EXHIBIT 1
Part 14 of 14

1 ♀ BORN 5-8-77 TO BLEED

EXPERIMENTAL ✱ G INJECTION

EPO β SPG POOLED I 6-22-77 UM-2 CONC

10/31/77	25 u/0.3 ml	11/11/77	25 u/0.3 ml
11/2/77	25 u/0.3 ml	11/13/77	25 u/0.3 ml
11/4/77	25 u/0.3 ml	11/16/77	25 u/0.3 ml
11/6/77	25 u/0.3 ml	11/18/77	25 u/0.3 ml
11/8/77	25 u/0.3 ml	11/21/77	25 u/0.3 ml

E.X. 10/31/77

Acc. # 77-794

HMR 935442

AM-ITC 01006743

AM670222076

PROJECT LOGBOOK C 23249

Subject [illegible] + Clinical Chemistry Determinations for 5 Hematocrits for Dr. Eugene Goldwasser Date 11/22/77 + 11/23/77 Page 15

Signature [illegible]

		A*	B	C	D*	E	F	G	H
Treatment Date	A(BH/11-16)								
Day in Study	I(BH/17-19)								
HEMATOLOGY: HCT (%)	I(H/20-23)	46	44	52	50	65	68	65	[illegible]
HGB (G %)	R(H/24-27)	16.2	15.6	15.2	17.2	21.2	22.7	22.7	19.8
RBC (10⁶/CUMM)	R(H/28-31)	8.36	8.23	8.11	7.26	8.89	8.53	9.04	8.16 X
WBC (10³/CUMM)	R(H/32-35)	7.1	6.6	8.4	8.0	17.8	19.0	19.7	4.2 X
RET (% RBC)	R(H/36-39)	1.3	1.0	0.5	1.5	2.3	2.4	4.1	1.6
Platelets (10³/CUMM)	I(H/40-43)								
Diff. %: Neut. I	I(H/44-45)	0	0	0	0	0	0	0	0
Neut. M	I(H/46-47)	53	12	9	16	9	19	17	9
Lympho.	I(H/48-49)	94	86	85	75	88	80	78	85
Eosino.	I(H/50-51)	3	2	3	5	0	0	2	2
Baso.	I(H/52-53)	0	0	0	0	0	0	0	0
Mono.	I(H/54-55)	1	0	3	4	3	1	3	4
Cells Observed (≠ 100)	I(H/56-58)	NR	NR	NR	NR	NR	NR	NR	NR
NRBC/100 WBC	I(H/59-60)	0	2	0	0	0	1	0	1
BLOOD CHEMISTRY: BUN (MG %)	I(B1/20-23)	25	24	25	22	28	37	36	28
BS (MG %)	I(B1/24-27)								
BSP (% RET/15 MIN)	I(B1/28-31)								
AP (I.U.)	I(B1/32-35)	37	58	65	51	49	24	36	27
SGOT (I.U.)	I(B1/36-39)	36	30	38	52	35	51	87	22
SGPT (I.U.)	I(B1/40-43)	27	26	27	39	30	30	41	24
PT (SEC)	R(B1/44-47)								
Creatinine (MG %)	R(B1/48-51)								
Bilirubin (MG %) T	R(B1/52-55)								
Bilirubin (MG %) D	R(B1/56-59)								
Na (MEQ/L)	I(B1/60-63)								
K (MEQ/L)	R(B1/64-67)								
Ca (MEQ/L)	R(B1/68-71)								
Cl (MEQ/L)	R(B1/72-75)								
Mg (MEQ/L)	R(B1/76-79)								
Sequence within day	I(B1/80)								
Weight (KG)	R(H/61-65)								
Sequence within day	I(H/75)								
Temperature	R(H/76-80)								

X - denotes duplicately run sample
* - denotes slightly clotted sample

HMR 935443

Read and Understood: Signature ______ Date ______

Comparative Pathology Report Form
A. J. CARLSON ANIMAL RESEARCH FACILITY
University of Chicago

