EXHIBIT 4

SECTION I

Form Approved OMB No. 0925-0001

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

APPLICATION FOR CONTINUATION GRANT

REVIEW GROUP	TYPE	ACTIVITY	GRANT NUMBER (Insert on all pages)
EH	5	R01	HL21676-06

TOTAL PROJECT PERIOD
From: 07/01/77 Through: 06/30/85

REQUESTED BUDGET PERIOD
From: 07/01/82 Through: 06/30/83

To Be Verified By Applicant. Check Information in Items 1 Through 6. If Incorrect, Furnish Correct Information in Item 13.

1. TITLE
ERYTHROPOIETIN: PURIFICATION, PROPERTIES, BIOGENESIS

2A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Name and Address, Street, City, State, Zip Code)
GOLDWASSER, EUGENE
UNIVERSITY OF CHICAGO
5801 SOUTH ELLIS AVENUE
CHICAGO, ILL 60637

4. APPLICANT ORGANIZATION (Name and Address, Street, City, State, Zip Code)
THE UNIVERSITY OF CHICAGO
5801 SOUTH ELLIS AVENUE
CHICAGO, ILL 60637

5. ENTITY IDENTIFICATION NUMBER
13621771394A1

2B. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT
BIOCHEMISTRY

2C. MAJOR SUBDIVISION
DIV OF BIOLOGICAL SCIENCES

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR INSTITUTIONAL GRANT (See Instructions)
01 SCHOOL OF MEDICINE

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION
DIRECTOR
OFFICE OF SPONSORED PROGRAMS
THE UNIVERSITY OF CHICAGO
5801 SOUTH ELLIS AVENUE
CHICAGO, ILL 60637

COMPLETE THE FOLLOWING (See Instructions)

7. HUMAN SUBJECTS, DERIVED MATERIAL OR DATA INVOLVED
☐ NO ☒ YES (If "YES," form HHS 596 required)

8. RECOMBINANT DNA RESEARCH SUBJECT TO NIH GUIDELINES
☒ NO ☐ YES

9. PERFORMANCE SITE(S)
The University of Chicago
920 East 58th Street
Chicago, Illinois 60637

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD
$164,023

11. INVENTIONS (See Instructions)
☒ NO ☐ Yes-not previously reported
☐ Yes-previously reported

TELEPHONE INFORMATION

	Area Code	Tele. No. & Ext.
12A. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Item 2a)	312	753-4911
12B. NAME OF BUSINESS OFFICIAL (Item 4) Donald S. Sigal	312	962-8604
12C. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 15) a) b) Same as 12B		

13. USE THIS SPACE FOR CORRECTIONS TO ITEMS 1 THROUGH 6. INDICATE THE NUMBER(S) WHERE ANSWER(S) APPLY.

2A The University of Chicago

TRIAL EXHIBIT OF 97-10814 WGY

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14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I Agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PERSON NAMED IN 2A (In ink. "Per" signature not acceptable)
Eugene Goldwasser

DATE
4/5/82

15. CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true and complete to the best of my knowledge, and accept the obligation to comply with the Public Health Service terms and conditions if a grant is awarded as the result of this application. A willfully false certification is a criminal offense. (U.S. Code, Title 18, Section 1001.)

SIGNATURE OF PERSON NAMED IN 12C (In ink. "Per" signature not acceptable)

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DEFENDANT'S EXHIBIT 193

DEFENDANT'S DEPOSITION EXHIBIT 30 10-13-99

PAGE 1

RETURN COMPLETED APPLICATION TO PHS AS SOON AS POSSIBLE: NO LATER THAN 1 MAY 1982

SECTION II

SECTION II—BUDGET (USUALLY 12 MONTHS) | FROM 07/01/82 | THROUGH 06/30/83 | GRANT NUMBER HL 21767-06

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD — DOLLAR AMOUNT REQUESTED (Omit cents)

PERSONNEL (Applicant organization only) (See instructions)

