SCIENTIFIC CORPORATION

510(k) Summary

SEP - 9 1997

(a) (1) **Submitter's name, address**

AVL Scientific Corporation
33 Mansell Court
Roswell, GA 30076

Contact Person

Randy Byrd
Quality Assurance Manager
(770) 587-4040 x 631

Date of preparation of this summary: 16 July 1997

(2) **Device trade or proprietary name:** AVL OMNI™ Combi Analyzer

Device common or usual name or classification name

Fully automatic, modular analyzer for the analysis of:

pH, Blood Gases
ion-selective Sodium Potassium Chloride, ionized Calcium
hematocrit, total hemoglobin, hemoglobin derivatives, Glucose and Lactate

	CLASSIFICATION		
PRODUCT NOMENCLATURE	NUMBER	CLASS	PANEL
ELECTRODE, ION-SPECIFIC, POTASSIUM	75 CEM	II	CHEMISTRY
ELECTRODE, ION-SPECIFIC, CALCIUM	75 JFP	II	CHEMISTRY
ELECTRODE, ION-SPECIFIC, SODIUM	75 JGS	II	CHEMISTRY
ELECTRODE, ION-SPECIFIC, CHLORIDE	75 CGC	II	CHEMISTRY
ELECTRODE, BLOOD PH	75 CHL	II	CHEMISTRY
BLOOD GASES/PH	75 CHL	II	CHEMISTRY
HEMOGLOBINOMETER, AUTOMATED	81 GKR	II	HEMATOLOGY
HEMATOCRIT, AUTOMATED	81 GKF	II	HEMATOLOGY
CARBOXYHEMOGLOBIN	81 GHS	II	HEMATOLOGY
OXIMETER, WHOLE BLOO	81 GLY	II	HEMATOLOGY
METHEMOGLOBIN	not known		
SULFHEMOGLOBIN	not known		
DEOXYHEMOGLOBIN	not known		
LACTATE OXIDASE	not known	II	CHEMISTRY
GLUCOSE OXIDASE, GLUCOSE	75 CGA	II	CHEMISTRY

(3) **Substantial Equivalence**

The AVL OMNI is substantially equivalent in function, safety and efficacy to a number of currently marketed devices known as 'Combi Analyzers.' Specifically: Radiometer 625 [K954612], NOVA Biomedical ULTRA [K960120], Chiron 865 [K946206] and Instrumentation Laboratories BGGE [K955793].

(4) Description of the new device

The AVL OMNI™ Analyzer is a fully-automatic, microprocessor-controlled system that can perform up to 16 tests per sample.

Versions	Parameter
AVL OMNI™ 1	BG (= pH, PO_2 and PCO_2)
AVL OMNI™ 2	BG and tHb
AVL OMNI™ 3	BG and COOX (= *c*tHb, HHb, O_2Hb, COHb, MetHb, SulfHb)
AVL OMNI™ 4	BG, Hct and ISE (= Na^+, K^+, Cl^-, iCa^{++})
AVL OMNI™ 5	BG and tHb, Hct and ISE
AVL OMNI™ 6	BG and COOX, Hct and ISE
AVL OMNI™ 7	BG, Hct, ISE and MSS (= Glu, Lac)
AVL OMNI™ 8	BG and tHb, Hct and ISE and MSS (= Glu, Lac)
AVL OMNI™ 9	BG and COOX, Hct and ISE and MSS (= Glu, Lac)

(5) Intended use of the device.

The AVL OMNI™ Analyzer is intended to be used for the measurement of pH , pCO_2, pCO_2 , sodium, potassium, ionized calcium, chloride, hematocrit and total hemoglobin and the hemoglobin derivatives: O_2Hb, COHb, MetHb, HHb,SulfHb and metabolites; glucose and lactate in samples of whole blood, serum, plasma, aqueous solutions as appropriate, in a clinical laboratory setting by personnel minimally qualified to perform and to report these results.

(6) Technological characteristics of the device.

