EXHIBIT 2
Part 3 of 3

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☐ FOLLOWUP ☐ REVISION

☒ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER

☐ NEW ☐ RENEWAL ☐ CONTINUATION

APPLICATION IDENTIFICATION NUMBER (If known)

STATEMENT OF POLICY: Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW 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 DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless the Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW 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 DHEW policy and regulation is the responsibility of the Office for Protection from Research Risks, National Institutes of Health, Bethesda, Md 20014.

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 6. 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 DHEW THAT APPLIES TO THIS APPLICATION OR ACTIVITY. ASSURANCE IS HEREBY GIVEN THAT THIS INSTITUTION WILL COMPLY WITH REQUIREMENTS OF *DHEW Regulation 45 CFR 46*, THAT IT HAS ESTABLISHED AN INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN SUBJECTS AND, WHEN REQUESTED, WILL SUBMIT TO DHEW 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 (DHEW ASSURANCE NUMBER G1626) OR AN ACTIVE SPECIAL ASSURANCE FOR THIS ONGOING ACTIVITY, ON FILE WITH DHEW. 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

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NEW-598 (Rev. 4-75)

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

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PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: Eugene Goldwasser

CHECKLIST

This is the required last page of the application.

Check the appropriate boxes and provide the information requested.

TYPE OF APPLICATION:

☐ NEW application (This application is being submitted to the PHS for the first time.)

☐ COMPETING CONTINUATION of grant number: _____
(This application is to extend a grant beyond its original project period.)

☒ SUPPLEMENT to grant number: HL 21676
(This application is for additional funds during a funded project period.)

☐ REVISION of application number: _____
(This application replaces a prior version of a new, competing continuation or supplemental application.)

☐ Change of Principal Investigator/Program Director.
Name of former Principal Investigator/Program Director: _____

ASSURANCES IN CONNECTION WITH:

Civil Rights	Handicapped Individuals	Sex Discrimination	Human Subjects General Assurance (If applicable)	Laboratory Animals (If applicable)
☒ Filed ☐ Not filed	☒ Filed ☐ Not filed	☒ Filed ☐ Not filed	☒ Filed ☐ Not filed	☒ Filed ☐ Not filed

INDIRECT COSTS:

Indicate the applicant organization's most recent indirect cost rate established with the appropriate DHHS Regional Office. If the applicant organization is in the process of initially developing or renegotiating a rate, or has established a rate with another Federal agency, it should, immediately upon notification that an award will be made, develop a tentative indirect cost rate proposal based on its most recently completed fiscal year in accordance with the principles set forth in the pertinent DHHS Guide for Establishing Indirect Cost Rates, and submit it to the appropriate DHHS Regional Office. Indirect costs will not be paid on foreign grants, construction grants, and grants to individuals, and usually not on grants in support of conferences.

☒ DHHS Agreement Dated: 07/06/81
_____ % Salary and Wages or 57 % [redacted] MTDC

Is this an off-site or other special rate, or is more than one rate involved? ☐ YES ☒ NO
Explanation: _____

☐ DHHS Agreement being negotiated with _____ Regional Office.

☐ No DHHS Agreement, but rate established with _____ Date _____

☐ No Indirect Costs Requested.

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Rev. 5/80

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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.

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Signature of Principal Investigator

April 8, 1982
Date

evised 9/77

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EXHIBIT A

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)

8-03698

DATE: 4 / 7 / 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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BSD
RECOMBINANT DNA RESEARCH

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 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.

April 8, 1982
Date

Eugene Goldwasser
Signature of Principal Investigator

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NOTICE: See instructions on reverse of last copy.

FORM APPROVED O.M.B. NO. 68-R0249

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

NOTICE OF RESEARCH PROJECT

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

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 Professor

NAME AND ADDRESS OF APPLICANT INSTITUTION.

The University of Chicago, 5801 S. Ellis Avenue, 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 kidney 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 sutdy of physiological properties. 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.

.8003700

PROFESSIONAL SCHOOL *(medical, dental, etc.)* WITH WHICH THIS PROJECT SHOULD BE IDENTIFIED	SIGNATURE OF PRINCIPAL INVESTIGATOR	DATE
01 School of Medicine	Eugene Goldwasser	4/7/82

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

PHS 186 REV. 5/80

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