Abstract
As the world’s population shifts toward increasing numbers of older citizens, long-held assumptions and methods in many fields are being reexamined. In the field of clinical test machines, Horiba has used its preeminent position and expertise in sensing technologies (especially in areas such as pH electrodes) to develop a wide variety of clinical test machines for the expanding market in human healthcare. The company has been very active in the fields of clinical blood testing and measurement since 1987 when Horiba introduced the ABX company’s automated blood cell counter to the Japanese market. The author describes the basic technology that supports Horiba’s clinical test machines, specifically the LC-270 automatic blood cell counter with CRP concentration measurement capability. The discussion concludes with four viewpoints on the company’s future product development efforts.
1. Introduction

In developed countries, the average life expectancy continues to rise and is now significantly longer than it was two generations ago. As a result of this trend, Japan expects to become a society made up of many more aging and elderly. Current trends suggest that by the year 2020 one fourth of the population will be 65 years old or older. By 2050, this number rises to one third.

As this situation develops, one of the crucial issues that the developed countries have to tackle is reducing the costs of providing medical care. Some nations, including the United States, have already started to reorganize their medical insurance systems. In 1983 the U.S. adopted a diagnosis-related-groups-based prospective payment system (DRG/PPS), and Japan is likely to follow.

While Japan reforms its healthcare system, the area of clinical test instruments is being forced to change radically. What is needed in the field is the development of tools that allow anyone to carry out fast and accurate examination regardless of time and location.

This report describes how Horiba, a manufacturer of analyzers and laboratory test instruments, is trying to meet the requirements for ideal testing machines and describes where the company is heading.

2. Development process

Horiba has brought a variety of analyzing instruments to the market since the company was founded in 1945. The analyzing technologies developed during this period have been applied to medical use.

In 1977 Horiba developed a first-in-the-industry, breakthrough product – the SERA series automatic electrolyte analyzer, which was capable of measuring sodium and potassium by using ion selective electrodes. This technology was an application of pH electrode technology, in which Horiba is a world leader. In 1987 Horiba entered the blood testing field by offering the blood cell counter developed by the French company ABX S.A.

The basic measurement principle of the ABX blood cell counter is the electric impedance method, in which the electric conductivity of a solution is measured. Measurement of electric conductivity of solutions is a key element of Horiba’s water analysis technology and experience with this technology has since helped the company develop and improve superior blood counter instruments.

At the same time, Horiba, in collaboration with Sankyo Co. Ltd., developed the Luminomaster™ model LE1A-2000, a fully automatic chemiluminescent EIA system, based on chemical luminescence analysis (CLA) technology. This product was based on the analysis technology for measuring atmospheric nitrogen oxides and automotive emissions in which Horiba had years of successful experience.

In addition to these sensing technologies, Horiba’s mechatronics technology, refined during the development of automatic samplers for benchtop pH/ion meters and reticle and mask contaminant inspection equipment, has been used in sampling-related applications.

3. Development of machines that can provide results promptly

Horiba has applied its analyzing technologies to products for use in medicine and the company expects to make future advances in this field. Horiba’s basic philosophy in terms of technology development will not change, but producing clinical test instruments takes more than advanced technology. In order to cope with a healthcare system that is on the verge of radical change, suppliers to the medical market should fully understand what is needed at the clinical level and take prompt action to meet these needs. Horiba, as a market leader, understands that the responsibility for the performance of clinical test machines rests primarily on the manufacturer.

The following sequence illustrates the typical steps that you may experience at a hospital when seeing a doctor:

You talk to a receptionist and are asked detailed questions about your condition and clinical history and your temperature is taken. If necessary, you may be asked to furnish a specimen for urinalysis. You then are sent to the consultation room, where you go through a set of diagnosis procedures including a check with a stethoscope. This may complete the consultation, but sometimes more steps are required. If the doctor thinks it is necessary, you will have your blood sampled and tested to confirm or rule out a suspected disease.

Recent clinical test instruments have high-speed processing capabilities and, unless a special procedure is required, it usually takes them only a few minutes to provide the result of a test after sample is set into the machines. Frequently the test instruments are placed in a remote area in the hospital or in a clinical examination center separate from the hospital. Because of this, it is
almost impossible to obtain the test results before the doctor finishes the consultation, and his or her diagnosis is usually made based on information other than the test results. There must be a large number of people who remember being told to visit the hospital again in the late afternoon or the next day. This delay creates inconvenience for patients and causes unnecessary anxiety. Patients want to have the cause of their symptoms accurately determined and receive proper medical treatment as soon as possible. From a manufacturer’s point of view, the demand for clinical test instruments that meet patients’ needs remains high.

4. Automatic blood cell counter and CRP measurement system

Horiba’s chief products for the clinical testing market are the LC series portable automatic blood cell counters. These machines are known as handy tools that can deliver immediate results in the presence of the patient. The FL-270CRP automatic blood cell counter and CRP measurement system has been gaining popularity as a handy test instrument for initial diagnosis since it was introduced to the market in 1998. The instrument can simultaneously count blood cells and measure the concentration of C-reactive protein (CRP) - an effective index for determining if a patient is suffering from acute inflammation.

