

CONTINUATION DOCUMENTS TO
NIH/NCI FOR COOPERATIVE
STUDY OF AIDS, 1984-85

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

APPLICATION
FOR CONTINUATION GRANT

REVIEW GROUP SSS 9	TYPE 5	ACTIVITY U01	GRANT NUMBER (Insert on all pages) CA34980-02
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TOTAL PROJECT PERIOD

From: 05/01/83 Through: 04/30/86

REQUESTED BUDGET PERIOD

From: 05/01/84 Through: 04/30/85

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

1. TITLE

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR
(name and address, street, city, state, zip code)

VOLBERDING, PAUL A
SAN FRANCISCO GENERAL HOSP
MEDICAL SERVICE,, 5H22
SAN FRANCISCO, CALIF 94110

4. APPLICANT ORGANIZATION (name and address, street, city,
state, zip code)

UNIV OF CALIF, SAN FRANCISCO
CANCER RESEARCH INST, M-1282
SAN FRANCISCO, CA 94143

5. ENTITY IDENTIFICATION NUMBER

1946036493A6

2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT
MEDICINE

2c. MAJOR SUBDIVISION
SCHOOL OF MEDICINE

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR
BIOMEDICAL RESEARCH SUPPORT GRANT (see instructions)

01 SCHOOL OF MEDICINE

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE
OF APPLICANT ORGANIZATION

CONTRACTS AND GRANTS OFFICER
OFFICE OF EXTRAMURAL SUPPORT
UNIVERSITY OF CALIFORNIA
SAN FRANCISCO, CA 94143

COMPLETE THE FOLLOWING (See Instructions)

7. HUMAN SUBJECTS

☐ NO ☐ YES

☐ OR
☐

Exemption # _____
Form HHS 596 enclosed

8. RECOMBINANT DNA

☐ NO ☐ YES

9. PERFORMANCE SITE(S) (organizations and addresses)

11. INVENTIONS (see instructions)

☐ NO ☐ YES

☐ OR
☐

Previously reported
Not previously reported

TELEPHONE INFORMATION

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD

12a. PRINCIPAL INVESTIGATOR

OR
PROGRAM DIRECTOR (Item 2a)

AREA
CODE

TELEPHONE NO.
AND EXTENSION

12b. NAME OF BUSINESS OFFICIAL
(Item 6)12c. NAME AND TITLE OF OFFICIAL
SIGNING FOR APPLICANT
ORGANIZATION (Item 15)

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

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. Willful provision of false information is a criminal offense (U.S. Code, Title 18, Section 1001).

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

DATE

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)

DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

REVIEW GROUP	TYPE	ACTIVITY	GRANT NUMBER (Insert on all pages)
			UOI CA34980

APPLICATION
FOR CONTINUATION GRANT

TOTAL PROJECT PERIOD

From: 5-1-84

Through: 4-30-86

REQUESTED BUDGET PERIOD

From: 5-1-84

Through: 4-30-85

1. TITLE

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR
(name and address, street, city, state, zip code)

VOLBERDING, PAUL A
ZIEGLER JOHN
SAN FRANCISCO GENERAL HOSP
DIVISION OF ONCOLOGY
WARD 86
995 POTRERO AVE.
SAN FRANCISCO CA 94110

4. APPLICANT ORGANIZATION (name and address, street, city, state, zip code)

UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO
CANCER RESEARCH INSTITUTE
M-1282
SAN FRANCISCO CA 94143

2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT
MEDICAL SERVICE

2c. MAJOR SUBDIVISION

DEPARTMENT OF MEDICINE

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR
BIOMEDICAL RESEARCH SUPPORT GRANT (see instructions)

School of Medicine

5. ENTITY IDENTIFICATION NUMBER

1946036493A6

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF
APPLICANT ORGANIZATION (415) 666-2977

LORRAINE M. PETRAKIS
CONSTRUCTS & GRANTS OFFICER
OFFICE OF EXTRAMURAL SUPPORT
UNIVERSITY OF CALIFORNIA
SAN FRANCISCO CA 94143

7. HUMAN SUBJECTS

☐ NO☒ YES

☐ Exemption # _____
OR
☐ Form HHS 596 enclosed

11. INVENTIONS (see instructions)

☒ NO☐ YES

☐ Previously reported
OR
☐ Not previously reported

8. RECOMBINANT DNA

☒ NO☐ YES

TELEPHONE INFORMATION

9. PERFORMANCE SITE(S) (organizations and addresses)

University of California, S.F.
Cancer Research Institute UCSF
Dept. of Pediatrics, UCSF
Division of Dermatology, UCSF
San Francisco General Hospital
Mt. Zion Hospital, San Francisco

12a. PRINCIPAL INVESTIGATOR

OR

PROGRAM DIRECTOR (Item 2a)

PAUL VOLBERDING, M.D.

AREA
CODETELEPHONE NO.
AND EXTENSION

415

666-4387

12b. NAME OF BUSINESS OFFICIAL
(Item 6)

LORRAINE PETRAKIS

415

666-2977

12c. NAME AND TITLE OF OFFICIAL
SIGNING FOR APPLICANT OR-
GANIZATION (Item 15)

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD

13. DO NOT USE THIS SPACE

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSUR-
ANCE: 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. Willful provision of false infor-
mation is a criminal offense. (U.S. Code, Title 18, Section 1001.)SIGNATURE OF PERSON NAMED IN 2a
(In ink. "Per" signature not acceptable)

DATE

2/29/84

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)

DATE

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA 34980 A	
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)	
PERSONNEL (Applicant organization only) (See instructions)			TIME/EFFORT		
NAME	TITLE OF POSITION	%	Hours per Week	SALARY	FRINGE BENEFITS
	Principal Investigator				
CLINIC	CONANT			42,199	12,220
EPIDEMIOLOGY	MOSS			24,678	7,157
IMMUNOLOGY	AMMANN			54,109	15,685
VIROLOGY I	LEVY			39,671	8,686
VIROLOGY II	DREW			46,607	13,364
THERAPY	VOLBERDING			65,057	15,983
SUBTOTALS				272,321	73,095
CONSULTANT COSTS (See instructions)					345,416
					0
EQUIPMENT (Itemize)					
CLINIC	5,000				
EPIDEMIOLOGY	0				
IMMUNOLOGY	0				
VIROLOGY I	5,000				
VIROLOGY II	0				
THERAPY	0				
					10,000
SUPPLIES (Itemize by category)					
CLINIC	1,000				
EPIDEM	0				
IMMUNOLOGY	3,008				
VIROLOGY I	34,050				
		VIROLOGY II	4,596		
		THERAPY	1,284		
					43,938
TRAVEL	DOMESTIC CLN 1,000-IM 1,500-VRI 1,100-THRP 1,605				5,205
	FOREIGN				0
PATIENT CARE COSTS	INPATIENT				0
	OUTPATIENT				0
ALTERATIONS AND RENOVATIONS (Itemize by category)					
					0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)					
VIROLOGY II					43,338
OTHER EXPENSES (Itemize by category)					
CLINIC	5,000		VRI	34,596	
EPI	0		VRII	383	
IMMUN	0		THRP	214	
					40,193
TOTAL DIRECT COST (Enter on Page 1, Item 10)					488,090

INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
	27.7%	5-1-84 to 6-30-84		
	31.87%	7-1-84 to 4-30-85		
	154,168	% TDC*		

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
UOI CA34980

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
1) CLINIC	CONANT, MARCUS	DIV. OF DERMATOLOGY UCSF
2) EPIDEMIOLOGY	MOSS, ANDREW	DEPT. OF EPIDEMIOLOGY "
3) IMMUNOLOGY	AMMAN, ARTHUR	DEPT. OF PEDIATRICS "
4) VIROLOGY I	LEVY, JAY	CANCER RESEARCH INST "
5) VIROLOGY II	DREW, LAWRENCE	MT ZION HOSPITAL/SFGH
6) THERAPY	VOLBERDING, PAUL	DIV OF ONCOLOGY/SFGH

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. **DO NOT EXCEED THE SPACE PROVIDED.**

For the second year of this grant we propose the following projects:
(1) continue epidemiologic surveillance studies of the sexual contacts of AIDS patients seen at the KS clinic, compare clinical features of KS in AIDS patients to the classical form, and provide tissue and serum specimens to the central tissue bank facility (MA Conant); (2) continue to collect incidence data for population-based analysis of morbidity and mortality, conduct pilot study of AIDS in intravenous drug-abusers, and contrive surveillance of non-Hodgkin's lymphoma in homosexual men (AR Moss); (3) immunologic and functional assays of T cell subsets and monocytes in pre-AIDS and AIDS patients to define immunopathogenesis, follow immune parameters in patients receiving interferon and IL2 therapy (AJ Amman); (4) continue studies of viral etiology of AIDS by inoculating AIDS tissues into Balb-C and CH3 mice and newborn hamsters, baboons and chimpanzees (JA Levy); (5) continue surveillance of CMV sero-negative homosexual men and conduct extensive immunologic studies when sero-conversion occurs, continue CMV analysis of homosexual men to determine strain variations and effects of multiple-strain infections (WL Drew); (6) continue to study natural history of KS and lymphadenopathy syndrome, initiate treatment protocols using ICRF-159, gamma-interferon, and interleukin-2, study natural history and treatment of non-Hodgkin's lymphoma in homosexual men (PA Volberding, JL Ziegler, DI Abrams).

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

UOI CA34980

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

SEE INDIVIDUAL SECTIONS FOR "NEXT BUDGET PERIOD" AND "NEXT BUDGET PERIOD" JUSTIFICATIONS.

DUE TO COST OF LIVING INCREASES IN SUPPLIES, TRAVEL, AND OTHER EXPENSES THESE SECTIONS WERE INCREASED BY 7%. THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO PERSONNEL SALARIES AND FRINGE BENEFITS WERE INCREASED ON AN AVERAGE OF 8% and 12%. THE RESULT OF THE INCREASE IS A TOTAL DIRECT COST OF \$488,090 FOR THE PROPOSED '84-'85 BUDGET PERIOD. THIS IS LESS THAN AN OVERALL 7% INCREASE OVER THE \$457,463 TOTAL DIRECT COSTS FOR THE '83-'84 BUDGET PERIOD.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA34980A
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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 (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	457,463	240,521	216,942	467,463	0
INDIRECT COSTS (as provided)	106,766	54,958	51,808	106,766	0
TOTALS →	564,229	295,479	268,750	564,229	0

B. THROUGH F.

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

SEE "CURRENT BUDGET PERIOD" PAGES IN EACH SECTION

SECTION IV
PROGRESS REPORT SUMMARY

GRANT NUMBER

UOI CA34980

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

PERIOD COVERED BY THIS REPORT

PAUL VOLBERDING JOHN ZIEGLER

FROM

THROUGH

NAME OF ORGANIZATION

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

5-1-83

4-30-84

TITLE (Repeat title shown in item 1 on first page)

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

(SEE INSTRUCTIONS)

SEE "PROGRESS REPORT SUMMARY" PAGE IN EACH SECTION.

REMOVE AND USE FOR DRAFT COPY

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM May 1, 1984	THROUGH April 30, 85	GRANT NUMBER 1 U01 CA34980 - 01		
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
M. Conant	Principal Investigator	10		6,000	1,560	7,560
P. Volberding	Co.- Investigator	10		5,000	1,300	6,300
F. Baumgartner		100	40	23,939	7,182	31,121
To be hired		50	20	7,260	2,178	6,300
SUBTOTALS				42,199	12,220	54,419
CONSULTANT COSTS (See instructions)						
EQUIPMENT (Itemize)						
Computer terminal stand/alterations						
Tissue holders for LN ₂						
LN ₂ Storage						5,000
SUPPLIES (Itemize or category)						
LN ₂						
Becksted (substrates, plastic, slides, chemicals, film)						
Knives (for Cryostat, pipettes, slides)						1,000
TRAVEL						
DOMESTIC : M. Conant						1,000
FOREIGN						
PATIENT CARE COSTS						
INPATIENT						
OUTPATIENT						
ALTERATIONS AND RENOVATIONS (Itemize by category)						
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						
OTHER EXPENSES (Itemize by category)						
Mailing; Xeroning; Graphic sildes presentations:						
Printing; Pathology processing						
Becksted (color plates, ect)						
Periodicals, and Books.						5,000
TOTAL DIRECT COST (Enter on Page 1, Item 10)						66,419

INDIRECT COST (See instructions)	% S&W*	If this is a special rate (for estimated expense)	Date of OHS agreement	☐ Not requested ☐ Under negotiation with:
	27.7%			
	% TOC*			
19,146				

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

1 U01 CA34980 - 01

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
Marcus A. Conant, M.D.	Assoc. Clin. Prof., UCSF	Dermatology, UCSF
Paul Volberding, M.D.	Asst. Prof. of Medicine, UCSF	School of Medicine, UCSF
John Greenspan, Ph.D	Prof. of Oral Biology & Oral Pathology	Division of Oral Biology, UCSF
Jay H. Beckstead, M.D.	Asst. Prof. of Pathology	Pathology, UCSF

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

I. To recruit more participants in each of our studies to continue to achieve our research objectives.

A. Contact Study

1. Presentations to professional groups
2. Media releases
3. Networking to outpatient facilities in the community by the Nurse Coordinator of the K.S. Clinic.
4. Networking through community resources to contact more participants, i.e. San Francisco Aids Foundation, Shanti Project, and Aids Coordination Committee of San Francisco, by Nurse Coordinator.

B. Traditional Study

1. Presentations to professional groups
2. Media releases
3. Networking to the private physicians communities of the bay area. coordinated through K.S. Nursing Coordinator.

C. K.S. Patient Study

1. Presentations to professional groups
2. Networking to the outpatient areas in the community and also the private physicians communities to serve as a resource and a referral to patients. This will be done by Nursing Coordinator.

II. To expand on patient Specimen Banking:

A. Speciman Bank

1. In collaboration with Dr. J. Greenspan the Nursing Coordinator will continue to coordinate specimen collection for the specimen bank.
2. The Nurse Coordinator and Principal investigator will establish new areas of specimen collection in the community.
3. The Nurse Coordinator will coordinate these new activities.

VERTEBRATE ANIMALS INVOLVED ☒ NO ☐ YES If "YES" identify by common names and underline primates.

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

1U01 CA 34980 - 01

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

SECTION III CURRENT BUDGET PERIOD	FROM May 1, 1983	THROUGH April 30, 1984	GRANT NUMBER 1 U01 CA34980 - 01
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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)	ACTUAL EXPENDITURES THRU (insert date) 01/31/84	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	68,451	37,878	30,573	68,451	-0-
INDIRECT COSTS (as provided)	16 932	10 492	6 440	16 932	
TOTALS →	85 383	48 340	37 013	85 383	

B. THROUGH F.

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

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER UOI CA34980	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR MARCUS A. CONANT, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UCSF, DIVISION OF DERMATOLOGY		FROM 5-1-83	THROUGH 4-30-84
TITLE (Repeat title shown in item 1 on first page) PRINCIPAL INVESTIGATOR			
(SEE INSTRUCTIONS)			

The general scientific goals of the Kaposi's Sarcoma clinic have not changed. They include the following:

1. To coordinate the studies of the epidemiology, etiology, and treatment of Kaposi's Sarcoma and AIDS.
2. To collect data on AIDS patients, KS patients, persons exposed to AIDS, and persons exposed to KS to understand the natural history of the diseases.
3. To develop a specimen bank for tissue and serum collection and to distribute materials for research.

The following studies are being conducted:

1. Fifty patients have been followed from August 1981 to the present.
 - A. Deceased 13 patients
 - B. Receiving treatment or have received treatment 31 patients
 - C. Never received treatment 6 patients
2. Since November 1982 we have staged approximately 99 patients through the KS clinic and are following them through the natural course of their disease.
3. The KS Clinic has been the primary source for patient material collection in the Specimen Bank. The Nursing Coordinator has scheduled and done the biopsies and serum collection during patients visits to the KS Clinic. Coordinated specimen collection from various facilities in the community. San Francisco General and the Veterans Administration Hospital of San Francisco have been participating in the specimen collection.

To date the Specimen Bank contains 200 tissue specimens divided in the following categories:

- | | |
|-----------------------|--------------------------|
| A. Lymph nodes | D. KS tumor bowel tissue |
| B. KS tumor skin | E. KS tumor spleen |
| C. Normal skin tissue | F. KS tumor tonsil |

In the Sera Bank 300 sera specimens have been collected from patients with the following

- | | |
|----------------------------|--------------------|
| A. AIDS | D. Lymphadenopathy |
| B. KS | E. ITP |
| C. AIDS related conditions | |

These specimens have been allocated and stored from 2 to 15cc per tube in lcc vials..

PUBLICATIONS

MARCUS CONANT, M.D.

Modlin, R., Meyer, P., Hofman, F., Mehlmauer, M., Levy, N., Lukes, R., Parker, J., Ammann, A., Conant, M., Rea, T. and Taylor, C.: T-Lymphocyte Subsets in Lymph Nodes from Homosexual Men. JAMA, 1983 Vol. 250:1302-05

Meyer, P., Modlin R., Mehlmauer, M., Taylor, C., Lukes, R., Conant, M. and Rea, T.: Immunologic Assessment of Thymus, Bursa and Macrophage Antigens in Homosexual Patients with Reactive Lymph Nodes, Lymph Nodes Containing Kaposi's Sarcoma and Malignant Lymphomas Compared with Reactive Tonsils and Lymph Nodes from Non-Homosexual patients. Clin. Res., 1983, Vol: 31 (1):39 A.

Colombe, B., conant, M., Volberding, P., and Garovoy, M.: Susceptibility of Kaposi's Sarcoma and HLa BW44. Clin. Res., 1983, Vol. 31:340

Volberding, P., Gottlieb, M., Bothman, J., Rudnick, S., Conant, M., Derezin, M., Weinstein, W. and Groopman, J.: Therapy of Kaposi's Sarcoma (KS) in Acquired Immune Deficiency (AIDS) with a -2Recombinant Interferon Amer. Soc. Clin. Oncology Proc., 1983, Vol. 2:C-206

Modlin, R., Conant, M., Taylor, C., Meyer, R., Hofman, F., Lukes, R., Parker, J., Ammann, A. and Rea, T.: T-Lymphocyte Subsets in Skin, Blood and Lymph Nodes from Homosexual Men with Kaposi's Sarcoma. J. Invest. Derm., 1983, Vol 80 (4):332

Moss, A., Bacchetti, P., gorman, M., Dritz, S., Conant, M., Abrams, D., Volberding, P., and Ziegler, J.: AIDS in the "Gay areas of San Francisco. The Lancet, April 1983, Vol. 1(8330):923-24

Ziegler, J., Conant M., Lutzner M. Kaposi's Sarcoma In T. Fitzpatrick Ed., Dermatology in General Medicine, McGraw Hill, New York, 1984 (3rd Edition) in press

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
A. R. Moss, Ph.D.	Adjunct Assistant Professor	Epidemiology & International Health, UCSF
N. Petrakis, M.D.	Professor, Chairman of Dept.	Epidemiology & International Health, UCSF
S. Dritz, M.D.	Deputy Chief	Bureau of Communicable Disease Control, S.F.
D. Osmond, M.A.	Assoc. Specialist, Epidemiology	Epidemiology & International Health, UCSF
P. Bacchetti, M.S.	Statistician	Epidemiology & International Health, UCSF
L. Swig, B.A.	Staff Research Associate	Epidemiology & International Health, UCSF

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

1. In association with Selma Dritz, M.D., we will continue to collect and analyze AIDS incidence and mortality data for San Francisco. We will report incidence data at six-monthly intervals, as of July 1, 1984 and January 1, 1985. We will carry out a population-based analysis of mortality among San Francisco-resident AIDS cases in Fall 1984.
2. In association with Dr. Dritz, we will continue to find AIDS cases for case-control and other-case-based epidemiological studies, using the collaborative UCSF-City of San Francisco AIDS casefinding process. (1) A case-control study of AIDS in homosexual men has been funded by the State of California and will continue through November 1984. (2) Pilot studies of AIDS in intravenous drug users are in progress. (3) A prospective study on AIDS risk in sexual partners of documented AIDS cases will be initiated in 1984-85.
3. In collaboration with Drs. J. Ziegler and D. Austin, AIDS incidence in San Francisco will be compared with incidence of other tumors believed to be associated with the acquired immune deficiency syndrome (including non Hodgkin's lymphomas and squamous cell tumors of the mouth and tongue) as reported by the California Tumor Registry.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II NEXT BUDGET PERIOD Follow instructions carefully	FROM May 1, 1984	THROUGH April 30, 1985	GRANT NUMBER CA 34980-02
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A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD DOLLAR AMOUNT REQUESTED (Omit cents)

PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
A.R. Moss, Ph.D.	Principal Investigator	25		-	-	
N. Petrakis, M.D.	Professor & Chairman	5		-	-	
S. Dritz, M.D.	Deputy Chief	-		-	-	
D. Osmond, M.A.	Assoc. Specialist	30		8,472	2,457	
L. Swig	Staff Research Assoc.	50		9,514	2,759	
P. Bacchetti	Statistician	25		6,692	1,941	
SUBTOTALS				24,678	7,157	31,835

CONSULTANT COSTS (See instructions)

EQUIPMENT (Itemize)

SUPPLIES (Itemize by category)

TRAVEL	DOMESTIC	
	FOREIGN	
PATIENT CARE COSTS	INPATIENT	
	OUTPATIENT	

ALTERATIONS AND RENOVATIONS (Itemize by category)

CONSORTIUM/CONTRACTUAL COSTS (See instructions)

OTHER EXPENSES (Itemize by category)

TOTAL DIRECT COST (Enter on Page 1, Item 10) 31,835

INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
	9,925			

SECTION III CURRENT BUDGET PERIOD	FROM 5/1/83	THROUGH 4/30/84	GRANT NUMBER CA 34980
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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)	ACTUAL EXPENDITURES THRU (insert date):	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	29,343	23,581	5,762	29,343	-
INDIRECT COSTS (as provided)	8,128	6,532	1,596	8,128	
TOTALS →	37,471	30,113	7,358	37,471	-

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	LESS THAN 25%	26-50%	51-75%	MORE THAN 75%
A. Moss,	Adjunct Assist, Professor	1	X			
N. Petrakis	Professor Chair. Dept.	1	X			
S. Dritz	Deputy Chief Communicable Disease Control		X			
D. Osmond	Associate Specialist	2		*		
L. Swig	Staff Research Assistant	2		*		
P. Bacchetti	Statistician	2	*			

F. Other Support

A. R. Moss, Ph.D.	NIOSH "Occupational Exposure in Adult Glioma Patients". \$95,997 State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$125,815
D. Osmond, M.A.	NIOSH "Occupational Exposure in Adult Glioma Patients" \$95,997 State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$125,815
L. Swig	City of San Francisco "Study of AIDS Partners and Relationships Between Lifestyle and Immune Status in Well Gay Men". \$78,936
P. Bacchetti, M.S.	NIOSH "Occupational Exposure in Adult Glioma Patients". \$95,997 State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$125,815

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER CA 34980	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR A. R. Moss, Ph.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION		FROM 5/1/83	THROUGH 4/30/84
TITLE (Repeat title shown in item 1 on first page)			

(SEE INSTRUCTIONS)

1. Introduction

Funding was received to assist Dr. Selma Dritz in the establishment of a system for analyzing AIDS surveillance data in San Francisco. No funds were received for specific projects based on the surveillance data. Partial support was received for a statistician, a field supervisor, and research associate.

2. Progress to Date

In association with Dr. Dritz, a computerized incidence file has been established for San Francisco-resident diagnosed AIDS cases. Using census based denominator data and a division of the city of San Francisco into demographically homogenous areas, a procedure has been developed to obtain incidence rates which can reasonably be assumed to estimate AIDS incidence in homosexual men. A preliminary report on this data was published in April 1983.¹

In the current project, a six-month schedule has been established for incidence reporting and a first report (as of July 1983) has been submitted for publication (Moss, Bacchetti, Osmond et al., attached). We propose to continue to examine AIDS incidence in detail on a six-month basis.

In association with Dr. Dritz and the AIDS clinic at San Francisco General Hospital, we have also established a mortality surveillance procedure for San Francisco-resident AIDS cases which allows us to obtain population-to-based mortality estimates. A first report (as if summer 1983) has been submitted for publication. (Moss, Volberding, McCallum et al., attached.) We propose to continue to report AIDS mortality on an annual basis.

A collaborative relationship with the California Tumor Registry has been established and in the coming year we plan to compare AIDS incidence with incidence rates for other tumors which may be associated with the syndrome on a census tract level. This study will be collaborative with Drs. Dritz, J. Ziegler and D. Austin.

3. Studies using the surveillance system for casefinding

The surveillance system established by us in collaboration with the San Francisco Department of Public Health serves as a casefinding mechanism for studies of the acquired immune deficiency syndrome. During the current project year, funding has been received for two studies based on this casefinding system. 1) A case-control study of 140 AIDS cases matched with clinic controls and randomly-selected neighborhood controls was funded by the State of California and is currently nearing completion. 2) A cross-sectional study of immune function in the controls for the case-control study was funded by the City of San Francisco and is currently in progress.

Although only a handful of AIDS cases in intravenous drug users has yet been reported in San Francisco, we expect more cases to be found in the coming year. We are currently conducting pilot studies for an AIDS case-control study in intravenous drug users. A formal study will be proposed in the coming year.

We are also conducting pilot studies of both male and female sexual partners of documented AIDS cases. In the coming year we expect to propose a formal study of this cohort.

-
1. Moss A.R., Bacchetti, P., Gorman, M., et al. AIDS in the "gay" areas of San Francisco Lancet 1983; ii:923-4.

Publications (cont'd)

AR MOSS

Moss AR, Bacchetti P, Osmond D et al. Incidence of the Acquired Immunodeficiency Syndrome in San Francisco 1980-1983. The Lancet (Submitted 2/84)

Moss AR, McCallum J, Volberding P, Bacchetti P, Dritz S., Mortality associated with the Acquired Immunodeficiency Syndrome. (In preparation)

Moss AR, Bacchetti P, Gorman M et al. AIDS in the "gay" areas of San Francisco. The Lancet 1983; 2:923-4

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SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

UOI CA34980

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
AMMANN AJ STITES D CASAVANT C	PRINCIPAL INVESTIGATOR CO-INVESTIGATOR CO-INVESTIGATOR	

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

Research will continue to analyze the specific immunologic abnormalities found in patients with AIDS and related disorders. Our current investigations suggest there is both a monocyte and T-cell defect present in the patients. The monocyte defect, if found to be an early abnormality may explain the inability of patients to respond to antigen with an appropriate antibody response. Defining the specific defect which is found in "pre AIDS" will have important implications regarding pathogenesis of the immunodeficiency. We continue to define T and B cell subset abnormalities in the groups of patients. The extent of these abnormalities and the specific patient populations in which these abnormalities are found are being utilized for correlation with epidemiologic and clinical data to improve diagnosis and therapeutic approaches. Detailed evaluation of the patients receiving immunotherapy is in progress. One hundred patient will be treated with 9 doses of recombinant DNA interleukin-2. Included in this study is an immunologic evaluation of patients before and during therapy as well as in vitro incubation studies to determine the correlation between in vitro response and subsequent in vivo response.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 3/1/84	THROUGH 4/30/85	GRANT NUMBER CA 34980A	
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED <i>(Omit cents)</i>	
PERSONNEL <i>(Applicant organization only) (See instructions)</i>		TIME/EFFORT		SALARY	FRINGE BENEFITS
NAME	TITLE OF POSITION	%	Hours per Week		TOTALS
Arthur J. Ammann	Principal Investigator	10%		N/A	
Daniel Stites	Co- Investigator	10%		N/A	
Conrad Casavant	CO- Investigator	10%		N/A	
Nanita Arias	Hos. Lab. Tech	100%	40	32,206	
Teresa Kadlecek	Staff. Res. Assoc.	100%	40	21,903	
SUBTOTALS →				54,109	15,685
CONSULTANT COSTS <i>(See instructions)</i>					-0-
EQUIPMENT <i>(Itemize)</i>					-0-
SUPPLIES <i>(Itemize by category)</i>					
Plastic Tissue culture supplies				3,008	3,008
TRAVEL	DOMESTIC 3 trip for investigators @ 500 each				1,500
	FOREIGN				
PATIENT CARE COSTS	INPATIENT				
	OUTPATIENT				
ALTERATIONS AND RENOVATIONS <i>(Itemize by category)</i>					
CONSORTIUM/CONTRACTUAL COSTS <i>(See instructions)</i>					
OTHER EXPENSES <i>(Itemize by category)</i>					
TOTAL DIRECT COST <i>(Enter on Page 1, Item 10)</i>					74,302
INDIRECT COST <i>(See instructions)</i>	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:	
	23,164				

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

CA 34980A

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

PERSONNEL:

Increased technician time: The present single FTE is divided between one principal investigator and two co-investigators. In the nearly one year that the grant has been in effect, the investigators have required two FTE technicians. The additional technician has been temporarily funded from a one year state grant which will not be available after this year. The number of studies which we are committed to performing to fulfill the objectives of the grant will require the additional FTE. A single technician can perform 20 functional assays of T cell immunity per week and analyze the data. This number is required to perform the initial and follow up studies on 100 patients with AIDS who are going to receive IL2 treatment beginning in April of 1984 and continuing for one year. Without the added FTE the studies cannot be performed and the effects of IL2 on the immunologic status of the patient cannot be assessed. This is critical information which must be obtained to determine if a clinical effect of IL2 can be correlated with an immunologic effect. Simultaneous studies in AIDS and AIDS related syndrome must also be performed utilizing lymphocyte phenotyping and monoclonal antibody. Because two technicians are therefore required we are requesting that all funding be applied to technical salaries. Funding for additional supplies will be obtained from other sources.

EQUIPMENT:

\$12,000 lease of B.D. Research Analyzer is deleted due to coverage from other sources. These funds are rebudgeted among personnel and remaining categories individually justified.

SECTION III CURRENT BUDGET PERIOD	FROM	THROUGH	GRANT NUMBER
	3/1/84	4/30/85	CA 34980A

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 (insert date): 1/31/84 (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	68,798	38,843.31		29,954.69	-0-
INDIRECT COSTS (as provided)	15,733	9,434.44		6,298.56	-0-
TOTALS →	84,531	48,277.75		36,253.25	-0-

B. THROUGH F.

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

B. Name	Title	Category	less than 25%	26-50%	51-75%	More than
Arthur J. Ammann	Professor	1	X			
Daniel Stites	Professor	1	X			
Conrad Casavant	Assoc. Clin Prof.	1	X			

C. Equipment:

1. Bechman Refrigerated Centrifuge \$4,362.52
* note BD Research Analyzer lease are covered from other funding sources
2. Ranna #8086 drives \$2,950

- D. 3 investigators will share travel money in the amount of \$1,000, used to partially defray the cost of attending research meetings for the presentation of research results.

E. None

F. OTHER SUPPORT

Arthur J. Ammann, M.D.
Northern California Sickie Cell Center, Grant # HL 20985, (100% Technician salary)
4/1/83 through 3/31/84 \$47,139

Arthur J. Ammann M.D.
State of California AIDS Research Grant, '(50% Technician)
\$25,000,

Daniel Stites
NICHD - 03939, Study of Fetal- Placental Maternal Interaction
\$100,000 7/1/83 through 6/30/84

Daniel Stites
NICHD-13543, Basic and Clinical studies of preterm parturition
\$45,753 4/1/83 through 3/31/84

Daniel Stites
State of California AIDS Research Grant
\$115,000 7/1/83 through 6/30/84

the amount of immunoglobulin detected. Elution studies have indicated that these immunoglobulins are not intrinsic but are fixed to the surface of the T lymphocytes. Whether these represent immune complexes, cytophilic antibodies or anti-lymphocyte antibodies will be further investigated.

Using simultaneous two-color fluorescence with phycoerythrin labeled and FITC labeled monoclonal antibodies, we have been able to detect large amounts of DR antigens on the surface of both helper and suppressor T-lymphocytes in these same patient groups. Again, there is a relative increase from health to full-blown AIDS in relation to these markers of activation. The significance of this finding remains unknown but will be further pursued by additional study.

We have studied a group of CMV negative individuals and found normal distributions of lymphocyte subsets. In a longitudinal study, some of these individuals have converted from sera positive to sera negative associated with profound changes in lymphocyte subsets. We are continuing to follow this interesting group of patients prospectively to see if these changes are progressive. It is clear that in normal healthy subjects, CMV infection results in similar changes which are transient.

A variety of support studies for the therapy section of the grant in following lymphocyte subsets in several trials of immuno-modulating agents are in progress.

Objectives For The Coming Year:

Research will continue to analyze the specific immunologic abnormalities found in patients with AIDS and related disorders. Our current investigations suggest there is both a monocyte and T-cell defect present in the patients. The monocyte defect, if found to be an early abnormality may explain the inability of patients to respond to antigen with an appropriate antibody response. Defining the specific defect which is found in "pre AIDS" will have important implications regarding pathogenesis of the immunodeficiency. We continue to define T and B cell subset abnormalities in the groups of patients. The extent of these abnormalities and the specific patient populations in which these abnormalities are found are being utilized for correlation with epidemiologic and clinical data to improve diagnosis and therapeutic approaches. Detailed evaluation of the patients receiving immunotherapy is in progress. One hundred patients will be treated with 9 doses of recombinant DNA Interleukin-2. Included in this study is an immunologic evaluation of patients before and during therapy as well as in vitro incubation studies to determine the correlation between in vitro response and subsequent in vivo response.

Research Involving Human Subjects:

Our laboratories utilize blood samples from patients and we have received human experimentation approval. The risks of obtaining blood samples are minimal. The potential benefit to the patient is great if improved immunologic diagnosis can be obtained.

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER UOI CA34980	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR ARTHUR J. AMMANN		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UNIVERSITY OF CALIFORNIA, SAN FRANCISCO		FROM 5-1-83	THROUGH 4-30-84
TITLE (Repeat title shown in item 1 on first page) Studies of Acquired Immune Deficiency Syndrome			
(SEE INSTRUCTIONS)			

The scientific goals of the project have not been altered since the submission of the grant. The following is a brief summary of the studies which have been completed during the award year.

