CHAPTER 7.17

ELECSYS® IMMUNOASSAY SYSTEMS

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The Elecsys family of automated immunoassay systems was designed to meet the needs for cost efficiency and standardized testing across small-, medium-, and high-volume laboratories in integrated health care networks, hospitals, and independent laboratories. More than 40 analytes are currently available, including cardiac markers (including NT-proBNP), tumor markers, bone markers, infectious diseases, thyroid function tests, anemia, and fertility tests.

The Elecsys family includes the Elecsys 1010 System (Fig. 1), the Elecsys 2010 System (Fig. 2), and the E 170 Elecsys Immunoassay Module. The Elecsys 1010 System is designed for small- and medium-volume laboratories. It is also suitable for dedicated applications such as STAT testing. The Elecsys 2010 System is engineered for continuous, random-access operation in medium- to large-volume laboratories. For expanding workloads, the Elecsys 2010 System can be equipped for sample rack handling with the capacity for 100 samples. Based on the same five-position sample rack used on Roche chemistry systems, the Elecsys 2010 rack system facilitates sample flow by allowing sample racks to be transferred directly from the Elecsys 2010 System to Roche systems.

For high-volume laboratories, the E 170 Elecsys Immunoassay Module for MODULAR *SYSTEMS*™ offers a throughput of up to 510 tests/h and 100 reagent packs onboard. The E 170 can be configured as a stand-alone system with up to three modules or as part of MODULAR *ANALYTICS* (cobas e) for integrated chemistry and immunodiagnostics testing (Fig. 3). The cobas 6000 analyzer series offers tailored configurations using flexible combinations of the clinical chemistry (cobas c 501) module and immunochemistry (cobas e 601) module. This concept allows serum samples to be processed, from centrifugation and decapping to final results, without manual handling.

Every Elecsys system is designed for simplicity of operation, training, and maintenance. All systems use the same liquid, ready-to-use reagents, with the same packaging, making it easy to standardize operation procedures, and compare patient results across different laboratories in an integrated health network.

The Elecsys systems use electrochemiluminescence (ECL) detection technology, which was developed by IGEN International, Inc. In 2004, Roche acquired IGEN International. Elecsys instrumentation was developed jointly by Roche Diagnostics and Hitachi. Hitachi manufactures the Elecsys 2010 and E 170 systems.

Elecsys reagents are developed and manufactured by Roche. The Elecsys family was launched globally in 1996.

TYPICAL ASSAY PROTOCOL

The Elecsys technology is very flexible and can be applied to sandwich assays for high-molecular-weight analytes, competitive assays for haptens, bridge assays for antibody measurement, and DNA/RNA probes.

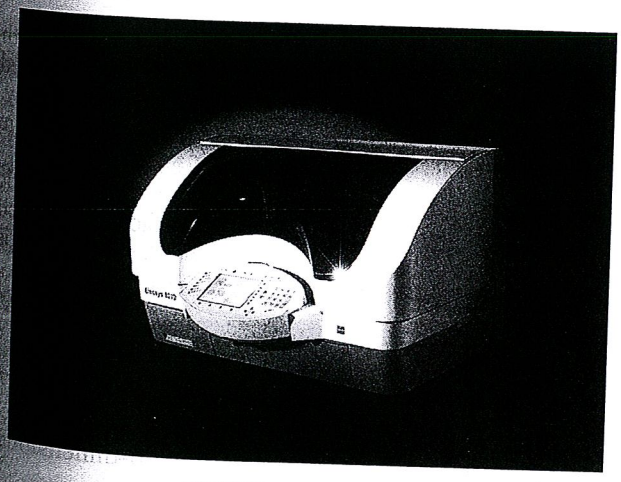

FIGURE 1 Elecsys 1010.

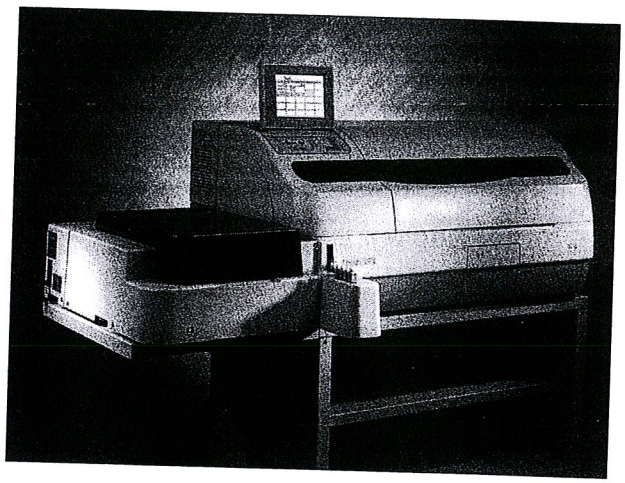

FIGURE 2 Elecsys 2010 rack system.