NAME	TITLE OF POSITION	TIME EFFORT %	TIME EFFORT Hours per Week	SALARY	FRINGE BENEFITS	TOTALS
Eugene Goldwasser	Principal Investigator	15		7,980	1,740	[redacted]
Fung-Fang Wang	Research Associate	100		18,836	3,428	
Charles Kung	Res. Technologist		40	26,347	4,796	
Annette Gardner	Res. Technician		40	19,090	3,474	
Carol Sims	Res. Technician		40	15,710	2,859	
Catherine Fowler	Lab. Assistant		40	13,515	2,460	
Yvonne Price	Secretary		20	6,503	1,184	
			SUBTOTALS	107,981	19,940	

(Indicate cost of each item listed below) TOTAL $127,921

CONSULTANT COSTS (See instructions) 0

EQUIPMENT (Itemize) [redacted] 0

SUPPLIES (Itemize by category) 200 rats @ 4.68 = $936, 300 mice @ 3.03 = $909, 100 nude mice @$ 49= $4900, Isotopes $4000, chemicals $2800, media $2200, glass and plastic ware $325, erythropoietin $16,000. [redacted] $32,070

TRAVEL — DOMESTIC 1 National meeting per investigator (E.G. & F.W.) 1,400; FOREIGN 0

PATIENT CARE COSTS — INPATIENT 0; OUTPATIENT 0

ALTERATIONS AND RENOVATIONS (Itemize by category) 0

CONTRACTUAL OR THIRD PARTY COSTS (See instructions) CONFIDENTIAL 0

OTHER EXPENSES (Itemize by category) Animal care $553, (4000 mouse days @ 0.091, $365; 1000 rat days @ 0.188, $188), maintenance contracts $1500, film badge service $150, postage $100, books and journals $140, Reprints $189. 2,632

TOTAL DIRECT COST (Enter on Page 1, Item 10) 164,023

INDIRECT COST (See instructions) — 57 % S&W* / % MTDC — Date of DHHS Agreement 07/06/81 — ☐ Not Requested ☐ Under negotiation with:

*If this is a special rate (e.g. off-site), explain.

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SECTION II—BUDGET (Continued)

Grant Number: HL 21767-06

B. Supplemental information regarding ITEMS in the proposed budget for the next period which require explanation or justification (See instructions)

"The inclusion of faculty salary in this budget is a policy of the Division of the Biological Sciences and The Pritzker School of Medicine. If an award is made in a reduced amount, the Principal Investigator will be asked to retain an appropriate amount of faculty salary support in the budget.

Most appointments in the Division of the Biological Sciences and the Pritzker School of Medicine are on a full-time, 12 month basis. Although salaries are assured on this basis, it is expected that investigators will recover reasonable and appropriate salary support from research grants and contracts proportionate to the fraction of their time and effort devoted to the research."

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SECTION III—DATA FOR CURRENT BUDGET PERIOD (USUALLY 12 MONTHS)	FROM:	THROUGH	GRANT NUMBER
	07/01/81	06/30/82	HL 21676-05

The following pertains to your CURRENT PHS budget. Do not include cost sharing funds. This information in conjunction with that provided on Page 2 will be used in determining the amount of support for the NEXT budget period.

A. BUDGET	CURRENT BUDGET (As approved by awarding unit) (1)	ACTUAL EXPENDITURES THRU 02/28/82 (Insert Date) (2)	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD (3)	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3) (4)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1) (5)
TOTAL DIRECT COSTS	153,751	102,908	42,843	145,751	+8,000
INDIRECT COSTS (As Provided)	91,015	58,542	24,421	82,963	+8,052
TOTALS	$ 244,766	$ 161,450	$ 67,264	$ 228,714	$ 16,052

B. THROUGH F.
See instructions and provide the information required in items B. through F. Use this page and continuation pages as necessary.