Principles of Measurement

The principles of measurement used in the AVL OMNI™ Combi Analyzer are essentially identical to those principles existing in the electrolyte analyzers to which substantial equivalence is claimed in paragraph (a)(3) above.

pH, PCO_2	potentiometric
PO_2	amperometric
Na, K, Cl, Ca	direct potentiometric
*c*tHb (AVL OMNI™ 2, 5)	photometric
COOX (AVL OMNI™ 3, 6)	spectrophotometric
Hct	conductance
Glu, Lac	amperometric

Calibration

The AVL OMNI™ Combi Analyzer uses a patented, liquid calibration system for all sensors, eliminating the use of any gas supply system and thus, eliminating the disadvantages coupled with gas supplies.

(b) (1)Summary of non-clinical tests submitted with the premarket notification for the device.

Following is a summary of non-clinical testing performed with this submission for the addition of Glucose and Lactate. Additional information is provided with previous submissions, K945915 and K954018.

Precision

Typical Within-Run (Swr), Between-Day (Sdd) and Total (ST) precision were determined from two runs per day with 2 replicates per run for 20 days on two AVL OMNI™ instruments using samples of each of the specimen types suitable for measurement on the AVL OMNI™.

Linearity in N.I.S.T. Standard Reference Materials

Evaluation of linearity of Sodium, Potassium and Lithium was made in accordance to recommendations by NCCLS[1] using N.I.S.T. SRM 956a Electrolyte in Human Serum and N.I.S.T. SRM 965 for Glucose.

Linearity in Aqeuous Solutions

Aqueous standard solutions were gravimetrically prepared, then diluted serially to obtain linearity standard solutions with a known range of values. These solutions were then measured on each of three AVL OMNI™ units.

Linearity in Plasma

Patient-Sample Pool. The ideal sample matrix is a pool of patient specimens with an analyte level up to 30 % higher than the upper linear limit to be diluted with another patient-sample pool with an analyte level at or below the claimed lower linear limit. The aliquots were then mixed in verying ratios to provide a lineat range of values for each of the metabolites, and measured in randomized order on two AVL OMNI™ instruments.

Interferences[2]

The effects of various analytes or drugs on the measurement of glucose and lactate were considered, including exogenous and endogenous substances, and the results included with this submission. No significant effects on measurement were demonstrated at the concentrations evaluated.

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[1] NCCLS. Standardization of Sodium and Potassium Ion-Selective Electrode Systems to the Flame Photometric Reference Method; Approved Standard. NCCLS Document C29-A. NCCLS, 771 East Lancaster Avenue, Villanova, Pennsylvania 19085, 1995.

[2] NCCLS. Interference Testing in Clinical Chemistry; Proposed Guideline. NCCLS Document EP7-P. NCCLS, 771 East Lancaster Avenue, Villanova, Pennsylvania 19085, 1986.

(b) (2) Summary of clinical tests submitted with the premarket notification for the device.

Clincial testing was conducted to demonstrate the correlation of AVL OMNI™ to legally marketed predicate devices in a clinical setting, operated by personnel trained to perform and report these analyses. Specimens analyzed in these tests were remnant from patient specimens of both whole blood and serum collected for routing analysis on existing instrumentation.

In all evaluations, there was no significant difference in mean values ($P<0.05$) obtained on measurement by the AVL OMNI™ .

(b) (3) Conclusions drawn from the clinical and nonclinical trials.

Analysis of the comparative measurement presented in the 510(k) for this device, together with the linearity and precision data collected during these clinical and non-clinical trials demonstrates that the AVL OMNI™, with the additional analytes, Glucose and Lactate, is safe and effective, and equivalent to those predicate devices to which it is compared.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP - 9 1997

Randy Byrd
Quality Assurance Manager
AVL Scientific Corporation
50 Mansell Court
Roswell, Georgia 30076

Re: K972733
AVL OMNI™ Combi Analyzer
Regulatory Class: II
Product Code: CGA, CGZ, CHL, GHS, GLY, JFP, JGS
Dated: July 16, 1997
Received: July 21, 1997

Dear Mr. Byrd:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known) K972733

Device Name: AVL OMNI™ Combi Analyzer

The AVL OMNI™ is a modular Critical Care Analyzer intended to be used for the measurement of pH, PCO_2, PO_2, ctHb, HHb, O_2Hb, COHb, MetHb, SulfHb, Na^+, K^+, Cl^-, ionized Ca^{++}, Hematocrit, glucose and lactate in whole blood, serum, plasma, dialysate and QC materials as appropriate by minimally trained personnel qualified to perform and to report these values in a clinical laboratory setting.