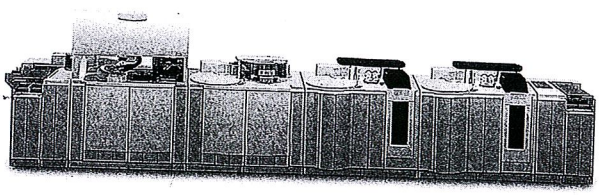

FIGURE 3 Integrated chemistry and immunochemistry MODULAR *ANALYTICS*.

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PRODUCT FEATURES

- Representative incubation times are 9 min for critical assays (e.g., CARDIAC T® troponin T assay, CK-MB, myoglobin, and hCG) and 18 min for routine tests.
- The Elecsys 1010 System features six assays onboard and a throughput of approximately 50 tests/h. There are 42 positions for primary tubes and 24 positions for secondary cups. STAT samples can be introduced into normal routine operation at any time and are assigned the highest priority for processing. Operator interface is *via* a graphical monitor with custom soft keys (Fig. 4).
- The Elecsys 2010 System features up to 15 assays onboard and a throughput of 88 tests/h. In addition to a 30-position sample disk, a 100-position rack is available. Primary tubes and secondary cups can be used without special adapters. STATs are processed with priority without interrupting the routine workflow. The operator interface consists of a color touch screen and customized keyboard (Fig. 5).
- E 170 Elecsys Module has a maximum sample throughput of 170 tests/h, and up to three modules can be connected in one system for a total throughput of 510 tests/h. As many as 25 different assays can be installed on each module. With three modules, the maximum number of reagent packs onboard is 75. STAT samples can be introduced at any time. Reruns are handled automatically. A single graphical interface controls up to six chemistry and/or E 170 modules plus ion-selective electrode (ISE).
- Liquid level detection, clot detection, and automated sample dilution are standard for all Elecsys systems.
- Liquid and ready-to-use reagents are available in packages of 100 or 200 test packs. Only two points are needed to confirm calibration since the master curve is encoded in the two-dimensional barcode on each reagent pack. Shelf-life of reagent kits is 18 months after manufacturing. Onboard stability for the majority of assays is 8 weeks.
- Elecsys systems provide programming-by-loading, a technology that initiates test and calibration selection when barcoded reagents and calibrators are placed on the system.
- All Elecsys systems support standard primary tube barcode symbologies.
- Disposable tips eliminate carryover.
- ECL technology provides a broad dynamic range, with a signal response that is linear over more than six orders of magnitude. Since the ECL reaction is initiated electrically, the imprecision inherent in enzyme detection systems is eliminated. The amplifying property of the label molecule permits the detection of extremely low concentrations of analyte.

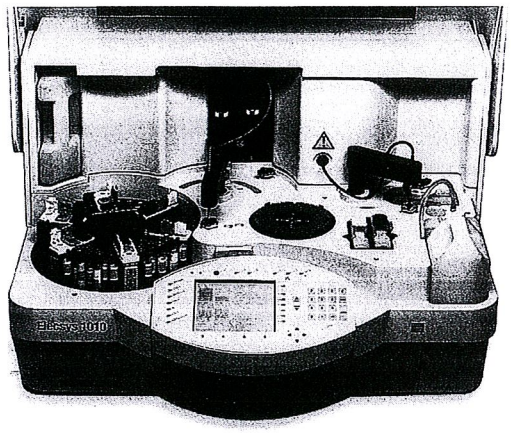

FIGURE 4 Elecsys 1010 System.

