Exhibit 21

to the Declaration of Cullen N. Pendleton in Support of Amgen's Opposition to Roche's Motion for Summary Judgment that Claim 7 of the '349 Patent is Invalid Under 35 USC §112 and is Not Infringed

EPO-Trac™
^{125}I RIA Kit

For the quantitative determination of
Erythropoietin in serum or plasma

Instruction Manual
Manuel d'Instructions
Testanleitung
Manual de Instrucciones
Manuale di Istruzioni
Manual de instruções
Εγχειρίδιο οδηγιών

REF: 23200

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EPO-Trac ^{125}I RIA KIT

1. INTENDED USE

FOR *IN VITRO* DIAGNOSTIC USE.

The EPO-Trac™ RIA kit is intended for the quantitative determination of erythropoietin (EPO) in serum or EDTA plasma by radioimmunoassay (RIA) as an aid in the diagnosis of anemias and polycythemias.

2. SUMMARY AND EXPLANATION

Erythropoietin (EPO) is a glycoprotein hormone (34,000 daltons) that stimulates the maturation of red blood cell precursors. EPO is secreted by the kidney in response to the blood's oxygen content. Normally when oxygen levels fall, as in physiological hypoxia, the level of EPO in the circulation system increases and stimulates the increased production of red blood cells.[1]

Abnormal blood levels of circulating EPO are characteristic of specific pathological disorders including various anemias, polycythemia and tumors. Overproduction of EPO has been associated with renal carcinoma. Some liver tumors and other organ tumors have been associated with ectopic erythropoietin production.[2]

Anemia is characterized by inadequate levels of red blood cells.[2] Anemic patients presenting with elevated EPO levels include aplastic anemia, iron deficiency anemia and hemolytic anemia. Anemia associated with chronic renal failure is a result of insufficient production of EPO by the kidney.

Overproduction of red blood cells is called polycythemia. In untreated polycythemia rubra vera, overproduction of red blood cells by hematopoietic progenitors occurs in the presence of low or undetectable EPO concentrations.[3]

Secondary (stress) polycythemia is caused by increased production and release of EPO resulting in increased red blood cell mass. Secondary polycythemia may be caused by various factors such as smoking, kidney stones, pulmonary fibrosis, cardiac disease, tumors, or defective hemoglobin.[2]

Several methods have been developed to measure erythropoietin in humans and animals. Initial assays development included and in vivo bioassay utilizing exhypoxic polycythemic live mice.[4,5] With the development of recombinant human erthropoietin, in vitro assays were also developed which were less time consuming and less expensive. These in vitro assays include radioimmunoassay (RIA) and enzyme immunoassay (EIA).

3. PRINCIPLE OF THE ASSAY

The DiaSorin EPO-Trac ^{125}I RIA procedure is a competitive binding, disequilibrium radio-immunoassay which utilizes recombinant human erythropoietin for both tracer and calibrators. Samples are incubated with the EPO-Trac primary goat antibody (goat anti-EPO) and allowed to react for 2 hours before EPO-Trac tracer labeled with iodine-125 is added. Following an overnight incubation, the donkey anti-goat precipitating complex (DAG-PPT) secondary antibody is added to the specific assay test tubes (TABLE I). The DAG-PPT is a donkey anti-goat serum that is pre-precipitated with a normal goat serum and a surfactant. The DAG-PPT is incubated with calibrators or samples, primary antibody and tracer, for thirty minutes before the test tubes are centrifuged to separate the bound from the unbound tracer. The unbound tracer is removed by decanting the supernatant from each test tube. The bound tracer in the remaining DAG-PPT complex pellets is counted in a gamma counter for 1 minute. The ^{125}I counts are inversely proportional to the amount of EPO present in each sample.

4. REAGENTS PROVIDED IN THE KIT

EPO-Trac Primary Antibody (BLUE)	1 vial/11 mL
EPO-Trac Calibrators (0-5)	1 vial/11 mL, 5 vials/2.1 mL
EPO-Trac DAG-ppt	2 vials/35 mLs
EPO-Trac Tracer (RED)	1 vial/11 mL
EPO-Trac Controls	2 vials/2.1 mL
Number of tests	100

STORAGE: Upon receipt, the kit should be stored at 2-8°C. After opening, store each reagent at 2-8° until the expiration date on the label. Reagents should not be used past the expiration date. The expiration date of the kit is reported on the external label and corresponds to the expiration date of the tracer.