B. Professional Personnel

NAME	TITLE	CATEGORY	-25%	75%+
1. Goldwasser, Eugene	Professor	1	*	
2. Wang, Fung-Fang	Res. Assoc.	2		*
3. Kung, Charles	Res. Tech.	2		*

C. Equipment: None

D. Travel
1) C. Kung: a) Int. Symp. on HPLC of Peptides and Proteins
b) 2 workshops at Argonne Natl Lab.
2) F. F. Wang: FASEB Meetings

E. Explanation of column 5

The projected direct cost balance results from agency approval of release of 1/2 of the funds formerly restricted to the purchase of erythropoietin. The anticipated indirect cost balance reflects a University wide rate change: from 90% of salaries to 57% of modified total direct costs, effective 7/1/81.

F. Other support: NIH: Grant CA 18375 Hemopoietic Stem Cells and Induced Differentiation. P.I. E. Goldwasser (20%). Annual direct cost $75,154.
Grant HL 16005. Part of Comprehensive Sickle Cell Center - Studies of Erythropoiesis in vitro P.I. E. Goldwasser (10%) and M. Gross. Annual direct cost $89,724 (approx. one-half of this is for Dr. Gross' lab).

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SECTION IV

APPLICANT REPEAT GRANT NUMBER SHOWN ON PAGE 1

SECTION IV—SUMMARY PROGRESS REPORT

GRANT NUMBER: HL 21676-06

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial): Goldwasser, Eugene

PERIOD COVERED BY THIS REPORT: FROM 03/20/81 THROUGH 03/31/82

NAME OF ORGANIZATION: The University of Chicago

TITLE (Repeat title shown in Item 1 on first page): Erythropoietin: Purification, Properties, Biogenesis

1. List all publications, not previously reported, resulting from work supported by this grant (author(s), title, page numbers, year, journal or book). List manuscripts separately as submitted for publication or accepted for publication.
2. Provide two reprints of publications not previously submitted to the awarding unit.
3. Progress Report. (See instructions)

PUBLICATIONS

B. D. Tong and E. Goldwasser
The Formation of erythrocyte membrane proteins during erythropoietin-induced differentiation. pp 12666-12672, (1981) J. Biol. Chem. Vol. 256.

E. Goldwasser
Erythropoietin and red cell differentiation. pp. 487-494, (1981) in Control of Cellular Division and Development. eds. Cunningham, Goldwasser, Watson and Fox. A. R. Liss.

T. L. Weiss and E. Goldwasser.
The biological properties of endotoxin-free human erythropoietin. pp 17-21, (1981). Biochem. J. Vol. 198.

H.P. Koeffler and E. Goldwasser. Erythropoietin radioimmunassay in evaluating patients with polycythemia. pp 44-47, (1981), Ann Int. Med. Vol. 94.

Submitted. T. L. Weiss, C. Kavinsky and E. Goldwasser. Characterization of a monoclonal antibody to human erythropoietin.

J.B. Sherwood and E. Goldwasser. The heterogeneity of immunoreactive human serum erythropoietin.

Progress Report

1) Goals: No change from original

2) We have succeeded in developing a hybridoma which secretes a monoclonal anti-erythropoietin (epo), have purified the immunoglobin and are making and testing an immunoaffinity column for the purification of epo. In our continuing study of the chemical properties of epo we found, with Dr. L. Hood of Cal Tech, that the epo presumed to be homogeneous had, in fact, only one N terminal amino acid, alanine. The α and β forms have identical sequences of 28 residues at the N termini.

Our earlier conclusion that there were three free sulfhydryl groups that were not required for biological activity, was erroneous. This artifact arose because although ^{14}C N-ethylmaleimide appeared to be bound, it was not by covalent bonds, and the SH groups were not alkylated. When epo is denatured and reduced, the reagent then reacts with the SH groups and causes inactivation. Thus, epo appears to have two disulfide bonds which are essential for its biological activity. These findings make all of our recent efforts to label epo, by reactions at the SH group futile. We did, however, find an interesting paradox; (N-dimethyl amino-4-methyl-coumarinyl) malemide which is an SH reagent, binds to epo to yield a fluorescent derivative with full biological activity. We have used this labeled epo to determine the frequency of bone marrow cells with epo receptors, despite the ambiguities in the chemistry.