ID # 0508 90977007953	MODE: C D E F M N P Q (R) S T ___	ACC. NO. 77-795
Acct # 38000163C116	AGE: NB I YA AD 6m	
User [illegible]	SEX: (M) F C S U H ___	
	ROOM: EM1	Hamster H

Supporting Studies:
___Micro ___Photo
___Paras ___EM
X Hemat ___U/A
___Sp St X Chem

Specimen:
___Live Animal ___ _____
X Carcass
___Fresh Tiss.
___Fixed Tiss.

Copy to CM _____
Copy to user _____
Phoned _____
Indexed _____

PRELIMINARY DIAGNOSIS:

COMMENTS:

James L. Kaplia D.V.M.
Prosector Date

FINAL DIAGNOSIS:

HMR 935444

Ward R Richter Mar 3-78

77-795

LAB REPORTS

Pro	WS	Tissue
✓	/	adipose
✓	/	adrenal
✓		aorta
✓	/	bladder
✓	/	bone
✓	/	brain
✓	/	caecum
✓	/	colon
✓	/	diaphragm
✓	/	duodenum
✓	/	esophagus
✓	/	eye
—		ear (mid)
✓	/	gall bladder
✓	/	gonad
✓	/	heart
✓		ileum
✓		jejunum
✓	/	kidney(s)
✓		larynx
✓	/	liver
✓	/	lung
✓		lymph node
✓		mammary glnd
—		med. l. node
✓	/	mes. l. node
✓	/	muscle
✓	/	pancreas
✓		parathyroid
✓	/	pituitary
✓		prostate
✓	/	saliv. glnd
~	/	sciatic n.
~	/	semin. ves.
✓	/	skin
✓	/	spinal cord
/	/	spleen
/	/	stomach
✓	/	trachea
~	/	thymus
/	/	thyroid
~		tongue
~		tonsils
~		ureters
~		urethra
—		uterus
—		vagina
JK		

DICTATION GUIDE

EXTERNAL APPEARANCE: hair, eyes, skin, nodes, extremities, rigidity, lividity, scalp, nares, perineum
PERITONEAL CAVITY: fat, fluid, adhesions, position of organs, hernias
PLEURAL CAVITIES & MEDIASTINUM: fluid, lung expansion, widening of med.
HEART & VESSELS: size, fat, color, smoothness of endo & epicardium, chambers, cordae tend., pap. mus., hemorrhages, thrombi, valves, thickenings, coronary arteries
RESPIRATORY TRACT: nasal cav., sinuses, larynx, trachea, lung consist., crepitation, pleural surfaces, cut surfaces
ALIMENTARY TRACT: oral cav., sal. glands, pharynx, esophagus, stomach, intestine, colon, anus, contents, serosa, mucosa, scars, Peyer's patches, mesenteric surface, vessels, nodes
LIVER: size, shape, color, surface, consistency, veins, arteries
BILIARY SYSTEM: patency, size, contents, serosa, mucosa, wall, color
PANCREAS: weight, color, consistency
URINARY TRACT: kidney--shape, wt., surface, size of cortex, contents of pelvis, arteries, veins, fat; bladder, urethra & ureter--contents, mucosa, serosa, patency
GENERATIVE ORGANS: prostate, semin. ves., testes, epididymes, vagina, uterus, fall. tubes, ovaries--size, shape, surface, content
SPLEEN: size, color, consistency, cut surface, shape
LYMPH NODES: superficial, mediastinal, periaortic, portal pelvic, mesenteric; TONSILS, THYMUS: size, color, consistency
BONE MARROW: ribs, vertebra, sternum; color, consistency
ENDOCRINE GLANDS: pituitary, thyroid, parathy., adrenals; symmetry, size, color, nodules
BONES, JOINTS, SYNOVIA: shape, size, contents
SKELETAL MUSCLES: symmetry, color, fibrosis, measure if a/hypertrophic
HEAD: scalp, galea, calvarium
BRAIN: CSF, color, consistency, dura, vessels
SPINAL CORD: dura, contents of space