Indications for Use[1,2]

pH

The pH value of the blood may be the single most valuable factor in the evaluation of the acid-base status of a patient. The pH value is an indicator of the balance between the buffer (blood), renal (kidney) and respiratory (lung) systems, and one of the most tightly controlled parameters in the body. The causes of abnormal blood pH values are generally classified as:

- primary bicarbonate deficit — metabolic acidosis
- primary bicarbonate excess — metabolic alkalosis
- primary hypoventilation — respiratory acidosis
- primary hyperventilation — respiratory alkalosis

An increase in blood, serum or plasma pH (*alkalemia*) may be due to increased plasma bicarbonate, or a feature of respiratory alkalosis due to an increased elimination of CO_2 due to hyperventilation.
A decrease of pH value (*acidemia*) in blood, serum or plasma may occur due to an increased formation of organic acids, an increased excretion of H^+-ions in certain renal disorders, an increased acid intake such as in salicylate poisoning or loss of alkaline body fluids. Respiratory acidosis is the result of a decreased alveolar ventilation and may be acute, as the result of pulmonary edema, airway obstruction or medication, or maybe be chronic, as the result of obstructive or restrictive respiratory diseases.
The composition of serous body fluids: pleural, pericardial, ascitic and cerebrospinal fluid, is similar to serum and plasma in electrolyte content and pH. The AVL OMNI™ may be used for the analysis of these fluids, limited to a pH in the range between 6 and 8, as long as care is taken to ensure the specimen to be analyzed is clear of fibrin clots or other debris which may block the sample transport system.

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[1] Tietz, Norbert W., Ed., Clinical Guide to Laboratory Tests, 2nd Ed., (Philadelphia: W.B.Saunders, Co., 1990) p.436.
[2] Burtis C, Ashwood E (Eds.), Tietz Textbook of Clinical Chemistry, 2nd Ed., (Philadelphia: W.B.Saunders, Co., 1994) pp.1354-1360,2180-2206.

Pleural fluid[3]

The pH measurement of pleural fluid can be a clinically useful tool in the management of patients with parapneumonic effusions. Patients with pneumonia may develop effusions when the infectious process extends to the visceral pleura, causing exudation of fluid into the pleural space. Fluids are divided into potentially benign and complicated effusions on the basis of pH. Fluids with a pH greater than 7.30 resolve spontaneously, whereas a pH less than 7.20 is an indication of tube drainage.

PCO_2

The PCO_2 value of arterial blood is used to assess how well the body eliminates carbon dioxide in relation to the metabolic rate of CO_2 production.
An arterial PCO_2 below the normal range is termed respiratory alkalosis and indicates *hypocapnia*, a condition caused by increased alveolar ventilation such as hyperventilation. An arterial PCO_2 above the normal range is termed respiratory acidosis and indicates *hypercapnia*, a sign of hypoventilation and failure, resulting from cardiac arrest, chronic obstructive lung disease, drug overdose, or chronic metabolic acid-base disturbances.

PCO_2

The PO_2 value of arterial blood has become the primary tool for the evaluation of arterial oxygenation status. Values below the normal arterial PO_2 (arterial *hypoxemia*) are usually caused by pulmonary, circulatory, or respiratory abnormalities (e.g. bronchial obstruction, vascular problems, decrease in cardiac output, increased oxygen demand, anatomical heart defect, low inspired O_2 content). Generally, PO_2 levels above 100 mmHg do not contribute significantly to the oxygen content since, with normal hemoglobin concentrations, 80 - 100 mmHg, PO_2 provides a 97 % saturation level, and a level greater than 100 % cannot be achieved.

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[3] Kaplan LA, Pesce AJ. Clinical Chemistry: Theory, analysis and correlation, 2nd Ed. (St.Louis: C.V.Mosby Co. 1989) p 590-591.

Sodium

Sodium is the major cation of extracellular fluid. Its primary functions in the body are to chemically maintain osmotic pressure and acid-base balance and to transmit nerve impulses. Sodium functions at the cell membrane level by creating an electrical potential between different cell membranes causing the transmission of nerve impulses and neuromuscular excitability to be maintained. Sodium is involved in some enzyme catalyzed reactions as a cofactor. The body has a strong tendency to maintain a total base content, and only slight changes are found even under pathologic conditions.