Categorization of the immunologic profile of patients with AIDS (Kaposi's sarcoma) and opportunistic infection (as well as AIDS related syndromes has been completed and the work has been published. A distinctive profile can be demonstrated in the patient groups of healthy homosexual controls, patients with lymphadenopathy syndrome, opportunistic infection or Kaposi's sarcoma. The degree of immunologic abnormalities can be ranked and correlates well with prognosis and survival. Functional impairment of T-cell immunity occurs in the most severely affected patients and when less than 10% of normal, usually indicates an immunologic state which is incompatible with survival beyond 1 year. Our studies also indicate that there is an impaired antibody response following specific immunization in patients with severe impairment of T-cell immunity. Many of these patients have a paradoxical increase in immunoglobulin levels. The impaired antibody response was demonstrated when patients were immunized with pneumococcal polysaccharide and a protein antigen, keyhole limpet hemocyanin. These studies provide important information in relation to appropriate approaches to treatment when reconstituting deficient immunity in this population of patients.

Additional AIDS related syndromes have been investigated to determine whether immunologic abnormalities in these groups of patients are consistent with AIDS. Two groups were defined, patients with hemophilia receiving concentrate factor VIII therapy and pediatric patients with blood transfusion related AIDS or AIDS acquired by means of vertical transmission from an IV drug addict mother. An analysis of additional patients who received blood products from patients with AIDS clearly indicates a significant risk in these populations for acquiring AIDS. The epidemiologic, clinical and immunologic findings in these groups of patients have been described and published and will serve as a continuing basis for investigation.

We have also investigated the distribution of B and T lymphocytes in the lymph nodes of homosexual men with Kaposi's sarcoma. The information obtained from these studies was utilized to compare with results of peripheral blood analysis of similar populations of cells. These studies have provided a basis for determining whether or not peripheral blood studies accurately reflect the distribution of immunologically competent cells within the tissue of affected patients.

Flow cytometric analysis using monoclonal antibodies to leukocyte subsets has revealed striking changes in the distribution of cells among patients with AIDS, the lymphadenopathy syndrome and normal homosexual controls. Large amounts of surface immunoglobulin are present on both T helper and T suppressor cells in these various groups. There is a quantitative increase from healthy to lymphadenopathy to full-blown AIDS in

Bibliography

1. Ammann AJ, Cowan MJ, Wara DW, Weintrub P, Dritz S, Goldman H, Perkins HA. Acquired immunodeficiency in an infant: Possible transmission by means of blood products. Lancet 1:956-958, 1983.
2. Ammann AJ, Abrams D, Conant M, Chudwin D, Cowan MJ, Volberding P, Lewis B, Casavant C. Acquired immune dysfunction in homosexual men: Immunologic Profiles. Clin. Immunol. Immunopath. 27:315-325, 1983.
3. Conte JE, Hadley WK, Sande M, Ammann AJ. Infection control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). New Eng. J. Med. 309:740-744, 1983.
4. Modlin RL, Meyer PR, Hofman FM, Mehlmauer M, Levy NB, Lukes RJ, Parker JW, Ammann AJ, Conant MA, Rhea TH, Taylor CR. T lymphocyte subsets in lymph nodes from homosexual men. JAMA 250:1302-1305, 1983.
5. Weintrub PS, Koerper MA, Addiego JE, Drew LW, Lenette ET, Miner R, Cowan MJ, Ammann AJ. Immunologic abnormalities in patients with hemophilia A. J. Pediat. 103:692-695, 1983.
6. Modlin RL, Meyer PR, Ammann AJ, Rea TH, Hofman FM, Vaccaro SA, Conant MA, Taylor CR. Altered distribution of B and T lymphocytes in lymph nodes from homosexual men with Kaposi's sarcoma. Lancet 2:768-771, 1983.
7. Jaffe HS, Ammann AJ, Abrams DI, Lewis B, Golden JA. Complications of co-trimoxazole in treatment of AIDS associated *Pneumocystis carinii* pneumonia in homosexual men. Lancet 2:1109-1111, 1983.
8. Abrams DI, Lewis BJ, Beckstead JH, Casavant H, Drew WL. Persistent diffuse lymphadenopathy in homosexual men: Endpoint or Prodrome? Ann. Int. Med. (in press).
9. Drew WL, Mills J, Dylewski J, Casavant H, Ammann A, Brodie H, Merigan T. CMV infection: Is the cause of abnormal T-lymphocyte subset ratios in homosexual men. (Submitted for publication).

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
Jay A. Levy	Principal Investigator	Department of Medicine Cancer Research Institute
John Morrow	Research Immunologist	Cancer Research Institute

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

The specific objective of this laboratory is to identify the infectious agent responsible for AIDS. Over the next year, we shall continue our efforts to isolate this agent using tissue culture and animal experimentation. For tissue culture studies, we shall employ a selected number of different animal cell lines which are susceptible to a variety of known viruses. These cells will be cocultivated with white cells and sperm from individuals with AIDS. In addition, the white cells of patients with AIDS will be cultured in the presence of IL2 to establish T cell lines, with B cell growth factor (when available) to cultivate B cells, and in human sera, to cultivate macrophages. The presence of an infectious agent in these cells will be assessed. In particular, over the next year we shall concentrate on the presence of retroviruses in the T cells of AIDS patients and the possibility of a new agent in cultured monocytes. Assays for HTLV and LAV-1 will be conducted.

For animal studies, mice and hamsters appear to be the most sensitive rodents to infections which may result from immune deficiency induced by the AIDS agent. We shall thus inoculate these animals with purified white cells from patients with AIDS, as well as the pellets of centrifuged serum samples. The animals will be followed for changes in immunologic parameters as well as for differences in their cell numbers as measured by immunofluorescence (FACS) using helper and suppressor T cell antisera. The end point will be the development of immunologic changes and opportunistic infections in these animals.

In all these studies, sera from patients with AIDS, a collection of sera from close intimate contacts of AIDS patients over at least six months, and normal healthy gay individuals will be used in an attempt to identify the agent responsible for the disease. The tests conducted will include immunofluorescence testing, hemagglutination, hemadsorption, reverse transcriptase assays and interferon assays, as well as electron microscopy.

Finally, we shall continue to establish and characterize cell lines derived from Kaposi's sarcomas. We ultimately want to develop a tumorigenic line that can be studied for its transformation properties and presence of oncogenic viruses.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☒ YES If "YES," identify by common names and underline primates.

Mice

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

UI CA 34980A

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

Equipment

We have requested \$5,000. to buy a Coulter Counter to be placed in our P-2 facility. At this time, we must take the white cells, after they are separated through Ficoll-Hypaque gradients and count them in a Coulter Counter in a lab situated at a distance from the P-2 facility. This procedure has alarmed some individuals in the other laboratory and also could present problems in the bio-safety requirements for separation of equipment used in AIDS research. We, thus, hope that funding for this important piece of equipment will be approved.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-83	THROUGH 4-30-84	GRANT NUMBER UI CA 34980A
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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)	ACTUAL EXPENDITURES THRU (insert date):	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	122,968	53,656	69,312	122,968	0
INDIRECT COSTS (as provided)	30,600	11,674	18,926	30,600	0
TOTALS →	153,568	65,330	88,238	153,568	0

B. THROUGH F.

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

PROFESSIONAL PERSONNEL

NAME	TITLE	CATEGORY	25%	26-50%	51-75%	MORE THAN 75%
J Levy	Assc. Prof	1	X			
J Morrow	"in training"	3		*		
J Landes	SRA I	2				*
T Shimobukaro	SRA I	2	*			
MSzoenyi	Lab Asst	2	*			

EQUIPMENT

Lease of Becton-Dickenson Research FACS Analyzer

TRAVEL

Domestic travel to the East coast for an AIDS Conference.

OTHER SUPPORT

J. Levy, M.D. State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$81,000

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Jay A. Levy, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION		FROM	THROUGH
TITLE (Repeat title shown in item 1 on first page) Isolation of Agent Responsible for AIDS			

(SEE INSTRUCTIONS)

1. Inoculation of concentrated white cells and sera from patients with AIDS into newborn animals from four different strains of mice, and from guinea pigs, hamsters, and rats. Over 1,000 animals have been inoculated and maintained for up to 1 year. Control animals have received white cells from healthy donors. Results show a 15% incidence of opportunistic infections in BALB/c mice and not in ICR, C37 black, or C3H mice. Control animals had less than 1% infection rate. Hamsters had a somewhat increased death rate compared to controls. Guinea pigs and rats showed no infection or mortality after 1 year.

2. Histologic examination of blood smears from the animals has indicated a reduction in lymphocytes in some of the mice and hamsters inoculated with AIDS material, but not in rat or guinea pigs. Thus, combined with the above mentioned results, we believe that mice may be a potential animal model for the study of AIDS.

3. In collaborative studies with Dr. Sy Kalter, Southwest Texas Foundation, we have inoculated AIDS blood into 4 baboons, one of which was a newborn. The first three animals inoculated all showed initially a lymphocytosis, with many atypical lymphocytes. In two animals, this picture has been maintained. Their blood contains no antibodies to CMV, EBV, or hepatitis B. Blood from one of the infected animals was inoculated into a newborn baboon, and the same pattern of lymphocytosis has been maintained in this animal after 9 months.

4. We have inoculated purified white cells from AIDS patients onto a variety of heterologous cell lines, including mink, dog, cat, mongoose, gazelle, chicken, human, chimp, rhesus monkey. They have also been cocultivated with the CEM and MOLT T cell lines and the U937 human macrophage cell line. In a limited number of studies conducted thus far, we can find no evidence of an infectious agent by CPE, hemagglutination or hemadsorption tests. Immunoflourescent studies using sera from a patient with AIDS has not indicated any presence of an agent in these cell lines, but these studies are only preliminary.

5. We have cocultivated AIDS white cells with the established T cell lines and attempted to induce interferon production in these cells. Thus far, no interferon has been noted in these cells after a short cocultivation period.

6. We have cultured over 50 T cell lines from patients with AIDS as well as controls and healthy gay donors. These cells have been studied by FACS for antigen markers after long term growth in culture. We have achieved 100% success in growing the cell lines in the presence of IL2. In those studied by FACS, we find that the helper cells are initially increased in number, but these then decrease after about 3 weeks. Suppressor T cells can be maintained in culture for several months. Macrophages and NK cells disappear after one week. We have maintained AIDS T cell lines in the presence of IL2 for over 90 days with good viability. As noted above, there is then a preponderance of suppressor T cells in culture.

7. In one lymphocyte culture, we have evidence that B cells remain and are making antibodies to T cells. By double labelling the presence of T cells carrying immunoglobulins on their surface have been noted even after three months in culture.

8. In about 5 out of 50 cultures we have detected the presence of HTLV by reverse transcriptase and immunofluorescent tests. Antibodies to HTLV have only been found in about 2 out of 20 AIDS patient's serum examined. We have confirmed the ability of HTLV to induce syncytial formation in XC and mink lung cells. We are perfecting this assay to use as one of the tests for HTLV. We have also noted that HTLV does not hemagglutinate goose, 1 day chick, adult chick, guinea pig, rat, rhesus monkey, human O, or sheep erythrocytes.

9. In some cultures, high reverse transcriptase activity has been noted without evidence of infection with HTLV. We are presently investigating whether LAV-1 (isolated first by Barre, et al.) is responsible for this RT activity.

10. We have noted that macrophages from AIDS patients adhere less readily to the cell culture as compared to controls. This may indicate either a difference in population of macrophages or an abnormality in their adherence potential.

11. We have noted after long term culture, the presence of dendritic -like cells growing in cultures of both AIDS patients and normal controls suggesting that IL2 enhances the growth of these cell populations. They become evident after long term culture.

12. We have established over 35 cell lines from Kaposi's sarcomas (KS) removed from patients with AIDS. These cells have been grown by selected techniques on plastic, and then analyzed for endothelial cell characteristics. They have been studied for prostaglandin and prostacycline production (with Dr. M. Goldyne). Over 80% of them produce Factor VIII and have some properties suggesting malignant potential. Moreover, our Kaposi's cell lines have been examined by various histochemical tests by Dr.

Jay Beckstead. These results have indicated that several of them have enzyme markers typical of endothelial cells. Nevertheless, none of these cell lines produced tumors in nude mice, nor have grown in methylcellulose. We have also attempted to grow the cell lines in nude mice in the presence of an angiogenesis-producing tumor (choriocarcinoma). These results, however, have also been unsuccessful. Nevertheless, we believe KS is a hormone-dependent tumor, and thus, the cells may only be tumorigenic when the proper growth factors are present in the host.

13. We have analyzed our Kaposi's sarcoma cell lines in collaboration with Drs. Nelson and MacDougall in Oregon, as well as individuals at UCSF (Dr. A. Geballe), for the presence of CMV, EBV and hepatitis B. In a limited number of studies, none of these agents have been definitively found in the cell lines, nor in fresh tumor tissue removed from the patients. Previous work indicated the presence of CMV, but when Dr. Nelson purified his probes further, and normal human sequences were eliminated, the positive results could not be confirmed. These studies continue to be conducted.

14. We have begun a collaborative work with Professor Keonig in the Dominican Republic as well as colleagues in Haiti examining blood from Haitian immigrants and patients for the presence of antibodies to HTLV, CMV, hepatitis B and EBV. These studies have indicated that Haitian coming from the provinces do not have the same high titer of antibodies to these agents as do those in the cities. These results suggest that AIDS was probably introduced into Haiti and did not result from the voodoo practices, come from animals, or from the population living in the provinces.

PUBLICATIONS

J LEVY

Marx, PA, Maul, DH, Osborn, KG, Lerche, NW, Moody, P, Lowenstine, LJ, Henrickson, RV, Arthur, LO, Gravel, M, London WT, Sever JL, Levy JA, Munn RJ, and Gardner MB. Simian AIDS: Isolation of a Type D Retrovirus and Disease Transmission. Science. In press.

Levy JA, Ziegler JL, Acquired immunodeficiency Syndrome in an opportunistic infection and Kaposi's Sarcoma results from secondary immune stimulation. Lancet 1983;2: 78-81

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

1 U01 CA34980-01

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
W. Lawrence Drew, M.D. Ph.D.	Associate Clinical Prof.	Medicine, Clinical Pathology & Laboratory Medicine, U.C.S.F.
John Mills, M.D.	Associate Professor	Medicine, U.C.S.F.
Alan Gottlieb, R.N.	Nurse Practitioner, II	Medicine, U.C.S.F.
Richard Miner, B.A.	Research Tech, IV	Pathology Research Mt. Zion Hospital
To Be Hired	Research Tech.	Medicine, U.C.S.F.

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

1. Enroll 60 additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
2. Collect sequential isolates of CMV from individual, healthy homosexual men and analyse them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

VERTEBRATE ANIMALS INVOLVED ☒ NO ☐ YES If "YES," identify by common names and underline primates.

PAGE 3

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5/01/84	THROUGH 4/30/85	GRANT NUMBER 1 U01 CA34980-01		
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
W. Lawrence Drew, M.D. Ph.D.	Principal Investigator	20	8	NONE	NONE	0.
R. Miner	Research Tech, IV	50	20	16,411.	3,692.	20,103.
SUBTOTALS →				16,411.	3,692.	20,103.
CONSULTANT COSTS (See instructions)						
N/A						
EQUIPMENT (Itemize)						
N/A						
SUPPLIES (Itemize by category)						
CO ₂ & liquid N ₂ 413.						
Tissue Culture 2,067.						
Media & Sera 1,654.						
Reagents (antisera, chemicals, etc.) 1,654.						
Plastic & Glassware 3,396.						9,184.
TRAVEL		DOMESTIC				
		FOREIGN International Congress of Virology				1,600.
PATIENT CARE COSTS		INPATIENT				
		OUTPATIENT				
ALTERATIONS AND RENOVATIONS (Itemize by category)						
N/A						
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						
N/A						
OTHER EXPENSES (Itemize by category)						
Computer Costs 1,650.						
Office Expenses 767.						
Statistical & Epidemiological Consultation 2,600.						
Indirect Costs 45.3% (16,411.) 7,434.						12,451.
TOTAL DIRECT COST (Enter on Page 1, Item 10).						43,338.
INDIRECT COST (See instructions)		45.3 % S&W*		Date of DHHS agreement 3/23/83		☐ Not requested ☐ Under negotiation with:
		% TDC*				

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

1 U01 CA34980-01

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

SALARY JUSTIFICATION

Increases in salary for the following U.C.S.F. personnel: John Mills, M.D. Alan Gottlieb, and To Be Hired Tech. Institutional increases of 11% for the above U.C.S.F. personnel constitute budgeted salary increases.

Two 50% Research Techs. will replace previously budgeted 100% SRA II, 5, because the work conducted in this study is divided between two locations. Typing of viruses is performed at Mount Zion Hospital and Medical Center as are all serologic studies, requiring one 50% tech (Research tech, IV). Viral cultures are performed at San Francisco General Hospital requiring another 50% tech (To Be Hired).

Increase of salary for 50% Research tech, IV at Mount Zion Hospital is due to higher skill and salary step level.

TRAVEL JUSTIFICATION

Invitation to present lecture on the relationship of cytomegalovirus and AIDS and to discuss the results of CMV researchers from Japan and European countries at the International Congress of Virology in Japan.

Other Category for next budget period has been reduced to appropriately cover Travel costs.

VIROLOGY II

SECTION III CURRENT BUDGET PERIOD	FROM 5/01/83	THROUGH 4/30/84	GRANT NUMBER 1 U01 CA 34980-01
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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 (insert date): 12/31/83 (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	89,403.	34,424.	54,979.	89,403.	0.
INDIRECT COSTS (as provided)	6,499.	2,882.	3,617.	6,499.	0.
TOTALS →	95,902.	37,306.	58,596.	95,902.	0.

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%	26-50%	51-75%	more than 75%
W. L. Drew	P.I.	1	X			
J. Mills	Co-Invest.	1	*			
A. Gottlieb	Nurse Pract.	2		*		
R. Miner	Tech IV	2		*		
M. Blair	Tech III	2				X
E. Mocarski	Consultant	1	X			
T. Merigan	Consultant	1	X			
To Be Hired	Tech	2		*		
K. Taylor	Secretary	2				X

C. EQUIPMENT N/A

D. TRAVEL

Invitation to present a lecture on the Relationship of Cytomegalovirus and AIDS and opportunity to discuss the results of CMV researchers from Japan and European countries at the International Congress of Virology to be held in Japan.

E. EXPLANATION OF COLUMN 5. N/A

F. OTHER SUPPORT See attached page.

F. OTHER SUPPORT FOR DR. W. LAWRENCE DREW:

- A. State of California State AIDS Center Grant Series -
University of California

Project Title: The Role of Cytomegalovirus in the
Etiology of AIDS.

Grant Period: 7/01/83 to 10/30/84

Annual Amount: \$135,000.

- B. Hoffmann LaRoche, Inc. Pending - Protocol 2563B

Project Title: Evaluation of the Tolerance and
Efficacy of Escalating Doses of
Recombinant Leukocyte A Interferon
(Ro 22-8181/001) Therapy of Decreasing
Titer of Virus in the Urine,
Blood or Semen of Patients with
Disseminated Cytomegalovirus Infections.

Annual Amount: Up to \$40,000., dependant upon
patient enrollment.

- C. Hoffmann LaRoche, Inc. Pending - Protocol 2564B

Project Title: Safety & Efficacy of Recombinant
Leukocyte A Interferon (Ro 22-
8181/001) in Patients with Acquired
Immunodeficiency and viral Infections.

Annual Amount: Up to \$45,000., dependant upon
patient enrollment.

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER 1 U01 CA34980-01	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR W. Lawrence Drew, M.D., Ph.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION Mount Zion Hospital and Medical Center		FROM 5/01/83	THROUGH 1/31/84
TITLE (Repeat title shown in item 1 on first page) Studies of Acquired Immune Deficiency Syndrome			

(SEE INSTRUCTIONS)

We have enrolled 40 CMV seronegative homosexual men in our prospective study. Ten have seroconverted and have lowered their H:S ratios from an average of 1.6 pre-infection to 0.6 post-infection. Three of the ten have been followed for more than or equal to 15 mos. and two continue to have H:S ratios less than 1.0. CMV infection was asymptomatic in all ten. To assess the possibility that homosexual men experience infection with more than one strain of CMV, we have analyzed, by restriction enzymes, multiple CMV isolates from four separate individuals with AIDS. In each patient at least two different strains were identified.

PUBLICATIONS

- Drew WL, Miner RC, Ziegler JL, Gullett JH, Abrams DI, Conant MA, Huang ES, Groundwater JR, Volberding P, Mintz L. Cytomegalovirus and Kaposi's Sarcoma in Young Homosexual Men. *Lancet* 1982, 2:125-127.
- Follansbee SE, Busch DF, Wofsy CB, Coleman DL, Gullet J, Aurigemma GP, Ross T, Hadley WK, Drew WL. An Outbreak of Pneumocystis carinii Pneumonia in Homosexual Men. *Ann Int Med* 1982, 96:705-713.
- Ziegler JL, Drew WL, Miner RC, Mintz L, Rosenbaum E, Gershow J, Lennette ET, Greenspan J, Shillitoe E, Beckstead J, Cassavant C, Yamamoto K. Outbreak of Burkitt's-like Lymphoma in Homosexual Men. *Lancet* 1982, 2:631-633.
- Black SB, Raas M, Mintz L, Shinefield JR, Drew WL. Indirect Hemagglutination Inhibition: A Direct Method for Detecting Cytomegalovirus Antigen. *J Clin Lab Med* 1983, 101:450-452.
- Drew WL, Mintz L. Cytomegaloviral Infection in Healthy and Immune Deficient Homosexual Men, in Ma P and Armstrong D (eds): The Acquired Immune Deficiency Syndrome and Infections of Homosexual Men. Yorke Medical Books, New York, New York, April 1983, 117-123.
- Mintz L, Drew WL, Sexually Transmitted Viral Infections in Homosexual Men, in de la Maza (ed): *Med Clin North Am; Medical Virology*. W. B. Saunders Company, Philadelphia, Pennsylvania, September 1983, 67/5:1093-1104.
- Mintz L, Drew WL, Miner RC, Braff EH. Cytomegalovirus infections in homosexual men: an epidemiological study. *Ann Intern Med* 1983, 99:326-329.
- Drew WL. Sexual Transmission of CMV and Its Relationship to Kaposi's Sarcoma in Homosexual Men, in Plotkin S (ed): Pathogenesis and Prevention of Human Cytomegalovirus Infection. In Press.
- Abrams DI, Lewis B, Beckstead J, Cassavant C, Drew WL. Persistent Diffuse Lymphadenopathy in Homosexual Men: Endpoint or Prodrome? Accepted for publication in the *Ann Int Med*.
- Drew WL, Mills J, Dylewski J, C Cassavant, A Ammann, H Brodie, T Merigan. Is CMV Infection the Cause of Abnormal T Lymphocyte Subset Ratios in Homosexual Men? Submitted for publication.
- Katznelson S, Drew WL, Mintz L. Efficacy of the Condom as a Barrier to the Transmission of Cytomegalovirus. Submitted for Publication.

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
UOI CA34980

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
VOLBERDING PA	PRINCIPAL INVESTIGATOR	DEPT OF MEDICINE/SFGH
ZIEGLER J	CO-PRINCIPAL INVESTIGATOR	DEPT OF MEDICINE/CRI
ABRAMS, DI	CO-INVESTIGATOR	DEPT OF MEDICINE/SFGH
LEWIS, BJ	CO-INVESTIGATOR	DEPT OF MEDICINE/CRI

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

In the second year of the NIH Grant we will continue to observe and record the natural history of patients with lymphadenopathy syndrome as well as AIDS associated Kaposi's sarcoma. We also will continue to collect material for banking for collaborative research into the pathogenesis and etiology of this syndrome. The specific objectives for each main patient group covered in this grant will include therapy of patients with diffuse lymphadenopathy with recominant alpha interferon and therapy of Kaposi's sarcoma with recominant gamma interferon and interleukin-2. Future chemotherapy trials after the conclusion of enrollment in INCRF-159 protocol serial immunologic monitoring.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II NEXT BUDGET PERIOD Follow instructions carefully	FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UI CA 34980A
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A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD	DOLLAR AMOUNT REQUESTED (Omit cents)
--	--------------------------------------

PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
P. VOLBERDING	Principal Investigator	20		12,360	2,802	
D. ABRAMS	CO-INVESTIGATOR	50		27,143	6,152	
J. ZEIGLER	CO-INVESTIGATOR	20		-	-	
B. LEWIS	CO-INVESTIGATOR	20		-	-	
G. GEE	ADM. NURSE II	50		16,998	4,676	
P. ROY	PR CLK	50		8,556	2,353	
SUBTOTALS →				65,057	15,983	81,040
CONSULTANT COSTS (See instructions)						0
EQUIPMENT (Itemize)						
SUPPLIES (Itemize by category)						
MAILING						
REPRO/PRINTING						
PHONE						
OFFICE SUPPLIES						
CLINIC SUPPLIES						1,284
TRAVEL	DOMESTIC P. VOLBERDING, D. ABRAMS, G. GEE					1,605
	FOREIGN					0
PATIENT CARE COSTS	INPATIENT					0
	OUTPATIENT					0
ALTERATIONS AND RENOVATIONS (Itemize by category)						0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						0
OTHER EXPENSES (Itemize by category)						
PHOTO PROCESSING						
BOOKS, PERIODICALS						214
TOTAL DIRECT COST (Enter on Page 1, Item 10)						84,143

INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of CHHS agreement	☐ Not requested ☐ Under negotiation with:
26,232	% TDC*			

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER
UI CA 34980A

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

PERSONNEL

P VOLBERDING 24% increase in salary since 5-1-83 due to promotional and cost of living increases.
D ABRAMS 50% increase in salary since 5-1-83 due to promotional reclassification to faculty status and cost of living adjustment. Paid time reduced to 50% to accommodate the salary increases.
G GEE 16% increase in salary due to promotional reclassification and cost of living adjustment.
P ROY 18% increase in salary due to promotional and cost of living adjustment.

FRINGE BENEFIT RATES

EFFECTIVE 1-1-84

EFFECTIVE 7-1-84

ACADEMIC PERSONNEL

26%

22%

STAFF PERSONNEL (CAREER)

30%

27%

EQUIPMENT IBM PC COMPUTER AND MONITOR TO BE USED FOR PATIENT DATA COLLECTION. \$3,750
PATIENT DATA COLLECTION NEEDS HAVE INCREASED TO THREE TIMES OF ORIGINAL EXPECTATIONS.

SUPPLIES To accommodate cost of living increases these
TRAVEL sections have been adjusted upwards
OTHER EXPENSES to 7%.

CONTRACTUAL

Mt Zion Hospital
Lawrence Drew, M.D.
In an effort to cover overhead costs at
Mt Zion Hospital Dr. Drew's virology section
will be listed as a sub-contract under
Dr. Paul Volberding's therapy section.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-83	THROUGH 4-30-84	GRANT NUMBER
--------------------------------------	----------------	--------------------	--------------

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)	ACTUAL EXPENDITURES THRU (insert date):	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	78,500	52,139	26,361	78,500	
INDIRECT COSTS (as provided)	21,135	13,944	7,191	21,135	
TOTALS →	99,635	66,083	33,552	99,635	

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	LESS 25%	26-50%	51-75%	MORE 75%
P VOLBERDING	ASST PROF MED	1	*			
D ABRAMS	CLN INSTR MED	1				*
J ZEIGLER	PROF MED	1	X			
B LEWIS	ASSC CLN PROF MEDICINE	1	X			
G GEE	ADM NURSE	2		*		
P ROY	PRIN CLK	2		*		

C. EQUIPMENT

Toshiba Pl350 printer and components to be used with IBM PC Computer
\$1,798.87

D. TRAVEL

P Volberding has used the travel money in the amount of \$1,500 to partially defray the cost of attending research meetings for the presentation of research results.

E. EXPLANATION OF COLUMN 5

None

F. OTHER SUPPORT

Paul A. Volberding, M.D.
City and County of San Francisco
Dept. of Public Health
"Study of AIDS - Outpatient Clinic"
7-1-83 to 6-30-84 Grant period
\$390,541

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER UOI CA34980	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR PAUL VOLBERDING, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UNIVERSITY OF CALIFORNIA, SAN FRANCISCO		FROM 5-1-83	THROUGH 4-30-84
TITLE (Repeat title shown in item 1 on first page) PRINCIPAL INVESTIGATOR (SEE INSTRUCTIONS)			

SEE ATTACHED SHEET

THERAPY OF AIDSOVERALL OBJECTIVES

The overall objectives of the therapy section of this grant have not changed. Because of work accomplished in the first grant year, the focus of Kaposi's sarcoma therapy protocols in this grant year will be on biologic response modifiers rather than cytotoxic chemotherapy. Also because of the number of cases of lymphadenopathy syndrome progressing to AIDS, therapy trials for this syndrome will also be conducted.

SUMMARY OF WORK ACCOMPLISHED

A number of original observations have been made from our center on the natural history of the lymphadenopathy syndrome and of the natural history and therapy of Kaposi's sarcoma in AIDS.

Lymphadenopathy Syndrome: Over two hundred patients with the syndrome of diffuse lymphadenopathy have been followed in the AIDS clinic at UCSF and San Francisco General Hospital. In contrast to our experience at the time of the original grant request, five of these patients have now progressed to AIDS as defined by the CDC. The careful clinical observations made on these patients prior to conversion should be important in helping predict the natural history of this extremely common syndrome. Also because of this conversion to AIDS, therapy trials of recombinant alpha two interferon as discussed in the original grant application are now being initiated. The serial evaluations of patients with lymphadenopathy syndrome has also provided access to specimens including serum and lymph node material. These are being collected on a regular basis from this cohort of patients and have proved valuable for collaborative research studies, many of which were summarized in virology immunology and epidemiology sections of this progress report.

Kaposi's Sarcoma: In the first year of this grant approximately 100 patients with Kaposi's sarcoma in AIDS have been evaluated in the Kaposi's sarcoma clinic at UCSF and the AIDS clinic at San Francisco General Hospital. A staging system devised in retrospect from analysis of these patients initial evaluation in clinical outcome is being developed. A preliminary analysis of 81 patients with Kaposi's sarcoma has revealed minimal impact on survival from the extent of Kaposi's sarcoma but a relatively greater impact from clinical features which may more directly reflect the status of immune competence. This has been reported in abstract form and a more complete analysis of 150 Kaposi's sarcoma patients is currently being conducted.

The natural history of Kaposi's sarcoma in AIDS has also been evaluated by studying those patients who have refused therapy of their tumor. A preliminary analysis of this experience reveals a broad spectrum of clinical aggressiveness of AIDS associated Kaposi's sarcoma. While essentially all patients have shown progression of their tumor, in several well-documented cases there was at most only minimal progression in twelve months of follow-up without therapy. This observation raises important implications for the design of prospective clinical trials which will be addressed in the next year of this grant.

Cytotoxic chemotherapy has been studied in the first year of the continuation of vinblastine therapy for all stages of Kaposi's sarcoma which demonstrates a 35% objective response in these patients. Also 25 patients have been entered onto a phase two trial of ICRF-159. Accrual to this study is being completed and early clinical results suggest that this drug is not more active than vinblastine in the treatment of Kaposi's sarcoma. If confirmed in a more complete analysis these results would suggest that the biology of AIDS associated Kaposi's sarcoma is unlike that of African Kaposi's sarcoma where ICRF-159 was extremely active.

In addition to trials of cytotoxic agents biologic response modifiers are also being tested in Kaposi's sarcoma associated with AIDS. Over 60 patients have been entered into trials of recombinant alpha interferon. As reported in several publications an objective response rate of approximately 40% was observed with this agent. Disappointingly, no immune restoration of clinical significance was observed in these trials. Future trials will continue with this and other biologic response modifiers including recombinant gamma-interferon and recombinant interleukin-2.

As was true of the patients with lymphadenopathy syndrome, patients with Kaposi's sarcoma have also been a valuable source of specimens for collaborative research studies with other components of this grant. Patients with Kaposi's sarcoma are followed serially and specimens including serum and tumor tissue are regularly preserved for future studies by the tissue and serum repository discussed in the first section of the grant.

OBJECTIVES FOR THE NEXT GRANT YEAR

In the second year of the NIH Grant we will continue to observe and record the natural history of patients with lymphadenopathy syndrome as well as AIDS associated Kaposi's sarcoma. We also will continue to collect material for banking for collaborative research into the pathogenesis and etiology of this syndrome. The specific objectives for each main patient group covered in this grant will include therapy of patients with diffuse lymphadenopathy.

alpha interferon & therapy of Kaposi's Sarcoma with recombinant gamma interferon & interleukin-2.
denopathy with recombinant interleukin-2. Future chemotherapy trials after the conclusion of enrollment in ICRF-159 protocol will continue to investigate single agent chemotherapy with serial immunologic monitoring.

HUMAN SUBJECT CONSIDERATION

Lymphadenopathy Syndrome: A protocol for the use of recombinant alpha interferon for patients with lymphadenopathy syndrome has been approved by the Human Subject's Committee at UCSF and a copy of the protocol is attached.

Kaposi's Syndrome: Three protocols are currently being developed and will be initiated shortly for the treatment of AIDS associated Kaposi's sarcoma. While discussed in brief in the original competitive review these protocols are much more complete at this stage and are included in this section. These include a controlled study of no therapy compared with alpha interferon or alpha interferon plus vinblastine for patients with minimal stage of Kaposi's sarcoma, recombinant gamma-interferon and recombinant interleukin-2. In these protocols, particularly in the last two, substantial efforts will be made to monitor the immunologic effects of these agents as they may prove helpful in immuneres-toration. A detailed analysis of the rationale for each agent is beyond the scope of this progress report but is included in each of the attached protocols.