The FL-270CRP (available through Fukuda Electric Corp.) uses measurement principles that are specifically suited to each type of measurement – the electric impedance method and the cyanmethemoglobin method for blood cell counting, and direct blood latex immunoturbidimetry for CRP. Horiba was the first in the industry to integrate these three different methods into one instrument. Before the introduction of the FL-270CRP, clinicians needed white blood cell counting and CRP measurement to diagnose inflammation, but the different measurement principles used to perform measurements were considered too unrelated or complicated to be covered by one unit.

Clinical test instruments currently in use come from many different branches of science and technology, and the variety of measurement technologies has led to an assumption that blood cell counting required a special unit using the electric impedance method, and CRP measurement required a separate unit using latex immunoturbidimetry. Based on this assumption, until recently blood cell counting and CRP measurement have been performed by separate specialized test machines. The FL-270CRP finally realized the physician’s dream and became the first unit ever to perform blood cell counting and CRP measurement at the same time – performance that allows small- to medium-scale hospitals to reduce costs and minimize benchtop space for clinical instruments.

One of the major benefits of the FL-270CRP instrument is that it works from a single sample of whole blood. A conventional instrument used several sample tubes containing different types of anticoagulants. The FL-270CRP uses only a single vacuum-type sample tube to extract the sample. As a result, a complicated serum separation process requiring the use of a centrifuge has been eliminated from the analysis procedure.

The outstanding features of the FL-270CRP place this instrument far ahead of those made by others. Users of the product benefit from design and performance improvements resulting from market research carried out at actual clinical testing sites by our sales department. (Visit our website for more information on the development of the FL-270CRP.)

While the FL-270 found wide use in many hospitals, growing numbers of physicians called for an even better product, one which could perform 3-part differential white blood counting. To meet this demand, in 1999 Horiba successfully developed the LC-170 automatic blood cell counter and CRP measurement system with a 3-part differential white blood counting function. This has extended the existing LC series, and allows Horiba to cover an even wider range of customers’ needs.

When it comes to the development of a clinical test instrument, the cost and performance of the machine are no longer the top priorities. What matters most is how the machine can contribute to the improvement of the total efficiency of the medical system. After all, a test device cannot be offered in the market without a demonstrated direct link to diagnosis and treatment – and diagnosis
and treatment are the essential parts of health care.

5. Four viewpoints that drive product development

In medicine, advances in analyzing living organisms and elements in vivo will continue in the future. However, what is needed for medical analysis is not just a device for measuring a certain item but a tool that serves many needs and helps improve the total medical system. In order to achieve the goal, manufacturers of clinical test machines should never fail to see things from the patients’ viewpoint. We believe that these items must be considered when developing clinical test instruments:

(1) Precision of the instrument

Accurate diagnoses will prevent unnecessary treatment and medication, leading to an improvement in the quality and a reduction in the cost of medical treatment. Horiba has confidence in making the most of its sensing technology to perform precise measurements.

(2) Early detection of disease

People are concerned with life-threatening diseases such as cancer and stroke, and debilitating diseases such as diabetes and osteoporosis. These concerns will result in growing demands for development and use of devices for early detection and early treatment of these diseases. Horiba has been developing an easy-to-operate analytical instrument that uses ultrasound to detect osteoporosis and the company expects this instrument will help clinicians detect the disease at an early stage so that treatment can begin promptly.

(3) Pain relief and reduction of costs

To achieve these goals, the clinical testing machine should use non-invasive or minimally invasive methods. Horiba’s current product line of automatic blood cell counters, including machines performing CRP measurements, are designed to make an accurate analysis using only a 10 µl blood sample. This means that instead of taking a blood sample using more costly and uncomfortable venipuncture methods, a tiny fingertip or earlobe blood sample may be used.

(4) Quality control

Illness can strike anywhere and anytime – this means that any clinical test instrument must be constantly operational. Although instruments require regular maintenance and occasional repair, the machines must be capable of performing around the clock. Horiba’s quality management system was certified as compliant with ISO 9001 in 1993. The company’s environmental management system was certified compliant to ISO 14001 in 1997 and since then Horiba has been working even harder to establish the highest quality control system to assure reliable products.

In addition to making quality control compliant with international standards, Horiba has been working on improving electromagnetic compatibility – an issue that has become important due to the rapid growth of sources of electromagnetic energy such as cellular phones and personal computers. Horiba has set several environment-related goals for new products under development, including a mandatory 5% reduction in power consumption.

6. Conclusion

This report has focused on compact blood cell counters as a way to summarize the basic technologies Horiba uses and our viewpoints on the development of Horiba’s clinical test instruments. Horiba’s attitude toward product development can be expressed in a short phrase: “harmonization of efforts to push the technological limit combined with thorough market surveys.” Horiba will keep making every effort to develop clinical products that help people improve and maintain their health.

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