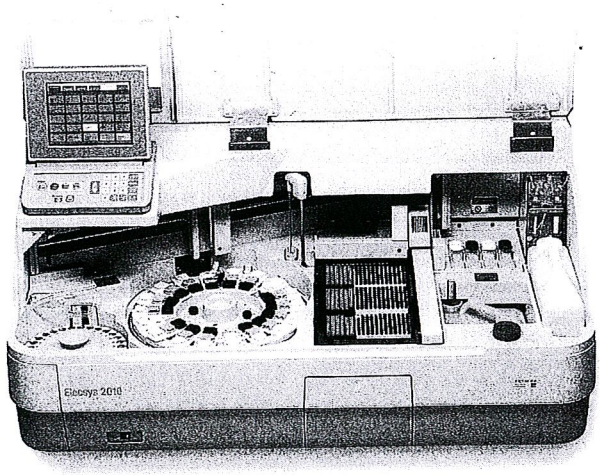

FIGURE 5 Elecsys 2010 Disk System.

ASSAY PRINCIPLE

The Elecsys assay combines conventional antigen–antibody reactions on the surface of a streptavidin-coated paramagnetic microparticle with electrochemical reaction on the surface of an electrode, which generates luminescence (Fig. 6).

- A biotin-labeled antibody and a ruthenium-labeled antibody are incubated with the sample analyte. An antigen or nucleic acid probe may be substituted for either antibody to accommodate other assay types.
- The immune complex is captured by the streptavidin-coated microparticles, which have a high biotin-binding capacity.
- Inside the ECL measuring cell, the microparticles with their bound immune complexes are uniformly deposited on the electrode. Unbound components are washed away.
- The sample analyte is quantitated by applying a voltage to the electrode and measuring the ECL signal.
- Once the ECL reaction is completed, the magnetic microparticles are released from the surface and washed away. The surface is thoroughly cleaned, and the cell is ready for another measurement (see Fig. 7).

CALIBRATION

Only two points are needed to confirm calibration since the master curve is encoded in the two-dimensional barcode on the reagent pack.

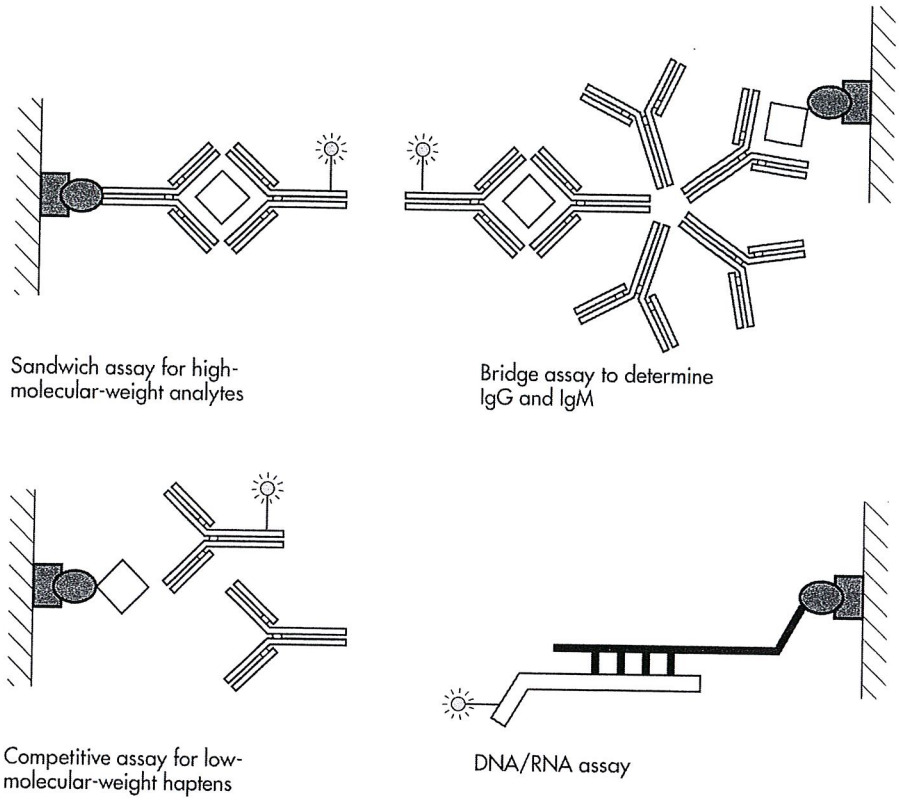

FIGURE 6 Elecsys assay formats.