PUBLICATIONS

PA VOLBERDING

Ziegler JL, Stites DP. Immunopathogenesis of acquired immunodeficiency syndrome: "host versus host" autoimmunity. JNCI (submitted 2/84)

Ziegler JL, Beckstead JA, Levine AM, et al. Non-Hodgkin's lymphoma in homosexual men with lymphadenopathy or AIDS. Clinical features in 90 patients from six insititutions. N England J Med (submitted, 3/84)

Diffuse, undifferentiated non-Hodgkin's lymphoma among homosexual males-United States. MMWR 1982;31:277-9

Ziegler JL, Drew WL, Miner RC et al. Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet 1982;2: 631-3

Ziegler JL, Bragg K, Abrams DI, et al. High-grade non-Hodgkin's lymphomas in patients with AIDS. Ann NY Acad Sci, in press

Ziegler JL, Templeton AC, Vogel CL. Kaposi's sarcoma: a comparison of classical endemic, and epidemic forms. Sem. Oncol (in press)

ABSTRACTS

1. Natural killer cell activity in homosexual men with Kaposi's sarcoma. Seaman, W., Ziegler, J., Volberding, P., Conant, M., Official Publication of the American Federation for Clinical Research, (in press) 1983.
2. Susceptibility to Kaposi sarcoma and HLA BW44. Colombe, B.W., Conant, M., Volberding, P., and Garovoy, M.R. American Federation for Clinical Research (in press) 1983.
3. Therapy of Kaposi's sarcoma (KS) in Acquired Immune Deficiency Syndrome with alpha-2 recombinant interferon. Volberding, P., Gottlieb, M., Rothman, J., Rudnick, S., Konnert, M., Derezin, M., Weinstein, W., Groopman, J. Proceedings: American Society of Oncology, Vol. 2, Pg. 53, 1983.
4. Single agent or combination chemotherapy of Kaposi's sarcoma in Acquired Immune Deficiency Syndrome. Lewis, B., Abrams, D. Ziegler, J., Conant, M., Gee, G., Silverberg, I., Volberding, P., Proceedings: American Society of Clinical Oncology, Vol. 2, pg. 59, 1983.
5. Immune thrombocytopenic purpura in homosexual men: Clinical manifestations and treatment results. Abrams, D., Voldberding, P., Linker, C., Kiproff, D., Moss, A., Sperling, J., and Embury, S. Blood, Vol. 62, No. 5, Supplement 1, pg. 108a, Nov. 1983.
6. Syngenic bone marrow transplantation for patients with AIDS and Kaposi's sarcoma. Mitsuyasu, R., Volberding, P., Groopman, J. Champlin, R. Blood, Vol. 62, No. 5, Supplement 1, pg. 226a.
7. Recombinant alpha-interferon therapy for Kaposi's sarcoma in Acquired Immune Deficiency Syndrome. Volberding, P., Moran, T., Rudinck, S., Rothman, J. Proceedings: Second European Conference in Clinical Oncology and Cancer Nursing, pg. 221, Nov. 1983.

**UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONTRACTS AND GRANTS APPROVAL FORM**

REVISED BUDGET

(SUBMIT NINE COPIES OF THIS FORM)

ATTACHED ARE _____ COPIES OF A PROPOSAL
(INCLUDE ONE COPY FOR CONTRACTS AND GRANTS)

PAUL A. VOLBERDING, M.D.

FROM: (PI) JOHN ZIEGLER, M.D.
(LIST PROFESSIONAL DEGREES)

ACADEMIC TITLE: ASST. PROF OF MED PROF OF MED

DEPARTMENT: DEPT MED/SEGH CRI

CAMPUS MAIL STOP: SEGH WARD 86 EXT. 4387

PERSON TO CONTACT WITH QUESTIONS ABOUT THIS

PROPOSAL: ROBERTA WILSON EXT. 4387

PROJECT DATES: 05-1-84 to 04-01-85
(FIRST 12 MONTHS)

FUNDS REQUESTED: 601,042
(FIRST 12 MONTHS INCLUDING INDIRECT COSTS)

PROJECT TITLE: STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

FUNDING AGENCY: NATIONAL INSTITUTES OF HEALTH

AGENCY ADDRESS: 5333 WESTBARD AVE.
BETHESDA MD 20205

AGENCY DEADLINE: _____

UNIVERSITY FRANKING NO: _____
(FOR 1ST CLASS MAILING)

ACCOUNT/FUND NO: _____
(FOR EXPRESS MAILING)

● TYPE OF PROPOSAL (CHECK ONE IN EACH COLUMN):

NEW

☐ CONTINUATION OF NO. _____

☐ RENEWAL OF NO. _____

☐ SUPPLEMENT TO NO. _____

☒ REVISION OF NO. U01 CA 34980 - 02

☒ RESEARCH

☐ TRAINING

☐ GRANT

☐ CAREER DEVELOPMENT

☐ PUBLIC SERVICE

☐ CONTRACT

☐ EQUIPMENT

☐ CONFERENCE

☐ SUBCONTRACT

☐ TRAVEL

● COMMITMENT OF SPACE: BEFORE A PROPOSAL IS SUBMITTED, IT IS THE RESPONSIBILITY OF THE DEPARTMENT TO ASSURE THAT APPROPRIATE SPACE WILL BE AVAILABLE FOR THE DURATION OF THE PROJECT.

SITE OF WORK: ☒ UCSF ☒ SEGH ☒ VAMC ☒ OTHER ☐ RENT/LEASE.

LIST BUILDINGS AND ROOM NUMBERS: SEGHWARD 86; UCSF, DERM CLN, M1273; MT ZION LABS

WHAT DEPARTMENT HAS SPACE ASSIGNMENT? MEDICINE

● INVENTIONS (FOR CONTINUATIONS AND RENEWALS): ARE THERE ANY INVENTIONS TO REPORT? ☐ NO ☐ YES

● COMPUTER: EQUIPMENT PURCHASES: \$ 0 EQUIPMENT LEASES: \$ 0

● SAFETY REQUIREMENTS: FOR EACH YES MARKED BELOW ATTACH A COPY OF THE APPROPRIATE APPROVAL TO EACH COPY OF THIS CONTRACTS AND GRANTS APPROVAL FORM.

INVOLVEMENT

REQUIRED ATTACHMENT

1. IONIZING RADIATION/RADIOISOTOPES:

NO YES

☒

☐

RADIOISOTOPE APPLICATION FORM

2. HUMAN SUBJECTS:

SPECIFIC RESEARCH PLAN(S) DESCRIBED

☐

☒

COMMITTEE ON HUMAN RESEARCH APPROVAL LETTER

MULTIPLE PROJECT OR UNSPECIFIED PLANS
(GENERAL APPROVAL)

☐

☒

COMMITTEE ON HUMAN RESEARCH APPROVAL LETTER

3. BIOSAFETY:

RECOMBINANT DNA

☒

☐

MUA OR RECOMBINANT DNA
REGISTRATION DOCUMENT

CLASS 1*, 2*, OR 3 INFECTIOUS AGENTS

☒

☐

1) INFECTIOUS AGENTS REVIEW FORM, AND
2) BIOLOGICAL LABORATORY INSPECTION
REPORT AND CERTIFICATION

CLASS 1 OR 2 INFECTIOUS AGENTS

☒

☐

BIOLOGICAL LABORATORY INSPECTION
REPORT AND CERTIFICATION

CELL CULTURE

☒

☐

BIOLOGICAL LABORATORY INSPECTION
REPORT AND CERTIFICATION

4. ANIMALS: LOCATION OF ANIMALS _____

☐

☒

VERTEBRATE ANIMAL USE SUMMARY FORM

5. CHEMICAL SAFETY:

CHEMICAL CARCINOGENS

☒

☐

CHEMICAL CARCINOGEN APPROVAL FORM

FLAMMABLE AND/OR TOXIC COMPRESSED GAS

☒

☐

COMPRESSED AND LIQUIFIED GAS
CYLINDERS APPROVAL FORM

FLAMMABLE SOLVENTS (OVER 10 GALLONS)

☒

☐

FLAMMABLE LIQUID STORAGE USE
APPROVAL FORM

PERCHLORIC ACID

☒

☐

PERCHLORIC ACID APPROVAL FORM

SUBMITTED BY: John C. Ziegler MD Paul Volberding
SIGNATURE, PRINCIPAL INVESTIGATOR

7-17-84
DATE

DEPARTMENT CHAIRMAN OR
INSTITUTE DIRECTOR

DATE

DEAN OF SCHOOL

DATE

SFGH, DEAN'S OFFICE

DATE

ACOS RESEARCH AND
DEVELOPMENT, VAMC

DATE

DETAILED BUDGET FOR FIRST 12-MONTH PERIOD:

(1) SALARIES: LIST ALL SALARIED, NON-SALARIED UC PERSONNEL. PROJECT MERIT, PROMOTIONAL INCREASES IN COMPUTATION. USE TIME FOR STAFF EMPLOYEES ONLY — USE EFFORT FOR ACADEMICS.

FRINGE BENEFITS ARE CALCULATED AT: _____% ACADEMICS. _____% STAFF.

Name and Title	Step	Time or Effort %	Based on Annual Rate	Actual Gross	Fringe Benefits	Total
(PI) CLINIC - CONANT			42,199	42,199	12,220	
EPIDEMIOLOGY - MOSS			22,746	22,746	6,597	
IMMUNOLOGY - AMMANN			49,728	49,728	13,670	
VIROLOGY I - LEVY			39,671	39,671	8,686	
VIROLOGY II - DREW			46,607	46,607	13,364	
THERAPY - VOLBERDING			62,669	62,669	15,397	
SUBTOTALS:				263,620	69,934	333,554
(2) CONSULTANT COSTS (ITEMIZE):						0
(3) EQUIPMENT- DEFINED AS COSTING \$500 AND MORE (ITEMIZE):						
CLINIC						
VIROLOGY I COULTER COUNTER						10,000
(4) SUPPLIES (ITEMIZE BY CATEGORY):						
CLINIC			1,000			
IMMUNOLOGY			3,008			
VIROLOGY I			34,050			
VIROLOGY II			--7.0			
THERAPY			999			
						39,827
(5) TRAVEL (DOMESTIC): CLN 1,000 IMMUN 1,500 VIRI 1,100 THER 1,605 (FOREIGN):						5,205
(6) PATIENT COSTS (INPATIENT): (OUTPATIENT):						
(7) ALTERATIONS AND RENOVATIONS:						0
(8) CONTRACTUAL OR THIRD PARTY COSTS: VIROLOGY II						29,080
(9) OTHER EXPENSES (ITEMIZE):						
CLINIC			5,000			
IMMUNOLOGY			1,030			
VIROLOGY I			36,741			
EPIDEMIOLOGY			138			
						42,909
(10) TOTAL DIRECT COST						460,575
(11) _____% INDIRECT COST .27-.7%5-1-84 to 6-30-84 31.87% 7-1-84 to 4-30-84						140,467
(12) TOTAL REQUESTED FOR EXTRAMURAL SUPPORT						601,042

IF MATCHING FUNDS ARE REQUIRED, INDICATE AMOUNT \$ SOURCE OF FUNDS

FACULTY EFFORT: LIST ALL ACTIVE OR PENDING GRANTS BY AGENCY, GRANT NUMBER OR TITLE AND PERCENT OF EFFORT DEVOTED TO EACH BY THE PRINCIPAL INVESTIGATOR (CONTINUE ON SEPARATE SHEET IF NECESSARY):

PENDING

--	--

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROTECTION OF HUMAN SUBJECTS
ASSURANCE/CERTIFICATION/DECLARATION

☐ ORIGINAL ☒ FOLLOWUP ☐ EXEMPTION
(previously undesignated)

☒ GRANT ☐ CONTRACT ☐ FELLOW ☐ OTHER
☐ New ☐ Competing continuation ☒ Noncompeting continuation ☐ Supplemental

APPLICATION IDENTIFICATION NO. (if known)

U01 CA 34980-02

POLICY: A research activity involving human subjects that is not exempt from HHS regulations may not be funded unless an Institutional Review Board (IRB) has reviewed and approved the activity in accordance with Section 474 of the Public Health Service Act as implemented by Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46—as revised). The applicant institution must submit certification of IRB approval to HHS unless the applicant institution has designated a specific exemption under Section 46.101(b) which applies to the proposed research activity. Institutions with an assurance of compliance on file with HHS which covers the proposed activity should submit certification of IRB review and approval with each application. (In exceptional cases, certification may be accepted up to 60 days after the receipt date for which the application is submitted.) In the case of institutions which do not have an assurance of compliance on file with HHS covering the proposed activity, certification of IRB review and approval must be submitted within 30 days of the receipt of a written request from HHS for certification.

1. TITLE OF APPLICATION OR ACTIVITY

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

2. PRINCIPAL INVESTIGATOR, PROGRAM DIRECTOR, OR FELLOW

PAUL A. VOLBERDING, M.D. & JOHN ZIEGLER, M.D.

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION (see reverse side)

4. HHS ASSURANCE STATUS

☐ This institution has an approved assurance of compliance on file with HHS which covers this activity.

_____ Assurance identification number _____ IRB identification number

☐ No assurance of compliance which applies to this activity has been established with HHS, but the applicant institution will provide written assurance of compliance and certification of IRB review and approval in accordance with 45 CFR 46 upon request.

5. CERTIFICATION OF IRB REVIEW OR DECLARATION OF EXEMPTION

☐ This activity has been reviewed and approved by an IRB in accordance with the requirements of 45 CFR 46, including its relevant Subparts. This certification fulfills, when applicable, requirements for certifying FDA status for each investigational new drug or device. (See reverse side of this form.)

_____ Date of IRB review and approval. (If approval is pending, write "pending." Followup certification is required.)
(month/day/year)

☐ Full Board Review☐ Expedited Review

☒ This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by 45 CFR 46 will be reviewed and approved before they are initiated and that appropriate further certification (Form HHS 596) will be submitted.

☐ Human subjects are involved, but this activity qualifies for exemption under 46.101(b) in accordance with paragraph _____ (insert paragraph number of exemption in 46.101(b), 1 through 5), but the institution did not designate that exemption on the application.

6. Each official signing below certifies that the information provided on this form is correct and that each institution assumes responsibility for assuring required future reviews, approvals, and submissions of certification.

APPLICANT INSTITUTION	COOPERATING INSTITUTION
NAME, ADDRESS, AND TELEPHONE NO. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO CANCER RESEARCH INSTITUTE M-1282 SAN FRANCISCO CA 94143	NAME, ADDRESS, AND TELEPHONE NO. NONE
NAME AND TITLE OF OFFICIAL (print or type) LORRAINE PETRAKIS, CONTRACTS AND GRANTS OFFICER	NAME AND TITLE OF OFFICIAL (print or type)
SIGNATURE OF OFFICIAL LISTED ABOVE (and date)	SIGNATURE OF OFFICIAL LISTED ABOVE (and date)

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION (from front side)

According to 45 CFR 46.121, if an application is made to HHS requiring certification and involving use of an investigational new drug or device, additional information is required. In addition, according to 21 CFR 312.1(a)(2), 30 days must elapse between date of receipt by FDA of Form FD-1571 and use of the drug, unless the 30 day delay period is waived by FDA.

3a. INVESTIGATIONAL NEW DRUG EXEMPTION (if more than one is involved, list others below under NOTES):

SPONSOR NAME

DRUG NAME

DATE OF END OF 30-DAY EXPIRATION OR WAIVER

NUMBER ISSUED

3b. INVESTIGATIONAL DEVICE EXEMPTION:

SPONSOR NAME

DEVICE NAME

Unless notified otherwise by FDA, under 21 CFR 812.2(b) (ii) a sponsor is deemed to have an approved IDE if: (1) the IRB has agreed with the sponsor that the device is a nonsignificant risk device; and (2) the IRB has approved the study. (Check applicable box.)

☐ The IRB agrees with the sponsor that this device is a nonsignificant risk device.

OR

☐ The IDE application was submitted to FDA on (date) _____. Number issued _____.

NOTES:

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICEAPPLICATION
FOR CONTINUATION GRANT

REVIEW GROUP	TYPE	ACTIVITY	GRANT NUMBER (Insert on all pages)
	5	U01	CA34980-02
TOTAL PROJECT PERIOD			
From: 05-01-83		Through: 04-30-86	
REQUESTED BUDGET PERIOD			
From: 05-01-84		Through: 04-30-85	

1. TITLE

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

(name and address, street, city, state, zip code)

SAN FRANCISCO GENERAL HOSPITAL
VOLBERDING, PAUL A. M.D.
DIV OF ONCOLOGY WARD 86
995 POTRERO AVE.
SAN FRANCISCO CA 94110 &
JOHN ZIEGLER, M.D.
SAN FRANCISCO VETERANS ADM. HOSP.
ROOM 141 SAN FRANCISCO CA

2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT
MEDICINE

2c. MAJOR SUBDIVISION

SCHOOL OF MEDICINE

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR
BIOMEDICAL RESEARCH SUPPORT GRANT (see instructions)4. APPLICANT ORGANIZATION (name and address, street, city, state,
zip code)

UNIVERSITY OF CALIF, SAN FRANCISCO
CANCER RESEARCH INSTITUTE M-1282
SAN FRANCISCO CA 94143

5. ENTITY IDENTIFICATION NUMBER

1946036493A6

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF
APPLICANT ORGANIZATION

CONTRACTS AND GRANTS OFFICER

UNIVERSITY OF CALIFORNIA
SAN FRANCISCO CA 94143

7. HUMAN SUBJECTS

☐ NO☒ YES☐ Exemption # _____

OR

☒ Form HHS 596 enclosed PENDING

11. INVENTIONS (see instructions)

☒ NO☐ YES☐ Previously reported

OR

☐ Not previously reported

8. RECOMBINANT DNA

☒ NO☐ YES

TELEPHONE INFORMATION

9. PERFORMANCE SITE(S) (organizations and addresses)

UNIVERSITY OF CALIFORNIA, S.F.
CANCER RESEARCH INSTITUTE UCSF
DEPT. OF PEDIATRICS, UCSF
DIVISION OF DERMATOLOGY, UCSF
SAN FRANCISCO GENERAL HOSPITAL
MT. ZION HOSPITAL, SAN FRANCISCO

12a. PRINCIPAL INVESTIGATOR

OR PAUL A. VOLBERDING

JOHN ZIEGLER, M.D.

AREA
CODE

415

TELEPHONE NO.
AND EXTENSION

666-4387

12b. NAME OF BUSINESS OFFICIAL
(Item 6)

LORRAINE PETRAKIS

415

666-2977

12c. NAME AND TITLE OF OFFICIAL
SIGNING FOR APPLICANT OR-
GANIZATION (Item 15)

LORRAINE M. PETRAKIS
CONTRACTS AND GRANTS OFFICER

(415)

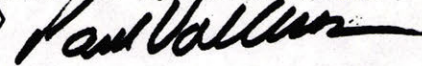
666-2977

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD

460,575

13. DO NOT USE THIS SPACE

14. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSUR-
ANCE: 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. Willful provision of false infor-
mation is a criminal offense. (U.S. Code, Title 18, Section 1001.)

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

DATE

7/17/84

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)

DATE

**UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONTRACTS AND GRANTS APPROVAL FORM**

(SUBMIT NINE COPIES OF THIS FORM)

ATTACHED ARE _____ COPIES OF A PROPOSAL
(INCLUDE ONE COPY FOR CONTRACTS AND GRANTS)

FUNDING AGENCY: National Institutes of Health

FROM: (PI) Paul A. Volberding, M.D.
(LIST PROFESSIONAL DEGREES)

AGENCY ADDRESS: 5333 Westbard Ave.
Bethesda MD 20205

ACADEMIC TITLE: Assistant Professor of Medicine

DEPARTMENT: Dept. of Medicine/SFGH

CAMPUS MAIL STOP: SFGH WARD 86 EXT. 6-4387

PERSON TO CONTACT WITH QUESTIONS ABOUT THIS

PROPOSAL: ROBERTA WILSON EXT. 4387

AGENCY DEADLINE: March 1, 1984

PROJECT DATES: MAY 1, 1984-APRIL 30, 1985
(FIRST 12 MONTHS)

UNIVERSITY FRANKING NO: _____
(FOR 1ST CLASS MAILING)

FUNDS REQUESTED: \$642,258
(FIRST 12 MONTHS INCLUDING INDIRECT COSTS)

ACCOUNT/FUND NO: _____
(FOR EXPRESS MAILING)

PROJECT TITLE: STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

● **TYPE OF PROPOSAL** (CHECK ONE IN EACH COLUMN):

☐ NEW

☒ CONTINUATION OF NO. UOI CA34980-o2

☐ RENEWAL OF NO. _____

☐ SUPPLEMENT TO NO. _____

☐ REVISION OF NO. _____

☐ RESEARCH

☐ TRAINING

☐ CAREER DEVELOPMENT

☐ PUBLIC SERVICE

☐ EQUIPMENT

☐ CONFERENCE

☐ TRAVEL

☒ GRANT

☐ CONTRACT

☐ SUBCONTRACT

● **COMMITMENT OF SPACE:** BEFORE A PROPOSAL IS SUBMITTED, IT IS THE RESPONSIBILITY OF THE DEPARTMENT TO ASSURE THAT APPROPRIATE SPACE WILL BE AVAILABLE FOR THE DURATION OF THE PROJECT.

SITE OF WORK: ☒ UCSF ☒ SFGH ☒ VAMC ☐ OTHER ☐ RENT/LEASE
LIST BUILDINGS AND ROOM NUMBERS: UCSF-Cancer Research Institute, Immunology Lab, Div. of Derm
SFGH-AIDS/KS CLINIC SFGH-Oncology Division Mt Zion Hosp-Viro-
WHAT DEPARTMENT HAS SPACE ASSIGNMENT? UCSF Dept of Medicine Immunology Lab
Cancer Research Institute

● **INVENTIONS** (FOR CONTINUATIONS AND RENEWALS): ARE THERE ANY INVENTIONS TO REPORT? ☒ NO ☐ YES

● **COMPUTER:** EQUIPMENT PURCHASES: \$ 0 EQUIPMENT LEASES: \$ 0

● **SAFETY REQUIREMENTS:** FOR EACH YES MARKED BELOW ATTACH A COPY OF THE APPROPRIATE APPROVAL TO EACH COPY OF THIS CONTRACTS AND GRANTS APPROVAL FORM.

	INVOLVEMENT		REQUIRED ATTACHMENT
	NO	YES	
1. IONIZING RADIATION/RADIOISOTOPES:	☒	☐	☐ RADIOISOTOPE APPLICATION FORM
2. HUMAN SUBJECTS:			
SPECIFIC RESEARCH PLAN(S) DESCRIBED	☐	☒	☐ COMMITTEE ON HUMAN RESEARCH APPROVAL LETTER
MULTIPLE PROJECT OR UNSPECIFIED PLANS (GENERAL APPROVAL)	☐	☒	☐ COMMITTEE ON HUMAN RESEARCH APPROVAL LETTER
3. BIOSAFETY:			
RECOMBINANT DNA	☒	☐	☐ MUA OR RECOMBINANT DNA REGISTRATION DOCUMENT
CLASS 1*, 2*, OR 3 INFECTIOUS AGENTS	☒	☐	☐ 1) INFECTIOUS AGENTS REVIEW FORM, AND 2) BIOLOGICAL LABORATORY INSPECTION REPORT AND CERTIFICATION
CLASS 1 OR 2 INFECTIOUS AGENTS	☒	☐	☐ BIOLOGICAL LABORATORY INSPECTION REPORT AND CERTIFICATION
CELL CULTURE	☒	☐	☐ BIOLOGICAL LABORATORY INSPECTION REPORT AND CERTIFICATION
4. ANIMALS: LOCATION OF ANIMALS <u>CANCER RESEARCH</u>	☐	☒	☐ VERTEBRATE ANIMAL USE SUMMARY FORM
5. CHEMICAL SAFETY: <u>INSTITUTE</u>			
CHEMICAL CARCINOGENS	☒	☐	☐ CHEMICAL CARCINOGEN APPROVAL FORM
FLAMMABLE AND/OR TOXIC COMPRESSED GAS	☒	☐	☐ COMPRESSED AND LIQUIFIED GAS CYLINDERS APPROVAL FORM
FLAMMABLE SOLVENTS (OVER 10 GALLONS)	☒	☐	☐ FLAMMABLE LIQUID STORAGE USE APPROVAL FORM
PERCHLORIC ACID	☒	☐	☐ PERCHLORIC ACID APPROVAL FORM

SUBMITTED BY: Paul Volberding, M.D.
Merle Sande, M.D. SIGNATURE, PRINCIPAL INVESTIGATOR

MARCH 1, 1984
DATE

MERLE SANDE, M.D. CHAIR, DEPT. OF MED/SFGH
DEPARTMENT CHAIRMAN OR
INSTITUTE DIRECTOR

DEAN OF SCHOOL

MARCH 1, 1984
DATE

SFGH, DEAN'S OFFICE

DATE

ACOS RESEARCH AND
DEVELOPMENT, VAMC

DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

APPLICATION
FOR CONTINUATION GRANT

REVIEW GROUP
SSS 9

5

ACTIVITY
001

GRANT NUMBER (Insert
on all pages)
CA34980-02

TOTAL PROJECT PERIOD

From: 05/01/83 Through: 04/30/86

REQUESTED BUDGET PERIOD

From: 05/01/84 Through: 04/30/85

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

1. TITLE

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR
(name and address, street, city, state, zip code)

VOLBERDING, PAUL A
SAN FRANCISCO GENERAL HOSP
MEDICAL SERVICE,, 5H22
SAN FRANCISCO, CALIF 94110

4. APPLICANT ORGANIZATION (name and address, street, city,
state, zip code)

UNIV OF CALIF, SAN FRANCISCO
CANCER RESEARCH INST, H-1282
SAN FRANCISCO, CA 94143

5. ENTITY IDENTIFICATION NUMBER

1946036493A6

2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT
MEDICINE

2c. MAJOR SUBDIVISION

SCHOOL OF MEDICINE

3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR
BIOMEDICAL RESEARCH SUPPORT GRANT (see instructions)

01 SCHOL OF MEDICINE

6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE
OF APPLICANT ORGANIZATION

CONTRACTS AND GRANTS OFFICER
OFFICE OF EXTRAMURAL SUPPORT
UNIVERSITY OF CALIFORNIA
SAN FRANCISCO, CA 94143

COMPLETE THE FOLLOWING (See Instructions)

7. HUMAN SUBJECTS

☐ NO ☐ YES

☐ OR
☐

Exemption # _____
Form HHS 596 enclosed

8. RECOMBINANT DNA

☐ NO ☐ YES

9. PERFORMANCE SITE(S) (organizations and addresses)

11. INVENTIONS (see instructions)

☐ NO ☐ YES

☐ OR
☐

Previously reported
Not previously reported

TELEPHONE INFORMATION

12a. PRINCIPAL INVESTIGATOR

OR
PROGRAM DIRECTOR (Item 2a)

AREA
CODE

TELEPHONE NO.
AND EXTENSION

12b. NAME OF BUSINESS OFFICIAL
(Item 6)12c. NAME AND TITLE OF OFFICIAL
SIGNING FOR APPLICANT
ORGANIZATION (Item 15)

10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD

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

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. Willful provision of false information is a criminal offense (U.S. Code, Title 18, Section 1001).

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

DATE

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).

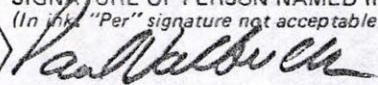
SIGNATURE OF PERSON NAMED IN 12c. (In ink.
"Per" signature not acceptable)

DATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICEAPPLICATION
FOR CONTINUATION GRANT

REVIEW GROUP	TYPE	ACTIVITY	GRANT NUMBER (Insert on all pages)
SSS 9	5	UOI	UOI CA34980 02
TOTAL PROJECT PERIOD			
From: 5-1-84		Through: 4-30-86	
REQUESTED BUDGET PERIOD			
From: 5-1-84		Through: 4-30-85	

1. TITLE STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME	
2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (name and address, street, city, state, zip code) VOLBERDING, PAUL A ZIEGLER JOHN SAN FRANCISCO GENERAL HOSP DIVISION OF ONCOLOGY WARD 86 995 POTRERO AVE. SAN FRANCISCO CA 94110	4. APPLICANT ORGANIZATION (name and address, street, city, state, zip code) UNIVERSITY OF CALIFORNIA, SAN FRANCISCO CANCER RESEARCH INSTITUTE M-1282 SAN FRANCISCO CA 94143
2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT MEDICAL SERVICE	5. ENTITY IDENTIFICATION NUMBER 1946036493A6
2c. MAJOR SUBDIVISION DEPARTMENT OF MEDICINE	6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION (415)666-2977 LORRAINE M. PETRAKIS CONSTRUCTS & GRANTS OFFICER OFFICE OF EXTRAMURAL SUPPORT UNIVERSITY OF CALIFORNIA SAN FRANCISCO CA 94143
3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR BIOMEDICAL RESEARCH SUPPORT GRANT (see instructions) School of Medicine	11. INVENTIONS (see instructions) ☒ NO ☐ YES { ☐ Previously reported OR ☐ Form HHS 596 enclosed ☐ Not previously reported
7. HUMAN SUBJECTS ☐ NO ☒ YES { ☐ Exemption # _____ OR ☐ Form HHS 596 enclosed	TELEPHONE INFORMATION
8. RECOMBINANT DNA ☒ NO ☐ YES	12a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Item 2a) PAUL VOLBERDING, M.D.
9. PERFORMANCE SITE(S) (organizations and addresses) University of California, S.F. Cancer Research Institute UCSF Dept. of Pediatrics, UCSF Division of Dermatology, UCSF San Francisco General Hospital Mt. Zion Hospital, San Francisco	AREA CODE 415 TELEPHONE NO. AND EXTENSION 666-4387
10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD 488,090	12b. NAME OF BUSINESS OFFICIAL (Item 6) LORRAINE PETRAKIS 415 666-2977
13. DO NOT USE THIS SPACE	12c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 15)

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. Willful provision of false information is a criminal offense. (U.S. Code, Title 18, Section 1001.)	SIGNATURE OF PERSON NAMED IN 2a (In ink. "Per" signature not acceptable) 	DATE 2/29/84
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)	DATE

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
1) CLINIC	CONANT, MARCUS	DIV. OF DERMATOLOGY UCSF
2) EPIDEMIOLOGY	MOSS, ANDREW	DEPT. OF EPIDEMIOLOGY "
3) IMMUNOLOGY	AMMAN, ARTHUR	DEPT. OF PEDIATRICS "
4) VIROLOGY I	LEVY, JAY	CANCER RESEARCH INST "
5) VIROLOGY II	DREW, LAWRENCE	MT ZION HOSPITAL/SFGH
6) THERAPY	VOLBERDING, PAUL	DIV OF ONCOLOGY/SFGH

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

For the second year of this grant we propose the following projects:

(1) continue epidemiologic surveillance studies of the sexual contacts of AIDS patients seen at the KS clinic, compare clinical features of KS in AIDS patients to the classical form, and provide tissue and serum specimens to the central tissue bank facility (MA Conant); (2) continue to collect incidence data for population-based analysis of morbidity and mortality, conduct pilot study of AIDS in intravenous drug-abusers, and contrive surveillance of non-Hodgkin's lymphoma in homosexual men (AR Moss); (3) immunologic and functional assays of T cell subsets and monocytes in pre-AIDS and AIDS patients to define immunopathogenesis, follow immune parameters in patients receiving interferon and IL2 therapy (AJ Amman); (4) continue studies of viral etiology of AIDS by inoculating AIDS tissues into Balb-C and CH3 mice and newborn hamsters, baboons and chimpanzees (JA Levy); (5) continue surveillance of CMV sero-negative homosexual men and conduct extensive immunologic studies when sero-conversion occurs, continue CMV analysis of homosexual men to determine strain variations and effects of multiple-strain infections (WL Drew); (6) continue to study natural history of KS and lymphadenopathy syndrome, initiate treatment protocols using ICRF-159, gamma-interferon, and interleukin-2, study natural history and treatment of non-Hodgkin's lymphoma in homosexual men (PA Volberding, JL Ziegler, DI Abrams).

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

REMOVE AND USE FOR DRAFT COPY

(1) SALARIES: LIST ALL SALARIED, NON-SALARIED UC PERSONNEL. PROJECT MERIT, PROMOTIONAL INCREASES IN COMPUTATION. USE TIME FOR STAFF EMPLOYEES ONLY — USE EFFORT FOR ACADEMICS.