We have reinvestigated the apparent molecular weight of epo. With an estimate of the partial specific volume, based on a carbohydrate content of 40% we now find a molecular weight of 34000. The carbohydrate compositions of the α and β forms were determined after developing micromethods based on chromatography of the trifluoroacetyl derivatives of the sugars. There is a significant difference between the N-acetylglucosamine and sialic acids of the two forms, with no difference in fucose, galactose, mannose and glucose. We found no N-acetylgalactosamine.

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PAGE 5 (Use Continuation Page as necessary)

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Continuation page

Goldwasser, Eugene
SOCIAL SECURITY NUMBER
494-14-6535

DO NOT TYPE IN THIS SPACE-BINDING MARGIN

We have prepared deglycosylated epo by two methods: solvolysis with pyridine in anhydrous HF and by use of mixed glycosidases. Approximately 80% of the carbohydrate was removed by these techniques with retention of about 80% of the biological activity.

Because some of the biological properties of crude epo have been found to be due to contaminant endotoxin, we prepared pure epo, freed of endotoxin and examined its biological effects. This epo supports the growth of erythroid bursts from mouse marrow cells, stimulates hemoglobin synthesis and transcription by marrow and stimulates the formation of the marrow cytoplasmic factor that acts on isolated nuclei to increase transcription. Thus, the properties previously ascribed to epo are not due to contaminants.

Using the radioimmunoassay (RIA) for epo to determine the serum titer in patients with chronic renal disease we found a discrepancy between that found by the bioassay and the RIA; the latter being considerably higher. Further study of this showed that the sera of these patients contained immunoreactive components of smaller size than native epo. The presence of these "fragments" may account for the discrepancy if they have no biological activity. This is still to be determined.

In the continued study of the clinical effect of epo in patients with chronic renal disease on dialysis, we found a clearance curve, after injection, that has a secondary rise after the initial rapid fall off. Samples from the first part of the curve consisted of about 75% native epo (by size) and 25% "fragments;" samples from secondary rise portion were about 25% native and 75% "fragments." These data suggest that, in these patients, epo is removed from the circulation, broken down and immunoreactive "fragments" released. We do not yet know whether this is true in normals.

We have studied the effects of epo on the biogenesis of rat red cell membrane constituents in vitro. Stimulated synthesis of glycophorin, was maximal 30 hours after the addition of epo and fell to control by 66 hours. Stimulated synthesis of band 3 started at 18 hours, was maximal at 66 hours and at control by 114 hours. In contrast, stimulated synthesis of hemoglobin did not start until 24 hours, was maximal at 96 hours and at control by 114 hours. There was also an effect of epo on the transient synthesis of some membrane proteins found in marrow cells but not in red cells.

Lastly, we have provided for distribution by an NIH committee, 305,660 units of a partially purified epo with a potency of about 1100 U/mg protein. It is free of endotoxin, colony-stimulating factor and burst-promoting activity, acts on mouse and human cells to support burst growth and is non-inhibitory up to 10 U/ml.

3) For the coming year we aim at determing at least another 30 residues of erythropoietin primary protein structure. We will have in place and operating an immunoaffinity column based on the monoclonal antibody and will have developed a more rapid, solid-state radioimmunoassay using the monoclonal antibody to generate specificity, rather than the antigen. Methods for the separation of the fragments of erythropoietin in serum and urine will be developed and their size and composition determined. As we obtain more pure erythropoietin we will continue the study of its clinical efficacy and resolve problems inherent in its rate of clearance from the circulation. We hope to generate additional anti-erythropoietin hybridomas and use the antibodies to study the protein domains with the intent of understanding the structural basis for its biological activity.