Reagents from different batches must not be mixed.

4.1 EPO-Trac Calibrators, 0-5: ready to use reagent
Six recombinant erythropoietin calibrators, at nominal concentrations ranging from approximately 0 to 280 mU/mL, are prediluted in buffered saline with protein stabilizers, anti-microbials and 0.1% sodium azide. Calibrators are referenced against World Health Organization (WHO) 2nd IRP Erythropoietin, HUM, Urinary/Bioassay 67/343[6] and WHO (IS) International Calibrator for Erythopoietin, Recombinant DNA (rDNA) - derived code #87/684. The kit calibrators demonstrate commutability with patient samples when used with reagents and operating procedure of this in vitro diagnostic test as recommended.

4.2 ^{125}I EPO-Trac: ready to use reagent
Human recombinant erythropoietin is labeled with iodine-125, 2 µCi (74 kBq), and diluted in buffered saline with protein stabilizers, antimicrobials, 0.1% sodium azide and Food, Drug and Cosmetic (FD & C) red dye No. 40.

4.3 EPO-Trac Primary Antibody: ready to use reagent
Goat anti-human EPO serum is diluted with buffered saline with protein stabilizers, anti-microbials, 0.1% sodium azide and FD & C blue dye No. 1.

4.4 EPO-Trac Precipitating Complex, DAG-PPT: lyophilized reagent
Donkey anti-goat serum is pre-precipitated with normal goat serum and surfactant, diluted in BSA-borate buffer with antimicrobials and 0.03% thimerosal and lyophilized. Reconstitute the vial with 35 mL of purified water; mix thoroughly until the suspension appears homogeneous and then allow it to stand for a minimum of 30 minutes at room temperature with occasional mixing. Swirl or mix with a small magnetic stirrer at very low speed while dispensing DAG-PPT into test tubes. If reagent shows evidence of rehydration prior to use, do not use.

4.5 EPO-Trac Controls, Levels 1 and 2: ready to use reagent
Human recombinant EPO is added to buffered saline with protein stabilizer to obtain a concentration within a specified range listed on the control vials. 0.1% sodium azide and other stabilizers are added.

5. WARNINGS AND PRECAUTIONS

FOR *IN VITRO* DIAGNOSTIC USE.
Not for internal or external use in humans or animals.

REAGENTS CONTAINING SODIUM AZIDE

CAUTION: Some reagents in this kit contain sodium azide. Sodium azide may react with lead or copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up. For further information, refer to "Decontamination of Laboratory Sink Drains to Remove Azide Salts," in the Manual Guide-Safety Management No. CDC-22 issued by the Centers for Disease Control and Prevention, Atlanta, GA, USA,1976.

European Communities Hazardous Substance Risk Phrases (Council Directive 1999/45/EC

R20/21/22 - Harmful by inhalation, in contact with skin and if swallowed.
R32 - Contact with acids liberates very toxic gas.
S28 - After contact with skin, wash immediately with plenty of water.

REAGENTS CONTAINING THIMEROSAL

Some reagents in this kit contain thimerosal which contains a mercury compound. Disposal of elemental mercury, inorganic mercury, mercury oxides and mercury compounds should be done in strict compliance with all local, state, and federal regulations.

WARNING: This product contains a chemical known to the State of California to cause birth defects or other reproductive harm.

REAGENTS CONTAINING IODINE-125

This kit contains radioactive material which does not exceed 2 µCi (74 kBq) of iodine-125. Appropriate precautions and good laboratory practices should be used in the storage, handling, and disposal of this material.