SPECIAL GROSS OBSERVATIONS: speculations, deduced conclusions

LABORATORY DETERMINATIONS:
MICROBIOLOGY: blood, organs, exudate, pul. nodes, CSF, stool, urine
PARASITOLOGY: fecal flotation
SEROLOGY:
VIROLOGY:

HISTOLOGIC ADJECTIVES: mild, moderate, severe, generalized, diffuse, focal, multifocal

lungs, bowel, bladder perfused

HMR 935445

77-795 NECROPSY REPORT

Post mortem interval: 5.5 to 6.5 hrs ♂ Weight: 125 (9) kg

ORGAN: OBSERVATION

✓ = W.N.L.

• ADRENALS	✓	R. 0.0002g, L. 0.0002g
AORTA	✓	
BLADDER	✓	
BONE	✓	
• BRAIN	✓	0.9095g
CAECUM	✓	
COLON	✓	
DUODENUM	✓	
ESOPHAGUS	✓	
EYE	✓	
GALL BLADDER	✓	
• GONADS	✓	R. 0.3438g, L. 0.4045g
• HEART	+	0.4440g
ILEUM	✓	
JEJUNUM	✓	
• KIDNEYS	✓	R. 0.3540g, L. 0.3338g
• LIVER	+	4.7750g
• LUNG	✓	1.3541g
LYMPH NODE	✓	
MES. NODE	✓	
MUSCLE	✓	
OPTIC NERVE	✓	
PANCREAS	✓	
PERIPHERAL NERVE	✓	
? PITUITARY	✓	Too small to weigh
PROSTATE	✓	
SALIVARY GLAND	✓	
SEMINAL VESICLE	✓	
SKIN	✓	
SPINAL CORD	✓	
• SPLEEN	✓	0.1212g
STERNUM	✓	
STOMACH	✓	
TRACHEA	✓	
THYMUS	✓	
THYROID	✓	
TONGUE	✓	
UTERUS	—	

Liver: mottled, enlarged, extends 2 cm beyond sternum at midline

Free blood in pleural cavity with clot over left ventricle

HMR 935446

-3-

☐cont'd p. 6

77-795 HISTOPATHOLOGIC EVALUATION

TISSUE: OBSERVATION

✓ = N.K.L	
ADRENALS	✓
AORTA	—
BLADDER	✓
BONE	✓
BRAIN	✓
CAECUM	✓
COLON	✓
DUODENUM	✓
ESOPHAGUS	✓
EYE	✓
GALL BLADDER	—
GONADS	+ moderate testicular degeneration + aspermia
HEART	+ subepicardial hemosiderosis, trace
ILEUM	—
JEJUNUM	—
KIDNEYS	✓
LIVER	✓
LUNG	✓
LYMPH NODE	—
MES. NODE	✓
MUSCLE	✓
OPTIC NERVE	✓
PANCREAS	✓
PERIPHERAL NERVE	✓
PITUITARY	✓
PROSTATE	✓
SALIVARY GLAND	✓
SEMINAL VESICLE	✓
SKIN	✓
SPINAL CORD	✓
SPLEEN	+ mild extramedullary hematopoiesis
STERNUM	+ 100% cellularity M/E ratio ≃ 1/3
STOMACH	✓
TRACHEA	✓
THYMUS	✓
THYROID	✓ small area examined
TONGUE	—
UTERUS	—

HMR 935447

☐cont'd p. 6

97-795 HISTORY AND CLINICAL SUMMARY

ID # Date_____ Euthanized _____

Acct. # Found dead ____am pm __/__/__ _____

User Last observed____am pm __/__/__

D.N.A.;