Name and Title	Step	Time or Effort %	Based on Annual Rate	Actual Gross	Fringe Benefits	Total
(PI) CLINIC - CONANT, M.			42,199	42,199	12,220	
EPIDEMIOLOGY - MOSS, A.			24,678	24,678	7,157	
IMMUNOLOGY			54,109	54,109	15,685	
VIROLOGY I - LEVY, J.			39,671	39,671	8,686	
VIROLOGY II - DREW, L.			46,607	46,607	13,364	
THERAPY - VOLBERDING, P.			65,057	65,057	15,983	
SUBTOTALS: →				272,321	73,095	345,416

5,000

43,938

5.205

0

0

0

0

43,338

40,193

488,090

154.168

~~642,258~~

FACULTY EFFORT: LIST ALL ACTIVE OR PENDING GRANTS BY AGENCY, GRANT NUMBER OR TITLE AND PERCENT OF EFFORT DEVOTED TO EACH BY THE PRINCIPAL INVESTIGATOR (CONTINUE ON SEPARATE SHEET IF NECESSARY):

PENDING

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA 34980 A 02		
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
	Principal Investigator					
CLINIC	CONANT			42,199	12,220	
EPIDEMIOLOGY	MOSS			24,678	7,157	
IMMUNOLOGY	AMMANN			54,109	15,685	
VIROLOGY I	LEVY			39,671	8,686	
VIROLOGY II	DREW			46,607	13,364	
THERAPY	VOLBERDING			65,057	15,983	
SUBTOTALS				272,321	73,095	345,416
CONSULTANT COSTS (See instructions)						0
EQUIPMENT (Itemize)						
CLINIC	5,000					
EPIDEMIOLOGY	0					
IMMUNOLOGY	0					
VIROLOGY I	5,000					
VIROLOGY II	0					
THERAPY	0					10,000
SUPPLIES (Itemize by category)						
CLINIC	1,000	VIROLOGY II	4,596			
EPIDEM	0	THERAPY	1,284			
IMMUNOLOGY	3,008					
VIROLOGY I	34,050					43,938
TRAVEL	DOMESTIC CLN 1,000-IM 1,500-VRI 1,100-THRP 1,605					5,205
	FOREIGN					0
PATIENT CARE COSTS	INPATIENT					0
	OUTPATIENT					0
ALTERATIONS AND RENOVATIONS (Itemize by category)						0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						
VIROLOGY II						43,338
OTHER EXPENSES (Itemize by category)						
CLINIC	5,000	VRI	34,596			
EPI	0	VR II	383			
IMMUN	0	THRP	214			40,193
TOTAL DIRECT COST (Enter on Page 1, Item 10)						488,090

INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
	27.7%	5-1-84 to 6-30-84		
	31.87%	7-1-84 to 4-30-85		
	154,168	% TDC		

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 05-01-84	THROUGH 04-30-85	GRANT NUMBER UOI CA349080-02	
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)	
PERSONNEL (Applicant organization only) (See instructions)			TIME/EFFORT		
NAME	TITLE OF POSITION	%	Hours per Week	SALARY	FRINGE BENEFITS
CONANT, M	Principal Investigator	10		6,000	1,560
VOLBERDING, P	CO-INVESTIGATOR	10		5,000	1,300
GREENSPAN, J	CO-INVESTIGATOR	10		-	-
BAUMGARTNER, F	NURSE PRACTITIONER	100		23,939	7,182
TO BE HIRED	CLK/DATA ENTRY	50		7,260	2,178
SUBTOTALS				42,199	12,220
CONSULTANT COSTS (See instructions)					0
EQUIPMENT (Itemize)					
COMPUTER TERMINAL STAND/ALTERATIONS					
TISSUE HOLDERS LN2					
LN _a STORAGE					5,000
SUPPLIES (Itemize by category)					
LN2					
KNIVES (FOR CRYOSTAT, PIPETTES, SLIDES)					1,000
TRAVEL	DOMESTIC CONANT, M				1,000
	FOREIGN				
PATIENT CARE COSTS	INPATIENT				
	OUTPATIENT				
ALTERATIONS AND RENOVATIONS (Itemize by category)					0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)					0
OTHER EXPENSES (Itemize by category)					
MAILING XEROXING GRAPHIC SLIDES					
PRINTING PATHOLOGY PROCESSING					
PERIODICALS AND BOOKS					5,000
TOTAL DIRECT COST (Enter on Page 1, Item 10)					66,419
INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain		Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
19,146	27.7%	5-1-84 to 6-30-84			
	31.8%	7-1-84 to 4-30-85			

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA349080-02	
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)	
PERSONNEL (Applicant organization only) (See instructions)			TIME EFFORT		SALARY
				FRINGE BENEFITS	
NAME	TITLE OF POSITION	%	Hours per Week		
MOSS, A	Principal Investigator	25	-	-	29,343
PETRAKIS, N	PROFESSOR & CHR	5	-	-	
DRITZ, S.	DEPUTY CHIEF	10	-	-	
OSMOND, D	ASSOC SPECLST	30		7,809	
SWIG, L	STAFF RES ASSC	50		8,769	
BACHETTI, P	STATISTICIAN	25		6,168	
SUBTOTALS				22,746	6,597
CONSULTANT COSTS (See instructions)					0
EQUIPMENT (Itemize)					0
SUPPLIES (Itemize by category)					0
TRAVEL					0
PATIENT CARE COSTS					0
ALTERATIONS AND RENOVATIONS (Itemize by category)					0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)					0
OTHER EXPENSES (Itemize by category)					138
MAILING, XEROXING EXPENSES					
TOTAL DIRECT COST (Enter on Page 1, Item 10)					29,481
INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain		Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
9,191	27.7	5-1-84 to 6-30-84			
	31.87	7-1-84 to 4-30-85			

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 05-01-84	THROUGH 04-30-85	GRANT NUMBER UOI CA349080-02	
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A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
LEVY, J	Principal Investigator	10		-	-	
MORROW, J	RES IMMUN	40		8,611	-	
LANDES, J	SRA I	100		21,792	6,102	
SHIMOBUKARO, T	SRA I	25		4,874	1,354	
SZOENYI, M	LAB ASST	25		4,394	1,230	
SUBTOTALS				39,671	8,686	48,357
CONSULTANT COSTS (See instructions)						0
EQUIPMENT (Itemize)						
COULTER COUNTER \$5,000						
SUPPLIES (Itemize by category)						
TISSUE CULTURE MEDIA AND FETAL CALF SERUM PLASTIC PIPETTES, SLIDES, FILTERS, FREEZING VIALS MASKS, STERILE ROBES, GLOVES BIOCHEMICAL SUPPLIES						
						34,050
TRAVEL		DOMESTIC				1,100
		FOREIGN				0
PATIENT CARE COSTS		INPATIENT				0
		OUTPATIENT				0
ALTERATIONS AND RENOVATIONS (Itemize by category)						0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						0
OTHER EXPENSES (Itemize by category)						
CO2 & LN2 TANK ANIMAL MAINTENANCE COSTS: MICE & GUINEA PIGS; ISOLATION CAGES GOWNS, CAPS, MASKS, SHOE COVERS, SECY COSTS, PUB COSTS						
						36,741
TOTAL DIRECT COST (Enter on Page 1, Item 10)						125,248

INDIRECT COST (See instructions)	*If this is a special rate (e.g. off-site) explain 27.7% 5-1-84 to 6-30-84 31.8% 7-1-84 to 4-30-85	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
	37,487		

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 05-01-84	THROUGH 04-30-85	GRANT NUMBER UOI CA349080-02		
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
AMMANN, A	Principal Investigator	10				
STITES, D	CO-INVESTIGATOR	10				
CASAVANT, C	CO-INVESTIGATOR	10				
ARIAS, N	HOSP LAB TECH	100		32,206	9,114	
KALECEK, T	STAFF RES ASSC	80		17,522	4,556	
SUBTOTALS →				49,728	13,670	63,398
CONSULTANT COSTS (See instructions)						0
EQUIPMENT (Itemize)						0
SUPPLIES (Itemize by category)						0
PLASTIC CULTURE SUPPLIES						3,008
TRAVEL		DOMESTIC 3 TRIPS FOR INVESTIGATORS @ 500 each				1,500
		FOREIGN				
PATIENT CARE COSTS		INPATIENT				
		OUTPATIENT				
ALTERATIONS AND RENOVATIONS (Itemize by category)						0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						0
OTHER EXPENSES (Itemize by category)						1,030
TOTAL DIRECT COST (Enter on Page 1, Item 10)						68,936
INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain 27.7% 5-1-84 to 6-30-84 31.8% 7-1-84 to 4-30-85		Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:	
	21,491					

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 05-01-84	THROUGH 04-30-85	GRANT NUMBER UOI CA349080-02	
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A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
DREW, L	Principal Investigator	20				
MILLS, J	CO-INVESTIGATOR	20	8	15,458	4,019	
GOTTLIEB, A	NURSE PRACTITIONER	50	20	17,617	5,285	
TBH	RESEARCH TECH	50	20	13,532	4,060	
SUBTOTALS →				46,607	13,364	59,971
CONSULTANT COSTS (See instructions)						0
EQUIPMENT (Itemize)						0
SUPPLIES (Itemize by category)						770
PLASTIC & GLASSWARE						
CO2 & LIQUID N2						
TISSUE CULTURES						
MEDIA & SERA						
REAGENTS (ANTISERA, CHEMICALS, ETC.)						
TRAVEL		DOMESTIC				
		FOREIGN				
PATIENT CARE COSTS		INPATIENT				
		OUTPATIENT				
ALTERATIONS AND RENOVATIONS (Itemize by category)						
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						
MT ZION HOSP SALARIES		16,411	INDIRECT COSTS 45.3%		7,434	
FRINGE BENEFIT		3,692	(S & W)			
SUPPLIES		1,543				29,080
OTHER EXPENSES (Itemize by category)						0
TOTAL DIRECT COST (Enter on Page 1, Item 10)						89,821

INDIRECT COST (See instructions)	28,001	27.7%	5-1-84 to 6-30-84	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
		31.87%	7-1-84 to 4-30-85		

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

PAGE 3

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

UOI CA34980 02

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

SEE INDIVIDUAL SECTIONS FOR "NEXT BUDGET PERIOD" AND "NEXT BUDGET PERIOD" JUSTIFICATIONS.

DUE TO COST OF LIVING INCREASES IN SUPPLIES, TRAVEL, AND OTHER EXPENSES THESE SECTIONS WERE INCREASED BY 7%. THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO PERSONNEL SALARIES AND FRINGE BENEFITS WERE INCREASED ON AN AVERAGE OF 8% and 12%. THE RESULT OF THE INCREASE IS A TOTAL DIRECT COST OF \$488,090 FOR THE PROPOSED '84-'85 BUDGET PERIOD. THIS IS LESS THAN AN OVERALL 7% INCREASE OVER THE \$457,463 TOTAL DIRECT COSTS FOR THE '83-'84 BUDGET PERIOD.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA34980A 02
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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 (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	457,463	240,521	216,942	467,463	0
INDIRECT COSTS (as provided)	106,766	54,958	51,808	106,766	0
TOTALS →	564,229	295,479	268,750	564,229	0

B. THROUGH F.

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

SEE "CURRENT BUDGET PERIOD" PAGES IN EACH SECTION

SECTION IV
PROGRESS REPORT SUMMARY

GRANT NUMBER

UOI CA34980 02

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

PERIOD COVERED BY THIS REPORT

PAUL VOLBERDING JOHN ZIEGLER

FROM

THROUGH

NAME OF ORGANIZATION

5-1-83

4-30-84

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

TITLE (Repeat title shown in item 1 on first page)

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

(SEE INSTRUCTIONS)

SEE "PROGRESS REPORT SUMMARY" PAGE IN EACH SECTION.

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SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

1 U01 CA34980 - 01

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
Marcus A. Conant, M.D.	Assoc. Clin. Prof., UCSF	Dermatology, UCSF
Paul Volberding, M.D.	Asst. Prof. of Medicine, UCSF	School of Medicine, UCSF
John Greenspan, Ph.D.	Prof. of Oral Biology & Oral Pathology	Division of Oral Biology, UCSF
Jay H. Beckstead, M.D.	Asst. Prof. of Pathology	Pathology, UCSF

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

I. To recruit more participants in each of our studies to continue to achieve our research objectives.

A. Contact Study

1. Presentations to professional groups
2. Media releases
3. Networking to outpatient facilities in the community by the Nurse Coordinator of the K.S. Clinic.
4. Networking through community resources to contact more participants, i.e. San Francisco Aids Foundation, Shanti Project, and Aids Coordination Committee of San Francisco, by Nurse Coordinator.

B. Traditional Study

1. Presentations to professional groups
2. Media releases
3. Networking to the private physicians communities of the bay area. coordinated through K.S. Nursing Coordinator.

C. K.S. Patient Study

1. Presentations to professional groups
2. Networking to the outpatient areas in the community and also the private physicians communities to serve as a resource and a referral to patients. This will be done by Nursing Coordinator.

II. To expand on patient Specimen Banking:

A. Speciman Bank

1. In collaboration with Dr. J. Greenspan the Nursing Coordinator will continue to coordinate specimen collection for the specimen bank.
2. The Nurse Coordinator and Principal investigator will establish new areas of specimen collection in the community.
3. The Nurse Coordinator will coordinate these new activities.

VERTEBRATE ANIMALS INVOLVED: YES NO YES NO YES NO Identify by common name and underline primates.

SECTION III
CURRENT BUDGET PERIOD

FROM
May 1, 1983

THROUGH
April 30, 1984

GRANT NUMBER
1 U01 CA34980 - 02

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)	ACTUAL EXPENDITURES THRU <u>01/31/84</u>	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	68,451	37,878	30,573	68,451	-0-
INDIRECT COSTS (as provided)	<u>16,932</u> 16,932	<u>10,492</u> 10,492	<u>6,440</u> 6,440	<u>16,932</u> 16,932	0
TOTALS →	<u>85,383</u> 85,383	<u>48,370</u> 48,370	<u>37,013</u> 37,013	<u>85,383</u> 85,383	0

B. THROUGH F.

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

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER UOI CA34980 02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR MARCUS A. CONANT, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UCSF, DIVISION OF DERMATOLOGY		FROM 5-1-83	THROUGH 4-30-84
TITLE (Repeat title shown in item 1 on first page) PRINCIPAL INVESTIGATOR			
(SEE INSTRUCTIONS)			

The general scientific goals of the Kaposi's Sarcoma clinic have not changed. They include the following:

1. To coordinate the studies of the epidemiology, etiology, and treatment of Kaposi's Sarcoma and AIDS.
2. To collect data on AIDS patients, KS patients, persons exposed to AIDS, and persons exposed to KS to understand the natural history of the diseases.
3. To develop a specimen bank for tissue and serum collection and to distribute materials for research.

The following studies are being conducted:

1. Fifty patients have been followed from August 1981 to the present.
 - A. Deceased 13 patients
 - B. Receiving treatment or have received treatment 31 patients
 - C. Never received treatment 6 patients
2. Since November 1982 we have staged approximately 99 patients through the KS clinic and are following them through the natural course of their disease.
3. The KS Clinic has been the primary source for patient material collection in the Specimen Bank. The Nursing Coordinator has scheduled and done the biopsies and serum collection during patients visits to the KS Clinic. Coordinated specimen collection from various facilities in the community. San Francisco General and the Veterans Administration Hospital of San Francisco have been participating in the specimen collection.

To date the Specimen Bank contains 200 tissue specimens divided in the following categories:

- | | |
|-----------------------|--------------------------|
| A. Lymph nodes | D. KS tumor bowel tissue |
| B. KS tumor skin | E. KS tumor spleen |
| C. Normal skin tissue | F. KS tumor tonsil |

In the Sera Bank 300 sera specimens have been collected from patients with the following

- | | |
|----------------------------|--------------------|
| A. AIDS | D. Lymphadenopathy |
| B. KS | E. ITP |
| C. AIDS related conditions | |

These specimens have been allocated and stored from 2 to 15cc per tube in lcc vials..

PUBLICATIONS

MARCUS CONANT, M.D.

Modlin, R., Meyer, P., Hofman, F., Mehlmauer, M., Levy, N., Lukes, R., Parker, J., Ammann, A., Conant, M., Rea, T. and Taylor, C.: T-Lymphocyte Subsets in Lymph Nodes from Homosexual Men. JAMA, 1983 Vol. 250:1302-05

Meyer, P., Modlin R., Mehlmauer, M., Taylor, C., Lukes, R., Conant, M. and Rea, T.: Immunologic Assessment of Thymus, Bursa and Macrophage Antigens in Homosexual Patients with Reactive Lymph Nodes, Lymph Nodes Containing Kaposi's Sarcoma and Malignant Lymphomas Compared with Reactive Tonsils and Lymph Nodes from Non-Homosexual patients. Clin. Res., 1983, Vol: 31 (1):39 A.

Colombe, B., conant, M., Volberding, P., and Garovoy, M.: Susceptibility of Kaposi's Sarcoma and HLa BW44. Clin. Res., 1983, Vol. 31:340

Volberding, P., Gottlieb, M., Bothman, J., Rudnick, S., Conant, M., Derezin, M., Weinstein, W. and Groopman, J.: Therapy of Kaposi's Sarcoma (KS) in Acquired Immune Deficiency (AIDS) with a -2Recombinant Interferon Amer. Soc. Clin. Oncology Proc., 1983, Vol. 2:C-206

Modlin, R., Conant, M., Taylor, C., Meyer, R., Hofman, F., Lukes, R., Parker, J., Ammann, A. and Rea, T.: T-Lymphocyte Subsets in Skin, Blood and Lymph Nodes from Homosexual Men with Kaposi's Sarcoma. J. Invest. Derm., 1983, Vol 80 (4):332

Moss, A., Bacchetti, P., gorman, M., Dritz, S., Conant, M., Abrams, D., Volberding, P., and Ziegler, J.: AIDS in the "Gay areas of San Francisco. The Lancet, April 1983, Vol. 1(8330):923-24

Ziegler, J., Conant M., Lutzner M. Kaposi's Sarcoma In T. Fitzpatrick Ed., Dermatology in General Medicine, McGraw Hill, New York, 1984 (3rd Edition) in press

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
A. R. Moss, Ph.D.	Adjunct Assistant Professor	Epidemiology & International Health, UCSF
N. Petrakis, M.D.	Professor, Chairman of Dept.	Epidemiology & International Health, UCSF
S. Dritz, M.D.	Deputy Chief	Bureau of Communicable Disease Control, S.F.
D. Osmond, M.A.	Assoc. Specialist, Epidemiology	Epidemiology & International Health, UCSF
P. Bacchetti, M.S.	Statistician	Epidemiology & International Health, UCSF
L. Swig, B.A.	Staff Research Associate	Epidemiology & International Health, UCSF

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

1. In association with Selma Dritz, M.D., we will continue to collect and analyze AIDS incidence and mortality data for San Francisco. We will report incidence data at six-monthly intervals, as of July 1, 1984 and January 1, 1985. We will carry out a population-based analysis of mortality among San Francisco-resident AIDS cases in Fall 1984.
2. In association with Dr. Dritz, we will continue to find AIDS cases for case-control and other-case-based epidemiological studies, using the collaborative UCSF-City of San Francisco AIDS casefinding process. (1) A case-control study of AIDS in homosexual men has been funded by the State of California and will continue through November 1984. (2) Pilot studies of AIDS in intravenous drug users are in progress. (3) A prospective study on AIDS risk in sexual partners of documented AIDS cases will be initiated in 1984-85.
3. In collaboration with Drs. J. Ziegler and D. Austin, AIDS incidence in San Francisco will be compared with incidence of other tumors believed to be associated with the acquired immune deficiency syndrome (including non Hodgkin's lymphomas and squamous cell tumors of the mouth and tongue) as reported by the California Tumor Registry.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline priorities

SECTION III CURRENT BUDGET PERIOD	FROM 5/1/83	THROUGH 4/30/84	GRANT NUMBER CA 34980 02
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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)	ACTUAL EXPENDITURES THRU (insert date)	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	29,343	23,581	5,762	29,343	-
INDIRECT COSTS (as provided)	8,128	6,532	1,596	8,128	
TOTALS →	37,471	30,113	7,358	37,471	-

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	LESS THAN 25%	26-50%	51-75%	MORE THAN 75%
A. Moss,	Adjunct Assist, Professor	1	X			
N. Petrakis	Professor Chair. Dept.	1	X			
S. Dritz	Deputy Chief Communicable Disease Control		X			
D. Osmond	Associate Specialist	2		*		
L. Swig	Staff Research Assistant	2		*		
P. Bacchetti	Statistician	2	*			

F. Other Support

A. R. Moss, Ph.D.	NIOSH "Occupational Exposure in Adult Glioma Patients". \$95,997 State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$125,815
D. Osmond, M.A.	NIOSH "Occupational Exposure in Adult Glioma Patients" \$95,997 State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$125,815
L. Swig	City of San Francisco "Study of AIDS Partners and Relationships Between Lifestyle and Immune Status in Well Gay Men". \$78,936
P. Bacchetti, M.S.	NIOSH "Occupational Exposure in Adult Glioma Patients". \$95,997 State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$125,815

SECTION IV
PROGRESS REPORT SUMMARY

GRANT NUMBER
CA 34980 02

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

A. R. Moss, Ph.D.

PERIOD COVERED BY THIS REPORT

FROM

THROUGH

NAME OF ORGANIZATION

5/1/83

4/30/84

TITLE (Repeat title shown in item 1 on first page)

(SEE INSTRUCTIONS)

1. Introduction

Funding was received to assist Dr. Selma Dritz in the establishment of a system for analyzing AIDS surveillance data in San Francisco. No funds were received for specific projects based on the surveillance data. Partial support was received for a statistician, a field supervisor, and research associate.

2. Progress to Date

In association with Dr. Dritz, a computerized incidence file has been established for San Francisco-resident diagnosed AIDS cases. Using census based denominator data and a division of the city of San Francisco into demographically homogenous areas, a procedure has been developed to obtain incidence rates which can reasonably be assumed to estimate AIDS incidence in homosexual men. A preliminary report on this data was published in April 1983.¹

In the current project, a six-month schedule has been established for incidence reporting and a first report (as of July 1983) has been submitted for publication (Moss, Bacchetti, Osmond et al., attached). We propose to continue to examine AIDS incidence in detail on a six-month basis.

In association with Dr. Dritz and the AIDS clinic at San Francisco General Hospital, we have also established a mortality surveillance procedure for San Francisco-resident AIDS cases which allows us to obtain population-to-based mortality estimates. A first report (as if summer 1983) has been submitted for publication. (Moss, Volberding, McCallum et al., attached.) We propose to continue to report AIDS mortality on an annual basis.

A collaborative relationship with the California Tumor Registry has been established and in the coming year we plan to compare AIDS incidence with incidence rates for other tumors which may be associated with the syndrome on a census tract level. This study will be collaborative with Drs. Dritz, J. Ziegler and D. Austin.

3. Studies using the surveillance system for casefinding

The surveillance system established by us in collaboration with the San Francisco Department of Public Health serves as a casefinding mechanism for studies of the acquired immune deficiency syndrome. During the current project year, funding has been received for two studies based on this casefinding system. 1) A case-control study of 140 AIDS cases matched with clinic controls and randomly-selected neighborhood controls was funded by the State of California and is currently nearing completion. 2) A cross-sectional study of immune function in the controls for the case-control study was funded by the City of San Francisco and is currently in progress.

Although only a handful of AIDS cases in intravenous drug users has yet been reported in San Francisco, we expect more cases to be found in the coming year. We are currently conducting pilot studies for an AIDS case-control study in intravenous drug users. A formal study will be proposed in the coming year.

We are also conducting pilot studies of both male and female sexual partners of documented AIDS cases. In the coming year we expect to propose a formal study of this cohort.

1. Moss A.R., Bacchetti, P., Gorman, M., et al. AIDS in the "gay" areas of San Francisco
Lancet 1983; ii:923-4.

Moss AR, Bacchetti P, Osmond D et al. Incidence of the Acquired Immunodeficiency Syndrome in San Francisco 1980-1983. The Lancet (Submitted 2/84)

Moss AR, McCallum J, Volberding P, Bacchetti P, Dritz S., Mortality associated with the Acquired Immunodeficiency Syndrome. (In preparation)

Moss AR, Bacchetti P, Gorman M et al. AIDS in the "gay" areas of San Francisco. The Lancet 1983; 2:923-4

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
AMMANN AJ STITES D CASAVANT C	PRINCIPAL INVESTIGATOR CO-INVESTIGATOR CO-INVESTIGATOR	

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

Research will continue to analyze the specific immunologic abnormalities found in patients with AIDS and related disorders. Our current investigations suggest there is both a monocyte and T-cell defect present in the patients. The monocyte defect, if found to be an early abnormality may explain the inability of patients to respond to antigen with an appropriate antibody response. Defining the specific defect which is found in "pre AIDS" will have important implications regarding pathogenesis of the immunodeficiency. We continue to define T and B cell subset abnormalities in the groups of patients. The extent of these abnormalities and the specific patient populations in which these abnormalities are found are being utilized for correlation with epidemiologic and clinical data to improve diagnosis and therapeutic approaches. Detailed evaluation of the patients receiving immunotherapy is in progress. One hundred patient will be treated with 9 doses of recombinant DNA interleukin-2. Included in this study is an immunologic evaluation of patients before and during therapy as well as in vitro incubation studies to determine the correlation between in vitro response and subsequent in vivo response.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

REMOVE AND USE FOR DRAFT COPY

SECTION II (continued)
NEXT BUDGET PERIOD

ACCOUNT NUMBER

CA 34980A 02

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

PERSONNEL:

Increased technician time: The present single FTE is divided between one principal investigator and two co-investigators. In the nearly one year that the grant has been in effect, the investigators have required two FTE technicians. The additional technician has been temporarily funded from a one year state grant which will not be available after this year. The number of studies which we are committed to performing to fulfill the objectives of the grant will require the additional FTE. A single technician can perform 20 functional assays of T cell immunity per week and analyze the data. This number is required to perform the initial and follow up studies on 100 patients with AIDS who are going to receive IL2 treatment beginning in April of 1984 and continuing for one year. Without the added FTE the studies cannot be performed and the effects of IL2 on the immunologic status of the patient cannot be assessed. This is critical information which must be obtained to determine if a clinical effect of IL2 can be correlated with an immunologic effect. Simultaneous studies in AIDS and AIDS related syndrome must also be performed utilizing lymphocyte phenotyping and monoclonal antibody. Because two technicians are therefore required we are requesting that all funding be applied to technical salaries. Funding for additional supplies will be obtained from other sources.

EQUIPMENT:

\$12,000 lease of B.D. Research Analyzer is deleted due to coverage from other sources. These funds are rebudgeted among personnel and remaining categories individually justified.

SECTION III CURRENT BUDGET PERIOD	FROM	THROUGH	GRANT NUMBER
	3/1/84	4/30/85	CA 34980A 02

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 (insert date): 1/31/84 (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	68,798	38,843.31		29,954.69	-0-
INDIRECT COSTS (as provided)	15,733	9,434.44		6,298.56	-0-
TOTALS →	84,531	48,277.75		36,253.25	-0-

B. THROUGH F.

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

B. Name	Title	Category	less than 25%	26-50%	51-75%	More than 75%
Arthur J. Ammann	Professor	1	X			
Daniel Stites	Professor	1	X			
Conrad Casavant	Assoc. Clin Prof.	1	X			

C. Equipment:

1. Bechman Refrigerated Centrifuge \$4,362.52
* note BD Research Analyzer lease are covered from other funding sources
2. Ranna #8086 drives \$2,950

- D. 3 investigators will share travel money in the amount of \$1,000, used to partially defray the cost of attending research meetings for the presentation of research results.

E. None

F. OTHER SUPPORT

Arthur J. Ammann, M.D.
Northern California Sickle Cell Center, Grant # HL 20985, (100% Technician salary)
4/1/83 through 3/31/84 \$47,139

Arthur J. Ammann M.D.
State of California AIDS Research Grant, '(50% Technician)
\$25,000.

Daniel Stites
NICHD - 03939, Study of Fetal- Placental Maternal Interaction
\$100,000 7/1/83 through 6/30/84

Daniel Stites
NICHD-13543, Basic and Clinical studies of preterm parturition
\$45,753 4/1/83 through 3/31/84

Daniel Stites
State of California AIDS Research Grant
\$115,000 7/1/83 through 6/30/84

the amount of Immunoglobulin detected. Elution studies have indicated that these Immunoglobulins are not intrinsic but are fixed to the surface of the T lymphocytes. Whether these represent immune complexes, cytophilic antibodies or anti-lymphocyte antibodies will be further investigated.

Using simultaneous two-color fluorescence with phycoerythrin labeled and FITC labeled monoclonal antibodies, we have been able to detect large amounts of DR antigens on the surface of both helper and suppressor T-lymphocytes in these same patient groups. Again, there is a relative increase from health to full-blown AIDS in relation to these markers of activation. The significance of this finding remains unknown but will be further pursued by additional study.

We have studied a group of CMV negative individuals and found normal distributions of lymphocyte subsets. In a longitudinal study, some of these individuals have converted from sera positive to sera negative associated with profound changes in lymphocyte subsets. We are continuing to follow this interesting group of patients prospectively to see if these changes are progressive. It is clear that in normal healthy subjects, CMV infection results in similar changes which are transient.

A variety of support studies for the therapy section of the grant in following lymphocyte subsets in several trials of immuno-modulating agents are in progress.

Objectives For The Coming Year:

Research will continue to analyze the specific immunologic abnormalities found in patients with AIDS and related disorders. Our current investigations suggest there is both a monocyte and T-cell defect present in the patients. The monocyte defect, if found to be an early abnormality may explain the inability of patients to respond to antigen with an appropriate antibody response. Defining the specific defect which is found in "pre AIDS" will have important implications regarding pathogenesis of the immunodeficiency. We continue to define T and B cell subset abnormalities in the groups of patients. The extent of these abnormalities and the specific patient populations in which these abnormalities are found are being utilized for correlation with epidemiologic and clinical data to improve diagnosis and therapeutic approaches. Detailed evaluation of the patients receiving immunotherapy is in progress. One hundred patients will be treated with 9 doses of recombinant DNA Interleukin-2. Included in this study is an immunologic evaluation of patients before and during therapy as well as in vitro incubation studies to determine the correlation between in vitro response and subsequent in vivo response.

Research Involving Human Subjects:

Our laboratories utilize blood samples from patients and we have received human experimentation approval. The risks of obtaining blood samples are minimal. The potential benefit to the patient is great if improved immunologic diagnosis can be obtained.

SECTION IV PROGRESS REPORT SUMMARY		COUNT NUMBER UOI CA34980 02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR ARTHUR J. AMMANN		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UNIVERSITY OF CALIFORNIA, SAN FRANCISCO		FROM 5-1-83	THROUGH 4-30-84
TITLE (Repeat title shown in item 1 on first page) Studies of Acquired Immune Deficiency Syndrome			
(SEE INSTRUCTIONS)			

The scientific goals of the project have not been altered since the submission of the grant. The following is a brief summary of the studies which have been completed during the award year.

Categorization of the immunologic profile of patients with AIDS (Kaposi's sarcoma) and opportunistic infection (as well as AIDS related syndromes) has been completed and the work has been published. A distinctive profile can be demonstrated in the patient groups of healthy homosexual controls, patients with lymphadenopathy syndrome, opportunistic infection or Kaposi's sarcoma. The degree of immunologic abnormalities can be ranked and correlates well with prognosis and survival. Functional impairment of T-cell immunity occurs in the most severely affected patients and when less than 10% of normal, usually indicates an immunologic state which is incompatible with survival beyond 1 year. Our studies also indicate that there is an impaired antibody response following specific immunization in patients with severe impairment of T-cell immunity. Many of these patients have a paradoxical increase in immunoglobulin levels. The impaired antibody response was demonstrated when patients were immunized with pneumococcal polysaccharide and a protein antigen, keyhole limpet hemocyanin. These studies provide important information in relation to appropriate approaches to treatment when reconstituting deficient immunity in this population of patients.

Additional AIDS related syndromes have been investigated to determine whether immunologic abnormalities in these groups of patients are consistent with AIDS. Two groups were defined, patients with hemophilia receiving concentrate factor VIII therapy and pediatric patients with blood transfusion related AIDS or AIDS acquired by means of vertical transmission from an IV drug addict mother. An analysis of additional patients who received blood products from patients with AIDS clearly indicates a significant risk in these populations for acquiring AIDS. The epidemiologic, clinical and immunologic findings in these groups of patients have been described and published and will serve as a continuing basis for investigation.

We have also investigated the distribution of B and T lymphocytes in the lymph nodes of homosexual men with Kaposi's sarcoma. The information obtained from these studies was utilized to compare with results of peripheral blood analysis of similar populations of cells. These studies have provided a basis for determining whether or not peripheral blood studies accurately reflect the distribution of immunologically competent cells within the tissue of affected patients.

Flow cytometric analysis using monoclonal antibodies to leukocyte subsets has revealed striking changes in the distribution of cells among patients with AIDS, the lymphadenopathy syndrome and normal homosexual controls. Large amounts of surface immunoglobulin are present on both T helper and T suppressor cells in these various groups. There is a quantitative increase from healthy to lymphadenopathy to full-blown AIDS in

Bibliography

1. Ammann AJ, Cowan MJ, Wara DW, Weintrub P, Dritz S, Goldman H, Perkins HA. Acquired Immunodeficiency in an infant: Possible transmission by means of blood products. Lancet 1:956-958, 1983.
2. Ammann AJ, Abrams D, Conant M, Chudwin D, Cowan MJ, Volberding P, Lewis B, Casavant C. Acquired immune dysfunction in homosexual men: Immunologic Profiles. Clin. Immunol. Immunopath. 27:315-325, 1983.
3. Conte JE, Hadley WK, Sande M, Ammann AJ. Infection control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). New Eng. J. Med. 309:740-744, 1983.
4. Modlin RL, Meyer PR, Hofman FM, Mehlmauer M, Levy NB, Lukes RJ, Parker JW, Ammann AJ, Conant MA, Rhea TH, Taylor CR. T lymphocyte subsets in lymph nodes from homosexual men. JAMA 250:1302-1305, 1983.
5. Weintrub PS, Koerper MA, Addiego JE, Drew LW, Lenette ET, Miner R, Cowan MJ, Ammann AJ. Immunologic abnormalities in patients with hemophilia A. J. Pediatr. 103:692-695, 1983.
6. Modlin RL, Meyer PR, Ammann AJ, Rea TH, Hofman FM, Vaccaro SA, Conant MA, Taylor CR. Altered distribution of B and T lymphocytes in lymph nodes from homosexual men with Kaposi's sarcoma. Lancet 2:768-771, 1983.
7. Jaffe HS, Ammann AJ, Abrams DI, Lewis B, Golden JA. Complications of co-trimoxazole in treatment of AIDS associated *Pneumocystis carinii* pneumonia in homosexual men. Lancet 2:1109-1111, 1983.
8. Abrams DI, Lewis BJ, Beckstead JH, Casavant H, Drew WL. Persistent diffuse lymphadenopathy in homosexual men: Endpoint or Prodrome? Ann. Int. Med. (In press).
9. Drew WL, Mills J, Dylewski J, Casavant H, Ammann A, Brodie H, Merigan T. CMV Infection: Is the cause of abnormal T-lymphocyte subset ratios in homosexual men. (Submitted for publication).

