
- Available for most infectious disease analytes
- Specifically formulated for manual and automated platforms
- Liquid, ready to use
- Stable at refrigerated temperatures

Ordering Information:

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<th>Product</th>
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<td>Anti-HAV IgG</td>
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<td>Anti-HAV IgM</td>
<td>A121-5001</td>
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<tr>
<td>Anti-HBc IgM</td>
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<tr>
<td>Anti-Hbc Total</td>
<td>A115-5001</td>
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<td>Anti-HBe</td>
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</tr>
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<td>A117-5001</td>
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<td>HBsAg</td>
<td>A110-5001</td>
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<tr>
<td>Anti-HBs</td>
<td>A125-5001</td>
<td>1 x 5.0 mL</td>
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</tbody>
</table>

ACCURUN 1® Hepatitis Controls

Convenient Multi-Marker positive and negative controls for automated and manual immunoassay procedures

Features and Benefits:
- Human based controls
  - *Closely mimics a patient sample*
- Low reactive positive controls
  - *Detect immediate errors*
- Independent external run controls
  - *Monitor assay performance over time*
- Multiple package and fill sizes
  - *Convenience for manual and automated systems*

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<tr>
<th>Product</th>
<th>Fill Size</th>
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<tr>
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<td>A51-5001, A51-5005</td>
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<tr>
<td>Designed for use with HBeAg, HBc IgM, and HAV IgM assay systems</td>
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<tr>
<td>ACCURUN 52 Hepatitis Multi-Marker Control 2</td>
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<td>A52-5001, A52-5005</td>
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<tr>
<td>Designed for use with anti-HBe, anti-HBs, and anti-HAV test systems</td>
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</tr>
<tr>
<td>ACCURUN 810 Multi-Marker Negative Control</td>
<td>1 x 5 mL, 6 x 3.5 mL</td>
<td>A810-0001, A810-0005</td>
</tr>
<tr>
<td>Designed for use with HAV, HAV IgM, HBC, HBcIgM, HBe, HBeAg, HBs, HBsAg, HCV, HIV-1, HIV-2, HTLV I, HTLV II, RPR, Syphilis IgG, CMV total, Lyme IgG and Lyme IgM test systems</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kindly contact All Eights (your local distributor) at tel. no. (03) 5633 4988 for more information on Accurun 1 Multi-Marker controls.
For 35 years - An Essential Tool in External Quality Assessment (EQA)
and Quality Improvement Through Accurate Diagnostic Testing

Viral Markers (Cat No. 775)

Five challenges each.

HbsAb
HAV
HCV
HbsAg
HBeAg
Anti-HBc
Anti-HIV

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550 AmniSure Fetal Membrane Rupture Test

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790 Anti-HIV Challenges
791 Anti-HIV

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832 i-STAT Chemistry (2 challenges)
843 Direct Bilirubin
856 Blood Oximetry
857 Blood Oximetry (Add-On)
864 Thyroid Antibodies
Establishing Quality Control Means and Standard Deviations for Hematology Instrumentation

One of the regulations found in the Clinical Laboratory Amendments Regulatory (CLIA) Programme is the use of Quality Control (QC) materials to access the validity of patients’ results. Laboratories are required to ensure that the means and standard deviations meet or exceed the requirements given by these agencies.

According to the CLIA regulations for hematology instruments, a laboratory must test, at a minimum, two levels of third party control materials each day. For each QC procedure employed, the laboratory must have appropriate QC ranges. Besides that, CLIA deems it good laboratory practice for the individual lab to establish its own means and ranges.

The assayed mean and ranges provided by the manufacturer should only be used as guides in setting the initial control limits for testing new control materials. This is because, when compared to the assayed ranges, a laboratory may find that the range spans more than the commonly used +/- 2SD. This range may be too broad and may not be effective in the detection of clinically significant errors.

As a result, a laboratory should establish their own mean and ranges with the criteria that the calculated mean falls within the range listed by the manufacturer. All QC results for an individual laboratory do not need to fall within the given assay range.