CLINICAL DIAGNOSIS:

HMR 935448

Clinician -5- cont'd: p. 6

77-795 CONTINUATION PAGE

☐ History ☐ Necropsy ☐ Histopath ☐ Comments

[redacted]

☐ History ☐ Necropsy ☐ Histopath ☐ Comments

[redacted]

HMR 935449

1 ♂ BORN 5-8-77

EXPERIMENTAL [redacted] TO BLEED

RPO INJECTION EPO/β Sat's Pooled I 6-22-77 UM-2 Conc

10/31/77	Bled	25u/0.3ml		11/77	25u/0.3ml
11/3/77		25u/0.3ml		11/13/77	25u/0.3ml
11/4/77		25u/0.3ml		11/16/77	25u/0.3ml
11/7/77		25u/0.3ml		11/18/77	25u/0.3ml
11/8/77		25u/0.3ml		11/21/77	25u/0.3ml

E.Y. 10/21/77

Accession # 77-795

HMR 935450

PROJECT LOGBOOK

C 23249

Subject [illegible] Date 11/22/77 & 11/23/77

Page 35

Signature [illegible]

			A*	B	C	D*	E	F	G	H
Treatment Date		A(BH/11-16)								
Day in Study		I(BH/17-19)								
HEMATOLOGY	HCT (%)	I(H/20-23)	46	44	52	50	65	68	65	
	HGB (G %)	R(H/24-27)	16.2	15.6	18.2	17.2	21.2	22.1	22.1	17.3
	RBC (10^6/CUMM)	R(H/28-31)	9.26	9.23	9.11	7.26	9.59	9.53	9.04	8.15
	WBC (10^3/CUMM)	R(H/32-35)	7.1	6.6	8.4	8.0	17.2	19.0	19.7	4.2
	RET (% RBC)	R(H/36-39)	1.3	1.0	0.8	1.5	2.3	2.9	4.1	1.6
	Platelets (10^3/CUMM)	I(H/40-43)								
DIH. %	Neut. I	I(H/44-45)	0	0	0	0	0	0	0	0
	Neut. M	I(H/46-47)	33	12	9	16	9	19	17	9
	Lympho.	I(H/48-49)	94	86	85	75	88	80	76	85
	Eosino.	I(H/50-51)	3	2	3	5	0	0	2	2
	Baso.	I(H/52-53)	0	0	0	0	0	0	0	0
	Mono.	I(H/54-55)	1	0	3	4	3	1	3	4
	Cells Observed (# 100)	I(H/56-58)	N2	N2	N2	N2	N2	N2	N2	N2
	NRBC/100 WBC	I(H/59-60)	0	2	0	0	0	1	0	1
BLOOD CHEMISTRY	BUN (MG %)	I(B1/20-23)	25	24	25	22	28	37	36	23
	BS (MG %)	I(B1/24-27)								
	BSP (% RET/15 MIN)	I(B1/28-31)								
	AP (I.U.)	I(B1/32-35)	37	58	65	51	49	24	36	27
	SGOT (I.U.)	I(B1/36-39)	36	30	38	52	35	51	87	22
	SGPT (I.U.)	I(B1/40-43)	27	26	29	39	30	30	41	24
	PT (SEC)	R(B1/44-47)								
	Creatinine (MG %)	R(B1/48-51)								
	Bilirubin T	R(B1/52-55)								
	(MG %) D	R(B1/56-59)								
	Na (MEQ/L)	I(B1/60-63)								
	K (MEQ/L)	R(B1/64-67)								
	Ca (MEQ/L)	R(B1/68-71)								
	Cl (MEQ/L)	R(B1/72-75)								
	Mg (MEQ/L)	R(B1/76-79)								
Sequence within day		I(B1/80)								
Weight (KG)		R(H/61-65)								
Sequence within day		I(H/75)								
Temperature		R(H/76-80)								