Low sodium values, *hyponatremia*, usually reflect a relative excess of body water rather than a low total body sodium. Reduced sodium levels may be associated with: low sodium intake; sodium losses due to vomiting or diarrhea with adequate water and inadequate salt replacement, diuretics abuse, or salt-losing nephropathy; osmotic diuresis, metabolic acidosis; adreocortical insufficiency; congenital adrenal hyperplasia; dilution type due to edema, cardiac failure, hepatic failure; and hypothyroidism.

Elevated sodium values, *hypernatremia*, are associated with conditions with water loss in excess of salt loss through profuse sweating, prolonged hyperpnea, severe vomiting or diarrhea, diabetes insipidus or diabetic acidosis; increased renal sodium conservation in hyperaldosteronism, Cushing's syndrome; inadequate water intake because of coma or hypothalamic diseases; dehydration; or excessive saline therapy.

The sodium value obtained may be used in the diagnosis or monitoring of all disturbances of the water balance, infusion therapies, vomiting, diarrhea, burns, heart and kidney insufficiencies, central or renal diabetes insipidus, endocrine disturbances and primary or secondary cortex insufficiency of the adrenal gland or other diseases involving electrolyte imbalance.

Potassium

Potassium is the major cation in the intracellular fluid and functions as the primary buffer within the cell itself. Ninety percent of potassium is concentrated within the cell, and damaged cells release potassium into the blood. Potassium plays an important role in nerve conduction, muscle function, and helps maintain acid-base balance and osmotic pressure.

Elevated potassium levels, *hyperkalemia*, can be found in oligouria, anemia, urinary obstruction, renal failure due to nephritis or shock, metabolic or respiratory acidosis, renal tubular acidosis with the K^+/H^+ exchange and hemolysis of the blood. Low potassium levels, *hypokalemia*, can be found in excessive loss of potassium through diarrhea or vomiting, inadequate intake of potassium, malabsorption, severe burns and increased secretion of aldosterone. High or low potassium levels may cause changes in muscle irritability, respiration and myocardial function.

The potassium value obtained may be used to monitor electrolyte imbalance in the diagnosis and treatment of infusion therapies, shock, heart or circulatory insufficiency, acid-base imbalance, therapy with diuretics, all kinds of kidney problems, diarrhea and hyper- and hypo-function of adrenal cortex and other diseases involving electrolyte imbalance.

Chloride

Chloride is an anion that exists predominantly in extracellular spaces. It maintains cellular integrity through its influence on osmotic pressure. It is also significant in monitoring acid-base balance and water balance. In metabolic acidosis, there is a reciprocal rise in chloride concentration when the bicarbonate concentration drops.

Decreased levels are found in severe vomiting, severe diarrhea, ulcerative colitis, pyloric obstruction, severe burns, heat exhaustion, diabetic acidosis, Addison's disease, fever and acute infections such as pneumonia.

Increased levels are found in dehydration, Cushing's syndrome, hyperventilation, eclampsia, anemia, cardiac decompensation.

ionized Calcium

Calcium in blood is distributed as free calcium ions (50 %), bound to protein, mostly albumin (40 %) and 10 % bound to anions such as bicarbonate, citrate, phosphate and lactate. However, only ionized calcium can be used by the body in such vital processes as muscular contraction, cardiac function, transmission of nerve impulses and blood clotting. The AVL OMNI™ measures the ionized portion of the total calcium. In certain disorders such as pancreatitis and hyperparathyroidism, ionized calcium is a better indicator for diagnosis than total calcium.

Elevated calcium, *hypercalcemia*, may be present in various types of malignancy, and calcium measurements may serve as biochemical markers. In general, while ionized calcium may be slightly more sensitive, either ionized or total calcium measurements have about equal utility in the detection of occult malignancy. Hypercalcemia occurs commonly in critically ill patients with abnormalities in acid-base regulation and losses of protein and albumin, which gave clear advantages to monitoring calcium status by ionized calcium measurements.