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
Jay A. Levy	Principal Investigator	Department of Medicine Cancer Research Institute
John Morrow	Research Immunologist	Cancer Research Institute

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

The specific objective of this laboratory is to identify the infectious agent responsible for AIDS. Over the next year, we shall continue our efforts to isolate this agent using tissue culture and animal experimentation. For tissue culture studies, we shall employ a selected number of different animal cell lines which are susceptible to a variety of known viruses. These cells will be cocultivated with white cells and sperm from individuals with AIDS. In addition, the white cells of patients with AIDS will be cultured in the presence of IL2 to establish T cell lines, with B cell growth factor (when available) to cultivate B cells, and in human sera, to cultivate macrophages. The presence of an infectious agent in these cells will be assessed. In particular, over the next year we shall concentrate on the presence of retroviruses in the T cells of AIDS patients and the possibility of a new agent in cultured monocytes. Assays for HTLV and LAV-1 will be conducted.

For animal studies, mice and hamsters appear to be the most sensitive rodents to infections which may result from immune deficiency induced by the AIDS agent. We shall thus inoculate these animals with purified white cells from patients with AIDS, as well as the pellets of centrifuged serum samples. The animals will be followed for changes in immunologic parameters as well as for differences in their cell numbers as measured by immunofluorescence (FACS) using helper and suppressor T cell antisera. The end point will be the development of immunologic changes and opportunistic infections in these animals.

In all these studies, sera from patients with AIDS, a collection of sera from close intimate contacts of AIDS patients over at least six months, and normal healthy gay individuals will be used in an attempt to identify the agent responsible for the disease. The tests conducted will include immunofluorescence testing, hemagglutination, hemadsorption, reverse transcriptase assays and interferon assays, as well as electron microscopy.

Finally, we shall continue to establish and characterize cell lines derived from Kaposi's sarcomas. We ultimately want to develop a tumorigenic line that can be studied for its transformation properties and presence of oncogenic viruses.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☒ YES If "YES," identify by common names and underline primates.

Mice

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

Equipment

We have requested \$5,000. to buy a Coulter Counter to be placed in our P-2 facility. At this time, we must take the white cells, after they are separated through Ficoll-Hypaque gradients and count them in a Coulter Counter in a lab situated at a distance from the P-2 facility. This procedure has alarmed some individuals in the other laboratory and also could present problems in the bio-safety requirements for separation of equipment used in AIDS research. We, thus, hope that funding for this important piece of equipment will be approved.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-83	THROUGH 4-30-84	GRANT NUMBER UI CA 34980A 02
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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)	ACTUAL EXPENDITURES THRU (insert date):	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE * (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	122,968	53,656	69,312	122,968	0
INDIRECT COSTS (as provided)	30,600	11,674	18,926	30,600	0
TOTALS →	153,568	65,330	88,238	153,568	0

B. THROUGH F.

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

PROFESSIONAL PERSONNEL

NAME	TITLE	CATEGORY	25%	26-50%	51-75%	MORE THAN 75%
J Levy	Assc. Prof	1	X			
J Morrow	"in training"	3		*		
J Landes	SRA I	2				*
T Shimobukaro	SRA I	2	*			
MSzoenyi	Lab Asst	2	*			

EQUIPMENT

Lease of Becton-Dickenson Research FACS Analyzer

TRAVEL

Domestic travel to the East coast for an AIDS Conference.

OTHER SUPPORT

J. Levy, M.D. State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$81,000

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER CA34980 02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Jay A. Levy, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION		FROM	THROUGH

TITLE (Repeat title shown in item 1 on first page)

Isolation of Agent Responsible for AIDS

(SEE INSTRUCTIONS)

1. Inoculation of concentrated white cells and sera from patients with AIDS into newborn animals from four different strains of mice, and from guinea pigs, hamsters, and rats. Over 1,000 animals have been inoculated and maintained for up to 1 year. Control animals have received white cells from healthy donors. Results show a 15% incidence of opportunistic infections in BALB/c mice and not in ICR, C37 black, or C3H mice. Control animals had less than 1% infection rate. Hamsters had a somewhat increased death rate compared to controls. Guinea pigs and rats showed no infection or mortality after 1 year.

2. Histologic examination of blood smears from the animals has indicated a reduction in lymphocytes in some of the mice and hamsters inoculated with AIDS material, but not in rat or guinea pigs. Thus, combined with the above mentioned results, we believe that mice may be a potential animal model for the study of AIDS.

3. In collaborative studies with Dr. Sy Kalter, Southwest Texas Foundation, we have inoculated AIDS blood into 4 baboons, one of which was a newborn. The first three animals inoculated all showed initially a lymphocytosis, with many atypical lymphocytes. In two animals, this picture has been maintained. Their blood contains no antibodies to CMV, EBV, or hepatitis B. Blood from one of the infected animals was inoculated into a newborn baboon, and the same pattern of lymphocytosis has been maintained in this animal after 9 months.

4. We have inoculated purified white cells from AIDS patients onto a variety of heterologous cell lines, including mink, dog, cat, mongoose, gazelle, chicken, human, chimp, rhesus monkey. They have also been cocultivated with the CEM and MOLT T cell lines and the U937 human macrophage cell line. In a limited number of studies conducted thus far, we can find no evidence of an infectious agent by CPE, hemagglutination or hemadsorption tests. Immunoflourescent studies using sera from a patient with AIDS has not indicated any presence of an agent in these cell lines, but these studies are only preliminary.

5. We have cocultivated AIDS white cells with the established T cell lines and attempted to induce interferon production in these cells. Thus far, no interferon has been noted in these cells after a short cocultivation period.

6. We have cultured over 50 T cell lines from patients with AIDS as well as controls and healthy gay donors. These cells have been studied by FACS for antigen markers after long term growth in culture. We have achieved 100% success in growing the cell lines in the presence of IL2. In those studied by FACS, we find that the helper cells are initially increased in number, but these then decrease after about 3 weeks. Suppressor T cells can be maintained in culture for several months. Macrophages and NK cells disappear after one week. We have maintained AIDS T cell lines in the presence of IL2 for over 90 days with good viability. As noted above, there is then a preponderance of suppressor T cells in culture.

7. In one lymphocyte culture, we have evidence that B cells remain and are making antibodies to T cells. By double labelling the presence of T cells carrying immunoglobulins on their surface have been noted even after three months in culture.

8. In about 5 out of 50 cultures we have detected the presence of HTLV by reverse transcriptase and immunofluorescent tests. Antibodies to HTLV have only been found in about 2 out of 20 AIDS patient's serum examined. We have confirmed the ability of HTLV to induce syncytial formation in XC and mink lung cells. We are perfecting this assay to use as one of the tests for HTLV. We have also noted that HTLV does not hemagglutinate goose, 1 day chick, adult chick, guinea pig, rat, rhesus monkey, human O, or sheep erythrocytes.

9. In some cultures, high reverse transcriptase activity has been noted without evidence of infection with HTLV. We are presently investigating whether LAV-1 (isolated first by Barre, et al.) is responsible for this RT activity.

10. We have noted that macrophages from AIDS patients adhere less readily to the cell culture as compared to controls. This may indicate either a difference in population of macrophages or an abnormality in their adherence potential.

11. We have noted after long term culture, the presence of dendritic -like cells growing in cultures of both AIDS patients and normal controls suggesting that IL2 enhances the growth of these cell populations. They become evident after long term culture.

12. We have established over 35 cell lines from Kaposi's sarcomas (KS) removed from patients with AIDS. These cells have been grown by selected techniques on plastic, and then analyzed for endothelial cell characteristics. They have been studied for prostaglandin and prostacycline production (with Dr. M. Goldyne). Over 80% of them produce Factor VIII and have some properties suggesting malignant potential. Moreover, our Kaposi's cell lines have been examined by various histochemical tests by Dr.

Jay Beckstead. These results have indicated that several of them have enzyme markers typical of endothelial cells. Nevertheless, none of these cell lines produced tumors in nude mice, nor have grown in methylcellulose. We have also attempted to grow the cell lines in nude mice in the presence of an angiogenesis-producing tumor (choriocarcinoma). These results, however, have also been unsuccessful. Nevertheless, we believe KS is a hormone-dependent tumor, and thus, the cells may only be tumorigenic when the proper growth factors are present in the host.

13. We have analyzed our Kaposi's sarcoma cell lines in collaboration with Drs. Nelson and MacDougall in Oregon, as well as individuals at UCSF (Dr. A. Geballe), for the presence of CMV, EBV and hepatitis B. In a limited number of studies, none of these agents have been definitively found in the cell lines, nor in fresh tumor tissue removed from the patients. Previous work indicated the presence of CMV, but when Dr. Nelson purified his probes further, and normal human sequences were eliminated, the positive results could not be confirmed. These studies continue to be conducted.

14. We have begun a collaborative work with Professor Keonig in the Dominican Republic as well as colleagues in Haiti examining blood from Haitian immigrants and patients for the presence of antibodies to HTLV, CMV, hepatitis B and EBV. These studies have indicated that Haitian coming from the provinces do not have the same high titer of antibodies to these agents as do those in the cities. These results suggest that AIDS was probably introduced into Haiti and did not result from the voodoo practices, come from animals, or from the population living in the provinces.

PUBLICATIONS

J LEVY

Marx, PA, Maul, DH, Osborn, KG, Lerche, NW, Moody, P, Lowenstine, LJ, Henrickson, RV, Arthur, LO, Gravel, M, London WT, Sever JL, Levy JA, Munn RJ, and Gardner MB. Simian AIDS: Isolation of a Type D Retrovirus and Disease Transmission. Science. In press.

Levy JA, Ziegler JL, Acquired immunodeficiency Syndrome in an opportunistic infection and Kaposi's Sarcoma results from secondary immune stimulation. Lancet 1983;2: 78-81

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

1 U01 CA34980-02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
W. Lawrence Drew, M.D. Ph.D.	Associate Clinical Prof.	Medicine, Clinical Pathology & Laboratory Medicine, U.C.S.F.
John Mills, M.D.	Associate Professor	Medicine, U.C.S.F.
Alan Gottlieb, R.N.	Nurse Practitioner, II	Medicine, U.C.S.F.
Richard Miner, B.A.	Research Tech, IV	Pathology Research Mt. Zion Hospital
To Be Hired	Research Tech.	Medicine, U.C.S.F.

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

1. Enroll 60 additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
2. Collect sequential isolates of CMV from individual, healthy homosexual men and analyse them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

VERTEBRATE ANIMALS INVOLVED ☒ NO ☐ YES If "YES" specify, by common names and underline primates.

[illegible]

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

SALARY JUSTIFICATION

Increases in salary for the following U.C.S.F. personnel: John Mills, M.D. Alan Gottlieb, and To Be Hired Tech. Institutional increases of 11% for the above U.C.S.F. personnel constitute budgeted salary increases.

Two 50% Research Techs. will replace previously budgeted 100% SRA II, 5, because the work conducted in this study is divided between two locations. Typing of viruses is performed at Mount Zion Hospital and Medical Center as are all serologic studies, requiring one 50% tech (Research tech, IV). Viral cultures are performed at San Francisco General Hospital requiring another 50% tech (To Be Hired).

Increase of salary for 50% Research tech, IV at Mount Zion Hospital is due to higher skill and salary step level.

TRAVEL JUSTIFICATION

Invitation to present lecture on the relationship of cytomegalovirus and AIDS and to discuss the results of CMV researchers from Japan and European countries at the International Congress of Virology in Japan.

Other Category for next budget period has been reduced to appropriately cover Travel costs.

VIROLOGY II

SECTION III CURRENT BUDGET PERIOD	FROM 5/01/83	THROUGH 4/30/84	GRANT NUMBER 1 U01 CA 34980-01
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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 (insert date) 12/31/83 (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	89,403.	34,424.	54,979.	89,403.	0.
INDIRECT COSTS (as provided)	6,499.	2,882.	3,617.	6,499.	0.
TOTALS —————→	95,902.	37,306.	58,596.	95,902.	0.

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%	26-50%	51-75%	more than 75%
W. L. Drew	P.I.	1	X			
J. Mills	Co-Invest.	1	*			
A. Gottlieb	Nurse Pract.	2		*		
R. Miner	Tech IV	2		*		
M. Blair	Tech III	2				X
E. Mocarski	Consultant	1	X			
T. Merigan	Consultant	1	X			
To Be Hired	Tech	2		*		
K. Taylor	Secretary	2				X

C. EQUIPMENT N/A

D. TRAVEL

Invitation to present a lecture on the Relationship of Cytomegalovirus and AIDS and opportunity to discuss the results of CMV researchers from Japan and European countries at the International Congress of Virology to be held in Japan.

E. EXPLANATION OF COLUMN 5. N/A

F. OTHER SUPPORT See attached page.

F. OTHER SUPPORT FOR DR. W. LAWRENCE DREW:

- A. State of California State AIDS Center Grant Series -
University of California

Project Title: The Role of Cytomegalovirus in the
Etiology of AIDS.

Grant Period: 7/01/83 to 10/30/84

Annual Amount: \$135,000.

- B. Hoffmann LaRoche, Inc. Pending - Protocol 2563B

Project Title: Evaluation of the Tolerance and
Efficacy of Escalating Doses of
Recombinant Leukocyte A Interferon
(Ro 22-8181/001) Therapy of Decreasing
Titer of Virus in the Urine,
Blood or Semen of Patients with
Disseminated Cytomegalovirus Infections.

Annual Amount: Up to \$40,000., dependant upon
patient enrollment.

- C. Hoffmann LaRoche, Inc. Pending - Protocol 2564B

Project Title: Safety & Efficacy of Recombinant
Leukocyte A Interferon (Ro 22-
8181/001) in Patients with Acquired
Immunodeficiency and viral Infections.

Annual Amount: Up to \$45,000., dependant upon
patient enrollment.

SECTION IV PROGRESS REPORT SUMMARY		CONT NUMBER 1 U01 CA34980-02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR W. Lawrence Drew, M.D., Ph.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION Mount Zion Hospital and Medical Center		FROM 5/01/83	THROUGH 1/31/84
TITLE (Repeat title shown in item 1 on first page) Studies of Acquired Immune Deficiency Syndrome			
(SEE INSTRUCTIONS)			

We have enrolled 40 CMV seronegative homosexual men in our prospective study. Ten have seroconverted and have lowered their H:S ratios from an average of 1.6 pre-infection to 0.6 post-infection. Three of the ten have been followed for more than or equal to 15 mos. and two continue to have H:S ratios less than 1.0. CMV infection was asymptomatic in all ten. To assess the possibility that homosexual men experience infection with more than one strain of CMV, we have analyzed, by restriction enzymes, multiple CMV isolates from four separate individuals with AIDS. In each patient at least two different strains were identified.

PUBLICATIONS

- Drew WL, Miner RC, Ziegler JL, Gullett JH, Abrams DI, Conant MA, Huang ES, Groundwater JR, Volberding P, Mintz L. Cytomegalovirus and Kaposi's Sarcoma in Young Homosexual Men. *Lancet* 1982, 2:125-127.
- Follansbee SE, Busch DF, Wofsy CB, Coleman DL, Gullet J, Aurigemma GP, Ross T, Hadley WK, Drew WL. An Outbreak of Pneumocystis carinii Pneumonia in Homosexual Men. *Ann Int Med* 1982, 96:705-713.
- Ziegler JL, Drew WL, Miner RC, Mintz L, Rosenbaum E, Gershow J, Lennette ET, Greenspan J, Shillito E, Beckstead J, Cassavant C, Yamamoto K. Outbreak of Burkitt's-like Lymphoma in Homosexual Men. *Lancet* 1982, 2:631-633.
- Black SB, Raas M, Mintz L, Shinefield JR, Drew WL. Indirect Hemagglutination Inhibition: A Direct Method for Detecting Cytomegalovirus Antigen. *J Clin Lab Med* 1983, 101:450-452.
- Drew WL, Mintz L. Cytomegaloviral Infection in Healthy and Immune Deficient Homosexual Men, in Ma P and Armstrong D (eds): The Acquired Immune Deficiency Syndrome and Infections of Homosexual Men. Yorke Medical Books, New York, New York, April 1983, 117-123.
- Mintz L, Drew WL, Sexually Transmitted Viral Infections in Homosexual Men, in de la Maza (ed): Med Clin North Am; Medical Virology. W. B. Saunders Company, Philadelphia, Pennsylvania, September 1983, 67/5:1093-1104.
- Mintz L, Drew WL, Miner RC, Braff EH. Cytomegalovirus infections in homosexual men: an epidemiological study. *Ann Intern Med* 1983, 99:326-329.
- Drew WL. Sexual Transmission of CMV and Its Relationship to Kaposi's Sarcoma in Homosexual Men, in Plotkin S (ed): Pathogenesis and Prevention of Human Cytomegalovirus Infection. In Press.
- Abrams DI, Lewis B, Beckstead J, Cassavant C, Drew WL. Persistent Diffuse Lymphadenopathy in Homosexual Men: Endpoint or Prodrome? Accepted for publication in the *Ann Int Med*.
- Drew WL, Mills J, Dylewski J, C Cassavant, A Ammann, H Brodie, T Merigan. Is CMV Infection the Cause of Abnormal T Lymphocyte Subset Ratios in Homosexual Men? Submitted for publication.
- Katznelson S, Drew WL, Mintz L. Efficacy of the Condom as a Barrier to the Transmission of Cytomegalovirus. Submitted for Publication.

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
VOLBERDING PA	PRINCIPAL INVESTIGATOR	DEPT OF MEDICINE/SFGH
ZIEGLER J	CO-PRINCIPAL INVESTIGATOR	DEPT OF MEDICINE/CRI
ABRAMS, DI	CO-INVESTIGATOR	DEPT OF MEDICINE/SFGH
LEWIS, BJ	CO-INVESTIGATOR	DEPT OF MEDICINE/CRI

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

In the second year of the NIH Grant we will continue to observe and record the natural history of patients with lymphadenopathy syndrome as well as AIDS associated Kaposi's sarcoma. We also will continue to collect material for banking for collaborative research into the pathogenesis and etiology of this syndrome. The specific objectives for each main patient group covered in this grant will include therapy of patients with diffuse lymphadenopathy with recominant alpha interferon and therapy of Kaposi's sarcoma with recominant gamma interferon and interleukin-2.. Future chemotherapy trials after the conclusion of enrollment in INCRF-159 protocol serial immunologic monitoring.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UL CA 34980A	
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)	
PERSONNEL (Applicant organization only) (See instructions)			TIME/EFFORT		TOTALS
NAME	TITLE OF POSITION	%	Hours per Week	SALARY	
P. VOLBERDING	Principal Investigator	20		12,360	2,802
D. ABRAMS	CO-INVESTIGATOR	50		27,143	6,152
J. ZEIGLER	CO-INVESTIGATOR	20		-	-
B. LEWIS	CO-INVESTIGATOR	20		-	-
G. GEE	ADM. NURSE II	50		16,998	4,676
P. ROY	PR CLK	50		8,556	2,353
SUBTOTALS				65,057	15,983
CONSULTANT COSTS (See instructions)					0
EQUIPMENT (Itemize)					
SUPPLIES (Itemize by category)					
MAILING					
REPRO/PRINTING					
PHONE					
OFFICE SUPPLIES					
CLINIC SUPPLIES					1,284
TRAVEL					
DOMESTIC P. VOLBERDING, D. ABRAMS, G. GEE					1,605
FOREIGN					0
PATIENT CARE COSTS					
INPATIENT					0
OUTPATIENT					0
ALTERATIONS AND RENOVATIONS (Itemize by category)					0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)					0
OTHER EXPENSES (Itemize by category)					
PHOTO PROCESSING					
BOOKS, PERIODICALS					214
TOTAL DIRECT COST (Enter on Page 1, Item 10)					84,143
INDIRECT COST (See instructions)		26,232	% SOC*	% TOC*	☐ Not requested ☐ Under negotiation with

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

PERSONNEL

P VOLBERDING 24% increase in salary since 5-1-83 due to promotional and cost of living increases.
D ABRAMS 50% increase in salary since 5-1-83 due to promotional reclassification to faculty status and cost of living adjustment. Paid time reduced to 50% to accomodate the salary increases.
G GEE 16% increase in salary due to promotional reclassification and cost of living adjustment.
P ROY 18% increase in salary due to promotional and cost of living adjustment.

<u>FRINGE BENEFIT RATES</u>	<u>EFFECTIVE 1-1-84</u>	<u>EFFECTIVE 7-1-84</u>
ACADEMIC PERSONNEL	26%	22%
STAFF PERSONNEL (CAREER)	30%	27%

EQUIPMENT IBM PC COMPUTER AND MONITOR TO BE USED FOR PATIENT DATA COLLECTION. \$3,750
PATIENT DATA COLLECTION NEEDS HAVE INCREASED TO THREE TIMES OF ORIGINAL EXPECTATIONS.

SUPPLIES To accomodate cost of living increases these
TRAVEL sections have been adjusted upwards
OTHER EXPENSES to 7%.

CONTRACTUAL

Mt Zion Hospital
Lawrence Drew, M.D.
In an effort to cover overhead costs at
Mt Zion Hospital Dr. Drew's virology section
will be listed as a sub-contract under
Dr. Paul Volberding's therapy section.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-83	THROUGH 4-30-84	GRANT NUMBER CA34980 02
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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 (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	78,500	52,139	26,361	78,500	
INDIRECT COSTS (as provided)	21,135	13,944	7,191	21,135	
TOTALS →	99,635	66,083	33,552	99,635	

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	LESS 25%	26-50%	51-75%	MORE 75%
P VOLBERDING	ASST PROF MED	1	*			
D ABRAMS	CLN INSTR MED	1				*
J ZEIGLER	PROF MED	1	X			
B LEWIS	ASSC CLN PROF MEDICINE	1	X			
G GEE	ADM NURSE	2		*		
P ROY	PRIN CLK	2		*		

C. EQUIPMENT

Toshiba P1350 printer and components to be used with IBM PC Computer
\$1,798.87

D. TRAVEL

P Volberding has used the travel money in the amount of \$1,500 to partially defray the cost of attending research meetings for the presentation of research results.

E. EXPLANATION OF COLUMN 5

None

F. OTHER SUPPORT

Paul A. Volberding, M.D.
City and County of San Francisco
Dept. of Public Health
"Study of AIDS - Outpatient Clinic"
7-1-83 to 6-30-84 Grant period
\$390,541

SECTION IV

PROGRESS REPORT SUMMARY

GRANT NUMBER

UOI CA34980 02

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

PERIOD COVERED BY THIS REPORT

PAUL VOLBERDING, M.D.

FROM

THROUGH

NAME OF ORGANIZATION

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

5-1-83

4-30-84

TITLE (Repeat title shown in item 1 on first page)

PRINCIPAL INVESTIGATOR

(SEE INSTRUCTIONS)

SEE ATTACHED SHEET

THERAPY OF AIDS

OVERALL OBJECTIVES

The overall objectives of the therapy section of this grant have not changed. Because of work accomplished in the first grant year, the focus of Kaposi's sarcoma therapy protocols in this grant year will be on biologic response modifiers rather than cytotoxic chemotherapy. Also because of the number of cases of lymphadenopathy syndrome progressing to AIDS, therapy trials for this syndrome will also be conducted.

SUMMARY OF WORK ACCOMPLISHED

A number of original observations have been made from our center on the natural history of the lymphadenopathy syndrome and of the natural history and therapy of Kaposi's sarcoma in AIDS.

Lymphadenopathy Syndrome: Over two hundred patients with the syndrome of diffuse lymphadenopathy have been followed in the AIDS clinic at UCSF and San Francisco General Hospital. In contrast to our experience at the time of the original grant request, five of these patients have now progressed to AIDS as defined by the CDC. The careful clinical observations made on these patients prior to conversion should be important in helping predict the natural history of this extremely common syndrome. Also because of this conversion to AIDS, therapy trials of recombinant alpha two interferon as discussed in the original grant application are now being initiated. The serial evaluations of patients with lymphadenopathy syndrome has also provided access to specimens including serum and lymph node material. These are being collected on a regular basis from this cohort of patients and have proved valuable for collaborative research studies, many of which were summarized in virology immunology and epidemiology sections of this progress report.

Kaposi's Sarcoma: In the first year of this grant approximately 100 patients with Kaposi's sarcoma in AIDS have been evaluated in the Kaposi's sarcoma clinic at UCSF and the AIDS clinic at San Francisco General Hospital. A staging system devised in retrospect from analysis of these patients initial evaluation in clinical outcome is being developed. A preliminary analysis of 81 patients with Kaposi's sarcoma has revealed minimal impact on survival from the extent of Kaposi's sarcoma but a relatively greater impact from clinical features which may more directly reflect the status of immune competence. This has been reported in abstract form and a more complete analysis of 150 Kaposi's sarcoma patients is currently being conducted.

The natural history of Kaposi's sarcoma in AIDS has also been evaluated by studying those patients who have refused therapy of their tumor. A preliminary analysis of this experience reveals a broad spectrum of clinical aggressiveness of AIDS associated Kaposi's sarcoma. While essentially all patients have shown progression of their tumor, in several well-documented cases there was at most only minimal progression in twelve months of follow-up without therapy. This observation raises important implications for the design of prospective clinical trials which will be addressed in the next year of this grant.

Cytotoxic chemotherapy has been studied in the first year of the continuation of vinblastine therapy for all stages of Kaposi's sarcoma which demonstrates a 35% objective response in these patients. Also 25 patients have been entered onto a phase two trial of ICRF-159. Accrual to this study is being completed and early clinical results suggest that this drug is not more active than vinblastine in the treatment of Kaposi's sarcoma. If confirmed in a more complete analysis these results would suggest that the biology of AIDS associated Kaposi's sarcoma is unlike that of African Kaposi's sarcoma where ICRF-159 was extremely active.

In addition to trials of cytotoxic agents biologic response modifiers are also being tested in Kaposi's sarcoma associated with AIDS. Over 60 patients have been entered into trials of recombinant alpha interferon. As reported in several publications an objective response rate of approximately 40% was observed with this agent. Disappointingly, no immune restoration of clinical significance was observed in these trials. Future trials will continue with this and other biologic response modifiers including recombinant gamma-interferon and recombinant interleukin-2.

As was true of the patients with lymphadenopathy syndrome, patients with Kaposi's sarcoma have also been a valuable source of specimens for collaborative research studies with other components of this grant. Patients with Kaposi's sarcoma are followed serially and specimens including serum and tumor tissue are regularly preserved for future studies by the tissue and serum repository discussed in the first section of the grant.

OBJECTIVES FOR THE NEXT GRANT YEAR

In the second year of the NIH Grant we will continue to observe and record the natural history of patients with lymphadenopathy syndrome as well as AIDS associated Kaposi's sarcoma. We also will continue to collect material for banking for collaborative research into the pathogenesis and etiology of this syndrome. The specific objectives for each main patient group covered in this grant will include therapy of patients with diffuse lymphadenopathy.

PROGRESS REPORT
(cont'd)

denopathy with recombinant alpha interferon and therapy of Kaposi's sarcoma with recombinant gamma interferon and interleukin-2. Future chemotherapy trials after the conclusion of enrollment in ICRF-159 protocol will continue to investigate single agent chemotherapy with serial immunologic monitoring.

HUMAN SUBJECT CONSIDERATION

Lymphadenopathy Syndrome: A protocol for the use of recombinant alpha interferon for patients with lymphadenopathy syndrome has been approved by the Human Subject's Committee at UCSF and a copy of the protocol is attached.

Kaposi's Syndrome: Three protocols are currently being developed and will be initiated shortly for the treatment of AIDS associated Kaposi's sarcoma. While discussed in brief in the original competitive review these protocols are much more complete at this stage and are included in this section. These include a controlled study of no therapy compared with alpha interferon or alpha interferon plus vinblastine for patients with minimal stage of Kaposi's sarcoma, recombinant gamma-interferon and recombinant interleukin-2. In these protocols, particularly in the last two, substantial efforts will be made to monitor the immunologic effects of these agents as they may prove helpful in immunorestitution. A detailed analysis of the rationale for each agent is beyond the scope of this progress report but is included in each of the attached protocols.

Ziegler JL, Stites DP. Immunopathogenesis of acquired immunodeficiency syndrome: "host versus host" autoimmunity. JNCI (submitted 2/84)

Ziegler JL, Beckstead JA, Levine AM, et al. Non-Hodgkin's lymphoma in homosexual men with lymphadenopathy or AIDS. Clinical features in 90 patients from six insititutions. N England J Med (submitted, 3/84)

Diffuse, undifferentiated non-Hodgkin's lymphoma among homosexual males-United States. MMWR 1982;31:277-9

Ziegler JL, Drew WL, Miner RC et al. Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet 1982;2: 631-3

Ziegler JL, Bragg K, Abrams DI, et al. High-grade non-Hodgkin's lymphomas in patients with AIDS. Ann NY Acad Sci, in press

Ziegler JL, Templeton AC, Vogel CL. Kaposi's sarcoma: a comparison of classical endemic, and epidemic forms. Sem. Oncol (in press)

ABSTRACTS

1. Natural killer cell activity in homosexual men with Kaposi's sarcoma. Seaman, W., Ziegler, J., Volberding, P., Conant, M., Official Publication of the American Federation for Clinical Research, (in press) 1983.
2. Susceptibility to Kaposi sarcoma and HLA BW44. Colombe, B.W., Conant, M., Volberding, P., and Garovoy, M.R. American Federation for Clinical Research (in press) 1983.
3. Therapy of Kaposi's sarcoma (KS) in Acquired Immune Deficiency Syndrome with alpha-2 recombinant interferon. Volberding, P., Gottlieb, M., Rothman, J., Rudnick, S., Konnent, M., Derezin, M., Weinstein, W., Groopman, J. Proceedings: American Society of Oncology, Vol. 2, Pg. 53, 1983.
4. Single agent or combination chemotherapy of Kaposi's sarcoma in Acquired Immune Deficiency Syndrome. Lewis, B., Abrams, D. Ziegler, J., Conant, M., Gee, G., Silverberg, I., Volberding, P., Proceedings: American Society of Clinical Oncology, Vol. 2, pg. 59, 1983.
5. Immune thrombocytopenic purpura in homosexual men: Clinical manifestations and treatment results. Abrams, D., Voldberding, P., Linker, C., Kiproff, D., Moss, A., Sperling, J., and Embury, S. Blood, Vol. 62, No. 5, Supplement 1, pg. 108a, Nov. 1983.
6. Syngenic bone marrow transplantation for patients with AIDS and Kaposi's sarcoma. Mitsuyasu, R., Volberding, P., Groopman, J. Champlin, R. Blood, Vol. 62, No. 5, Supplement 1, pg. 226a.
7. Recombinant alpha-interferon therapy for Kaposi's sarcoma in Acquired Immune Deficiency Syndrome. Volberding, P., Moran, T., Rudinck, S., Rothman, J. Proceedings: Second European Conference in Clinical Oncology and Cancer Nursing, pg. 221, Nov. 1983.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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SANTA BARBARA • SANTA CRUZ

SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

SAN FRANCISCO, CALIFORNIA 94143

March 1, 1984

U.S. Department of Health and
Human Services
Public Health Service
Division of Research Grants
National Institutes of Health
5333 Westbard Ave.
Bethesda MD 20205

Dear Sirs:

Please note that this noncompeting continuation of Grant Number 5 UOI CA 34980-02 is one day late. Due to various changes with regards to the subcontract for Mt. Zion Hospital the continuation completion was not available for the due date of March 1, 1984.

Your consideration in the matter of making funding available by the scheduled May 1, 1984 start date would be appreciated. Every effort was made to meet the deadline.

Thank you for your attention to this matter.

Sincerely,

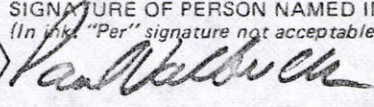
A handwritten signature in dark ink, reading "Paul Volberding", is written over the typed name.