X - denotes duplicately run sample
* - denotes slightly clotted sample

HMR 935451

Read and [illegible] Signature [illegible] Date [illegible]

AM670222085

AM-ITC 01006752

Reprinted from ENDOCRINOLOGY, August 1975
Vol. 97, No. 2

An Assay for Erythropoietin *in Vitro* at the Milliunit Level

E. GOLDWASSER, J. F. ELIASON,[1] AND D. SIKKEMA

Department of Biochemistry, University of Chicago, and [2] The Franklin McLean Memorial Research Institute, Chicago, Illinois 60637

ABSTRACT. A method is described for the assay of erythropoietin using primary cultures of adult rat bone marrow cells. Either total labeled iron uptake by the cells or hematin synthesis from labeled iron may be used as the measure of erythropoietin action. The method is useful in the range 0.001 to 0.010 U, where the log response is linear with the log dose, and can be carried out in 2 working days. This method has the disadvantage of detecting asialoerythropoietin which has no activity *in vivo*. (*Endocrinology* 97: 315, 1975)

THE need for a rapid, sensitive, and precise method of assay for erythropoietin has been apparent for a long time. Conventional bioassay methods, based on measurement of increased rates of red cell formation, require either too much erythropoietin, too much time, or both, in addition to having a low degree of precision. In the 11 years since we published data showing that rat bone marrow cells, in primary culture, respond to graded amounts of erythropoietin with a dose-response curve similar to that found *in vivo* (1), there have been several reports (2–5) showing that marrow or fetal liver cells can be used *in vitro* for the quantitative estimation of erythropoietin. In this paper, we describe an *in vitro* method for the routine, rapid determination of erythropoietin in the range from 0.001 to 0.01 U.

Materials and Methods

Cells. Femora and tibiae from male Sprague-Dawley rats (10 to 12 weeks old) are the source of marrow cells. Cells are removed sterilely by flushing out the bones after puncturing one end with a 22 gauge needle and injecting medium into the other end. Several flushings are needed to maximize the yield, which should be 4–5 × 10^8 nucleated cells per rat. The cell clumps are dispersed by repeated gentle ejection from a dropper or pipet. Rat marrow cells tend to aggregate very readily, and repeated dispersal is required to yield reproducible aliquots. Before the final dilution is made, the cell suspension is filtered through a sterile stainless steel screen (100 mesh) to remove bits of bone and connective tissue.

Medium. The basic constituents of the medium are NCTC 109, fetal calf serum, and rat serum. As long as the original NCTC 109 is used, rather than the modification, NCTC 135, the source of supply is immaterial. Tests of additions to the NCTC 109 formulation are described below.

The fetal calf serum is heat inactivated at 56 C for 30 min before use, in order to minimize the loss of erythrocytes during the culture period due to complement-promoted lysis. Each new lot of serum must be tested for adequacy of cellular response to erythropoietin before it can be used routinely. We have found that lots of serum from K. C. Biological Inc., Lenexa, Kansas; International Scientific Industries Inc., Cary, Illinois; Baltimore Biological Laboratories, Cockeysville, Maryland; and Reheis Chemical Company, Kankakee, Illinois, were all suitable.

Rat serum is used as a source of transferrin, both for unlabeled iron, which is required for optimal response by the cells (6), and for labeled iron. Data from this laboratory have shown that rat marrow cells utilize iron from rat transferrin to a considerably greater extent than from transferrins of other species, although human transferrin can also be used (7). As a source of unlabeled iron we use unhemolyzed rat serum to which 73 nmoles of ferric nitrate per ml have been added. Rat transferrin is labeled with radioiron as follows: to 5.0 ml of frozen, unhemolyzed serum are added 4.0 ml of NCTC 109, 0.5 ml of 0.9M $NaHCO_3$, and 0.5 ml

Received September 13, 1974.
[1] Supported by Training Grant No. GM 424 from The National Institute of General Medical Sciences.
[2] Operated by the University of Chicago for the United States Atomic Energy Commission.
This work was supported, in part, by USPHS grant HC-16005.