For practitioners or institutions receiving radioisotopes under a general license:

This radioactive material may be received, acquired, possessed and used only by physicians, veterinarians in the practice of veterinary medicine, clinical laboratories or hospitals, and only for *in vitro* clinical or laboratory tests not involving internal or external administration of the material, or the radiation therefrom, to human beings or animals. Its receipt, acquisition, possession, use and transfer are subject to the regulations and the general license of the U.S. Nuclear Regulatory Commission or of the state with which the Commission has entered into an agreement for the exercise of regulatory authority.

1. Storage of radioactive material should be limited to a specifically designated area.
2. Access to radioactive materials must be limited to authorized personnel only.
3. Do not pipette radioactive material by mouth.
4. Do not eat or drink within designated radioactive work areas.
5. Areas where spills may occur should be wiped up, then washed with an alkali detergent or radiological decontamination solution. Any glassware used must be rinsed completely with water before washing with other laboratory glassware.

For practitioners or institutions receiving radioisotopes under a specific license:

The receipt, use, transfer and disposal of radioactive materials are subject to the regulations and conditions of your specific license.

WARNING: This product contains a chemical known to the State of California to cause cancer.

ATTENTION: Radioactivity printed in the package insert may be slightly different from the radioactivity printed on the box label and on the tracer vial label. The box label and the tracer vial label indicate the actual amount of radioactivity at the calibration date where the package insert indicates the theoretical radioactivity of the kit.

ADDITIONAL WARNINGS

1. Avoid splashing or generating aerosols.
2. Incubation times or temperatures other than those specified may give erroneous results.
3. Microbial contamination of reagents may give incorrect results.
4. Do not substitute reagents with those from other lots or other manufacturers.

6. SPECIMEN REQUIREMENTS

CAUTION: Patient specimens and all materials coming into contact with them should be handled as if capable of transmitting infection and disposed of with proper precautions.

COLLECTION AND STORAGE OF SERUM OR PLASMA

An adequate sample of blood should be collected aseptically by venipuncture in a 5 or 10 mL evacuated sterile glass tube to yield a minimum of 400 µL of serum or EDTA plasma per assay (for 2 replicates). Care should be taken to remove the serum from the clot promptly by centrifugation to avoid hemolysis. Centrifuge serum or plasma at room temperature for 10 minutes at 760 x g*. EDTA (72 mg/5 mL blood) should be used as the anticoagulant for plasma. No further additives or preservatives are required to maintain sample integrity.

Serum or EDTA plasma should be placed in sterile covered storage tubes. Serum is stable up to 7 days at 4°C. For longer storage, freeze at -20°C in a non self-defrosting freezer. DiaSorin has shown serum samples to be stable up to 18 months when frozen continuously at -20°C. Serum samples should not be repeatedly frozen and thawed. All plastics, glassware or other material coming in contact with the specimen should be entirely free from contamination.

Fasting samples are recommended, but not required, to avoid unforeseen interference from lipid-soluble substances. Visibly hemolyzed samples should be discarded. Bilirubin (<5 mg/dL) has not been shown to interfere with this assay. No drugs have been examined for interference.

7. EQUIPMENT AND MATERIALS REQUIRED, BUT NOT SUPPLIED

7.1 Rubber/latex gloves to wear while performing the test.

7.2 Disposable borosilicate glass tubes, 12 x 75 mm.

7.3 Temperature controlled centrifuge (20-25°C) to accommodate 12 x 75 mm tubes spun at 1600 ±20 g*.

7.4 Gamma scintillation counter calibrated and capable of counting iodine-125.

7.5 Vortex mixer.

7.6 Pipetting devices:

- **a.** Micropipettors calibrated to deliver 200 (±4) µL.
- **b.** Repeating dispensers calibrated to deliver 100 (±2) µL and 500 (±5) µL.

7.7 Purified water to dilute DAG-PPT.

7.8 Timer to accurately time to ±2 minutes.

7.9 Three cycle semi-log graph paper.

8. ASSAY PROCEDURE

8.1 Prepare unknown samples.

8.2 Set up labeled 12 x 75 mm disposable glass tubes in duplicate according to the Scheme of the Assay, on the back page.