Paul A. Volberding, M.D.
Assistant Professor of Medicine
PRINCIPAL INVESTIGATOR, Studies of AIDS, CA 34980-02

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICEAPPLICATION
FOR CONTINUATION GRANT

REVIEW GROUP	TYPE	ACTIVITY	GRANT NUMBER (Insert on all pages)
SSS 9	5	UOI	UOI CA34980 02
TOTAL PROJECT PERIOD			
From: 5-1-84		Through: 4-30-86	
REQUESTED BUDGET PERIOD			
From: 5-1-84		Through: 4-30-85	

1. TITLE STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME	
2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (name and address, street, city, state, zip code) VOLBERDING, PAUL A ZIEGLER JOHN SAN FRANCISCO GENERAL HOSP DIVISION OF ONCOLOGY WARD 86 995 POTRERO AVE. SAN FRANCISCO CA 94110	4. APPLICANT ORGANIZATION (name and address, street, city, state, zip code) UNIVERSITY OF CALIFORNIA, SAN FRANCISCO CANCER RESEARCH INSTITUTE M-1282 SAN FRANCISCO CA 94143
2b. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT MEDICAL SERVICE	5. ENTITY IDENTIFICATION NUMBER 1946036493A6
2c. MAJOR SUBDIVISION DEPARTMENT OF MEDICINE	6. TITLE AND ADDRESS OF OFFICIAL IN BUSINESS OFFICE OF APPLICANT ORGANIZATION (415) 666-2977 LORRAINE M. PETRAKIS CONSTRUCTS & GRANTS OFFICER OFFICE OF EXTRAMURAL SUPPORT UNIVERSITY OF CALIFORNIA SAN FRANCISCO CA 94143
3. ORGANIZATIONAL COMPONENT TO RECEIVE CREDIT FOR BIOMEDICAL RESEARCH SUPPORT GRANT (see instructions) School of Medicine	11. INVENTIONS (see instructions) ☒ NO ☐ YES { ☐ Previously reported OR ☐ Form HHS 596 enclosed
7. HUMAN SUBJECTS ☐ NO ☒ YES { ☐ Exemption # _____ OR ☐ Form HHS 596 enclosed	TELEPHONE INFORMATION
8. RECOMBINANT DNA ☒ NO ☐ YES	12a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Item 2a) PAUL VOLBERDING, M.D. 415 666-4387
9. PERFORMANCE SITE(S) (organizations and addresses) University of California, S.F. Cancer Research Institute UCSF Dept. of Pediatrics, UCSF Division of Dermatology, UCSF San Francisco General Hospital Mt. Zion Hospital, San Francisco	12b. NAME OF BUSINESS OFFICIAL (Item 6) LORRAINE PETRAKIS 415 666-2977
10. DIRECT COSTS REQUESTED FOR BUDGET PERIOD	12c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 15)
13. DO NOT USE THIS SPACE	

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. Willful provision of false information is a criminal offense. (U.S. Code, Title 18, Section 1001.)	SIGNATURE OF PERSON NAMED IN 2a (In ink. "Per" signature not acceptable) 	DATE 4/29/84
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)	DATE

SECTION I (continued)

SUMMARY OF PROPOSED WORK

GRANT NUMBER

UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
1) CLINIC	CONANT, MARCUS	DIV. OF DERMATOLOGY UCSF
2) EPIDEMIOLOGY	MOSS, ANDREW	DEPT. OF EPIDEMIOLOGY "
3) IMMUNOLOGY	AMMAN, ARTHUR	DEPT. OF PEDIATRICS "
4) VIROLOGY I	LEVY, JAY	CANCER RESEARCH INST "
5) VIROLOGY II	DREW, LAWRENCE	MT ZION HOSPITAL/SFGH
6) THERAPY	VOLBERDING, PAUL	DIV OF ONCOLOGY/SFGH

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. **DO NOT EXCEED THE SPACE PROVIDED.**

For the second year of this grant we propose the following projects:

(1) continue epidemiologic surveillance studies of the sexual contacts of AIDS patients seen at the KS clinic, compare clinical features of KS in AIDS patients to the classical form, and provide tissue and serum specimens to the central tissue bank facility (MA Conant); (2) continue to collect incidence data for population-based analysis of morbidity and mortality, conduct pilot study of AIDS in intravenous drug-abusers, and contrive surveillance of non-Hodgkin's lymphoma in homosexual men (AR Moss); (3) immunologic and functional assays of T cell subsets and monocytes in pre-AIDS and AIDS patients to define immunopathogenesis, follow immune parameters in patients receiving interferon and IL2 therapy (AJ Amman); (4) continue studies of viral etiology of AIDS by inoculating AIDS tissues into Balb-C and CH3 mice and newborn hamsters, baboons and chimpanzees (JA Levy); (5) continue surveillance of CMV sero-negative homosexual men and conduct extensive immunologic studies when sero-conversion occurs, continue CMV analysis of homosexual men to determine strain variations and effects of multiple-strain infections (WL Drew); (6) continue to study natural history of KS and lymphadenopathy syndrome, initiate treatment protocols using ICRF-159, gamma-interferon, and interleukin-2, study natural history and treatment of non-Hodgkin's lymphoma in homosexual men (PA Volberding, JL Ziegler, DI Abrams).

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

REMOVE AND USE FOR DRAFT COPY

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA 34980 A 02		
A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
	Principal Investigator					
CLINIC	CONANT			42,199	12,220	
EPIDEMIOLOGY	MOSS			24,678	7,157	
IMMUNOLOGY	AMMANN			54,109	15,685	
VIROLOGY I	LEVY			39,671	8,686	
VIROLOGY II	DREW			46,607	13,364	
THERAPY	VOLBERDING			65,057	15,983	
SUBTOTALS →				272,321	73,095	345,416
CONSULTANT COSTS (See instructions)						0
EQUIPMENT (Itemize)						
CLINIC	5,000					
EPIDEMIOLOGY	0					
IMMUNOLOGY	0					
VIROLOGY I	5,000					
VIROLOGY II	0					
THERAPY	0					10,000
SUPPLIES (Itemize by category)						
CLINIC	1,000	VIROLOGY II	4,596			
EPIDEM	0	THERAPY	1,284			
IMMUNOLOGY	3,008					
VIROLOGY I	34,050					43,938
TRAVEL	DOMESTIC CLN 1,000-IM 1,500-VRI 1,100-THRP 1,605					5,205
	FOREIGN					0
PATIENT CARE COSTS	INPATIENT					0
	OUTPATIENT					0
ALTERATIONS AND RENOVATIONS (Itemize by category)						0
CONSORTIUM/CONTRACTUAL COSTS (See instructions)						
VIROLOGY II						43,338
OTHER EXPENSES (Itemize by category)						
CLINIC	5,000	VRI	34,596			
EPI	0	VRII	383			
IMMUN	0	THRP	214			40,193
TOTAL DIRECT COST (Enter on Page 1, Item 10)						488,090

INDIRECT COST (See instructions)	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
	27.7%	5-1-84 to 6-30-84		
	31.87%	7-1-84 to 4-30-85		
	154,168	% TDC*		

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

UOI CA34980 02

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

SEE INDIVIDUAL SECTIONS FOR "NEXT BUDGET PERIOD" AND "NEXT BUDGET PERIOD" JUSTIFICATIONS.

DUE TO COST OF LIVING INCREASES IN SUPPLIES, TRAVEL, AND OTHER EXPENSES THESE SECTIONS WERE INCREASED BY 7%. THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO PERSONNEL SALARIES AND FRINGE BENEFITS WERE INCREASED ON AN AVERAGE OF 8% and 12%. THE RESULT OF THE INCREASE IS A TOTAL DIRECT COST OF \$488,090 FOR THE PROPOSED '84-'85 BUDGET PERIOD. THIS IS LESS THAN AN OVERALL 7% INCREASE OVER THE \$457,463 TOTAL DIRECT COSTS FOR THE '83-'84 BUDGET PERIOD.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-84	THROUGH 4-30-85	GRANT NUMBER UOI CA34980A 02
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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 (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	457,463	240,521	216,942	467,463	0
INDIRECT COSTS (as provided)	106,766	54,958	51,808	106,766	0
TOTALS →	564,229	295,479	268,750	564,229	0

B. THROUGH F.

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

SEE "CURRENT BUDGET PERIOD" PAGES IN EACH SECTION

SECTION IV
PROGRESS REPORT SUMMARY

GRANT NUMBER

UOI CA34980 02

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

PERIOD COVERED BY THIS REPORT

PAUL VOLBERDING JOHN ZIEGLER

FROM

THROUGH

NAME OF ORGANIZATION

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

5-1-83

4-30-84

TITLE (Repeat title shown in item 1 on first page)

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

(SEE INSTRUCTIONS)

SEE "PROGRESS REPORT SUMMARY" PAGE IN EACH SECTION.

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SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

1 U01 CA34980 - 01

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
Marcus A. Conant, M.D.	Assoc. Clin. Prof., UCSF	Dermatology, UCSF
Paul Volberding, M.D.	Asst. Prof. of Medicine, UCSF	School of Medicine, UCSF
John Greenspan, Ph.D	Prof. of Oral Biology & Oral Pathology	Division of Oral Biology, UCSF
Jay H. Beckstead, M.D.	Asst. Prof. of Pathology	Pathology, UCSF

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

I. To recruit more participants in each of our studies to continue to achieve our research objectives.

A. Contact Study

1. Presentations to professional groups
2. Media releases
3. Networking to outpatient facilities in the community by the Nurse Coordinator of the K.S. Clinic.
4. Networking through community resources to contact more participants, i.e. San Francisco Aids Foundation, Shanti Project, and Aids Coordination Committee of San Francisco, by Nurse Coordinator.

B. Traditional Study

1. Presentations to professional groups
2. Media releases
3. Networking to the private physicians communities of the bay area. coordinated through K.S. Nursing Coordinator.

C. K.S. Patient Study

1. Presentations to professional groups
2. Networking to the outpatient areas in the community and also the private physicians communities to serve as a resource and a referral to patients. This will be done by Nursing Coordinator.

II. To expand on patient Specimen Banking:

A. Speciman Bank

1. In collaboration with Dr. J. Greenspan the Nursing Coordinator will continue to coordinate specimen collection for the specimen bank.
2. The Nurse Coordinator and Principal investigator will establish new areas of specimen collection in the community.
3. The Nurse Coordinator will coordinate these new activities.

VERTEBRATE ANIMALS INVOLVED ☒ NO ☐ YES IF "YES" identify by common names and underline primates.

SECTION III
CURRENT BUDGET PERIOD

FROM
May 1, 1983

THROUGH
April 30, 1984

GRANT NUMBER
1 U01 CA34980 -02

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)	ACTUAL EXPENDITURES THRU <u>01/31/84</u> (date)	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	68,451	37,878	30,573	68,451	-0-
INDIRECT COSTS (as provided)	16,932	10,492	6,440	16,932	0
TOTALS →	85,383	48,370	37,013	85,383	0

B. THROUGH F.

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

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER UOI CA34980 02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR MARCUS A. CONANT, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION UCSF, DIVISION OF DERMATOLOGY		FROM 5-1-83	THROUGH 4-30-84
TITLE (Repeat title shown in item 1 on first page) PRINCIPAL INVESTIGATOR			
(SEE INSTRUCTIONS)			

The general scientific goals of the Kaposi's Sarcoma clinic have not changed. They include the following:

1. To coordinate the studies of the epidemiology, etiology, and treatment of Kaposi's Sarcoma and AIDS.
2. To collect data on AIDS patients, KS patients, persons exposed to AIDS, and persons exposed to KS to understand the natural history of the diseases.
3. To develop a specimen bank for tissue and serum collection and to distribute materials for research.

The following studies are being conducted:

1. Fifty patients have been followed from August 1981 to the present.
 - A. Deceased 13 patients
 - B. Receiving treatment or have received treatment 31 patients
 - C. Never received treatment 6 patients
2. Since November 1982 we have staged approximately 99 patients through the KS clinic and are following them through the natural course of their disease.
3. The KS Clinic has been the primary source for patient material collection in the Specimen Bank. The Nursing Coordinator has scheduled and done the biopsies and serum collection during patients visits to the KS Clinic. Coordinated specimen collection from various facilities in the community. San Francisco General and the Veterans Administration Hospital of San Francisco have been participating in the specimen collection.

To date the Specimen Bank contains 200 tissue specimens divided in the following categories:

- | | |
|-----------------------|--------------------------|
| A. Lymph nodes | D. KS tumor bowel tissue |
| B. KS tumor skin | E. KS tumor spleen |
| C. Normal skin tissue | F. KS tumor tonsil |

In the Sera Bank 300 sera specimens have been collected from patients with the following

- | | |
|----------------------------|--------------------|
| A. AIDS | D. Lymphadenopathy |
| B. KS | E. ITP |
| C. AIDS related conditions | |

These specimens have been allocated and stored from 2 to 15cc per tube in lcc vials..

PUBLICATIONS

MARCUS CONANT, M.D.

Modlin, R., Meyer, P., Hofman, F., Mehlmauer, M., Levy, N., Lukes, R., Parker, J., Ammann, A., Conant, M., Rea, T. and Taylor, C.: T-Lymphocyte Subsets in Lymph Nodes from Homosexual Men. JAMA, 1983 Vol. 250:1302-05

Meyer, P., Modlin R., Mehlmauer, M., Taylor, C., Lukes, R., Conant, M. and Rea, T.: Immunologic Assessment of Thymus, Bursa and Macrophage Antigens in Homosexual Patients with Reactive Lymph Nodes, Lymph Nodes Containing Kaposi's Sarcoma and Malignant Lymphomas Compared with Reactive Tonsils and Lymph Nodes from Non-Homosexual patients. Clin. Res., 1983, Vol: 31 (1):39 A.

Colombe, B., conant, M., Volberding, P., and Garovoy, M.: Susceptibility of Kaposi's Sarcoma and HLA BW44. Clin. Res., 1983, Vol. 31:340

Volberding, P., Gottlieb, M., Bothman, J., Rudnick, S., Conant, M., Derezin, M., Weinstein, W. and Groopman, J.: Therapy of Kaposi's Sarcoma (KS) in Acquired Immune Deficiency (AIDS) with a -2Recombinant Interferon Amer. Soc. Clin. Oncology Proc., 1983, Vol. 2:C-206

Modlin, R., Conant, M., Taylor, C., Meyer, R., Hofman, F., Lukes, R., Parker, J., Ammann, A. and Rea, T.: T-Lymphocyte Subsets in Skin, Blood and Lymph Nodes from Homosexual Men with Kaposi's Sarcoma. J. Invest. Derm., 1983, Vol 80 (4):332

Moss, A., Bacchetti, P., gorman, M., Dritz, S., Conant, M., Abrams, D., Volberding, P., and Ziegler, J.: AIDS in the "Gay areas of San Francisco. The Lancet, April 1983, Vol. 1(8330):923-24

Ziegler, J., Conant M., Lutzner M. Kaposi's Sarcoma In T. Fitzpatrick Ed., Dermatology in General Medicine, McGraw Hill, New York, 1984 (3rd Edition) in press

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
A. R. Moss, Ph.D.	Adjunct Assistant Professor	Epidemiology & International Health, UCSF
N. Petrakis, M.D.	Professor, Chairman of Dept.	Epidemiology & International Health, UCSF
S. Dritz, M.D.	Deputy Chief	Bureau of Communicable Disease Control, S.F.
D. Osmond, M.A.	Assoc. Specialist, Epidemiology	Epidemiology & International Health, UCSF
P. Bacchetti, M.S.	Statistician	Epidemiology & International Health, UCSF
L. Swig, B.A.	Staff Research Associate	Epidemiology & International Health, UCSF

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

1. In association with Selma Dritz, M.D., we will continue to collect and analyze AIDS incidence and mortality data for San Francisco. We will report incidence data at six-monthly intervals, as of July 1, 1984 and January 1, 1985. We will carry out a population-based analysis of mortality among San Francisco-resident AIDS cases in Fall 1984.
2. In association with Dr. Dritz, we will continue to find AIDS cases for case-control and other-case-based epidemiological studies, using the collaborative UCSF-City of San Francisco AIDS casefinding process. (1) A case-control study of AIDS in homosexual men has been funded by the State of California and will continue through November 1984. (2) Pilot studies of AIDS in intravenous drug users are in progress. (3) A prospective study on AIDS risk in sexual partners of documented AIDS cases will be initiated in 1984-85.
3. In collaboration with Drs. J. Ziegler and D. Austin, AIDS incidence in San Francisco will be compared with incidence of other tumors believed to be associated with the acquired immune deficiency syndrome (including non Hodgkin's lymphomas and squamous cell tumors of the mouth and tongue) as reported by the California Tumor Registry.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION III CURRENT BUDGET PERIOD	FROM 5/1/83	THROUGH 4/30/84	GRANT NUMBER CA 34980 02
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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)	ACTUAL EXPENDITURES THRU (insert date):	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	29,343	23,581	5,762	29,343	-
INDIRECT COSTS (as provided)	8,128	6,532	1,596	8,128	
TOTALS →	37,471	30,113	7,358	37,471	-

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	LESS THAN 25%	26-50%	51-75%	MORE THAN 75%
A. Moss,	Adjunct Assist, Professor	1	X			
N. Petrakis	Professor	1	X			
S. Dritz	Chair. Dept. Deputy Chief Communicable Disease Control		X			
D. Osmond	Associate Specialist	2		*		
L. Swig	Staff Research Assistant	2		*		
P. Bacchetti	Statistician	2	*			

F. Other Support

A. R. Moss, Ph.D.	NIOSH	"Occupational Exposure in Adult Glioma Patients".	\$95,997
	State of California	"A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases".	\$125,815
D. Osmond, M.A.	NIOSH	"Occupational Exposure in Adult Glioma Patients"	\$95,997
	State of California	"A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases".	\$125,815
L. Swig	City of San Francisco	"Study of AIDS Partners and Relationships Between Lifestyle and Immune Status in Well Gay Men".	\$78,936
P. Bacchetti, M.S.	NIOSH	"Occupational Exposure in Adult Glioma Patients".	\$95,997
	State of California	"A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases".	\$125,815

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER CA 34980 02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR A. R. Moss, Ph.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION		FROM 5/1/83	THROUGH 4/30/84
TITLE (Repeat title shown in item 1 on first page)			

(SEE INSTRUCTIONS)

1. Introduction

Funding was received to assist Dr. Selma Dritz in the establishment of a system for analyzing AIDS surveillance data in San Francisco. No funds were received for specific projects based on the surveillance data. Partial support was received for a statistician, a field supervisor, and research associate.

2. Progress to Date

In association with Dr. Dritz, a computerized incidence file has been established for San Francisco-resident diagnosed AIDS cases. Using census based denominator data and a division of the city of San Francisco into demographically homogenous areas, a procedure has been developed to obtain incidence rates which can reasonably be assumed to estimate AIDS incidence in homosexual men. A preliminary report on this data was published in April 1983.¹

In the current project, a six-month schedule has been established for incidence reporting and a first report (as of July 1983) has been submitted for publication (Moss, Bacchetti, Osmond et al., attached). We propose to continue to examine AIDS incidence in detail on a six-month basis.

In association with Dr. Dritz and the AIDS clinic at San Francisco General Hospital, we have also established a mortality surveillance procedure for San Francisco-resident AIDS cases which allows us to obtain population-to-based mortality estimates. A first report (as if summer 1983) has been submitted for publication. (Moss, Volberding, McCallum et al., attached.) We propose to continue to report AIDS mortality on an annual basis.

A collaborative relationship with the California Tumor Registry has been established and in the coming year we plan to compare AIDS incidence with incidence rates for other tumors which may be associated with the syndrome on a census tract level. This study will be collaborative with Drs. Dritz, J. Ziegler and D. Austin.

3. Studies using the surveillance system for casefinding

The surveillance system established by us in collaboration with the San Francisco Department of Public Health serves as a casefinding mechanism for studies of the acquired immune deficiency syndrome. During the current project year, funding has been received for two studies based on this casefinding system. 1) A case-control study of 140 AIDS cases matched with clinic controls and randomly-selected neighborhood controls was funded by the State of California and is currently nearing completion. 2) A cross-sectional study of immune function in the controls for the case-control study was funded by the City of San Francisco and is currently in progress.

Although only a handful of AIDS cases in intravenous drug users has yet been reported in San Francisco, we expect more cases to be found in the coming year. We are currently conducting pilot studies for an AIDS case-control study in intravenous drug users. A formal study will be proposed in the coming year.

We are also conducting pilot studies of both male and female sexual partners of documented AIDS cases. In the coming year we expect to propose a formal study of this cohort.

-
1. Moss A.R., Bacchetti, P., Gorman, M., et al. AIDS in the "gay" areas of San Francisco Lancet 1983; ii:923-4.

Moss AR, Bacchetti P, Osmond D et al. Incidence of the Acquired Immunodeficiency Syndrome in San Francisco 1980-1983. The Lancet (Submitted 2/84)

Moss AR, McCallum J, Volberding P, Bacchetti P, Dritz S., Mortality associated with the Acquired Immunodeficiency Syndrome. (In preparation)

Moss AR, Bacchetti P, Gorman M et al. AIDS in the "gay" areas of San Francisco. The Lancet 1983; 2:923-4

SUMMARY OF PROPOSED WORK

GRANT NUMBER

UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
AMMANN AJ STITES D CASAVANT C	PRINCIPAL INVESTIGATOR CO-INVESTIGATOR CO-INVESTIGATOR	

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

Research will continue to analyze the specific immunologic abnormalities found in patients with AIDS and related disorders. Our current investigations suggest there is both a monocyte and T-cell defect present in the patients. The monocyte defect, if found to be an early abnormality may explain the inability of patients to respond to antigen with an appropriate antibody response. Defining the specific defect which is found in "pre AIDS" will have important implications regarding pathogenesis of the immunodeficiency. We continue to define T and B cell subset abnormalities in the groups of patients. The extent of these abnormalities and the specific patient populations in which these abnormalities are found are being utilized for correlation with epidemiologic and clinical data to improve diagnosis and therapeutic approaches. Detailed evaluation of the patients receiving immunotherapy is in progress. One hundred patient will be treated with 9 doses of recombinant DNA interleukin-2. Included in this study is an immunologic evaluation of patients before and during therapy as well as in vitro incubation studies to determine the correlation between in vitro response and subsequent in vivo response.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

PAGE 38

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

CA 34980A 02

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

PERSONNEL:

Increased technician time: The present single FTE is divided between one principal investigator and two co-investigators. In the nearly one year that the grant has been in effect, the investigators have required two FTE technicians. The additional technician has been temporarily funded from a one year state grant which will not be available after this year. The number of studies which we are committed to performing to fulfill the objectives of the grant will require the additional FTE. A single technician can perform 20 functional assays of T cell immunity per week and analyze the data. This number is required to perform the initial and follow up studies on 100 patients with AIDS who are going to receive IL2 treatment beginning in April of 1984 and continuing for one year. Without the added FTE the studies cannot be performed and the effects of IL2 on the immunologic status of the patient cannot be assessed. This is critical information which must be obtained to determine if a clinical effect of IL2 can be correlated with an immunologic effect. Simultaneous studies in AIDS and AIDS related syndrome must also be performed utilizing lymphocyte phenotyping and monoclonal antibody. Because two technicians are therefore required we are requesting that all funding be applied to technical salaries. Funding for additional supplies will be obtained from other sources.

EQUIPMENT:

\$12,000 lease of B.D. Research Analyzer is deleted due to coverage from other sources. These funds are rebudgeted among personnel and remaining categories individually justified.

SECTION III CURRENT BUDGET PERIOD	FROM	THROUGH	GRANT NUMBER
	3/1/84	4/30/85	CA 34980A 02

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 (insert date): 1/31/84 (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	68,798	38,843.31		29,954.69	-0-
INDIRECT COSTS (as provided)	15,733	9,434.44		6,298.56	-0-
TOTALS →	84,531	48,277.75		36,253.25	-0-

B. THROUGH F.

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

B. Name	Title	Category	less than 25%	26-50%	51-75%	More than 75%
Arthur J. Ammann	Professor	1	X			
Daniel Stites	Professor	1	X			
Conrad Casavant	Assoc. Clin Prof.	1	X			

C. Equipment:

1. Bechman Refrigerated Centrifuge \$4,362.52
* note BD Research Analyzer lease are covered from other funding sources
2. Ranna #8086 drives \$2,950

- D. 3 investigators will share travel money in the amount of \$1,000, used to partially defray the cost of attending research meetings for the presentation of research results.

E. None

F. OTHER SUPPORT

Arthur J. Ammann, M.D.
Northern California Sickle Cell Center, Grant # HL 20985, (100% Technician salary)
4/1/83 through 3/31/84 \$47,139

Arthur J. Ammann M.D.
State of California AIDS Research Grant, '(50% Technician)
\$25,000,

Daniel Stites
NICHD - 03939, Study of Fetal- Placental Maternal Interaction
\$100,000 7/1/83 through 6/30/84

Daniel Stites
NICHD-13543, Basic and Clinical studies of preterm parturition
\$45,753 4/1/83 through 3/31/84

Daniel Stites
State of California AIDS Research Grant
\$115,000 7/1/83 through 6/30/84

the amount of immunoglobulin detected. Elution studies have indicated that these immunoglobulins are not intrinsic but are fixed to the surface of the T lymphocytes. Whether these represent immune complexes, cytophilic antibodies or anti-lymphocyte antibodies will be further investigated.

Using simultaneous two-color fluorescence with phycoerythrin labeled and FITC labeled monoclonal antibodies, we have been able to detect large amounts of DR antigens on the surface of both helper and suppressor T-lymphocytes in these same patient groups. Again, there is a relative increase from health to full-blown AIDS in relation to these markers of activation. The significance of this finding remains unknown but will be further pursued by additional study.

We have studied a group of CMV negative individuals and found normal distributions of lymphocyte subsets. In a longitudinal study, some of these individuals have converted from sera positive to sera negative associated with profound changes in lymphocyte subsets. We are continuing to follow this interesting group of patients prospectively to see if these changes are progressive. It is clear that in normal healthy subjects, CMV infection results in similar changes which are transient.

A variety of support studies for the therapy section of the grant in following lymphocyte subsets in several trials of immuno-modulating agents are in progress.

Objectives For The Coming Year:

Research will continue to analyze the specific immunologic abnormalities found in patients with AIDS and related disorders. Our current investigations suggest there is both a monocyte and T-cell defect present in the patients. The monocyte defect, if found to be an early abnormality may explain the inability of patients to respond to antigen with an appropriate antibody response. Defining the specific defect which is found in "pre AIDS" will have important implications regarding pathogenesis of the immunodeficiency. We continue to define T and B cell subset abnormalities in the groups of patients. The extent of these abnormalities and the specific patient populations in which these abnormalities are found are being utilized for correlation with epidemiologic and clinical data to improve diagnosis and therapeutic approaches. Detailed evaluation of the patients receiving immunotherapy is in progress. One hundred patients will be treated with 9 doses of recombinant DNA Interleukin-2. Included in this study is an immunologic evaluation of patients before and during therapy as well as in vitro incubation studies to determine the correlation between in vitro response and subsequent in vivo response.

Research Involving Human Subjects:

Our laboratories utilize blood samples from patients and we have received human experimentation approval. The risks of obtaining blood samples are minimal. The potential benefit to the patient is great if improved immunologic diagnosis can be obtained.

SECTION IV
PROGRESS REPORT SUMMARY

GRANT NUMBER

UOI CA34980 02

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

ARTHUR J. AMMANN

PERIOD COVERED BY THIS REPORT

NAME OF ORGANIZATION

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

FROM

5-1-83

THROUGH

4-30-84

TITLE (Repeat title shown in item 1 on first page)

Studies of Acquired Immune Deficiency Syndrome

(SEE INSTRUCTIONS)

The scientific goals of the project have not been altered since the submission of the grant. The following is a brief summary of the studies which have been completed during the award year.

Categorization of the immunologic profile of patients with AIDS (Kaposi's sarcoma) and opportunistic infection (as well as AIDS related syndromes has been completed and the work has been published. A distinctive profile can be demonstrated in the patient groups of healthy homosexual controls, patients with lymphadenopathy syndrome, opportunistic infection or Kaposi's sarcoma. The degree of immunologic abnormalities can be ranked and correlates well with prognosis and survival. Functional impairment of T-cell immunity occurs in the most severely affected patients and when less than 10% of normal, usually indicates an immunologic state which is incompatible with survival beyond 1 year. Our studies also indicate that there is an impaired antibody response following specific immunization in patients with severe impairment of T-cell immunity. Many of these patients have a paradoxical increase in immunoglobulin levels. The impaired antibody response was demonstrated when patients were immunized with pneumococcal polysaccharide and a protein antigen, keyhole limpet hemocyanin. These studies provide important information in relation to appropriate approaches to treatment when reconstituting deficient immunity in this population of patients.

Additional AIDS related syndromes have been investigated to determine whether immunologic abnormalities in these groups of patients are consistent with AIDS. Two groups were defined, patients with hemophilia receiving concentrate factor VIII therapy and pediatric patients with blood transfusion related AIDS or AIDS acquired by means of vertical transmission from an IV drug addict mother. An analysis of additional patients who received blood products from patients with AIDS clearly indicates a significant risk in these populations for acquiring AIDS. The epidemiologic, clinical and immunologic findings in these groups of patients have been described and published and will serve as a continuing basis for investigation.

We have also investigated the distribution of B and T lymphocytes in the lymph nodes of homosexual men with Kaposi's sarcoma. The information obtained from these studies was utilized to compare with results of peripheral blood analysis of similar populations of cells. These studies have provided a basis for determining whether or not peripheral blood studies accurately reflect the distribution of immunologically competent cells within the tissue of affected patients.

Flow cytometric analysis using monoclonal antibodies to leukocyte subsets has revealed striking changes in the distribution of cells among patients with AIDS, the lymphadenopathy syndrome and normal homosexual controls. Large amounts of surface immunoglobulin are present on both T helper and T suppressor cells in these various groups. There is a quantitative increase from healthy to lymphadenopathy to full-blown AIDS in

Bibliography

1. Ammann AJ, Cowan MJ, Wara DW, Weintrub P, Dritz S, Goldman H, Perkins HA. Acquired immunodeficiency in an infant: Possible transmission by means of blood products. Lancet 1:956-958, 1983.
2. Ammann AJ, Abrams D, Conant M, Chudwin D, Cowan MJ, Volberding P, Lewis B, Casavant C. Acquired immune dysfunction in homosexual men: Immunologic Profiles. Clin. Immunol. Immunopath. 27:315-325, 1983.
3. Conte JE, Hadley WK, Sande M, Ammann AJ. Infection control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). New Eng. J. Med. 309:740-744, 1983.
4. Modlin RL, Meyer PR, Hofman FM, Mehlmauer M, Levy NB, Lukes RJ, Parker JW, Ammann AJ, Conant MA, Rhea TH, Taylor CR. T lymphocyte subsets in lymph nodes from homosexual men. JAMA 250:1302-1305, 1983.
5. Weintrub PS, Koerper MA, Addiego JE, Drew LW, Lenette ET, Miner R, Cowan MJ, Ammann AJ. Immunologic abnormalities in patients with hemophilia A. J. Pediat. 103:692-695, 1983.
6. Modlin RL, Meyer PR, Ammann AJ, Rea TH, Hofman FM, Vaccaro SA, Conant MA, Taylor CR. Altered distribution of B and T lymphocytes in lymph nodes from homosexual men with Kaposi's sarcoma. Lancet 2:768-771, 1983.
7. Jaffe HS, Ammann AJ, Abrams DI, Lewis B, Golden JA. Complications of co-trimoxazole in treatment of AIDS associated *Pneumocystis carinii* pneumonia in homosexual men. Lancet 2:1109-1111, 1983.
8. Abrams DI, Lewis BJ, Beckstead JH, Casavant H, Drew WL. Persistent diffuse lymphadenopathy in homosexual men: Endpoint or Prodrome? Ann. Int. Med. (In press).
9. Drew WL, Mills J, Dylewski J, Casavant H, Ammann A, Brodie H, Merigan T. CMV Infection: Is the cause of abnormal T-lymphocyte subset ratios in homosexual men. (Submitted for publication).

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER
CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
Jay A. Levy	Principal Investigator	Department of Medicine Cancer Research Institute
John Morrow	Research Immunologist	Cancer Research Institute

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

The specific objective of this laboratory is to identify the infectious agent responsible for AIDS. Over the next year, we shall continue our efforts to isolate this agent using tissue culture and animal experimentation. For tissue culture studies, we shall employ a selected number of different animal cell lines which are susceptible to a variety of known viruses. These cells will be cocultivated with white cells and sperm from individuals with AIDS. In addition, the white cells of patients with AIDS will be cultured in the presence of IL2 to establish T cell lines, with B cell growth factor (when available) to cultivate B cells, and in human sera, to cultivate macrophages. The presence of an infectious agent in these cells will be assessed. In particular, over the next year we shall concentrate on the presence of retroviruses in the T cells of AIDS patients and the possibility of a new agent in cultured monocytes. Assays for HTLV and LAV-1 will be conducted.

For animal studies, mice and hamsters appear to be the most sensitive rodents to infections which may result from immune deficiency induced by the AIDS agent. We shall thus inoculate these animals with purified white cells from patients with AIDS, as well as the pellets of centrifuged serum samples. The animals will be followed for changes in immunologic parameters as well as for differences in their cell numbers as measured by immunofluorescence (FACS) using helper and suppressor T cell antisera. The end point will be the development of immunologic changes and opportunistic infections in these animals.

In all these studies, sera from patients with AIDS, a collection of sera from close intimate contacts of AIDS patients over at least six months, and normal healthy gay individuals will be used in an attempt to identify the agent responsible for the disease. The tests conducted will include immunofluorescence testing, hemagglutination, hemadsorption, reverse transcriptase assays and interferon assays, as well as electron microscopy.

Finally, we shall continue to establish and characterize cell lines derived from Kaposi's sarcomas. We ultimately want to develop a tumorigenic line that can be studied for its transformation properties and presence of oncogenic viruses.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☒ YES If "YES," identify by common names and underline primates.

Mice

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

UI CA 34980A 02

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

Equipment

We have requested \$5,000. to buy a Coulter Counter to be placed in our P-2 facility. At this time, we must take the white cells, after they are separated through Ficoll-Hypaque gradients and count them in a Coulter Counter in a lab situated at a distance from the P-2 facility. This procedure has alarmed some individuals in the other laboratory and also could present problems in the bio-safety requirements for separation of equipment used in AIDS research. We, thus, hope that funding for this important piece of equipment will be approved.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-83	THROUGH 4-30-84	GRANT NUMBER UI CA 34980A 02
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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)	ACTUAL EXPENDITURES THRU (insert date):	ESTIMATED ADDITIONAL EXPENDITURES AND OBLIGATIONS FOR REMAINDER OF CURRENT BUDGET PERIOD	TOTAL ESTIMATED EXPENDITURES AND OBLIGATIONS (Col. 2 plus Col. 3)	ESTIMATED UNOBLIGATED BALANCE (Subtract Col. 4 from Col. 1)
	(1)	(2)	(3)	(4)	(5)
TOTAL DIRECT COSTS	122,968	53,656	69,312	122,968	0
INDIRECT COSTS (as provided)	30,600	11,674	18,926	30,600	0
TOTALS →	153,568	65,330	88,238	153,568	0

B. THROUGH F.

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

PROFESSIONAL PERSONNEL

NAME	TITLE	CATEGORY	25%	26-50%	51-75%	MORE THAN 75%
J Levy	Assc. Prof	1	X			
J Morrow	"in training"	3		*		
J Landes	SRA I	2				*
T Shimobukaro	SRA I	2	*			
MSzoenyi	Lab Asst	2	*			

EQUIPMENT

Lease of Becton-Dickenson Research FACS Analyzer

TRAVEL

Domestic travel to the East coast for an AIDS Conference.