THE JOURNAL OF BIOLOGICAL CHEMISTRY
Vol. 252, No. 15, Issue of August 10, pp. 5558-5564, 1977
Printed in U.S.A.

Purification of Human Erythropoietin*

(Received for publication, January 26, 1977, and in revised form, April 11, 1977)

TAKAJI MIYAKE,‡ CHARLES K.-H. KUNG, AND EUGENE GOLDWASSER

From the Department of Biochemistry, University of Chicago, and The Franklin McLean Memorial Research Institute,§ Chicago, Illinois 60637

Human erythropoietin, derived from urine of patients with aplastic anemia, has been purified to apparent homogeneity. The seven-step procedure, which included ion exchange chromatography, ethanol precipitation, gel filtration, and adsorption chromatography, yielded a preparation with a potency of 70,400 units/mg of protein in 21% yield. This represents a purification factor of 930. The purified hormone has a single electrophoretic component in polyacrylamide gels at pH 9, in the presence of sodium dodecyl sulfate at pH 7, and in the presence of Triton X-100 at pH 6. Two fractions of the same potency and molecular size, by sodium dodecyl sulfate gel electrophoresis, but differing slightly in mobility at pH 9, were obtained at the last step of fractionation. The nature of the difference between these two components is not yet understood.

Erythropoietin is an acidic glycoprotein that is present at a very low concentration in plasma under normal conditions. Under anemic or anoxic stress, it is found in relatively large amount in the plasma and is also excreted in the urine. Erythropoietin is the substance that is responsible, in large part, for the regulation of normal red blood cell differentiation. Because of this function, and because it may have a role in replacement therapy of some kinds of anemia, it is important to have pure erythropoietin in an amount sufficient for chemical characterization. Reports on the purification of human (1) and sheep (2) erythropoietin have been published. In the former, the evidence for homogeneity was not convincing, and in the latter, the total amount was too low for adequate characterization. We report in this paper on the preparation of milligram quantities of human urinary erythropoietin in a state of apparent homogeneity.

EXPERIMENTAL PROCEDURES

Bioassay—The fasted rat method of bioassay (3),[1] in which the incorporation of labeled iron into circulating red cells is measured, was used routinely to quantitate the amount of erythropoietin activity. Samples for assay were dissolved in 0.1% bovine serum albumin in 0.15 M NaCl, 0.01 M $CaCl_2$. Over the 18-month period covered by this work, the ln dose-ln response curve obtained when 1, 1.5, 2, and 3 units of erythropoietin[1]/rat were used had the following characteristics: slope, 1.11 ± 0.34; intercept, 0.75 ± 0.39; correlation coefficient, 0.96 ± 0.10. The assay values found for the two final hydroxylapatite fractions were confirmed by the polycythemic mouse method (3) which agreed closely with the other two assay methods. We are indebted to Dr. Walter Fried of the Michael Reese Hospital for doing the mouse assays. For the iodinated preparation and for the assay of activity recovered from polyacrylamide gels, biological activity was measured by the marrow cell culture method (4). This procedure, in which both the total uptake of radio-iron and its incorporation into hemoglobin are used as quantitative indicators of erythropoietin activity, is about 1000 times more sensitive than the fasted rat method, but does not distinguish between native erythropoietin and the asialo form, which is inactive *in vivo*.