Patients with renal disease caused by glomular failure often have altered concentrations of calcium, phosphate, albumin, magnesium and pH. Since these conditions tend to change ionized calcium independently of total calcium, ionized calcium is the preferred method for accurately monitoring calcium status in renal disease[4].

Ionized calcium is important for diagnosis or monitoring of: hypertension management, parathyroidism, renal diseases, inadequate calcium intake, vitamin D

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[4] Burritt MF, Pierides AM, Offord KP: Comparative studies of total and ionized serum calcium values in normal subjects and in patients with renal disorders. Mayo Clinic Proc. 55:606, 1980.

monitoring, dialysis patients, cancer, pancreatitis, effect of diuretics, malnutrition, kidney stones, multiple myeloma and diabetes mellitus.

total Hemoglobin concentration (ctHb)

The hemoglobin is the main component of erythrocytes. It serves as the vehicle for transportation of oxygen within the bloodstream and each gram/dL of hemoglobin can carry 1.39 mL of oxygen. The oxygen combining capacity of the blood is directly proportional to the hemoglobin concentration rather than to the number of red blood cells (RBC), because some red cells contain more hemoglobin than the others.

Although oxygen transport is the main function of hemoglobin, it also serves as an important buffer in the extracellular fluid. Decreases in the amount of hemoglobin can come about as a result of a decreased concentration of hemoglobin in the erythrocytes, or a decreased number of erythrocytes that contain a normal concentration of hemoglobin.

Decreased levels are found in anemia states, hyperthyroidism, severe hemorrhage and hemolytic reactions due to transfusions of incompatible blood, reaction to chemical, infectious and physical agents as well as various systemic diseases. Increased levels are found in hemoconcentration of the blood, chronic obstructive pulmonary disease and congestive heart failure.
*c*tHb gives valuable information in an emergency situation if interpreted not in an isolated fashion but in conjunction with other pertinent laboratory data.
*c*tHb is used to screen for disease associated with anemia, to determine the severity of anemia, to follow the response to treatment for anemia and to evaluate polycythemia.

Hemoglobin derivatives

Each hemoglobin molecule is composed of four heme groups, each containing
an iron atom. These iron atoms may exist in either a ferrous (reduced) or ferric (oxidized) state. In their ferrous state, each iron atom of reduced hemoglobin (HHb) may be reversibly associated with molecular oxygen (O_2Hb) or carbon monoxide (COHb) or irreversibly with sulfur as sulfhemoglobin (SulfHb). In its ferric, oxidized state it is termed methemoglobin (MetHb), and may be associated with hydroxyl ions, cyanide or sulfur compounds. The fraction of the total hemoglobin content which is bound to oxygen is the *oxyhemoglobin fraction,* FO_2Hb, and used to assess the amount of oxygen available to the tissues and, together with tHb and PO_2, is used to calculate the oxygen content. The degree of association between oxygen and hemoglobin is determined by the PO_2 and the affinity of hemoglobin for oxygen and is quantified as oxygen saturation. The plot of oxygen saturation (SO_2) against PO_2 results in a sigmoidal curve known as the O_2 dissociation curve, and the shape of this curve arises as a function of the affinity of the hemoglobin in the blood for O_2.

The affinity of hemoglobin for oxygen is dependent on five factors: temperature, pH PCO_2, concentration of 2,3-DPG and the type of hemoglobin. Hemoglobin which is capable of combining with oxygen is termed *functional hemoglobin*, and decreased amounts of functional hemoglobin can occur when quantities of hemoglobin are converted into nonfunctional, *carboxyhemoglobin, methemoglobin, sulfhemoglobin or cyanmethemoglobin*. Impairment of the ability to transfer oxygen from the lung to the hemoglobin, inadequate circulation or shunt, may result in a decrease in PO_2, a decrease in oxygen saturation, and ultimately a decrease in the delivery of oxygen to the tissues. Clinically, it is important to distinguish between *hypoxia* (decrease oxygen availability due to a decrease in PO_2 and oxygen saturation) and *cyanosis* (decrease in oxygen saturation because of abnormally high concentrations of deoxyhemoglobin or the dysfunctional hemoglobin derivatives, methemoglobin or sulfhemoglobin). Cyanosis is generally described to occur when the capillary content of deoxyhemoglobin exceeds 5 g/100 mL. This may occur when the arterial hemoglobin is not saturated, or when tissue extraction of oxygen from the blood is high. However, due to the altered color characteristics of sulfhemoglobin and methemoglobin, comparable degrees of cyanosis may occur with 1.5 g MetHb/dL of blood or 0.5 g SulfHb/dL of blood. The presence of abnormally high concentrations of MetHb or SulfHB generally result from reactions to drugs or chemicals, although congenital methemoglobinanemia does occur infrequently.