4) There has been no change in the protocols for research involving normal subjects.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☒ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☒ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☒ CONTINUATION

APPLICATION IDENTIFICATION NUMBER (If known)

H1 21676-06

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHHS is primarily the responsibility of the institution which receives or is accountable to DHHS for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHHS that no activity involving human subjects to be supported by DHHS grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHHS a certification of such review and approval, in accordance with the requirements of Public Law 93-348, as implemented by Part 46 of Title 45 of the Code of Federal Regulations, as amended, (45 CFR 46). Administration of the DHHS policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, MD 20205.

1. TITLE OF PROPOSAL OR ACTIVITY

Erythropoietin: Purification, Properties, Biogenesis

2. PRINCIPAL INVESTIGATOR/ACTIVITY DIRECTOR/FELLOW

Eugene Goldwasser

3. DECLARATION THAT HUMAN SUBJECTS EITHER WOULD OR WOULD NOT BE INVOLVED

☐ A. NO INDIVIDUALS WHO MIGHT BE CONSIDERED HUMAN SUBJECTS, INCLUDING THOSE FROM WHOM ORGANS, TISSUES, FLUIDS, OR OTHER MATERIALS WOULD BE DERIVED, OR WHO COULD BE IDENTIFIED BY PERSONAL DATA, WOULD BE INVOLVED IN THE PROPOSED ACTIVITY. (IF NO HUMAN SUBJECTS WOULD BE INVOLVED, CHECK THIS BOX AND PROCEED TO ITEM 7. PROPOSALS DETERMINED BY THE AGENCY TO INVOLVE HUMAN SUBJECTS WILL BE RETURNED.)

☒ B. HUMAN SUBJECTS WOULD BE INVOLVED IN THE PROPOSED ACTIVITY AS EITHER: ☒ NONE OF THE FOLLOWING, OR INCLUDING: ☐ MINORS, ☐ FETUSES, ☐ ABORTUSES, ☐ PREGNANT WOMEN, ☐ PRISONERS, ☐ MENTALLY RETARDED, ☐ MENTALLY DISABLED. UNDER SECTION 8. COOPERATING INSTITUTIONS, ON REVERSE OF THIS FORM, GIVE NAME OF INSTITUTION AND NAME AND ADDRESS OF OFFICIAL(S) AUTHORIZING ACCESS TO ANY SUBJECTS IN FACILITIES NOT UNDER DIRECT CONTROL OF THE APPLICANT OR OFFERING INSTITUTION.

4. DECLARATION OF ASSURANCE STATUS/CERTIFICATION OF REVIEW

☐ A. THIS INSTITUTION HAS NOT PREVIOUSLY FILED AN ASSURANCE AND ASSURANCE IMPLEMENTING PROCEDURES FOR THE PROTECTION OF HUMAN SUBJECTS WITH THE DHHS THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHHS Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHHS DOCUMENTATION AND CERTIFICATION OF SUCH REVIEWS AND PROCEDURES AS MAY BE REQUIRED FOR IMPLEMENTATION OF THIS ASSURANCE FOR THE PROPOSED PROJECT OR ACTIVITY.

☒ B. THIS INSTITUTION HAS AN APPROVED GENERAL ASSURANCE (DHHS ASSURANCE NUMBER 01626) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHHS. THE SIGNER CERTIFIES THAT ALL ACTIVITIES IN THIS APPLICATION PROPOSING TO INVOLVE HUMAN SUBJECTS HAVE BEEN REVIEWED AND APPROVED BY THIS INSTITUTION'S INSTITUTIONAL REVIEW BOARD IN A CONVENED MEETING ON THE DATE OF 12/1/81 IN ACCORDANCE WITH THE REQUIREMENTS OF THE *Code of Federal Regulations on Protection of Human Subjects (45 CFR 46)*. THIS CERTIFICATION INCLUDES, WHEN APPLICABLE, REQUIREMENTS FOR CERTIFYING FDA STATUS FOR EACH INVESTIGATIONAL NEW DRUG TO BE USED (SEE REVERSE SIDE OF THIS FORM).

THE INSTITUTIONAL REVIEW BOARD HAS DETERMINED, AND THE INSTITUTIONAL OFFICIAL SIGNING BELOW CONCURS THAT:

EITHER ☒ HUMAN SUBJECTS WILL NOT BE AT RISK; OR ☐ HUMAN SUBJECTS WILL BE AT RISK.

