SECTION I

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

APPLICATION FOR RESEARCH GRANT

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TYPE	PROGRAM	NUMBER
2	RO1	HD 00045-03
REVIEW GROUP		FORMERLY
DC		
COUNCIL (Month, Year)		DATE RECEIVED
June 66		1/3/66
APPLICANT CODE		D CODE

TO BE COMPLETED BY PRINCIPAL INVESTIGATOR (Items 1 through 9 and 17A)

1. ABBREVIATED TITLE OF RESEARCH PROPOSAL (Do not exceed 53 typewriter spaces)
Kindred Patterns (Mentally Retarded; Control)

2. TYPE OF APPLICATION (Check one)
☐ NEW PROJECT
☒ RENEWAL OF PHS GRANT NO. HD-00045
☐ REVISION OF PHS APPLICATION NO. _____
☐ SUPPLEMENT TO PHS GRANT NO. _____

3. DATES OF ENTIRE PROPOSED PROJECT PERIOD (This application)

FROM	THROUGH
June 1, 1966	May 31, 1969

4. TOTAL AMOUNT REQUESTED FOR PERIOD IN ITEM 3
$ 256.014.-

5. AMOUNT REQUESTED FOR FIRST 12-MONTH PERIOD
$ 83.614.-

6A. NAME OF PRINCIPAL INVESTIGATOR (Last, First, Initial)
Lederberg, Joshua

B. DEGREE: Ph.D.

C. SOCIAL SECURITY NO. [redacted]

D. TELEPHONE DATA: Area Code 415 | Telephone Number 321-1200 5049

E. TITLE OF POSITION
Professor and Executive Head
Department of Genetics

F. DEPARTMENT, SERVICE, LABORATORY OR EQUIVALENT (See Instructions)
Genetics Department

G. MAJOR SUBDIVISION (See Instructions)
School of Medicine

H. MAILING ADDRESS OF PRINCIPAL INVESTIGATOR (Street, City, State, Zip Code)
Department of Genetics
School of Medicine 94304
Stanford University, Palo Alto, Calif.

7A. IDENTIFY ORGANIZATIONAL COMPONENT RESPONSIBLE FOR CONDUCT OF SCIENTIFIC ASPECTS OF PROJECT
School of Medicine

B. DEPARTMENT
Genetics Department

8. ADDRESS WHERE RESEARCH WILL BE CONDUCTED If same as Item 6H, check box ☒

9. ARE FEDERAL FACILITIES TO BE USED FOR THIS RESEARCH?
☒ NO ☐ YES _____% OF TIME

TO BE COMPLETED BY RESPONSIBLE ADMINISTRATIVE AUTHORITY (Items 10 through 15 and 17B)

10. APPLICANT ORGANIZATION (Name and Address-Street, City, State, Zip Code) (See Instructions)
Stanford University
Stanford, California 94304

12. TYPE OF ORGANIZATION (Check applicable item) ☐ INDIVIDUAL
PUBLIC INSTITUTION: ☐ FEDERAL ☐ STATE ☐ LOCAL ☐ OTHER
PRIVATE INSTITUTION: ☒ NONPROFIT ☐ PROFIT

13. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Earl G. L. Cilley
Assistant Research Administrator

11. NAME, TITLE AND ADDRESS OF OFFICIAL TO WHOM CHECKS SHOULD BE MAILED
Mr. Kenneth D. Creighton, Controller
Encina Hall, Stanford University
Stanford, California

14. PHS ACCOUNT NUMBER (Enter if known)
458210

15. ESTABLISHED PHS INDIRECT COST RATE (Enter if known)
20 %

16. TERMS AND CONDITIONS. The undersigned accept, as to any grant awarded, the obligation to comply with Public Health Service Research Project Grant Regulations in effect at the time of the award (42 CFR, Part 52), the terms and conditions in the Grants for Research Projects Policy Statement, and the undersigned agree to comply with Title VI of the Civil Rights Act of 1964 (P.L. 88-352), and the Regulation issued pursuant thereto and state that our formally filed Assurance of Compliance with such Regulation (Form HEW-441) applies to this project. The undersigned also certify that they have no commitments or obligations, including those with respect to inventions, inconsistent with compliance with such Regulations, the Manual, and the Act.