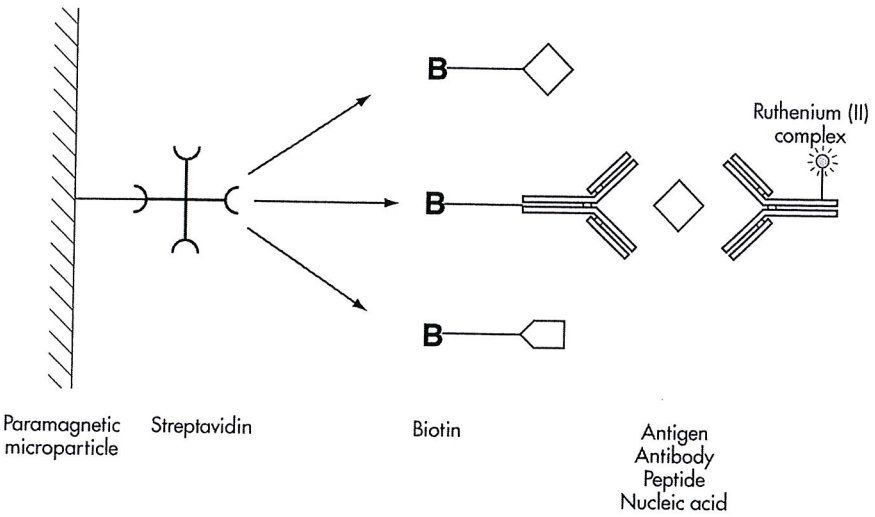

FIGURE 7 Elecsys assay principle.

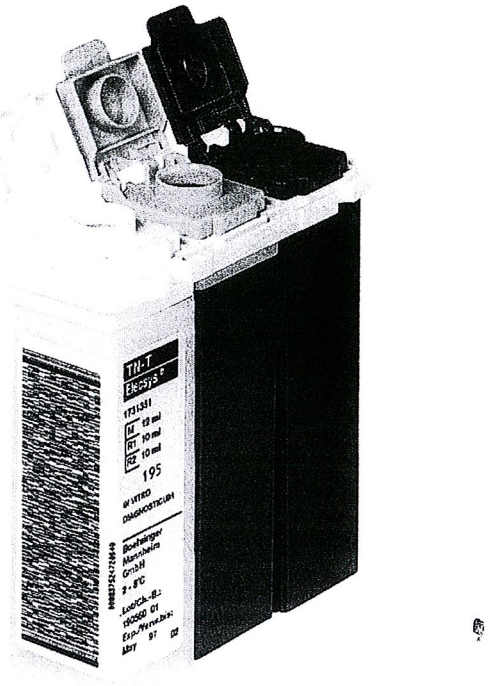

FIGURE 8 Elecsys reagent pack, showing two-dimensional barcode.

A lot-specific master calibration curve (n = 5 or 6) is generated at the manufacturing site using lot-specific test kit reagents and master calibrators. The data characterizing this curve are stored in the reagent barcode. Calibrator values are assigned based on the master calibration curve and are encoded in the calibrator barcode (Fig. 8).

At the customer site, results from the two-point calibration are combined mathematically with the encoded master curve data, based on which analyte concentration is calculated.

Calibration frequency varies but is typically once per lot, every month (same lot) or every 7 days (same kit on the system).

Antibodies

Antibodies are carefully selected to optimize assay performance. About 75% of the Elecsys assays use monoclonal antibodies. Examples are troponin T, thyroid stimulating hormone, and prostate-specific antigen. The remaining 25% use polyclonal antibodies selected for specificity to the analyte. Examples are triiodothyronine (T_3) and thyroxine (T_4). Monoclonal antibodies offer many advantages. Increased sensitivity and specificity along with consistency in manufacturing are primarily the reasons for the migration from polyclonal antibody use. Monoclonal antibodies, however, are more susceptible to heterophilic antibody interference than polyclonals. Elecsys assays that utilize monoclonal antibodies have additives to either minimize the effects of heterophilic antibodies or adsorb out the heterophilic reactive antibodies. In addition, the emergence of human/mouse chimeric antibodies has been shown to be more effective in neutralizing heterophilic interference than the addition of mouse serum or purified mouse IgG. The chimeric antibody, by its design, does not afford a binding site for the heterophilic antibody thereby eliminating the interference. The Elecsys carcinoembryonic antigen assay utilizes chimeric antibodies.