The actual mean and standard deviation must be established by serial testing in the laboratory. The brief procedure below can be use:

1. Analyse the control a minimum of 20 times.
2. Calculate the average of these runs.
3. This average value should be within the range given by the manufacturer.
4. If the average mean is within the range, it will be considered as the “new mean”.
5. Calculate a two standard deviation from the new mean.
6. The mean and SD values should be recalculated periodically during the life of the control lot.

In an instrument that is working properly, the SD should not change significantly from lot to lot. Below is the procedure that can be used to set a preliminary mean until 20 runs have been completed from the new lot of control:

1. From the new lot, analyse the control 10 times.
2. Calculate the average of these runs.
3. This average values should be within the range given by the manufacturer and be considered as the “temporary mean”.
4. The established SD (from the same level of control) from the previous lot of control can be used as the “temporary SD”.
5. After 20 runs, the above procedure should be utilized to establish the actual mean for the lot of control.

When analysers with two sample modes are concerned, QC is required for each sample mode according to the parameters established in the hematology standards. This would mean performance of at least one control every eight hours of patient testing and performance of at least two levels of controls every 24 hours of patient testing.

Text excerpted from: Establishing Quality Control Means and Standards Deviations for Hematology Instrumentation, www.streck.com
Control and Calibrator

Multi-parameter assayed hematology control for instruments offering a three-part differential.

Para 12
- Control with three distinct population of lymphocytes, mononuclears and granulocytes
- Has low and high abnormal ranges to test the linearity of the instrument
- Assay includes the following instruments as well as manual methods:
  - Beckman Coulter MD Series, T Series and A·T™ Series, A·T diff™, A·T diff2™, Abbott CELL-DYN® 1400, 1600, 1700 and 1800, ABX Diagnostic Microm 60, Drew™ Datacel™ I 18, Datacel™ 18MS/18MS Plus, Datacell™ 16CP and Excell™ 16, InfoLab I-1800, I-1800MS/MS Plus, I-1600, and Excell 16, Mindray BC-3200
- Closed vial stability: 110 days
- Open-vial stability: 14 days

Cal-Chex
- Efficient, cost effective alternative to whole blood calibration procedures
- System specific values are available for many of the same instrument models for which Para 12 is assayed

Ordering Information:

<table>
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<tr>
<th>Para 12</th>
<th>Description</th>
<th>Catalog#</th>
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<td>218512</td>
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<tr>
<td>6 Low, 6 Normal, 6 High (w/Disk)</td>
<td>18 x 2.5 ml</td>
<td>218108</td>
</tr>
<tr>
<td>2 Low, 2 Normal, 2 High</td>
<td>6 x 2.5 ml</td>
<td>218506</td>
</tr>
<tr>
<td>6 Normal</td>
<td>6 x 2.5 ml</td>
<td>218516</td>
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<tr>
<td>* Other packing options are available</td>
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<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Cal-Chex</th>
<th>Catalog #</th>
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<tr>
<td>1 x 3.0 ml</td>
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<tr>
<td>3 x 3.0 ml</td>
<td>221103</td>
</tr>
<tr>
<td>1 x 3.0 ml w/disk</td>
<td>221100</td>
</tr>
</tbody>
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Hematology External Quality Assurance Programme

- Over 2000 number of participants worldwide
- 12 samples per cycle, 2 cycles per year
- Reports every 2 weeks

Parameters
- Haemoglobin (Hb)
- Haematocrit (HCT)
- Mean Cell Volume (MCV)
- Mean Cell Haemoglobin (MCH)
- Mean Cell Haemoglobin Concentration (MCHC)
- Platelets (PLT)
- Red Blood Cell Count (RBC)
- Total White Blood Cell Count (WBC)

As part of an ongoing development, RIQAS is launching a pilot study for 3 new parameters on the Hematology Programme. These new parameters are Red Blood cell Distribution Width (RDW), Mean Platelet Volume (MPV) and Packed Cell Volume (PCV).

Current RIQAS participants may register for this pilot study at no extra cost.

Ordering Information:

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<tbody>
<tr>
<td>RQ9118</td>
<td>RIQAS Hematology Programme</td>
</tr>
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</table>

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