Oxyhemoglobin (O_2Hb)

When each heme group of the hemoglobin molecule is associated with one molecule of oxygen, the hemoglobin is referred to as oxyhemoglobin (O_2Hb). The amount of oxyhemoglobin, expressed as a fraction of the total hemoglobin is termed, oxyhemoglobin fraction of total hemoglobin (FO_2Hb).[5] The largest portion (about 98%) of blood oxygen content is the oxygen bound to hemoglobin. The reference interval for arterial blood from healthy adults is typically 94 to 98%[4].

Deoxyhemoglobin (HHb)

Deoxyhemoglobin is the hemoglobin with the iron molecule in the heme group in its ferrous state and not associated with any other molecule, thus, capable of carrying one oxygen molecule. The sum of deoxyhemoglobin and oxyhemoglobin, those derivatives capable of oxygen transport within the blood, is termed, *functional hemoglobin*.

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[5] Siggaard-Andersen O, Durst RA, Maas AHJ. IFCC/IUPAC approved recommendation (1984) on phyicochemical quantities and units in clinical chemistry. *J Clin Chem Clin Biochem.* 25:369-391, 1987.

Carboxyhemoglobin (COHb)

Hemoglobin has the capacity to combine with carbon monoxide in the same proportion as with oxygen, that is, one heme group can associate with one carbon monoxide molecule. However, the hemoglobin molecule has an affinity for carbon monoxide 200-300 times greater than its affinity for oxygen. Due to this high affinity of carbon monoxide to the oxygen binding site, it successfully competes with oxygen to form carboxyhemoglobin. This explains why a spurious concentration of carbon monoxide may result in life-threatening levels of COHb. Levels of approximately 6% are seen in the blood of moderate smokers. Blood concentrations of 10 to 20 % are associated with headaches and mild dyspnea. 30 to 40 % COHb causes weakness, nausea, vomiting and visual disturbances, at a 40 to 50 % level the clinical findings are characterized by tachypnea, tachycardia, ataxia and syncopes. Between 50 and 70 % seizures, coma and compromized overall heart and lung functions become apparent, higher levels usually cause death. Clinical diagnosis requires CO-Oximetry, since calculated oxygen saturation from blood gas and acid base measurements are misleadingly high[6]. Small amounts of carbon monoxide are produced in the body in the conversion of heme to biliverdin and, this small amount of endogenous carbon monoxide production is accelerated in hemolytic anemias.[7]

Methemoglobin (MetHb)

In methemoglobin, the central iron atom is oxidized to its ferric state. Because of the loss of an electron, methemoglobin is incapable of reversibly binding oxygen or carbon monoxide. It is formed spontaneously especially from deoxyhemoglobin, which is more readily subject to rapid autooxydation. Therefore it is found increased in chronic hypoxemia and in residents at high altitude. Methemoglobin is also formed by a number of organic and inorganic oxidants[8] and may be induced by drugs such as primaquine, dapsone, aniline and nitrates[9]. It also occurs in patients with hereditary structural abnormalities of the hemoglobin. MetHb levels up to 20% are usually well tolerated, levels of 30 to 40% cause dyspnea and headaches, levels above 40% require therapy, usually with intravenous methylene blue treatment, which acts as an activator of the NADPH dehydrogenase. In patients with certain enzyme deficiencies, methemoglobin can rise up to 70%.

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[6] Meigs JW, Hughes JPW (1952) Acute carbon monoxide poisoning- an analysis of five hundred cases. AMA Arch Ind Hvg 6: 344

[7] Burtis C, Ashwood E (Eds.), Tietz Textbook of Clinical Chemistry, 2nd Ed., (Philadelphia: W.B.Saunders, Co., 1994) pp.1178-1179.