17. SIGNATURES (Use ink. "Per" signatures are acceptable)

A. SIGNATURE OF PERSON NAMED IN ITEM 6A: Joshua Lederberg — DATE 12/28/65

B. SIGNATURE OF PERSON NAMED IN ITEM 13: Earl L Cilley — DATE 12/30/65

PHS-398 (REV. 1-65)
(All previous editions obsolete)

Form Approved
Budget Bureau No. 68-R140

SECTION 1

NOT FOR PUBLICATION OR PUBLICATION REFERENCE.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

RESEARCH OBJECTIVES

LEAVE BLANK - (For office use only)
SIE PROJECT NUMBER

ABBREVIATED TITLE OF PROJECT
Kindred Patterns (Mentally Retarded; Control)

NAME, SOCIAL SECURITY NUMBER, OFFICIAL TITLE AND DEPARTMENT OF ALL PROFESSIONAL PERSONNEL ENGAGED ON PROJECT

Joshua Lederberg [redacted] Professor and Executive Head, Department of Genetics
Walter F. Bodmer [redacted] Assistant Professor, Department of Genetics
Albert Jacquard (no S.S. not yet) Res. Associate, Department of Genetics

NAME AND ADDRESS OF APPLICANT ORGANIZATION

Stanford University
Stanford California

USE THIS SPACE TO MAKE A BROAD STATEMENT OF YOUR RESEARCH OBJECTIVES

Census data will be acquired and tabulated that will allow the statistical analysis of reproductive patterns - the temporal distribution of birth, marriage and birth of offspring (and number of offspring) - in relation to socio-economic variables. Similar data will be obtained on kindreds of mentally retarded patients in State institutions. Computer studies will be made to establish the optimum means of retrieval and presentation of complex data. Relationships to fertility, maternal age effects on infant performance, seasonal variations in birth incidence, and the extent of endogamous stratification in the samples of the U.S. population are expected.

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Research Plan and Supporting Data, including Progress Report:

The first phase of this project is coterminous with the current funding, expiring May 31, 1966. This has consisted predominantly of the processing of the 1960 Census 5% Population Sample for a detailed report on child spacing. This work is being carried out in close cooperation with the Bureau of the Census. Technical operations in programming the data processing are carried out here at Stanford under the supervision of Mr. William Buell, seconded from the Bureau. This has been a very satisfactory arrangement, as it reconciles needs for (a) control of confidentiality of the files, (b) the Bureau's interests in the detail of the report, (c) access by our staff to the summary data, (d) supervision for later research requirements of data reduction and preparation of summary files, and (e) efficient communication with the Bureau staff on technical details.

The main results of the first phase will be the mentioned report, to be published by the Bureau as a volume in its regular report series. Perhaps equally important as a research resource will be a summary file of manageable size (10-20 tapes) for more leisurely and independent reevaluation of the data used in the report. We have maintained a purposely hostile and critical attitude about every aspect of these data. The ultimate limitations of Census data have been stressed by the Bureau itself, and its quality control is a subject of considerable effort and review on its part. Several considerations limit the value of these data for health research.

1.) Relevance of the questionnaire

The most important gaps are (a) linkage to mortality and morbidity data and (b) family versus household data

2.) Precision of the responses; completeness of enumeration

3.) Techniques used to compensate for missing data.

We can do little more than (sympathetically) deplore the first two items, but our final reports will attempt to evaluate these for a quantitative perspective on the quality of the data base. Item 3 offers a more tangible operational challenge. Historically, the Bureau has interpreted missing data on a pragmatic basis, so that its reports would return consistent figures for totals. The credibility of this procedure will vary according to the sample; unfortunately, the usual form of publication makes it impossible to recover the original data for reevaluation. Since childspacing is an analysis of the relationships of specific individuals to one another, it is, of course, especially sensitive to biases in imputation. The allocation of a suitable birthdate is a particularly critical procedure, now done by extrapolation from a totally inadequate sample base.

Without interfering with the production of the conventional tables, we are therefore paying special attention to the preservation of the actual recorded data in the summary files. A concrete model for estimation is appended.