8.3 Add reagents as follows:

- **a. Total count tubes**
  Set aside until step 6 (used for quality control calculations - see Quality Control section)
- **b. Nonspecific binding tubes (NSB)**
  200 µL of calibrator 0 per tube
- **c. Calibrator 0**
  200 µL of Calibrator 0 per tube

* $g = (1118 \times 10^{-8})$ (radius in cm $(rpm)^2$

d. EPO-Trac Calibrators (1-5)
200 µL of calibrator per tube

e. Controls and unknown samples
200 µL of each sample or control per tube

8.4 Add 100 µL of EPO primary goat antibody (blue) to each tube except the total count and NSB tubes.

8.5 Vortex the tubes gently and incubate for 2 hours (±10 minutes) at room temperature (20-25°C).

8.6 Add 100 µL of EPO tracer (red) to all tubes.

8.7 Vortex the tubes gently and incubate for 16-24 hours at 2-8°C.

8.8 Vigorously mix the DAG-PPT before dispensing. Swirl or mix DAG-PPT with a small magnetic stirrer at very low speed while dispensing 500 µL to all the tubes except the total count tubes.

8.9 Vortex; then incubate the tubes for 30 (±5) minutes at room temperature (20-25°C).

8.10 Centrifuge the tubes for 20 minutes using 1600 x g* at 20-25°C.

8.11 Set aside the total count tubes; then decant the supernatant from the remaining tubes into an appropriate radioactive waste container. Blot the tubes upside down on absorbent paper to remove any drops of supernatant that may be remaining on the rims before turning the tubes upright.

8.12 Using a gamma scintillation counter, count the precipitate of each tube and the total count tubes for 1 minute.

9. PROCEDURAL COMMENTS

9.1 Add each aliquot of reagent to the lower third of the assay tubes to ensure complete mixing of reagents.

9.2 If tubes cannot be decanted within 5 minutes after centrifugation is completed, the tubes should be re-centrifuged before decanting supernatant.

9.3 To completely monitor the consistent performance of an RIA there are additional factors which may be checked. DiaSorin suggests a regular check of the following parameters to assure consistent kit performance.

a. Total Counts

b. Maximum Binding
Average counts per minute (CPM) of Calibrator 0 Tubes / Average CPM of the Total Count Tubes.

c. Nonspecific Binding

Average CPM of NSB tubes / Average CPM of the Total Count Tubes.

d. Slope of Calibrator Curve

For example, monitor the 80%, 50% and 20% suppression points of the calibrator line.

* $g = (1118 \times 10^{-8})$ (radius in cm $(rpm)^2$

10. QUALITY CONTROL

Each laboratory must include at least two controls in every assay to monitor assay performance. Commercially available controls or the two reference controls or the two reference controls provided with the kit may be utilized. The kit controls contain EPO at two concentrations. The kit controls have been evaluated by DiaSorin using the DiaSorin EPO-Trac ^{125}I RIA Kit. Ranges determined by DiaSorin are provided on the control vials. Quality control charts should be maintained to follow control performance. Acceptable performance limits should be determined by each individual laboratory for each level of control using statistically based methods designed to detect both systematic and random errors. Control results must meet the laboratory's criteria for acceptability prior to reporting patient test results.[19,20,21]

11. CALCULATIONS OF RESULTS

There are many methods in existence for calculating results of RIAs. Each is based on obtaining a calibration curve by plotting the extent of binding against stated concentrations of the calibration calibrators. This graph may be either a linear or logarithmic scale. Each of these methods gives essentially the same values for controls and samples, although certain assays may "fit" better into one particular method versus another. The calculation method for the DiaSorin Quality Control Laboratory is % B/B_0 [amount of tracer bound by sample (B), divided by the amount of tracer bound by the zero calibrator (B_0) x 100] (see step 3 below) versus log concentration.

11.1 Calculate the average (CPM) for each calibrator, control, and unknown sample.

11.2 Subtract the average CPM of the Non Specific Binding (NSB) tubes from all counts.

11.3 Divide the corrected CPM of each calibrator, control, or sample, by the corrected CPM of the Calibrator 0.

$$\% \, B/B_0 = \frac{\text{CPM of Calibrator or Unknown Sample} - \text{CPM of NSB}}{\text{CPM of Calibrator 0} - \text{CPM of NSB}} \times 100$$

11.4 Using three cycle semi-log graph paper, plot percent B/B_0 for the EPO-Trac calibrators (vertical axis) versus the concentration printed on the quality control specification sheet (horizontal axis).