OTHER SUPPORT

J. Levy, M.D. State of California "A Case-Control Study of Acquired Immune Deficiency Syndrome Diseases". \$81,000

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER CA34980 02	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Jay A. Levy, M.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION		FROM	THROUGH
TITLE (Repeat title shown in item 1 on first page) Isolation of Agent Responsible for AIDS			

(SEE INSTRUCTIONS)

1. Inoculation of concentrated white cells and sera from patients with AIDS into newborn animals from four different strains of mice, and from guinea pigs, hamsters, and rats. Over 1,000 animals have been inoculated and maintained for up to 1 year. Control animals have received white cells from healthy donors. Results show a 15% incidence of opportunistic infections in BALB/c mice and not in ICR, C37 black, or C3H mice. Control animals had less than 1% infection rate. Hamsters had a somewhat increased death rate compared to controls. Guinea pigs and rats showed no infection or mortality after 1 year.

2. Histologic examination of blood smears from the animals has indicated a reduction in lymphocytes in some of the mice and hamsters inoculated with AIDS material, but not in rat or guinea pigs. Thus, combined with the above mentioned results, we believe that mice may be a potential animal model for the study of AIDS.

3. In collaborative studies with Dr. Sy Kalter, Southwest Texas Foundation, we have inoculated AIDS blood into 4 baboons, one of which was a newborn. The first three animals inoculated all showed initially a lymphocytosis, with many atypical lymphocytes. In two animals, this picture has been maintained. Their blood contains no antibodies to CMV, EBV, or hepatitis B. Blood from one of the infected animals was inoculated into a newborn baboon, and the same pattern of lymphocytosis has been maintained in this animal after 9 months.

4. We have inoculated purified white cells from AIDS patients onto a variety of heterologous cell lines, including mink, dog, cat, mongoose, gazelle, chicken, human, chimp, rhesus monkey. They have also been cocultivated with the CEM and MOLT T cell lines and the U937 human macrophage cell line. In a limited number of studies conducted thus far, we can find no evidence of an infectious agent by CPE, hemagglutination or hemadsorption tests. Immunofluorescent studies using sera from a patient with AIDS has not indicated any presence of an agent in these cell lines, but these studies are only preliminary.

5. We have cocultivated AIDS white cells with the established T cell lines and attempted to induce interferon production in these cells. Thus far, no interferon has been noted in these cells after a short cocultivation period.

6. We have cultured over 50 T cell lines from patients with AIDS as well as controls and healthy gay donors. These cells have been studied by FACS for antigen markers after long term growth in culture. We have achieved 100% success in growing the cell lines in the presence of IL2. In those studied by FACS, we find that the helper cells are initially increased in number, but these then decrease after about 3 weeks. Suppressor T cells can be maintained in culture for several months. Macrophages and NK cells disappear after one week. We have maintained AIDS T cell lines in the presence of IL2 for over 90 days with good viability. As noted above, there is then a preponderance of suppressor T cells in culture.

7. In one lymphocyte culture, we have evidence that B cells remain and are making antibodies to T cells. By double labelling the presence of T cells carrying immunoglobulins on their surface have been noted even after three months in culture.

8. In about 5 out of 50 cultures we have detected the presence of HTLV by reverse transcriptase and immunofluorescent tests. Antibodies to HTLV have only been found in about 2 out of 20 AIDS patient's serum examined. We have confirmed the ability of HTLV to induce syncytial formation in XC and mink lung cells. We are perfecting this assay to use as one of the tests for HTLV. We have also noted that HTLV does not hemagglutinate goose, 1 day chick, adult chick, guinea pig, rat, rhesus monkey, human O, or sheep erythrocytes.

9. In some cultures, high reverse transcriptase activity has been noted without evidence of infection with HTLV. We are presently investigating whether LAV-1 (isolated first by Barre, et al.) is responsible for this RT activity.

10. We have noted that macrophages from AIDS patients adhere less readily to the cell culture as compared to controls. This may indicate either a difference in population of macrophages or an abnormality in their adherence potential.

11. We have noted after long term culture, the presence of dendritic -like cells growing in cultures of both AIDS patients and normal controls suggesting that IL2 enhances the growth of these cell populations. They become evident after long term culture.

12. We have established over 35 cell lines from Kaposi's sarcomas (KS) removed from patients with AIDS. These cells have been grown by selected techniques on plastic, and then analyzed for endothelial cell characteristics. They have been studied for prostaglandin and prostacycline production (with Dr. M. Goldyne). Over 80% of them produce Factor VIII and have some properties suggesting malignant potential. Moreover, our Kaposi's cell lines have been examined by various histochemical tests by Dr.

Jay Beckstead. These results have indicated that several of them have enzyme markers typical of endothelial cells. Nevertheless, none of these cell lines produced tumors in nude mice, nor have grown in methylcellulose. We have also attempted to grow the cell lines in nude mice in the presence of an angiogenesis-producing tumor (choriocarcinoma). These results, however, have also been unsuccessful. Nevertheless, we believe KS is a hormone-dependent tumor, and thus, the cells may only be tumorigenic when the proper growth factors are present in the host.

13. We have analyzed our Kaposi's sarcoma cell lines in collaboration with Drs. Nelson and MacDougall in Oregon, as well as individuals at UCSF (Dr. A. Geballe), for the presence of CMV, EBV and hepatitis B. In a limited number of studies, none of these agents have been definitively found in the cell lines, nor in fresh tumor tissue removed from the patients. Previous work indicated the presence of CMV, but when Dr. Nelson purified his probes further, and normal human sequences were eliminated, the positive results could not be confirmed. These studies continue to be conducted.

14. We have begun a collaborative work with Professor Keonig in the Dominican Republic as well as colleagues in Haiti examining blood from Haitian immigrants and patients for the presence of antibodies to HTLV, CMV, hepatitis B and EBV. These studies have indicated that Haitian coming from the provinces do not have the same high titer of antibodies to these agents as do those in the cities. These results suggest that AIDS was probably introduced into Haiti and did not result from the voodoo practices, come from animals, or from the population living in the provinces.

PUBLICATIONS

J LEVY

Marx, PA, Maul, DH, Osborn, KG, Lerche, NW, Moody, P, Lowenstine, LJ, Henrickson, RV, Arthur, LO, Gravel, M, London WT, Sever JL, Levy JA, Munn RJ, and Gardner MB. Simian AIDS: Isolation of a Type D Retrovirus and Disease Transmission. Science. In press.

Levy JA, Ziegler JL, Acquired immunodeficiency Syndrome in an opportunistic infection and Kaposi's Sarcoma results from secondary immune stimulation. Lancet 1983;2: 78-81

SECTION I (continued)
SUMMARY OF PROPOSED WORK

GRANT NUMBER

1 U01 CA34980-02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
W. Lawrence Drew, M.D. Ph.D.	Associate Clinical Prof.	Medicine, Clinical Pathology & Laboratory Medicine, U.C.S.F.
John Mills, M.D.	Associate Professor	Medicine, U.C.S.F.
Alan Gottlieb, R.N.	Nurse Practitioner, II	Medicine, U.C.S.F.
Richard Miner, B.A.	Research Tech, IV	Pathology Research Mt. Zion Hospital
To Be Hired	Research Tech.	Medicine, U.C.S.F.

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

1. Enroll 60 additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
2. Collect sequential isolates of CMV from individual, healthy homosexual men and analyse them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

VERTEBRATE ANIMALS INVOLVED ☒ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II NEXT BUDGET PERIOD Follow instructions carefully		FROM 5/01/84	THROUGH 4/30/85	GRANT NUMBER 1 U01 CA34980-012		
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A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD				DOLLAR AMOUNT REQUESTED (Omit cents)		
PERSONNEL (Applicant organization only) (See instructions)		TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week			
W. Lawrence Drew, M.D. Ph.D.	Principal Investigator	20	8	NONE	NONE	0
R. Miner	Research Tech, IV	50	20	16,411.	3,692.	20,103.
SUBTOTALS →				16,411.	3,692.	20,103.

CONSULTANT COSTS (See instructions)		
N/A		

EQUIPMENT (Itemize)		
N/A		

SUPPLIES (Itemize by category)		
CO ₂ & liquid N ₂	413.	
Tissue Culture	2,067.	
Media & Sera	1,654.	
Reagents (antisera, chemicals, etc.)	1,654.	
Plastic & Glassware	3,396.	
		9,184.

TRAVEL	DOMESTIC	
	FOREIGN International Congress of Virology	1,600.
PATIENT CARE COSTS	INPATIENT	
	OUTPATIENT	

ALTERATIONS AND RENOVATIONS (Itemize by category)		
N/A		

CONSORTIUM/CONTRACTUAL COSTS (See instructions)		
N/A		

OTHER EXPENSES (Itemize by category)		
Computer Costs		1,650.
Office Expenses		767.
Statistical & Epidemiological Consultation		2,600.
Indirect Costs 45.3% (16,411.)		7,434.
		12,451.

TOTAL DIRECT COST (Enter on Page 1, Item 10)		43,338.
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INDIRECT COST (See instructions)	45.3 % S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement 3/23/83	☐ Not requested ☐ Under negotiation with:
	% TDC*			

SECTION 1 (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

U01 CA34980-02

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

SALARY JUSTIFICATION

Increases in salary for the following U.C.S.F. personnel: John Mills, M.D. Alan Gottlieb, and To Be Hired Tech. Institutional increases of 11% for the above U.C.S.F. personnel constitute budgeted salary increases.

Two 50% Research Techs. will replace previously budgeted 100% SRA II, 5, because the work conducted in this study is divided between two locations. Typing of viruses is performed at Mount Zion Hospital and Medical Center as are all serologic studies, requiring one 50% tech (Research tech, IV). Viral cultures are performed at San Francisco General Hospital requiring another 50% tech (To Be Hired).

Increase of salary for 50% Research tech, IV at Mount Zion Hospital is due to higher skill and salary step level.

TRAVEL JUSTIFICATION

Invitation to present lecture on the relationship of cytomegalovirus and AIDS and to discuss the results of CMV researchers from Japan and European countries at the International Congress of Virology in Japan.

Other Category for next budget period has been reduced to appropriately cover Travel costs.

VIROLOGY II

SECTION III CURRENT BUDGET PERIOD	FROM 5/01/83	THROUGH 4/30/84	GRANT NUMBER 1 U01 CA 34980-01
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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 (insert date): 12/31/83 (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	89,403.	34,424.	54,979.	89,403.	0.
INDIRECT COSTS (as provided)	6,499.	2,882.	3,617.	6,499.	0.
TOTALS —————→	95,902.	37,306.	58,596.	95,902.	0.

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%	26-50%	51-75%	more than 75%
W. L. Drew	P.I.	1	X			
J. Mills	Co-Invest.	1	*			
A. Gottlieb	Nurse Pract.	2		*		
R. Miner	Tech IV	2		*		
M. Blair	Tech III	2				X
E. Mocarski	Consultant	1	X			
T. Merigan	Consultant	1	X			
To Be Hired	Tech	2		*		
K. Taylor	Secretary	2				X

C. EQUIPMENT N/A

D. TRAVEL

Invitation to present a lecture on the Relationship of Cytomegalovirus and AIDS and opportunity to discuss the results of CMV researchers from Japan and European countries at the International Congress of Virology to be held in Japan.

E. EXPLANATION OF COLUMN 5. N/A

F. OTHER SUPPORT See attached page.

F. OTHER SUPPORT FOR DR. W. LAWRENCE DREW:

- A. State of California State AIDS Center Grant Series -
University of California
- Project Title: The Role of Cytomegalovirus in the
Etiology of AIDS.
- Grant Period: 7/01/83 to 10/30/84
- Annual Amount: \$135,000.
- B. Hoffmann LaRoche, Inc. Pending - Protocol 2563B
- Project Title: Evaluation of the Tolerance and
Efficacy of Escalating Doses of
Recombinant Leukocyte A Interferon
(Ro 22-8181/001) Therapy of Decreasing
Titer of Virus in the Urine,
Blood or Semen of Patients with
Disseminated Cytomegalovirus Infections.
- Annual Amount: Up to \$40,000., dependant upon
patient enrollment.
- C. Hoffmann LaRoche, Inc. Pending - Protocol 2564B
- Project Title: Safety & Efficacy of Recombinant
Leukocyte A Interferon (Ro 22-
8181/001) in Patients with Acquired
Immunodeficiency and viral Infections.
- Annual Amount: Up to \$45,000., dependant upon
patient enrollment.

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER 1 U01 CA34980-01	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR W. Lawrence Drew, M.D., Ph.D.		PERIOD COVERED BY THIS REPORT	
NAME OF ORGANIZATION Mount Zion Hospital and Medical Center		FROM 5/01/83	THROUGH 1/31/84
TITLE (Repeat title shown in item 1 on first page) Studies of Acquired Immune Deficiency Syndrome			
(SEE INSTRUCTIONS)			

We have enrolled 40 CMV seronegative homosexual men in our prospective study. Ten have seroconverted and have lowered their H:S ratios from an average of 1.6 pre-infection to 0.6 post-infection. Three of the ten have been followed for more than or equal to 15 mos. and two continue to have H:S ratios less than 1.0. CMV infection was asymptomatic in all ten. To assess the possibility that homosexual men experience infection with more than one strain of CMV, we have analyzed, by restriction enzymes, multiple CMV isolates from four separate individuals with AIDS. In each patient at least two different strains were identified.

PUBLICATIONS

- Drew WL, Miner RC, Ziegler JL, Gullett JH, Abrams DI, Conant MA, Huang ES, Groundwater JR, Volberding P, Mintz L. Cytomegalovirus and Kaposi's Sarcoma in Young Homosexual Men. *Lancet* 1982, 2:125-127.
- Follansbee SE, Busch DF, Wofsy CB, Coleman DL, Gullet J, Aurigemma GP, Ross T, Hadley WK, Drew WL. An Outbreak of Pneumocystis carinii Pneumonia in Homosexual Men. *Ann Int Med* 1982, 96:705-713.
- Ziegler JL, Drew WL, Miner RC, Mintz L, Rosenbaum E, Gershow J, Lennette ET, Greenspan J, Shillitoe E, Beckstead J, Cassavant C, Yamamoto K. Outbreak of Burkitt's-like Lymphoma in Homosexual Men. *Lancet* 1982, 2:631-633.
- Black SB, Raas M, Mintz L, Shinefield JR, Drew WL. Indirect Hemagglutination Inhibition: A Direct Method for Detecting Cytomegalovirus Antigen. *J Clin Lab Med* 1983, 101:450-452.
- Drew WL, Mintz L. Cytomegaloviral Infection in Healthy and Immune Deficient Homosexual Men, in Ma P and Armstrong D (eds): The Acquired Immune Deficiency Syndrome and Infections of Homosexual Men. Yorke Medical Books, New York, New York, April 1983, 117-123.
- Mintz L, Drew WL, Sexually Transmitted Viral Infections in Homosexual Men, in de la Maza (ed): *Med Clin North Am; Medical Virology*. W. B. Saunders Company, Philadelphia, Pennsylvania, September 1983, 67/5:1093-1104.
- Mintz L, Drew WL, Miner RC, Braff EH. Cytomegalovirus infections in homosexual men: an epidemiological study. *Ann Intern Med* 1983, 99:326-329.
- Drew WL. Sexual Transmission of CMV and Its Relationship to Kaposi's Sarcoma in Homosexual Men, in Plotkin S (ed): Pathogenesis and Prevention of Human Cytomegalovirus Infection. In Press.
- Abrams DI, Lewis B, Beckstead J, Cassavant C, Drew WL. Persistent Diffuse Lymphadenopathy in Homosexual Men: Endpoint or Prodrome? Accepted for publication in the *Ann Int Med*.
- Drew WL, Mills J, Dylewski J, C Cassavant, A Ammann, H Brodie, T Merigan. Is CMV Infection the Cause of Abnormal T Lymphocyte Subset Ratios in Homosexual Men? Submitted for publication.
- Katznelson S, Drew WL, Mintz L. Efficacy of the Condom as a Barrier to the Transmission of Cytomegalovirus. Submitted for Publication.

SUMMARY OF PROPOSED WORK

GRANT NUMBER

UOI CA34980 02

KEY PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

NAME	POSITION TITLE	DEPARTMENT AND ORGANIZATION
VOLBERDING PA	PRINCIPAL INVESTIGATOR	DEPT OF MEDICINE/SFGH
ZIEGLER J	CO-PRINCIPAL INVESTIGATOR	DEPT OF MEDICINE/CRI
ABRAMS, DI	CO-INVESTIGATOR	DEPT OF MEDICINE/SFGH
LEWIS, BJ	CO-INVESTIGATOR	DEPT OF MEDICINE/CRI

Give a brief summary of plans for the next year of support, including the objectives and specific aims as well as the methodology to be used to achieve these aims. DO NOT EXCEED THE SPACE PROVIDED.

In the second year of the NIH Grant we will continue to observe and record the natural history of patients with lymphadenopathy syndrome as well as AIDS associated Kaposi's sarcoma. We also will continue to collect material for banking for collaborative research into the pathogenesis and etiology of this syndrome. The specific objectives for each main patient group covered in this grant will include therapy of patients with diffuse lymphadenopathy with recombinant alpha interferon and therapy of Kaposi's sarcoma with recombinant gamma interferon and interleukin-2. Future chemotherapy trials after the conclusion of enrollment in INCRF-159 protocol serial immunologic monitoring.

VERTEBRATE ANIMALS INVOLVED ☐ NO ☐ YES If "YES," identify by common names and underline primates.

SECTION II (continued)
NEXT BUDGET PERIOD

GRANT NUMBER

UI CA 34980A 02

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

PERSONNEL

P VOLBERDING 24% increase in salary since 5-1-83 due to promotional and cost of living increases.
D ABRAMS 50% increase in salary since 5-1-83 due to promotional reclassification to faculty status and cost of living adjustment. Paid time reduced to 50% to accommodate the salary increases.
G GEE 16% increase in salary due to promotional reclassification and cost of living adjustment.
P ROY 18% increase in salary due to promotional and cost of living adjustment.

FRINGE BENEFIT RATES

EFFECTIVE 1-1-84

EFFECTIVE 7-1-84

ACADEMIC PERSONNEL

26%

22%

STAFF PERSONNEL (CAREER)

30%

27%

EQUIPMENT IBM PC COMPUTER AND MONITOR TO BE USED FOR PATIENT DATA COLLECTION. \$3,750
PATIENT DATA COLLECTION NEEDS HAVE INCREASED TO THREE TIMES OF
ORIGINAL EXPECTATIONS.

SUPPLIES To accommodate cost of living increases these
TRAVEL sections have been adjusted upwards
OTHER EXPENSES to 7%.

CONTRACTUAL

Mt Zion Hospital
Lawrence Drew, M.D.
In an effort to cover overhead costs at
Mt Zion Hospital Dr. Drew's virology section
will be listed as a sub-contract under
Dr. Paul Volberding's therapy section.

SECTION III CURRENT BUDGET PERIOD	FROM 5-1-83	THROUGH 4-30-84	GRANT NUMBER CA34980 02
--------------------------------------	----------------	--------------------	----------------------------

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 (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	78,500	52,139	26,361	78,500	
INDIRECT COSTS (as provided)	21,135	13,944	7,191	21,135	
TOTALS →	99,635	66,083	33,552	99,635	

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	LESS 25%	26-50%	51-75%	MORE 75%
P VOLBERDING	ASST PROF MED	1	*			
D ABRAMS	CLN INSTR MED	1				*
J ZEIGLER	PROF MED	1	X			
B LEWIS	ASSC CLN PROF MEDICINE	1	X			
G GEE	ADM NURSE	2		*		
P ROY	PRIN CLK	2		*		

C. EQUIPMENT

Toshiba P1350 printer and components to be used with IBM PC Computer
\$1,798.87

D. TRAVEL

P Volberding has used the travel money in the amount of \$1,500 to partially defray the cost of attending research meetings for the presentation of research results.

E. EXPLANATION OF COLUMN 5

None

F. OTHER SUPPORT

Paul A. Volberding, M.D.
City and County of San Francisco
Dept. of Public Health
"Study of AIDS - Outpatient Clinic"
7-1-83 to 6-30-84 Grant period
\$390,541

SECTION IV
PROGRESS REPORT SUMMARY

GRANT NUMBER

UOI CA34980 02

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR

PERIOD COVERED BY THIS REPORT

PAUL VOLBERDING, M.D.

FROM

THROUGH

NAME OF ORGANIZATION

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

5-1-83

4-30-84

TITLE (Repeat title shown in item 1 on first page)

PRINCIPAL INVESTIGATOR

(SEE INSTRUCTIONS)

SEE ATTACHED SHEET

THERAPY OF AIDS

OVERALL OBJECTIVES

The overall objectives of the therapy section of this grant have not changed. Because of work accomplished in the first grant year, the focus of Kaposi's sarcoma therapy protocols in this grant year will be on biologic response modifiers rather than cytotoxic chemotherapy. Also because of the number of cases of lymphadenopathy syndrome progressing to AIDS, therapy trials for this syndrome will also be conducted.

SUMMARY OF WORK ACCOMPLISHED

A number of original observations have been made from our center on the natural history of the lymphadenopathy syndrome and of the natural history and therapy of Kaposi's sarcoma in AIDS.

Lymphadenopathy Syndrome: Over two hundred patients with the syndrome of diffuse lymphadenopathy have been followed in the AIDS clinic at UCSF and San Francisco General Hospital. In contrast to our experience at the time of the original grant request, five of these patients have now progressed to AIDS as defined by the CDC. The careful clinical observations made on these patients prior to conversion should be important in helping predict the natural history of this extremely common syndrome. Also because of this conversion to AIDS, therapy trials of recombinant alpha two interferon as discussed in the original grant application are now being initiated. The serial evaluations of patients with lymphadenopathy syndrome has also provided access to specimens including serum and lymph node material. These are being collected on a regular basis from this cohort of patients and have proved valuable for collaborative research studies, many of which were summarized in virology immunology and epidemiology sections of this progress report.

Kaposi's Sarcoma: In the first year of this grant approximately 100 patients with Kaposi's sarcoma in AIDS have been evaluated in the Kaposi's sarcoma clinic at UCSF and the AIDS clinic at San Francisco General Hospital. A staging system devised in retrospect from analysis of these patients initial evaluation in clinical outcome is being developed. A preliminary analysis of 81 patients with Kaposi's sarcoma has revealed minimal impact on survival from the extent of Kaposi's sarcoma but a relatively greater impact from clinical features which may more directly reflect the status of immune competence. This has been reported in abstract form and a more complete analysis of 150 Kaposi's sarcoma patients is currently being conducted.

The natural history of Kaposi's sarcoma in AIDS has also been evaluated by studying those patients who have refused therapy of their tumor. A preliminary analysis of this experience reveals a broad spectrum of clinical aggressiveness of AIDS associated Kaposi's sarcoma. While essentially all patients have shown progression of their tumor, in several well-documented cases there was at most only minimal progression in twelve months of follow-up without therapy. This observation raises important implications for the design of prospective clinical trials which will be addressed in the next year of this grant.

Cytotoxic chemotherapy has been studied in the first year of the continuation of vinblastine therapy for all stages of Kaposi's sarcoma which demonstrates a 35% objective response in these patients. Also 25 patients have been entered onto a phase two trial of ICRF-159. Accrual to this study is being completed and early clinical results suggest that this drug is not more active than vinblastine in the treatment of Kaposi's sarcoma. If confirmed in a more complete analysis these results would suggest that the biology of AIDS associated Kaposi's sarcoma is unlike that of African Kaposi's sarcoma where ICRF-159 was extremely active.

In addition to trials of cytotoxic agents biologic response modifiers are also being tested in Kaposi's sarcoma associated with AIDS. Over 60 patients have been entered into trials of recombinant alpha interferon. As reported in several publications an objective response rate of approximately 40% was observed with this agent. Disappointingly, no immune restoration of clinical significance was observed in these trials. Future trials will continue with this and other biologic response modifiers including recombinant gamma-interferon and recombinant interleukin-2.

As was true of the patients with lymphadenopathy syndrome, patients with Kaposi's sarcoma have also been a valuable source of specimens for collaborative research studies with other components of this grant. Patients with Kaposi's sarcoma are followed serially and specimens including serum and tumor tissue are regularly preserved for future studies by the tissue and serum repository discussed in the first section of the grant.

OBJECTIVES FOR THE NEXT GRANT YEAR

In the second year of the NIH Grant we will continue to observe and record the natural history of patients with lymphadenopathy syndrome as well as AIDS associated Kaposi's sarcoma. We also will continue to collect material for banking for collaborative research into the pathogenesis and etiology of this syndrome. The specific objectives for each main patient group covered in this grant will include therapy of patients with diffuse lymphadenopathy.

PROGRESS REPORT
(cont'd)

denopathy with recombinant alpha interferon and therapy of Kaposi's sarcoma with recombinant gamma interferon and interleukin-2. Future chemotherapy trials after the conclusion of enrollment in ICRF-159 protocol will continue to investigate single agent chemotherapy with serial immunologic monitoring.

HUMAN SUBJECT CONSIDERATION

Lymphadenopathy Syndrome: A protocol for the use of recombinant alpha interferon for patients with lymphadenopathy syndrome has been approved by the Human Subject's Committee at UCSF and a copy of the protocol is attached.

Kaposi's Syndrome: Three protocols are currently being developed and will be initiated shortly for the treatment of AIDS associated Kaposi's sarcoma. While discussed in brief in the original competitive review these protocols are much more complete at this stage and are included in this section. These include a controlled study of no therapy compared with alpha interferon or alpha interferon plus vinblastine for patients with minimal stage of Kaposi's sarcoma, recombinant gamma-interferon and recombinant interleukin-2. In these protocols, particularly in the last two, substantial efforts will be made to monitor the immunologic effects of these agents as they may prove helpful in immunorestitution. A detailed analysis of the rationale for each agent is beyond the scope of this progress report but is included in each of the attached protocols.

ABSTRACTS

1. Natural killer cell activity in homosexual men with Kaposi's sarcoma. Seaman, W., Ziegler, J., Volberding, P., Conant, M., Official Publication of the American Federation for Clinical Research, (in press) 1983.
2. Susceptibility to Kaposi sarcoma and HLA BW44. Colombe, B.W., Conant, M., Volberding, P., and Garovoy, M.R. American Federation for Clinical Research (in press) 1983.
3. Therapy of Kaposi's sarcoma (KS) in Acquired Immune Deficiency Syndrome with alpha-2 recombinant interferon. Volberding, P., Gottlieb, M., Rothman, J., Rudnick, S., Konnent, M., Derezin, M., Weinstein, W., Groopman, J. Proceedings: American Society of Oncology, Vol. 2, Pg. 53, 1983.
4. Single agent or combination chemotherapy of Kaposi's sarcoma in Acquired Immune Deficiency Syndrome. Lewis, B., Abrams, D. Ziegler, J., Conant, M., Gee, G., Silverberg, I., Volberding, P., Proceedings: American Society of Clinical Oncology, Vol. 2, pg. 59, 1983.
5. Immune thrombocytopenic purpura in homosexual men: Clinical manifestations and treatment results. Abrams, D., Voldberding, P., Linker, C., Kiproff, D., Moss, A., Sperling, J., and Embury, S. Blood, Vol. 62, No. 5, Supplement 1, pg. 108a, Nov. 1983.
6. Syngenic bone marrow transplantation for patients with AIDS and Kaposi's sarcoma. Mitsuyasu, R., Volberding, P., Groopman, J. Champlin, R. Blood, Vol. 62, No. 5, Supplement 1, pg. 226a.
7. Recombinant alpha-interferon therapy for Kaposi's sarcoma in Acquired Immune Deficiency Syndrome. Volberding, P., Moran, T., Rudinck, S., Rothman, J. Proceedings: Second European Conference in Clinical Oncology and Cancer Nursing, pg. 221, Nov. 1983.

Ziegler JL, Stites DP. Immunopathogenesis of acquired immunodeficiency syndrome: "host versus host" autoimmunity. JNCI (submitted 2/84)

Ziegler JL, Beckstead JA, Levine AM, et al. Non-Hodgkin's lymphoma in homosexual men with lymphadenopathy or AIDS. Clinical features in 90 patients from six insititutions. N England J Med (submitted, 3/84)

Diffuse, undifferentiated non-Hodgkin's lymphoma among homosexual males-United States. MMWR 1982;31:277-9

Ziegler JL, Drew WL, Miner RC et al. Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet 1982;2: 631-3

Ziegler JL, Bragg K, Abrams DI, et al. High-grade non-Hodgkin's lymphomas in patients with AIDS. Ann NY Acad Sci, in press

Ziegler JL, Templeton AC, Vogel CL. Kaposi's sarcoma: a comparison of classical endemic, and epidemic forms. Sem. Oncol (in press)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

NOTICE OF GRANT AWARD

DATE ISSUED: **SEP 10 1984**

GRANT NUMBER: SSS-9
5 U01 CA34980-02

TOTAL PROJECT PERIOD: *ps.*
From 05/01/83 Through 04/30/86

TYPE OF AWARD: COOPERATIVE AGREEMENTS
AUTHORIZED BY: 42 USC 241 42 PART 52 & PL 95-224
AWARDED BY:

NATIONAL CANCER INSTITUTE

Title of Project or Area of Training

STUDIES OF ACQUIRED IMMUNE DEFICIENCY SYNDROME

Grantee Institution

UNIV OF CALIF, SAN FRANCISCO
CANCER RESEARCH INST, M-1282
SAN FRANCISCO, CA 94143

Principal Investigator/Program Director/Awardee

VOLBERDING, PAUL A MD
SAN FRANCISCO GENERAL HOSP
995 POTRERO AVE/DIV OF ONC #86
SAN FRANCISCO, CALIF 94110

APPROVED BUDGET

FOR BUDGET PERIOD 05/01/84 Through 04/30/85
Salaries and Wages\$ 263,620
Fringe Benefits 69,934
Total Personnel Costs\$ 333,554
Consultant Costs
Equipment 10,000
Supplies 39,827
Travel - Domestic 5,205
- Foreign
Patient Care - Inpatient
- Outpatient
Alterations and Renovations
Contractual or Third Party Costs 29,080
Other 42,909
Trainee Stipends
Trainee Tuition and Fees
Trainee Travel

AWARD COMPUTATION

1. DIRECT COSTS\$ 460,575
2. INDIRECT COSTS\$ **
(Calculated at _____ rate)
3. TOTAL\$ 460,575
4. Less Unobligated Balance From
Prior Budget Period(s)\$
5. AMOUNT OF THIS AWARD → \$ 460,575

COST SHARING (1) Per Instl. agreement dated 07/01/73
CONTRIBUTION (2) Per Indiv. agreement, minimum

SUPPORT RECOMMENDED FOR REMAINDER OF PROJECT PERIOD*
Budget Total Direct Costs
Period (Includes Stipends)
03 487,220
04 NONE

TOTAL DIRECT COSTS → \$ 460,575

When PHS Prior Approval is required for rebudgeting, submit request to Grants Management Official below. #SEE REMARKS

*Subject to availability of funds and satisfactory progress.

REMARKS:
**INDIRECT COSTS FOR THIS AWARD ARE EXPECTED TO BE \$ 101,750. ACTUAL INDIRECT COSTS WILL BE PROVIDED ON A SUMMARY NOTICE.

REFER TO ADDITIONAL TERMS AND CONDITIONS OF AWARD.

#GRANTS MANAGEMENT CONTACT: MS. MARY NIEMIEC *mn* PHONE: 301 496-7444
THIS AWARD IS FUNDED UNDER HHS SINGLE LETTER OF CREDIT NO. 75-08-1471.

TERMS OF ACCEPTANCE: By acceptance of funds awarded under this grant, the grantee acknowledges that it will comply with terms and conditions in the following: (1) Legislation cited above; (2) Regulations cited above; (3) Provisions on or attached to this award notice and signed by the official(s) named below; (4) PHS Grants Administration Manual Chapters in effect on the beginning date of the grant Budget Period; (5) PHS Grants Policy Statement in effect on the beginning date of the grant Budget Period; (6) 45 CFR Part 74. The above order of precedence shall prevail.

FY - Common Accounting Number	CRS/Entity Identification No.	PHS List No./Object Class Code	Document Number
4-8422928	1946036493A6	/41.4 F	(08)U1CA34980A

PROGRAM OFFICIAL FOR THIS GRANT

PHS Grants Management Official

JACK GRUBER, PH.D.
DIVISION OF CANCER ETIOLOGY, NCI
301 496-9740

Leo F. Buscher, Jr.
LEO F. BUSCHER, JR.
GRANTS MANAGEMENT OFFICER
NATIONAL CANCER INSTITUTE

5 U01 34980-02

TERMS OF AWARD

This award has been negotiated between Mary Niemiec of the National Cancer Institute and Roberta Wilson on July 17, 1984.

This project has been identified as one involving hazardous or potentially hazardous agents. Attention is called to the National Institutes of Health publications, "National Cancer Institute Safety Standards for Research Involving Oncogenic Viruses," and "NIH Guidelines for the Laboratory Use of Chemical Carcinogens." These pamphlets may be obtained from the Division of Safety, Room 2E43, Building 13, National Institutes of Health, Bethesda, MD 20205, (301) 496-1357. Procedures used should be representative of accepted microbiological techniques applicable to the handling of materials containing hepatitis B virus or other infectious agents which may be transmitted by ingestion, parenteral inoculation, or exposure of mucous membranes to infectious droplets. As an additional precaution, it may be advisable to use a biological safety cabinet. The recommended procedures and precautions are cited in Centers for Disease Control Morbidity and Mortality Weekly Report, Vol. 31, No. 43, page 577, November 5, 1982. The report of Interagency Recommendations on the prevention of Acquired Immune Deficiency Syndrome (AIDS) is reported in CDC Morbidity and Mortality Weekly Report, Vol. 32, No. 8, page 101, March 4, 1983.

The indirect costs for Mt. Zion Hospital are awarded as direct costs and are based on the approved budget using the negotiated indirect cost rate(s) available at the time of award. Funds awarded for indirect costs may not be used for any other purpose without the authorization of the National Cancer Institute.

The amount of indirect costs charged must be based on actual direct cost expenditures, but is limited to the amount awarded. No additional funds will be awarded for indirect costs.