5. AND 6. SEE REVERSE SIDE

7. NAME AND ADDRESS OF INSTITUTION

The University of Chicago, 5801 South Ellis, Chicago, Illinois 60637

8. TITLE OF INSTITUTIONAL OFFICIAL	TELEPHONE NUMBER
SIGNATURE OF INSTITUTIONAL OFFICIAL	DATE

NIH-596 (Rev. 5-80)

ENCLOSE THIS FORM WITH THE PROPOSAL OR RETURN IT TO REQUESTING AGENCY.

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BSD

RECOMBINANT DNA RESEARCH

Principal Investigator: Eugene Goldwasser

Department: Biochemsitry

Title of Application: Erythropoietin: Purification, Properties, Biogenesis

Sponsoring Agency: NIH

(External, Departmental, Other, Etc.)

(This form MUST be completed and submitted with all grant and contract applications, befor processing in the Dean's Office. Additionally, one copy of this form must be submitted to the Institutional Biosafety Committee (IBC) if any recombinant DNA research is proposed in your application.)

Check the following statements that pertain to your application.

1. _X_ Experiments with recombinant DNA molecules[1] are not included in this application.

2. _____ Experiments with recombinant DNA molecules are included. According to the NIH Guidelines of January 1980, these experiments fall into one or more of the following categories:

(a) _____ Exempt from the Guidelines[2]. If so, provide the following information:

Nature of DNA sequences to be cloned _____

Source of DNA (organism) _____

Vector _____

Host _____

(b) _____ Governed by the Guidelines although an MUA need not be submitted[3]. If this is the case, provide the following information:

Nature of DNA sequence to be cloned _____

Source of DNA (organism) _____

Vector _____

Host _____

(Note that this signed form containing the requested information serves as the required registration document.)

(c) _____ Governed by the Guidelines and requiring submission of an MUA[4]. If this is the case, an MUA must be prepared according to the format required by the IBC and the NIH Guidelines of January 1980 and submitted to the IBC Chairman for review and approval by the Committee.

NOTE THAT YOU MAY HAVE PROPOSED EXPERIMENTS IN ALL 3 OF THESE CATEGORIES.

1 April 1982
Date

Eugene Goldwasser
Signature of Principal Investigator

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THE UNIVERSITY OF CHICAGO

STATEMENT TO ACCOMPANY APPLICATION FOR CONTRACT, GRANT OR AWARD

TO NIH
(Sponsoring Agency or Organization)

PROPOSAL TITLE:

Erythropoietin: Purification, Properties, Biogenesis

PRINCIPAL INVESTIGATOR(S): (Please type)

(1) Eugene Goldwasser

(2)

(3)

DATE: 3 / 31 / 82

The Principal Investigator(s) understand that any invention made or discovered by the Principal Investigator(s) or other staff in the course of activities encompassed by this application is subject to the terms of the University contract, grant or award document and rights shall be assigned and processed in accordance with the University Statute on patents now in effect. The Principal Investigator(s) agrees to ensure that all appropriate individuals working or consulting on this project shall be aware of this patent disclosure and assignment requirement.

Signed by Principal Investigator(s):

(1) Eugene Goldwasser

(2)

(3)

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A 91631

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PROTECTION OF HUMAN SUBJECTS

Principal Investigator: Eugene Goldwasser

Department: Biochemistry

Title of Application: Erythropoietin: Purification, Properties, Biogenesis

Sponsoring Agency: NIH (External, Departmental, Other, Etc.)

(This form MUST be completed and submitted with all grant and contract applications, before processing in the Dean's Office. Additionally, one copy of this form must be submitted to the CIC when submitting any protocol involving Human Subjects for review.)

Check the following statements that pertain to your application:

1. ____ Human subjects are not included in this application.