As indicated earlier, our main interests in the analysis of the completed data files are:

1.) Fitting mathematical models of family structure

2.) A critical examination of the variance of fertility

3.) Seasonality of birth in relation to socio-economic and to other seasonal parameters (marriage; birth of siblings)

The studies are the main objectives of the continuation of this research. They represent the main commitment to population study in this department, and in this way serve indirectly for advanced research training of participating students and fellows, whether or not listed in the formal roster (e.g., Drs. Sved, Kessler, and Mr. Fischer).

One of the important uses of an analysis of the variance of fertility is the estimation of the limits of the rate of natural selection in man. This was pointed out by Professor Crow some years ago, and has been the subject of considerable discussion since that time. The variance of fertility, however, includes a term of unknown magnitude for environmental effects which would play no part in the dynamics of gene frequencies in evolution. It is, however, very difficult to point to any attribute which is even reasonably free from genotypic influence. However, rank of birth within a family may be such an attribute, since the children within a kindred have, to a first approximation, the same expectation of genotype. A current population survey covering some 39,000 families has provided some information for this purpose; a special study is obviously required covering at least two generations in order to assess any significant performance of individuals in relation to their birth rank. We were not able to find any gross effects of birth rank on fertility, or on general socio-economic performance. However, the effect of birth rank should not be considered only by itself, but also for its impact on the correlation between parent and offspring. As folklore would have predicted, and as the present data clearly show, at least in certain occupational categories, the firstborn tends to follow the parents' occupation, significantly more frequently than other members of the kindred. At least this was undeniably apparent for farmers and for professional occupations. The expected effect of rank of birth should then be to increase the apparent heritability for a number of traits without necessarily influencing the mean level of performance over all individuals of a given rank.

In addition we have made some incursions into other data, such as the file from Pacific State Hospital. These patient files have now been completely coded and the last few data bugs are being weeded out. Some preliminary runs have been made, e.g., on kindreds of admissions for Down's syndrome. As Penrose had anticipated long ago, maternal age and <u>not</u> parity is a decisive etiological factor. We have found no support for the contention that impaired fertility and spontaneous abortion are premonitions of a trisomic birth. However, the control set has not been matched to the extent we intend before insisting on this conclusion.

Further analysis of day-of-week effect on total births supports elective induction as the main culprit. The missing births (after holidays) appear on following days; we are waiting momentarily for some additional information in which the management of the delivery has been detailed to nail this down once and for all. Non-whites do not show this deficiency in weekend births. Perhaps surprisingly, however, there is no evidence, at least from mortality statistics, of any disadvantage to babies who insist on being born on inconvenient days from the standpoint of hospital routine. An earlier thought that this weekly birth cycle might be related to a conception

cycle was a fantasy: the variance of gestation time would have to be 2 - 3 days, rather than 15, to fit the distribution; also holidays are comparable to weekends. However, there is no factual information on conception statistics. Howbeit, no model can be quite complete without them.

A study of twin data has shown a surprising clustering in time of these statistics. They may well be artifacts, but we are in any event trying to sort out the time series of mono- and dizygotic types. Even as artifacts, these series may afford controls or cautions for the statistical treatment of current reports on clustering of chromosome abnormalities. The operational budget is intended to cover the statistical analysis of the summary tapes. Our access to these and related background data will be facilitated by the renewal of our agreement with the Bureau of the Census for stationing a representative here and for furnishing various data files on a cost-reimbursement basis.

We solicit the interest of other investigators in the summary tapes and will endeavor to assist their access to them, subject only to the recovery of added costs and Census Bureau policies on confidentiality.

In previous reports we have mentioned our expectations for real-time access to the data so that we could analyze these files on a conversational basis. We have so far implemented this only to a very limited extent, namely, a facility to permit scope display of the data tapes themselves on a local, readily available LINC computer. We had originally intended to program some routine statistical operations on the LINC, but have decided to postpone this in favor of work on a very much more powerful time-shared computer facility that is now planned for installation in the Medical School starting approximately June 1966. This facility, which will center on an IBM 360-50 computer operated under a general time-sharing system, will be so much more powerful than the LINC that it would be a waste of effort to attempt to program the latter for the sake of the few months lead time. It will be necessary, however, to put together a rather sophisticated terminal to take full advantage of these capabilities. The financial arrangements for the Medical School computer are not yet fully crystallized. For that reason, the budget item of $15,000 computer time may be represented in charges on exactly that basis, or may be reallocated to the lease or purchase of terminal equipment dedicated to the project. Our plans for this type of interrogation of statistical data have been of some interest to the Bureau, and we remain in close contact about this. Until the new facilities are working smoothly, we will continue our data processing on the campus Computation Center's IBM 7090, and this will in any event require at least a portion of the budget for computer time.