11.5 Draw a best-fit line through the points (FIGURE 1).

11.6 Interpolate the levels of erythropoietin in the unknown samples from the plot.

11.7 If any unknown sample reads <4.4 mU/mL, the limit of detection of this test, report value as <4.4 mU/mL.

11.8 If any unknown sample reads greater than the highest calibrator, it should be diluted with EPO-Trac Calibrator 0, Cat. No. 23211 and reassayed. Dilutions of 1:2 and 1:5 will be sufficient for most samples.

12. LIMITATIONS OF THE PROCEDURE

12.1 The results of this assay should be used in conjunction with information available from clinical evaluations and other diagnostic procedures.

12.2 No drugs have been tested for assay interference.

TABLE II
DiaSorin EPO-Trac™ RIA Sample Data

Tube	CPM (mU/mL)	Average CPM	Average (CPM-NSB) (B)	Percent Bound (B/T)**	Percent Bound (B/B_0)	Conc. (mU/mL)	*Corr. Conc.
Total Count	14,823						
(T)14,270	14,546						
NSB	492						
	447	470		3.2**			
Calibrator 0	4,783						
	4,904	4,844	4,374 (B_0)	33**	100.0	0	
Calibrators							
1	4,321						
	4,273	4,297	3,827		87.5	9.0	
2	3,832						
	3,773	3,803	3,333		76.2	19.0	
3	2,896						
	2,920	2,908	2,438		55.7	39.0	
4	1,645						
	1,669	1,657	1,187		27.1	83.0	
5	865						
	932	898	428		9.8	290.0	
Control Level 1	3,924						
	3,877	3,901	3,431		74.4	16.9	
Control Level 2	1,918						
	1,935	1,927	1,457		33.3	69.3	
UKN No. 1	1,217						
	1,232	1,225	755		17.3	127	
1:2	1,832						
	1,873	1,853	1,383		31.6	72.6	124.8
UKN No. 2	1,508						
	1,437	1,472	1,002		22.9	96.6	
1:2	2,264						
	2,309	2,286	1,816		41.5	56.0	91.6

Typical sample data and a calibrator curve are shown in TABLE II and FIGURE 1; this information is for reference only and should not be used for the calculation of any value.

* Corr. conc. = Corrected concentration; for diluted samples only.

** These parameters are monitored for quality control purposes (see Quality Control section).

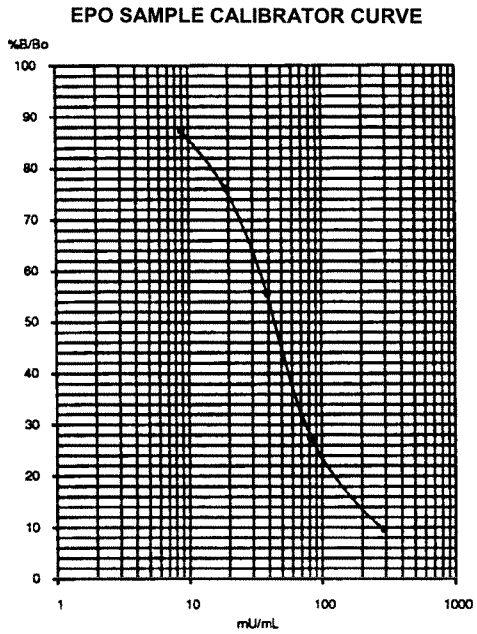

FIGURE 1

* This graph is generated from the Sample Data (TABLE II) and is for reference only. Do not use it for calculating your assay values.

13. EXPECTED VALUES

13.1 Normal Range

EACH LABORATORY SHOULD ESTABLISH ITS OWN NORMAL RANGE.