Separation

The streptavidin-coated microparticles bound with the antigen–antibody complexes are magnetically captured onto the surface of the working electrode by introduction of a magnetic field. A system buffer (ProCell) is used to wash the particles on the working electrode and to flush out the excess reagent and sample materials from the measuring cell.

Signal Generation and Detection

Two electrochemically active substances, the ruthenium label and tripropylamine (TPA), are involved in the reactions leading to the emission of light. The reactions occur at the electrode surface inside the measuring cell.

As an electrical potential is applied, the ruthenium label is oxidized at the electrode surface; simultaneously, TPA is oxidized to a radical cation that spontaneously loses a proton. The resulting TPA radical reacts with oxidized ruthenium, resulting in the excited state of the ruthenium label, which decays with the emission of a photon (620 nm). As the ruthenium label returns to ground state, it is regenerated and available to perform multiple light-generating cycles (Fig. 9).

The subsequent light emission is then detected by the photomultiplier tube and converted to an electrical signal based on which analytes are quantitated.

Data Processing

Data transmission to and from the analyzer, results evaluation, documentation, and quality control are performed automatically by the system software, which also manages the data interface with the laboratory information system (LIS).

Interfacing with LISs

Elecsys systems feature a bidirectional interface with host query capability for connecting to LISs.

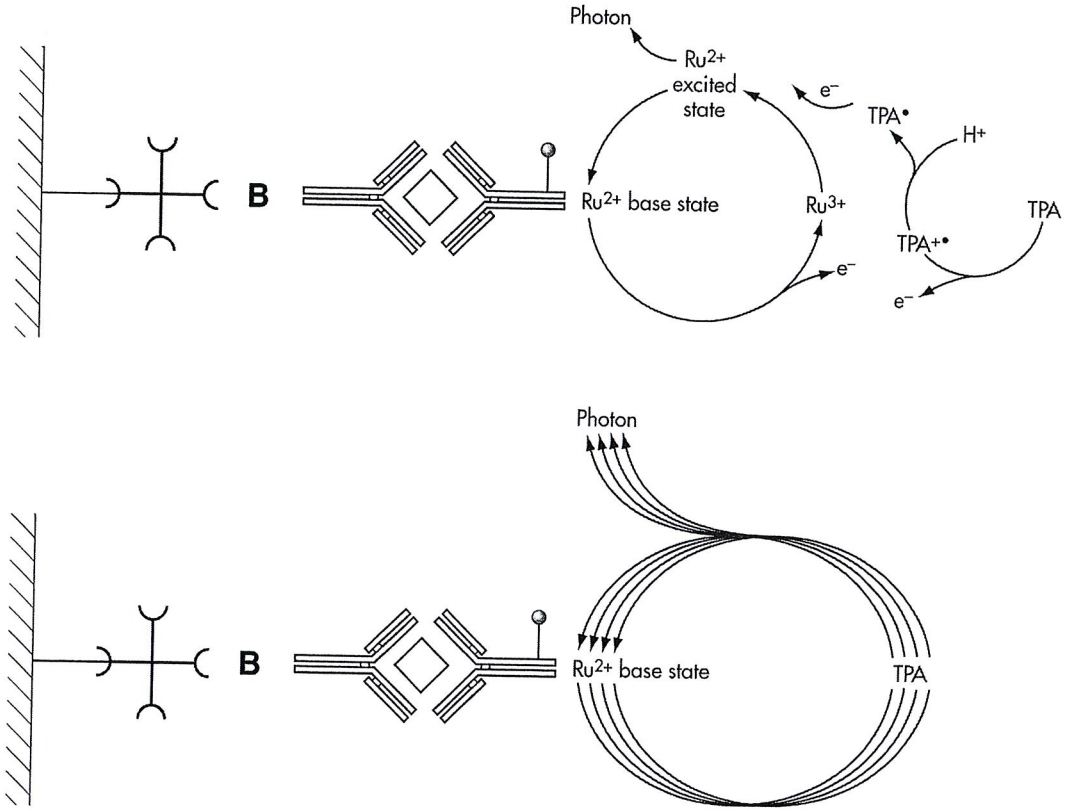

FIGURE 9 ECL signal generation and detection.

References and Further Reading

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