[8] Jaffe ER (1981) Methemoglobinemia. J Clin Haematol 10: 99

[9] Shapiro BA, Peruzzi WT, Kozelowski-Templin R. Clinical Application of Blood Gases, 5th Ed.,(Chicago: Mosby, 1994), pp.200-201.

Sulfhemoglobin (SulfHb)

Sulfhemoglobin is formed as the product of sulphur ligand binding to the heme iron in sulphide intoxications and with toxic side effects of drugs such as sulfonamides, dapsone, acetanilid and phenacetin. It is frequently misdiagnosed through the disability of older spectrophotometric CO- Oximeters to separate it from other derivatives, especially MetHb[10].
SulfHb is irreversibly unfunctional and does not disappear from the circulation until the erythrocytes have completed their life cycle and SulfHb is metabolized.

Hematocrit

Hematocrit, sometimes denoted as packed cell volume (PCV), is the volumetric fraction occupied by the red blood cells. The Hct is expressed either in percentage or fraction.
Decreased levels are an indicator for anemia (a condition where there is a reduction in Hct, tHb and RBCs), leukemia, hyperthyroidism, cirrhosis, acute massive blood loss as well as hemolytic reactions due to transfusions of incompatible blood, reaction to chemical, infectious and physical agents.
Increased levels are found in polycythemia, erythrocytosis, severe dehydration and shock.

Glucose

Hyperglycemia can be due to a number of causes which can be sub-divided into those due to *diabetes mellitus* or those due to non-diabetic causes. Diabetes mellitus is a syndrome of chronic hyperglycemia which is due to either absolute insulin deficiency or reduced tissue response to insulin, or both. It is a common condition which is diagnosed according to strict criteria that rely upon measurement of the blood glucose level. Nondiabetic causes of hyperglycaemia include *postprandial* (occurs immediately after a carbohydrate-containing meal), *factitious* (blood taken from an arm where glucose is being infused), *drugs* (produce a tissue insensitivity to insulin), *non-pancreatic endocrine disease* (excessive production of anti-insulin hormones), *pancreatic disorders* (secondary diabetes mellitus), and *stress* (physical and psychogenic types causing excess secretion of cortisol and catecholamines.

Hypoglycemia is an acute medical condition with a number of characteristic signs and symptoms which are accompanied by biochemical hypoglycamia and which are relieved by the administration of glucose. The causes of hypoglycaemia can be divided into three groups: Medication/Toxins, Reactive Hypoglycemia; Fasting Hypoglycemia. Hypoglycemia due to excessive amounts of certain *Medications or Toxins* include insulin (insulin overdose is the commonest cause of hypoglycemia), oral hypoglycaemics or suphonylureas, ethanol and other drugs such as salicylate and propanalol. *Reactive Hypoglycemia* occur, within 5-hours of a carbohydrate meal in otherwise normal subjects, in patients with early adult-onset diabetes

[10] Park CM, Nagel RL (1984) Sulfhemoglobinemia. N Engl J Med 310:1579

mellitus and in patients who have had gastric surgery. *Fasting Hypoglycemia* can be due to insulinomas, non-pancreatic tumors, endocrine disorders, liver failure, sepsis, renal failure or autoimmune disorders

Lactate

Causes of an increased lactate or lactic acidosis can be divided into two general groups:
Type A causes are those in which there is overt evidence of hypoxia and are the most causes of a lactic acidosis. Insufficient tissue oxygenation to meet the metabolic needs of the patient can arise due to *severe exercise; poor tissue perfusion* such as in shock; or due to *reduced arterial oxygen content* such as in asphyxia or hypoxemia.
Type B causes are those where there is no overt evidence of hypoxia and can occur in association with a wide variety of discases and toxins/chemicals. In these cases the mechanism is unclear but it is thought to be due to impaired tissue oxygen utilisation. Causes include *drugs and toxins* such as ethanol, methanol and phenformin; *predisposing diseases* such as respiratory alkalosis and diabetes mellitus, liver failure and sepsis; inborn or *congenital errors* in carbohydrate metabolism.
In all of the above cases the excess lactate is of the laevo or L-form. Dextro or D-lactic acidosis can occur when there is overgrowth of certain bacteria in a gut which has been shortened through surgery. The bacteria produce excessive quantities of D-lactate.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K972733