Serum erythropoietin levels were measured in one hundred and four (104) normal males and females (45 M, 61 F) from Minneapolis, Minnesota using the EPO-Trac RIA. The average EPO value was found to be 17.7 ±7.5 mU/mL. Individual values ranged from a minimum of 4.9 to a maximum of 52.7 mU/mL. The average serum EPO value for normal females was 18.3, with 16.6 mU/mL for normal males. No statistical difference ($p = 0.27$) was observed between male and female EPO levels.

Several other investigations of normals, using in-house EPO RIAs found average EPO levels similar in magnitude to the above study.[2, 4, 5] Some of these studies found significant but small differences between males and females, with females having slightly higher values than males.[8, 9] The results of these studies are summarized in the following table:

Study	Sex	n=	Mean ±1 S.D.
Koeffler 1981[2]	both	26	14.9 ±4.2 mU/mL
Garcia 1982[4]	males	364	17.2 ±5.5 mU/mL
	females	199	18.8 ±6.2 mU/mL
Ryner 1989[5]	males	50	8.0 ±3.2 mU/mL
	females	50	11.3 ±3.4 mU/mL

13.2 Disease State Values

Abnormal circulating EPO concentrations, when examined with other clinical information, may be characteristic of specific disease conditions.

Patients with polycythemia rubra vera typically present with normal or below serum EPO when measured with in-house RIA's.[8, 9] Those patients with secondary polycythemia brought on by hypoxia, as in congestive heart failure or chronic obstructive pulmonary disease, present with elevated EPO levels.[3, 8, 9] Ectopic EPO production can sometimes result in elevated serum EPO and subsequent secondary polycythemia in patients with uterine myoma, cerebellar hemangioblastoma, hepatic carcinoma, and pheochromocytoma. Renal tumors, including hypernephroma, adenoma and sarcoma, can result in similar EPO-related erythrocytosis.[2]

Most anemic patients have elevated serum EPO although the extent of elevation is dependent on the degree and type of anemia. Elevations in serum EPO may be found in patients with sickle cell anemia or with HIV infection although EPO levels, on average, are less pronounced than in other anemias.[10, 11]

The anemias found in renal disease patients are thought to result from deficient erythropoietin production by diseased or absent kidneys. Anephric anemic dialysis patients have low or undetectable EPO levels.[12] On the other hand, dialysis-dependent patients, with end stage renal disease, usually have normal or elevated serum EPO. The levels of serum EPO seen in these patients, however, are thought to be inappropriately low for their degree of anemia.[12, 13] Patients with recent kidney transplants sometimes have elevated serum EPO in response to their anemia.[14]

In a clinical study in Minneapolis, Minnesota, EPO levels were measured by the EPO-Trac RIA in twenty eight (28) nephric dialysis patients with end-stage renal disease. Serum EPO levels averaged 38.4 ± 67.1 mU/mL (range: 10.4-360.6 mU/mL), while hemoglobin levels averaged 9.4 ±1.6 g/dL (range: 6.9 to 12.3 g/dL). This value was considered to be inappropriately low for a patient population having an equivalent degree of anemia, but normal renal function.[12, 15] This study confirmed findings by previous investigators of relative erythropoietin deficiency in dialysis dependent patients.[15, 16] Additionally, erythropoietin levels were determined in a number of patient groups. The following table shows the average EPO levels measured. Patient controls were randomly selected from the patient population evaluated.

Summary table of mean EPO levels in various patient groups using the EPO-Trac RIA Kit

Diagnosis	n	Mean EPO (mU/mL)	S.D.
Normals	36	15.7	10.5
Patient Controls	18	18.6	11.3
Dialysis Patients	28	38.4	67.1
Myelodysplasia	2	651.0	887.2
Myelofibrosis	2	116.0	147.5
Erythroid Hypoplasia/Aplasia	4	1545	1213
Non-Hodgkin's Lymphoma	15	26.4	13.8
Hodgkin's Disease	3	29.8	31.3
Chronic Lymphocytic Leukemia	3	17.4	9.7
Macroglobulinemia	2	30.2	15.1
Myeloma	3	49.7	52.3
Hemolytic Anemia	3	51.4	29.2
Miscellaneous Anemias	10	32.2	18.9
Erythrocytotic Patients	6	14.6	8.5
Polycythemia Vera Patients	6	20.7	4.9

Erythropoietin levels exhibited above may or may not be consistent with the disease states listed. All patients were in various stages of treatment which may alter the erythropoietin level expected for their specific disease state. Consideration must be given to individual patient status and health of their erythropoietic system when interpreting specific erythropoietin levels.