Materials—Sodium dodecyl sulfate and DEAE-agarose were bought from Bio-Rad Laboratories, Richmond, Calif., as was hydroxylapatite (Bio-Gel HT, Control 12746); we found no significant difference between several different lots which we used. Sulfopropyl Sephadex (Lot 7963) and Sephadex G-100 (Lot 5011) were bought from Pharmacia Inc., Piscataway, N. J. Materials for gel electrophoresis (acrylamide, *N,N,N',N'*-tetramethylethylenediamine and *N,N'*-methylenebisacrylamide) and Triton X-100, scintillation grade, were bought from Eastman Kodak Co., Rochester, N. Y. Labeled iodide was obtained from Amersham-Searle Corp., Arlington Heights, Ill. Other reagents used were of the best quality commercially available. Ultrafilters were bought from Amicon Corp., Lexington, Mass. PBS is used to designate a solution consisting of 0.15 M NaCl, 0.01 M sodium phosphate buffer, pH 7.0.

Iodination—Labeling with ^{125}I (5, 6) was done as follows. To 20 μl of an erythropoietin solution containing 20 μg of protein, 2 μl of 0.5 M phosphate, pH 7.0, and 20 μl of dimethylsulfoxide were added. One microliter of $Na^{125}I$ (100 μCi, equivalent to 7.14 ng of iodide or 57 pg atoms) was then added, followed by 1 μl of freshly prepared chloramine-T (10 mg/ml in water). The mixture was allowed to stand at 24° for 10 min, after which 10 μl of $Na_2S_2O_5$ (25 mg/ml in water) were added. The solution was mixed and allowed to stand for 1 min; then 200 μl of KI (10 mg/ml in 0.05 M phosphate, pH 7.4) were added and mixed for 1 min at 24°, followed by addition of 50 μl of 7% (w/w) bovine serum albumin. The mixture was put on a Sephadex G-10 column (25 × 0.9 cm diameter), which had been equilibrated with PBS, being washed over to the column with two 200-μl washes of KI solution (10 mg/ml). The erythropoietin was separated from unreacted iodide by elution with PBS and collection of 0.3-ml fractions. The major peak material of large molecular weight label (Tubes 18 to 28) was pooled and dialyzed. The final volume of 4.1 ml contained 5.8 × 10^6 cpm of ^{125}I (2.9 × 10^6 cpm/μg of protein, equivalent to 0.1 g atom of iodine/mol of protein).

Because our previous experience showed that sheep erythropoietin was completely inactivated upon iodination using chloramine-T, we used the method of Stagg *et al.* (5), in which the presence of

* This work was supported in part by United States Public Health Service Grant HL 16005-03.

‡ Present address, Second Department of Internal Medicine, Kumamoto University Medical School, Kumamoto, Japan.

§ Operated by the University of Chicago for the United States Energy Research and Development Administration under contract EY-76-C-02-0069.

[1] One unit of erythropoietin is defined as the biological activity present in one-tenth of the contents of an ampule of the International Reference Preparation distributed by the World Health Organization. In the routine assay, we used, as a working standard, a preparation of sheep erythropoietin that had been standardized against the International Reference Preparation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service
Center for Drug Evaluation and Research
Office of Training and Communication
Freedom of Information HFD-205
5600 Fishers Lane 12 B 05
Rockville, Maryland 20857

August 23, 2000

In Response Refer to File : F99-23832

Kleinfeld Kaplan and Becker
Peter Safir
1140 19th Street, N.W., Suite 900
Washington, D.C. 20036-6601

Dear Mr. Safir:

This is in response to your request of November 5, 1999, in which you requested a copy of IND 16234. Your request was received in the Center for Drug Evaluation and Research on November 10, 1999.

The documents you have requested are enclosed.

Charges of $ 108.70(Search $87.00, Review $7.50, Reproduction $14.20, Computer time $0.00) will be included in a monthly invoice. **DO NOT SEND ANY PAYMENT UNTIL YOU RECEIVE AN INVOICE.**

If there are any problems with this response, please notify us in writing of your specific problem(s). Please reference the above file number.

This concludes the response for the Center for Drug Evaluation and Research.

Sincerely,

Roy V. Castle, Jr.,M.S.,P.D.
Freedom of Information Officer
Office of Training and Communication
Division of Freedom of Information HFD-205

HMR 935455