Reimbursement to Mt. Zion Hospital shall be made on the basis of approved certified vouchers, signed by the principal investigator and approved by an administrative official of the grantee institution.

The third party costs for Mt. Zion Hospital are apportioned as follows:

Personnel	\$20,103
Supplies	<u>1,543</u>
Total Direct Costs	21,646
Indirect Costs	<u>7,434</u>
TOTAL COSTS	\$29,080

This award is issued as a cooperative agreement in response to the NCI RFA "Studies of Acquired Immuno-deficiency Syndrome (Kaposi's Sarcoma and Opportunistic Infections)."

Nature of Collaboration with NCI Staff: Terms of Award

This section outlines the collaboration between recipients of these cooperative agreements and NCI program staff.

1. Scientific Resources.

- A. The Awardees shall develop research protocols and plans in accord with their individual interests and strengths as well as the minimum requirements included in these terms of award.
- B. The NCI Staff will serve as a resource of information on the activities of various members of the working group and will act to facilitate collaboration among involved researchers. It is in the context of the Working Group semi-annual meetings that the awardees, with the assistance of NCI staff, will identify and develop these collaborative areas.

2. Treatment Studies

NCI approval will be required for all treatment protocols developed following award. NCI staff will hold regular protocol review meetings chaired by the Associate Director, Cancer Therapy Evaluation Program, NCI, or his designee. The primary purposes of this review are 1) to assure that the proposed research is in compliance with all FDA requirements for NCI-funded clinical treatment research and 2) to identify and prevent undesirable duplication of efforts. Protocols may be disapproved by NCI on the basis of patient safety and toxicity, obvious duplication, or failure to meet FDA regulations, particularly those concerning NCI-sponsored investigational drugs.

If a proposed protocol is found to be unacceptable for any of the above reasons, the specific reasons for lack of approval will be communicated to the investigator within 30 days of protocol receipt by the NCI. NCI staff will work with the investigators to develop a mutually acceptable protocol compatible with the research interests and needs of the working group and the NCI.

NCI will establish an appeals process for determining the suitability of treatment protocols it has found unacceptable on initial review, and for which a mutually acceptable protocol cannot be arrived at through discussions between the group and NCI staff. An arbitration panel composed of one working group participant, one NCI nominee, and a third member with clinical trials expertise chosen by the other two members will be formed to review NCI decisions. This NCI arbitration process in no way affects the right of a recipient to subsequently appeal an adverse determination using the NIH informal appeals system and the formal Department of Health and Human Services procedures. If the investigator proceeds with performance of a protocol disapproved by the arbitration panel, the results of that study will be subject to careful monitoring and targeted for peer review when the competitive renewal application is under consideration. In addition, the NCI may withdraw the portion of funding designated for a disapproved protocol, if the grounds for disapproval are patient safety and toxicity, or unnecessary duplication.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO



SANTA BARBARA • SANTA CRUZ

SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

SAN FRANCISCO, CALIFORNIA 94143

August 27, 1984

John Klimec
Grants Management Analyst
Contracts and Grants
UCSF

Dear Mr. Klimec:

Enclosed you will find a copy of the Consortium Agreement between the University of California, San Francisco and Mt. Zion Hospital for grant U01 CA34980-02 Studies of AIDS.

The original should be sent to on to Mary Niemiec at the NIH. I've enclosed an envelope. According to my information the letter includes the appropriate information as requested by the NIH. If there is anything remiss please let me know.

Once again, John, I would like to express my appreciation for the help that you have given with regards to the Mt. Zion section of the NIH AIDS grant.

Sincerely,

Bobbi

Roberta Gonzales-Wilson
Admn Analyst
Div of Oncology/AIDS Clinical Outpatient Services
SFGH



Mount Zion Hospital and Medical Center

1600 Divisadero Street, San Francisco/Telephone (415) 567-6600
Mailing Address: Post Office Box 7921, San Francisco, California 94120-7921

August 2, 1984

Mary Niemiec
Grants Management
National Institute of Health
Westwood Building, Room 853
Bethesda, Maryland 20205

Dear Ms. Niemiec:

This letter represents the *Consortium Agreement between the University of California, San Francisco, Studies of AIDS, Grant U01 CA34980-02 and Dr. W. Lawrence Drew of Mount Zion Hospital and Medical Center, San Francisco. Dr. Drew, Principal Investigator of the Virology II Section of grant U01 CA34980-02 has agreed to perform the following for year two, 5/1/84-4/30/85.

1. Enroll 40 additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
2. Collect sequential isolates of CMV from individual, healthy homosexual men and analyse them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

He has furthermore agreed to perform the above for the total second year award amount of \$89,821., an abbreviated Virology II budget follows:

Personnel -	San Francisco General Hospital (UCSF)	\$59,971.
Supplies -	San Francisco General Hospital (UCSF)	\$ 770.
	Subtotal	\$60,741.

*Consortium/Contractual Costs - Mount Zion Hospital		
Salary + Fringe for one Research Technologist IV - 50%	\$20,103.	
Supplies	\$ 1,243.	
Indirect Costs 45.3% (\$16,411)	\$ 7,434.	
	Subtotal	\$29,080.
	Sumtotal	\$89,521.

Sincerely,

W. Lawrence Drew, M.D., Ph.D.
Principal Investigator, Virology II

Dr. Paul Volberding
Principal Investigator, Studies of AIDS
Mr. William H. Gurtner
President, Mount Zion Hospital

KT

cc: John Mills, M.D.



Mount Zion Hospital and Medical Center

1600 Divisadero Street, San Francisco/Telephone (415) 567-6600
Mailing Address: Post Office Box 7921, San Francisco, California 94120-7921

March 7, 1985

Ms. Mary Niemiec
Grants Management
National Institutes of Health
Westwood Building, Room 853
Bethesda, Maryland 20205

Dear Ms. Niemiec:

This letter represents the *Consortium Agreement between the University of California, San Francisco, Studies of AIDS, Grant U01 CA34980-03 and Dr. W. Lawrence Drew, of Mount Zion Hospital and Medical Center, San Francisco. Dr. Drew, Principal Investigator of the Virology II Section of this grant has agreed to perform the following for year three, 5/1/85 through 4/30/86.

1. Enroll additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
2. Collect sequential isolates of CMV from individual healthy homosexual men and analyze them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

He has furthermore agreed to perform the above for the total third year award amount of \$89,873., an abbreviated Virology II budget follows:

Personnel - San Francisco General Hospital (UCSF) \$50,010.

*Consortium/Contractual Costs - Mount Zion Hospital

Mt. Zion Salaries + Fringe Benefits	\$26,336.
Supplies	\$ 3,721.
Indirect Costs	\$ 9,806.
SUBTOTAL	\$39,863.
SUMTOTAL	\$89,873.

Sincerely,

W. Lawrence Drew, M.D., Ph.D.
Principal Investigator, Virology II

Paul Volberding, M.D.
Principal Investigator, Studies of AIDS

Lorraine M. Petrakis
Contracts and Grants Officer, UCSF

Mr. William H. Gurtner
President, Mount Zion Hospital



Mount Zion Hospital and Medical Center

To Bobbi Wilson
Ward 86-San Francisco General Hospital

From Karen Taylor 
Pathology Research

Subject: N.I.H. Grant CA34980-03

Date January 28, 1985

Enclosed is Dr. W. Lawrence Drew's renewal forms.

I have also attached a letter which we mailed to Mary Niemiec, Grants Management, N.I.H., last year which described the consortium agreement which would be forthcoming. This year we will again have to tell N.I.H. that the consortium agreement is forthcoming because as you will see from the second letter to Ms. Niemiec dated August 2, 1984, we need to get Mr. Gurtner's signature. Before that happens the 03 renewal must pass through the Mt. Zion review committee and that generally takes 1 month. So, please inform N.I.H. that this years consortium agreement is forthcoming and call me if you have questions.

Sorry for the delay, but I believe you will find Dr. Drew's papers conveniently in order so as not to cause further delay.

Thank you.



SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

SAN FRANCISCO, CALIFORNIA 94143

*Consortium letter
by Helen 7/31*

July 17, 1984

Mary Niemiec
Grants Management
National Institute of Health
Westwood Bldg Room 853
Bethesda MD

Dear Ms. Niemiec:

This letter is with regards to the University of California, San Francisco Studies of AIDS Grant U01 CA34980-02. The letter regarding the consortium with Mt. Zion Hospital is forthcoming. Dr. Lawrence Drew, Principal Investigator of the Virology II section will forward the agreement letter on July 27. The agreement will be in accordance with the Virology II budget as it has been submitted to you, in the amount of \$89,821 with \$29,080 contracted to Mt. Zion.

If you have any questions regarding this arrangement, please feel free to contact me at (415)666-4387.

Sincerely,

Roberta

Roberta Gonzales-Wilson
Adm. Asst.
Division of Oncology/SFGH-UCSF

cc: P Volberding M.D.
L Drew M.D.
K Taylor ✓



Mount Zion Hospital and Medical Center

1600 Divisadero Street, San Francisco/Telephone (415) 567-6600
Mailing Address: Post Office Box 7921, San Francisco, California 94120-7921

August 2, 1984

Mary Niemiec *Grant's Inquiry #3012446-7441*
Grants Management
National Institute of Health
Westwood Building, Room 853
Bethesda, Maryland 20205

Copy to Georgetown 8/7/84

Dear Ms. Niemiec:

This letter represents the *Consortium Agreement between the University of California, San Francisco, Studies of AIDS, Grant U01 CA34980-02 and Dr. W. Lawrence Drew of Mount Zion Hospital and Medical Center, San Francisco. Dr. Drew, Principal Investigator of the Virology II Section of grant U01 CA34980-02 has agreed to perform the following for year two, 5/1/84-4/30/85.

1. Enroll 40 additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
2. Collect sequential isolates of CMV from individual, healthy homosexual men and analyse them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

He has furthermore agreed to perform the above for the total second year award amount of \$89,821., an abbreviated Virology II budget follows:

Personnel - San Francisco General Hospital (UCSF)	\$59,971.
Supplies - San Francisco General Hospital (UCSF)	\$ 770.
Subtotal	\$60,741.

*Consortium/Contractual Costs - Mount Zion Hospital	
Salary + Fringe for one Research Technologist IV - 50%	\$20,103.
Supplies	\$ 1,243.
Indirect Costs 45.3% (\$16,411)	\$ 7,434.
Subtotal	\$29,080.
Sumtotal	\$89,521.

Sincerely,

W. Lawrence Drew, M.D., Ph.D.
Principal Investigator, Virology II

Dr. Paul Volberding
Principal Investigator, Studies of AIDS

Mr. William H. Gurtner
President, Mount Zion Hospital

KT

cc:John Mills, M.D.

Med. & W. 5

P.F. - Volkerding, Paul

AGREEMENT BETWEEN
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
AND
MOUNT ZION HOSPITAL AND MEDICAL CENTER

Prime Grant No. 5 U01 CA34980-02

AGREEMENT NUMBER 1081SC

This Agreement between The Regents of the University of California (hereinafter called the University), and Mount Zion Hospital and Medical Center (hereinafter called the Collaborating Institution).

WHEREAS, the University has received grant number CA34980 with the Department of Health and Human Services, National Cancer Institute (hereinafter referred to as the prime grant), and,

WHEREAS, the parties hereto desire to enter into an Agreement calling for collaboration on the project "Studies of Acquired Immune Deficiency Syndrome" as detailed in the revised application submitted to the National Institutes of Health on July 30, 1984,

IN WITNESS WHEREOF, the parties hereto have executed this agreement on the month, day and year specified below:

THE REGENTS OF THE UNIVERSITY
OF CALIFORNIA

MOUNT ZION HOSPITAL AND
MEDICAL CENTER

BY Lorraine M. Petrakis

BY William H. Ginter

Lorraine M. Petrakis
Contracts & Grants Officer

DATE 10/17/84

DATE October 8, 1984

ARTICLE I - SCOPE OF WORK

The Collaborating Institution will:

- 1) Enroll 40 additional CMV seronegative homosexual men and correlate acquisition of CMV with the development of abnormal H:S ratios.
- 2) Collect sequential isolates of CMV from individual, healthy homosexual men and analyse them by restriction enzymes to determine if these healthy individuals are also infected by multiple, different strains of CMV.

ARTICLE II - PERIOD OF PERFORMANCE

This Agreement shall become effective May 1, 1984 and terminate April 30, 1985 unless extension is agreed upon in writing by both parties. The Collaborating Institution shall submit a continuation application to the University in the form and time designated by the University if renewal is intended beyond the above referenced termination date.

ARTICLE III - COMPENSATION

The total amount available to the Collaborating Institution for the period reflected in ARTICLE II and itemized in Exhibit A is \$29,080. This amount shall not be exceeded without written authorization of the University.

ARTICLE IV - PRINCIPAL INVESTIGATOR

W. Lawrence Drew, M.D., Ph.D. has been designated by the Collaborating Institution as the Principal Investigator who shall be responsible for the scientific conduct of the project covered by this Agreement. In the event a change in principal investigator is necessary the University must be notified immediately and shall have the right to approve any successor.

ARTICLE V - PROJECT DIRECTOR

Paul A. Volberding, M.D. is the project director designated for the University. Any significant changes in the performance of this agreement as outlined in the Collaborating Institution's proposal and/or budget incorporated herein, require authorization by the Project Director.

ARTICLE VI - PUBLICATION

Publication of project results shall be in conformance with NIH policies (DHHS Publication No. (OASH) 82-50,000) and shall acknowledge support from NIH Grant No. CA34980 awarded to the University from the National Institutes of Health. Four reprints

of publications resulting from work performed in whole or part under this Agreement shall be submitted to the University's Project Director. Three copies will be transmitted to NIH to fulfill their requirement.

ARTICLE VII - METHOD OF PAYMENT, FINANCIAL REPORT REQUIREMENTS

The Collaborating Institution will be provided with quarterly payments, upon receipt from the Collaborating Institution, in triplicate, a statement of the current quarter's expenditures (in the following detail: salaries & wages, consultants, equipment, supplies, travel, patient costs, other direct costs and indirect costs). The itemized statement should be sent to the attention of:

Mr. Lawrence Johns
Accounting Officer
322 C.E.D.
University of California, San Francisco
San Francisco, California 94143

All costs incurred under this Agreement must be based on actual costs. Substantiating documents, e.g., travel receipts, invoices, etc., shall be retained and the Collaborating Institution is expected to keep an accurate accounting of all costs incurred in the performance of this Agreement.

All costs incurred under this Agreement will be subject to audit by the University's cognizant Federal Audit Agency. The Collaborating Institution shall provide the cognizant government auditors and/or University financial representatives access to records where necessary to support costs relating to this Agreement.

The final invoice shall be submitted in a timely manner so payment can be made; such payment to be included in the final report of expenditures due at the awarding agency ninety days after the close of the budget period set forth in Article II. If this information cannot be submitted to the University within this time, the Collaborating Institution will notify the University immediately, indicating the reason for the delay; otherwise funds may not be available due to close out of the grant.

ARTICLE VIII - PROVISIONS APPLICABLE TO DIRECT COSTS

Unless otherwise expressly provided elsewhere in this Agreement or in any amendment thereto, the costs of the following items or activities shall be unallowable as direct costs under this Agreement:

- 1) Purchase or lease of any item of general purpose office furniture or equipment.

- 2) Alteration or renovation of the Collaborating Institution's facilities. If funds are provided elsewhere for this purpose, the award amount may not be increased without prior University approval.
- 3) Foreign travel, herein defined as travel outside the United States, its Territories and Possessions, and Canada, shall not be performed and the costs thereof shall not be allowable without the prior written approval of the University and the National Institutes of Health.

ARTICLE IX - REBUDGETING

Public Health Service policy is hereby incorporated and made a part of this Agreement. The Collaborating Institution must implement the guidelines of this policy prior to any direct cost rebudgeting under this Agreement. However, any restrictions on rebudgeting listed elsewhere in this Agreement shall take precedence over the Public Health Service policy, provided the minimum requirements of the PHS Grants Policy Statement have been met. All requests for rebudgeting must be directed to the University's designated administrator for consideration.

ARTICLE X - EQUIPMENT ACCOUNTABILITY

The Collaborating Institution shall utilize sound purchasing and inventory procedures and maintain adequate records to account for the purchase, inventory and disposition of equipment acquired under this Agreement. Title to equipment shall reside with the University during the period of performance of this Agreement. Final disposition will be determined by the University upon conclusion of the project.

ARTICLE XI - PROGRESS REPORTING REQUIREMENTS

Interim progress reports are required if renewal is intended beyond the termination date (Article II) and shall be submitted at the time of continuation application (Article II).

Terminal progress reports must be submitted to the University within 90 days after the end of the Agreement. The report should include a summary statement of progress toward the achievement of the originally stated aims, a list of the results, positive or negative, considered significant by the investigator, and a list of publications resulting from the project with plans (if any) for further publication. All progress reports shall be submitted to the University's Project Director.

ARTICLE XII - GRANT-RELATED INCOME

The Collaborating Institution is accountable to the University for any grant-related income generated by activities

performed under this Agreement. Disposition of such income will be made by the University by one of the following options:

- 1) Treated as an offset to expenditures incurred
- 2) Treated as partial payment to the succeeding Agreement, if any
- 3) Returned to the University

The Collaborating Institution shall maintain adequate financial records of the receipts and disposition of grant-related income. Such income may not be used to fulfill the cost sharing requirements of this Agreement, if applicable.

ARTICLE XIII - GENERAL CONDITIONS

DHHS Publication No. (OASH) 82-50,000 "Public Health Service Grants Policy Statement" is incorporated herein and made a part of this Agreement; however, the Agreement shall take precedence over this publication.

ARTICLE XIV - PATENTS AND INVENTIONS

Patent Rights for the Collaborating Institution shall be in agreement with P.L. 96-517, Patent Rights, (Small Business Firms and Nonprofit Organizations) as implemented by OMB Circular A-124.

ARTICLE XV - TERMINATION

This Agreement may be cancelled prior to the termination date by either the Collaborating Institution or the University upon written notice 60 days before the proposed early termination date.

In the event of cancellation of this Agreement prior to the termination date, the Collaborating Institution agrees to deliver such information and items which, if the Agreement had been completed, would have been required to be furnished to the University, including partially completed plans, drawings, data, documents, surveys, maps, reports and models.

ARTICLE XVI - CARE AND TREATMENT OF LABORATORY ANIMALS

The Collaborating Institution shall comply with applicable portions of the Animal Welfare Act (P.L. 89-544 as amended) and to follow the guidelines prescribed in DHEW Publication No. 78-23, revised 1978, formerly PHS Publication No. 1024, Guide for the Care and Use of Laboratory Animals.

ARTICLE XVI - PROTECTION OF HUMAN SUBJECTS

A. The Collaborating Institution shall submit to the University an assurance, reviewed and approved by an appropriate institutional committee, that the rights and welfare of any human subjects involved in this project are adequately protected in accordance with the Federal Register dated 1/26/81: Vol. 46, No. 16:8386-8391.

B. In the event this Agreement is extended by mutual consent beyond the current period of performance, the Collaborating Institution shall submit to the University a certification that the continuation application will be reviewed in accordance with "A" above.

ARTICLE XVIII - CIVIL RIGHTS AND EQUAL EMPLOYMENT OPPORTUNITY

The Collaborating Institution must comply with Title VI of the Civil Rights Act of 1964 and Executive Order 11246 and have on file with the DHEW an Assurance of Compliance with the Civil Rights Act of 1964 (Form HEW 441).

SECTION II
NEXT BUDGET PERIOD
Follow instructions carefully

FROM 5-01-84

THROUGH 04-30-85

GRANT NUMBER #1081SC

Exhibit A

A. ITEMIZE DIRECT COSTS REQUESTED FOR NEXT BUDGET PERIOD					DOLLAR AMOUNT REQUESTED (Omit cents)			
PERSONNEL (Applicant organization only) (See instructions)				TIME/EFFORT		SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE OF POSITION	%	Hours per Week					
W. Lawrence Drew, M.D. Ph.D.	Principal Investigator	20	8	0	0			
R. Miner	Research Tech	50	20	16,411	3,692			
SUBTOTALS					16,411	3,692	20,103	
CONSULTANT COSTS (See instructions)								
N/A								
EQUIPMENT (Itemize)								
N/A								
0								
SUPPLIES (Itemize by category)								
PLASTIC & GLASSWARE								
CO2 & LIQUID N2								
MEDIA & SERA								
REAGENTS (ANTISERA, CHEMICALS, ETC.)								
1,543								
TRAVEL		DOMESTIC						
		FOREIGN						
PATIENT CARE COSTS		INPATIENT						
		OUTPATIENT						
ALTERATIONS AND RENOVATIONS (Itemize by category)								
N/A								
CONSORTIUM/CONTRACTUAL COSTS (See instructions)								
N/A								
OTHER EXPENSES (Itemize by category)								
Indirect costs 45.3% (16,411)								
7,434 7,434								
TOTAL DIRECT COST (Enter on Page 1, Item 10)								
29,080								

INDIRECT COST (See instructions)	45.3	% S&W*	*If this is a special rate (e.g. off-site) explain	Date of DHHS agreement	☐ Not requested ☐ Under negotiation with:
		% IDC*			



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20205

October 9, 1984

Our Reference: 5 U01 CA 34980-02

Ms. Roberta Gonzales-Wilson
Administrative Assistant
Division of Oncology
San Francisco General Hospital
University of California
San Francisco, California 94143

Dear Ms. Gonzales-Wilson:

Please forward an updated "Protection of Human Subjects" form (HHS 596) to indicate that Dr. Volberding has received IRB full board approval on all his projects involving human subjects for the current grant budget period.

This request is a follow-up to our previous conversations regarding this NIH annual requirement.

Sincerely,

A handwritten signature in cursive script, reading "Mary V. Niemiec", is written over a faint, circular embossed seal of the National Cancer Institute.

Mary V. Niemiec
Grants Management Specialist
National Cancer Institute
(301) 496-7444

Principal Paul Volberding, M.D. Univ Asst. Professor of Med CRI/Dept. Med
Investigator John Ziegler, M.D. Title Professor of Med Dept CRI/Dept. Med
Mailing San Francisco General Hospital Div of OncSubmission
Address 995 Potrero Ave. Ward P86 (415) 666-4387 Date May 1, 1984
Grant San Francisco CA 94110
Title STUDIES OF AIDS

Application to the CHR is New ☒ Renewal of Approval # 240890-01
Application to the agency is New ☒ Renewal of Grant # U01 CA34980-01
Funding year May 1 '84 to May 1 '85 Agency NIH

Short summary of subject area of grant:

For the second year of this grant we propose the following projects: (1) continue epidemiologic surveillance studies of the sexual contacts of AIDS patients seen at the KS clinic, compare clinical features of KS in AIDS patients to the classical form, and provide tissue and serum specimens to the central tissue bank facility: (2) continue to collect incidence data for population-based analysis of morbidity and mortality, conduct pilot study of AIDS in intravenous drug abusers, and contrive surveillance of non-Hodgkin's lymphoma in homosexual men (3) immunologic and functional assays of T cell subsets and monocytes in pre-AIDS and AIDS patients to define immunopathogenesis, follow immune parameters in patients receiving interferon and IL2 therapy: (4) continue studies of viral etiology of AIDS by inoculating AIDS tissues into Balb-G and CH3 mice and newborn hamsters, baboons and chimpanzees: (5) continue surveillance of CMV sero-negative homosexual men and conduct extensive immunologic studies when sero-conversion occurs, continue CMV analysis of homosexual men to determine strain variations and natural history of KS and lymphadenopathy syndrome, initiate treatment protocols using ICRF-159, gamma interferon, and interleukin-2, study natural history and treatment of non-Hodgkin's lymphoma in homosexual men.

List of ALL projects discussed in grant application.		CHR	CHR
Project	Project	Approval	Expir
Investigator	Title	Number	Date

SEE ATTACHED PAGE

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7/29/84
Date

Paul Volberding
Signature of P.I.

Comments:

Principal Paul Volberding, M.D. Univ Asst. Professor of Med CRI/Dept. Med
Investigator John Ziegler, M.D. Title Professor of Med Dept CRI/Dept. Med
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Program project
 X Research grant
 Training
 Development
 BRSG
 ?

List of ALL projects discussed in grant application. - - - - - CHR - - - - - CHR - - - - -
Project Project Approval Expir
Investigator Title Number Date

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Date

Signature of P.I.

Comments:

PROTOCOL FOR THE CLINICAL STUDY OF AIDS AT UCSF

INTRODUCTION

The Acquired Immune Deficiency Syndrome or AIDS is a serious new disease in which the cellular immune system regulation appears to be altered increasing dramatically the rate of malignancies, including Kaposi's sarcoma and non-Hodgkin's lymphoma and a variety of severe life threatening opportunistic infections, especially pneumocystis carinii pneumonia.

Because of the serious nature of this illness and the rapid spread of the epidemic, and because of the probability that the study of AIDS will result in advancement in our knowledge of the relationship between the immune system and cancers, extensive research projects are underway. Numerous investigators at UCSF, other UC campuses, and other medical centers across the country are interested in studying the epidemiology, etiology and immunology of this disease.

Because San Francisco represents a major focus of this epidemic and because of the coordination of AIDS activities at UCSF, numerous requests are received to provide patient material for these studies. To coordinate the collection and distribution of these specimens a Tissue Committee of the UCSF AIDS Working Group has been established. The chair of this committee is Dr. Paul Volberding.

In addition, a tissue and serum bank has been organized under the direction of Dr. John Greenspan to coordinate the optimum storage and processing of these specimens with appropriate biohazard precautions. To minimize the inconvenience of multiple studies to patients with AIDS and to prevent confusion among collaborating investigators, this protocol is intended to serve as a method for the centralization of this collection process. This protocol is not intended to give permission for any therapy studies. Additionally, any invasive tests that are not specifically outlined in this proposal will have separate protocols and consents approved through the Human Research Committee.

PROTOCOL

At the time of initial evaluation patients with AIDS or AIDS related conditions as defined by the CDC, will be asked to participate in an ongoing research effort. This will consist of collection of approximately 45cc's of blood on the first clinic visit and if the person has Kaposi's sarcoma will also include a biopsy of a Kaposi's lesion and adjacent normal skin. These specimens will be preserved by the Tissue and Serum Bank with code numbers to preserve patient confidentiality. In addition, at the initial clinic visit baseline, chest x-ray and pulmonary function tests will be obtained. Any other studies indicated for the patient's clinical condition will also be collected.

Patients will be followed as clinically indicated for their illness and will have additional blood collected for preservation in the Tissue Bank every 3 to 6 months. At no time will the amount of blood collected for this purpose exceed 30cc's. In addition, 10 follow-up patients will receive serial pulmonary function testing every 4 months. Subsequent biopsies of tumors may be performed, but only if clinically indicated, to assess response to therapy.

Any other invasive testing that is not of routine clinical utility will require a separate consent from each patient.

CONFIDENTIALITY

Because of the nature of AIDS and the risk groups involved in the epidemic, confidentiality concerns have been raised by a number of groups. To insure confidentiality of specimens collected on this protocol, no specimen will be identified by the patient's name. Code numbers will be used for this purpose as provided by the City Health Department AIDS Registry. This system of coding has been in place for the past several months and has been deemed acceptable by the Centers for Disease Control.

SUMMARY OF AIDS CLINICAL RESEARCH PROTOCOL

A DIAGNOSIS ON FIRST VISIT

	<u>AMOUNT</u>
BLOOD:	
STUDIES AS INDICATED CLINICALLY (CBC, CHEM PANELS ETC)	approx 20cc
BLOOD (SERUM) FOR PRESERVATION IN SPECIMEN BANK	approx 20cc
BIOPSY:	
SKIN BIOPSY FOR DIAGNOSIS OF SUSPICIOUS LESION	- 4mm punch
SKIN BIOPSY OF LESION FOR PRESERVATION/ RESEARCH	- 4mm punch
BIOPSY OF NORMAL SKIN FOR PRESERVATION/RESEARCH	- 4mm punch
BIOPSY OF LYMPH NODE FOR DIAGNOSIS AS CLINICALLY INDICATED	
PORTION OF NODE TO BE PRESERVED FOR RESEARCH (NO BIOPSY OF NODE FOR RESEARCH ONLY)	

PULMONARY FUNCTION TESTING: BASELINE TESTING

TESTING IN FOLLOW-UP PERIOD

	<u>AMOUNT</u>	<u>FREQUENCY</u>
BLOOD:		
BLOOD (SERUM) FOR PRESERVING/RESEARCH	20 cc	3-6 months
BIOPSY:		
KS LESIONS BIOPSIED FOR CLINICAL INDICATIONS:	- 4 mm punch	clinically as indicated
LYMPH NODE BIOPSIED FOR CLINICAL INDICATIONS:	portion of biopsy	as indicated
PULMONARY FUNCTION TESTS:		4 months



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20205

October 9, 1984

Our Reference: 5 U01 CA 34980-02

Ms. Roberta Gonzales-Wilson
Administrative Assistant
Division of Oncology
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Dear Ms. Gonzales-Wilson:

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Sincerely,

Mary V. Niemiec
Grants Management Specialist
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(301) 496-7444

10/17
Susan
Please call
for status
THX
Bb-

Principal Paul Volberding, M.D. Univ Asst. Professor of Med CRI/Dept. Med
Investigator John Ziegler, M.D. Title Professor of Med Dept CRI/Dept. Med
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Program project
☒ Research grant
Training
Development
BRSG
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7/29/84
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Paul Volberding
Signature of P.I.

Comments:

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PROTOCOL

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PULMONARY FUNCTION TESTS:		4 months

UCSF COMMITTEE ON HUMAN RESEARCH
GENERAL APPROVAL APPLICATION FORM

Principal Paul Volberding, M.D. Univ Asst. Professor of Med CRI/Dept. Med
Investigator John Ziegler, M.D. Title Professor of Med Dept CRI/Dept. Med
Mailing San Francisco General Hospital Div of OncSubmission
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determine strain variations and natural history of KS and lymphadenopathy
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CONFIDENTIALITY

Because of the nature of AIDS and the risk groups involved in the epidemic, confidentiality concerns have been raised by a number of groups. To insure confidentiality of specimens collected on this protocol, no specimen will be identified by the patient's name. Code numbers will be used for this purpose as provided by the City Health Department AIDS Registry. This system of coding has been in place for the past several months and has been deemed acceptable by the Centers for Disease Control.

SUMMARY OF AIDS CLINICAL RESEARCH PROTOCOL

A DIAGNOSIS ON FIRST VISIT

	<u>AMOUNT</u>
BLOOD:	
STUDIES AS INDICATED CLINICALLY (CBC, CHEM PANELS ETC)	approx 20cc
BLOOD (SERUM) FOR PRESERVATION IN SPECIMEN BANK	approx 20cc
BIOPSY:	
SKIN BIOPSY FOR DIAGNOSIS OF SUSPICIOUS LESION	- 4mm punch
SKIN BIOPSY OF LESION FOR PRESERVATION/ RESEARCH	- 4mm punch
BIOPSY OF NORMAL SKIN FOR PRESERVATION/RESEARCH	- 4mm punch
BIOPSY OF LYMPH NODE FOR DIAGNOSIS AS CLINICALLY INDICATED	
PORTION OF NODE TO BE PRESERVED FOR RESEARCH (NO BIOPSY OF NODE FOR RESEARCH ONLY)	

PULMONARY FUNCTION TESTING: BASELINE TESTING

TESTING IN FOLLOW-UP PERIOD

	<u>AMOUNT</u>	<u>FREQUENCY</u>
BLOOD:		
BLOOD (SERUM) FOR PRESERVING/RESEARCH	20 cc	3-6 months
BIOPSY:		
KS LESIONS BIOPSIED FOR CLINICAL INDICATIONS:	- 4 mm punch	clinically as indicated
LYMPH NODE BIOPSIED FOR CLINICAL INDICATIONS:	portion of biopsy	as indicated
PULMONARY FUNCTION TESTS:		4 months

SFGH Wd 86

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CONTRACTS AND GRANTS OFFICE
SAN FRANCISCO, CALIFORNIA 94143
(415) 666-2977

m

July 30, 1984

Ms. Mary Niemiec
Grants Management
NIH/NCI
5333 Westwood Avenue, Room 853
Bethesda, MD 20205

Dear Sir or Madam:

We are presenting for your review, a request for support of the following project:

PROJECT TITLE Studies of Acquired Immune Deficiency Syndrome

PRINCIPAL INVESTIGATOR Paul A. Volberding, M.D.

TYPE OF PROPOSAL

- ☐ New
☐ Continuation of No. _____
☐ Renewal of No. _____
☐ Supplement to No. _____
☒ Revision of No. CA34980-02

- ☐ Contract
☒ Grant
☐ Subcontract
☐ Fellowship

AMOUNT REQUESTED

First 12 Months \$561,408.00 (Including indirect cost)
Total _____ Direct Cost Only

INDIRECT COST RATE USED

22.7 % Total Direct Cost (22% for period 5/1/84 - 6/30/84)

PROJECT PERIOD

First 12 Mo. 5/1/84 - 4/30/85
Total Period _____

Your favorable consideration will be appreciated. If the request meets with your approval, or if you have any questions, please communicate with this office.

Sincerely yours,

Lorraine M. Petrakis
Contracts and Grants Officer

Attachments

DATE: December 28, 1983
TO: PRINCIPAL INVESTIGATOR Dr. Paul A. Volberding SFGH 5H22
FROM: CONTRACTS AND GRANTS OFFICE

Your application kit, Form PHS 2590-1, for the noncompeting continuation of Grant Number 5 U01 CA 34980-02 is available at the Contracts and Grants, 145 Irving Street (2nd Floor). The completed application must be in this office at least two weeks prior to the agency's deadline of March 1, 1984.

Applications must be received by NIH on the deadline or a delay in funding may result.

APPLICATIONS WILL NOT BE MAILED. They must be picked up at 145 Irving Street.

Inquiries should be addressed to our office at extension x-2977.

cc: Departmental Assistant Frank Cook M-997