14. PERFORMANCE DATA

14.1 Reproducibility

Within-assay variation Serum (Values = mU/mL)

	Mean Value	S.D.	%C.V.**	N
LOW	11.1	1.3	11.9	20
LOW	12.4	1.2	10.0	20
LOW	22.9	1.2	5.2	10
MEDIUM	39.9	1.9	4.8	10
HIGH	106.5	5.1	4.8	10
HIGH	254.6	29.8	11.7	20

Between-assay variation Serum (Values = mU/mL)

	Mean Value	S.D.	%C.V.**	N
LOW	9.8	1.4	14.3	5
LOW	13.2	1.6	12.1	5
LOW	19.0	1.3*	6.7	5
MEDIUM	40.9	1.4	3.5	5
HIGH	147.6	15.7	10.6	5
HIGH	220.2	26.9	12.2	5

* Samples were run in five separate assays (n = 5)

** % C.V. = (S.D. ÷ Mean) 100

14.2 TRUENESS: THE ASSAY TRUENESS HAS BEEN CHECKED BY THE LINEARITY AND THE RECOVERY TEST.

Dilution Parallelism

Serial Dilution Study of Unknown Serum Samples

Sample	Dilution	EPO Mean (mU/mL)	% mean/ 0 Dilution Mean
1	0	15.6*	-
	1:2	17.4	111.5
2	0	127.1	-
	1:2	124.8	98.2
	1:4	141.2	111.1
	1:8	152.0	119.6
3	0	96.6	-
	1:2	91.6	94.8
	1:4	100.4	103.9
	1:8	100.0	103.5
4	0	51.3	-
	1:2	52.8	102.9
	1:4	38.4	74.9
			Mean = 102.3

* Zero dilution values were measured values prior to dilution with DiaSorin serum diluent.

Accuracy

Recovery Study Serum (Values = mU/mL)

Set No.	Background*	EPO Calibrator Added	Measured Value**	Percent Recovery ***
1	8.9	19.5	27.3	94.4
	8.9	41.5	51.9	103.6
	8.9	145.0	182.0	119.4
2	18.1	19.5	37.3	98.5
	18.1	41.5	66.0	115.4
	18.1	145.0	205.6	129.3
3	44.3	19.5	62.9	95.4
	44.3	41.5	87.6	104.3
	44.3	145.0	158.5	78.8
4	80.8	19.5	101.3	105.1
	80.8	41.5	127.1	111.6
	80.8	145.0	210.7	89.6
				Mean = 103.8

* Assayed sample value divided by 2.

** Equal volume of EPO-Trac calibrator 3, 4, and 5, and patient sample combined.

*** %Recovery = [(measured-background)/EPO added] x 100

14.3 Analytical Sensitivity (Limits of Detection)

The minimum detectable concentration of EPO is 4.4 mU/mL, when defined as the apparent concentration at 3 calibrator deviations from the counts at maximum or zero binding. Unknown samples reading less than the sensitivity of this assay should be reported as <4.4 mU/mL.

14.4 Analytical Specificity

Results from a cross-reactivity experiment using the EPO-Trac RIA system and 8 naturally occurring serum proteins showed <0.001% cross-reactivity when measured at the sensitivity of the assay (4.4 mU/mL).

Substances	% Cross-reactivity
Human albumin	<0.001
Granulocytic macraphage-colony stimulating factor (GM-CSF)	<0.001
Interleukin-3	<0.001
Alpha-1 antitrypsin	<0.001
Human chorionic gonadotropin	<0.001
Alpha-1 acid glycoprotein	<0.001
Human IgG	<0.001
Human IgM	<0.001

The gene sequence of erythropoietin was compared to all human gene sequences in the Genbank and EMBL data bases. The search found no genes to be significantly similar to the erythropoietin gene sequence.