2. _x_ Human Subjects Involved:

None of the following	(x)
Minors	( )
Fetuses	( )
Abortuses	( )
Pregnant Women	( )
Prisoners	( )
Mentally Retarded	( )
Mentally Disabled	( )

(cannot understand the proposed course of treatment)

3. _x_ Human subjects are involved in this application. The protocol has been reviewed and approved by our Clinical Investigation Committee.

Date reviewed: 12/1/81 Protocol # 2399

4. ____ This research protocol was reviewed and approved by our Clinical Investigation Committee at the time I applied to another agency for funding:

Specify other agency: _____

Title of Application: _____

Date reviewed: _____ Protocol # _____

5. ____ This application includes human subjects, but has not received approval by the Clinical Investigation Committee, and therefore, must be submitted. (This will be handled by the Dean's Office.)

6. ____ Do you intend to obtain informed consent in writing? Yes _x_ No _____

7. ____ If the informed consent is obtained in writing, will you devise a special form? Yes _____ No _x_. If the answer is yes, please enclose a copy of the intended statement.

8. ____ If research subjects are to be paid, please give us the details (budget page does not reach Clinical Investigation Committee.) Please indicate whether these subjects are patient volunteers or non-patient volunteers.

Eugene Goldwasser
Signature of Principal Investigator

1 April 1982
Date

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Revised 9/77

CONFIDENTIAL A 91632

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Prepared for the Science Information Exchange. Not for publication or publication reference.

U. S. Department of
HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

NOTICE OF RESEARCH PROJECT

PROJECT NO. (DO NOT USE THIS SPACE)

TITLE OF PROJECT

Erythropoietin: Purification, Properties, Biogenesis

GIVE NAMES, DEPARTMENTS, AND OFFICIAL TITLES OF PRINCIPAL INVESTIGATORS OR PROJECT DIRECTORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT.

Eugene Goldwasser, Department of Biochemistry, Professor
Fung Wang, Department of Biochemistry, Research Associate

NAME AND ADDRESS OF APPLICANT INSTITUTION.

The University of Chicago, 5801 S. Ellis Aveneu, Chicago, Il. 60637

SUMMARY OF PROPOSED WORK—*(200 words or less) — Omit Confidential data.)*
In the Science Information Exchange summaries of work in progress are exchanged with government and private agencies supporting research in the bio-sciences and are forwarded to investigators who request such information. Your summary is to be used for these purposes.

We propose to continue to prepare and distribute pure human erythropoietin and to study possible improvements in fractionation methods. These improvements may include affinity chromatography using lectins and/or monoclonal anti-erythropoietin, as well as high liquid chromatography. We will also study possible alternative large scale sources of erythropoietin, such as kideny extraction and cell culture methods. We will use the newly developed radioimmunoassay for screening. Successful erythropoietin production in cell culture may also permit study of its biogenesis and regulation. Improvement in the specificity of the radioimmunoassay will also be studied. We will continue to work on finding a method for radioiodination of erythropoietin with retention of biological activity, and to use such labeled material for the study of physiological propoerties. Stimultaneously, we will continue the investigation of the chemical properties of erythropoietin with the intention of understanding the structural requirements for its biological activity, as a prerequisite for its eventual synthesis.

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PROFESSIONAL SCHOOL *(medical, dental, etc.)* WITH WHICH THIS PROJECT SHOULD BE IDENTIFIED	SIGNATURE OF PRINCIPAL INVESTIGATOR	DATE
01 School of Medicine	Eugene Goldwasser	3/31/82

DO NOT WRITE BELOW THIS LINE — FOR OFFICE USE ONLY

SUPPORTING AGENCY

METHOD OF SUPPORT *(Check one)*
☐ Agency Staff (intramural) ☐ Negotiated Contract ☐ Special Project Grant ☐ Research Grant ☐ Other (Specify)

FUNDS OBLIGATED CURRENT F.Y.	NUMBER OF FUTURE YEARS TENTATIVELY ASSURED	BEGINNING DATE	ESTIMATED COMPLETION DATE

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Rev. 6/69

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