14.5 Interference

Studies were evaluated according to NCCLS methods to determine interference of hemoglobin, tryglyceride, and bilirubin. These studies indicate that no interference was observed.

14.6 Sample Type

Paired Plasma EDTA and Serum samples were shown to be highly correlated.

Y (SERUM) = 0.9 + 0.993 (PLASMA); r = 0.93 (range: 4.7 - 42.5 mU/mL; serum).

SEE LAST PAGE FOR REFERENCES

REFERENCES/BIBLOGRAPHIE/LITERATUR/BIBLIOGRAFÍA/BIBLIOGRAFIA/ REFERÊNCIAS/ΒΙΒΛΙΟΓΡΑΦΙΑ

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SYMBOLS USED WITH DEVICES

	English	Français	Deutsch	Español	Italiano
CE	European Conformity	Conformité aux normes européennes	CE – Konformitäts-kennzeichnung	Conformidad europea	Conformità europea
	Expiration Date	Date limite d'utilisation	Mindesthaltbar-keitsdatum	Fecha de caducidad	Data di scadenza
	Manufacturer	Fabricant	Hersteller	Fabricante	Fabbricante
	Consult Instructions for Use	Consulter les instructions d'utilisation	Gebrauchsanwei-sung beachten	Consulte las instrucciones de uso	Consultare le istruzioni per l'uso
IVD	In vitro diagnostic.	Diagnostic in vitro.	In-vitro-Diagnostikum.	Diagnóstico in vitro.	Diagnostica in vitro.
LOT	Lot No.	No. de lot	Chargen-Nr.	Número de lote	Lotto n°
	Temperature limitation.	Limitation de température.	Temperaturbereich	Limitación de temperatura	Limite della temperatura
Ab	Antiserum	Antisérum	Antiserum	Antisuero	Antisiero
Ab PEG	Precipitating reagent	Réactif précipitant	Fällungsreagenz	Reactivo precipitante	Reagente precipitante
Ag ^{125}I	Tracer: antigen labelled with ^{125}I	Traceur : antigène marqué à l'iode ^{125}	Tracer: ^{125}I-markiertes Antigen	Trazador: antígeno etiquetado con ^{125}I	Tracciatore: antigene etichettato con ^{125}I
CAL	Calibrator	Étalon	Kalibrator	Calibrador	Calibratore
CONTROL	Control serum	Sérum de contrôle	Kontrollserum	Suero de control	Siero di controllo
DNR	Dry Natural Rubber	Caoutchouc naturel sec	Trockener Naturkautschuk	Goma natural seca	Gomma naturale secca
	Radioactive	Radioactif	Radioaktiv	Radiactivo	Radioattivo
Xn	Harmful	Nocif	Gesundheits-schädlich	Nocivo	Nocivo

SYMBOLS USED WITH DEVICES CONTINUED ON NEXT PAGE.

CONTINUED FROM PREVIOUS PAGE - SYMBOLS USED WITH DEVICES

	Português	Ελληνικά
CE	Conformidade com as normas europeias	Ευρωπαϊκή Συμμόρφωση
	Prazo de validade	Ημερομηνία Λήξης
	Fabricante	Κατασκευαστής
	Consulte as instruções de utilizaçäo	Συμβουλευτείτε τις Οδηγίες Χρήσης
IVD	Diagnóstico in vitro.	In vitro διαγνωστικό ιατροτεχνολογικό προϊόν.
LOT	N.º do lote	Αρ. παρτίδας
	Limite de temperatura.	Περιορισμοί θερμοκρασίας
Ab	Anti-soro	Αντιορός
Ab PEG	Precipitado no reagente	Αντιδραστήριο καθίζησης
Ag ^{125}I	Traçador: antígeno marcado com ^{125}I	Ιχνηθέτης: Αντιγόνο σημασμένο με ^{125}I
CAL	Calibrador	Βαθμονομητής
CONTROL	Soro de controlo	Ορός μάρτυρα
DNR	Borracha natural seca	Ξηρό φυσικό καουτσούκ
	Radioactivo	Ραδιενεργό
Xn	Nocivo	Επιβλαβής

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