To anticipate a question that previous experience suggests will always be brought up, the computing services on this campus to which time charges are attached are already the subject of detailed audit by government agencies. The charges already include provision for overhead and are therefore excluded from the base for indirect cost allowances.

APPENDIX

Estimation of birth interval distributions for families with children absent from the home at the time of the census

A major possible source of bias for family studies with census data arises from the fact that they are collected by the household rather than the family. Information on children who have left the household is missed, though the total number of children ever born to each female is, of course, recorded. There are many socio-economic and cultural factors (including, for example, mental retardation) which are correlated with the age at which children leave the parental household. The average characteristics of families with all children present may, therefore, differ markedly from those with one or more children absent. It will, in practice, be impossible to control (or perhaps even determine) all the variables which may influence such a bias. There may also be inherent ascertainment biases in the birth interval distributions obtained from such household data, which are not due to socio-economic and other stratifications. Thus if, for example, the age of the child were the main factor determining when it leaves a household, families from recently married couples with all children ever born present would be biased toward longer birth intervals. A preliminary attempt to determine the possible magnitude of such biases has been based on the construction of model populations having birth interval distributions corresponding to those observed in the August 1959 CPS, and incorporating various rules for when children leave the household. The indications, so far, are that these ascertainment biases do not present a serious problem. There is, generally, from Census data, a conflict between obtaining information on the complete family and obtaining information from women whose fertility history is completed.

There is an obvious need to try to obtain some information on the characteristics of the birth interval distributions for families with children missing from the household. Following previous practice in analogous situations, the Census Bureau has suggested procedures for "allocating" information on missing children based on tables constructed from sample surveys (August 1959 CPS) which specifically provide information on the distribution of birth intervals for children absent from home. These are considered unsatisfactory for the following three main reasons:

1. The allocation distributions are based mostly on sub-classification only by race and marital status. A bias may thus be introduced when these allocations distributions are used for more complex cross classifications such as will be required in the analysis of the 5% sample of the 1960 population census.

2. Many of the allocations are based on small numbers leading possibly to relatively large random errors when they are applied to a considerably larger body of data.

3. There may be a bias in the source data for the allocation tables, for example, if these changed from the 1959 CPS to the 1960 population census.

The allocation procedure actually combines data from complete families with the allocation distributions, which latter may be both biased and subject to relatively large random variation due to small numbers in the August 1959 CPS relative to the amount of information available from the 1960 census on the completed families. The confounding of these two sources of information dilutes the value of the actual data from the completed families.

We shall now outline formally a procedure for estimating birth intervals for families with children absent from home, using only the information contained in the 1960 population census.

The estimation problem is considered for a given category, by which is meant a particular set of cross classifications (i.e., cells) for which child spacing distributions

are desired. Thus, for example, we may be interested in these distributions for women classified by educational status, by age of marriage, and by epoch. To illustrate the method we consider first the case of families with two children ever born. As indicated in Table I, there are four types of families according to which child is present or absent. Families of type 2 and 3 cannot be distinguished in the census data as collected. We thus observe directly only the quantitites p_1, $p_2 + p_3$, p_4, the distribution of the interval from marriage to the first child and from the first child to the second child for completed families (type 1) and the distribution of the interval from marriage to the child which is present for families of types 2 and 3. Our concern in trying to obtain some estimate of the interval distributions for families of types 2 and 3 with one child missing is, of course, in case they differ significantly from those observed for the completed families. If this were the case, then these differences would have to be taken into account in describing the interval distributions for the particular category under consideration. It is clear that no information can be obtained on the interval distribution for families of type 4 where both children are missing. Possible biases introduced by using only data from the completed families will of course be minimized when the proportions p_2, p_3, and p_4 are small.

The observed distribution of the interval from marriage to the child present for families with one child missing will be a weighted combination of the distribution of the interval from marriage to the first child for families of type 2 and the distribution of the interval from marriage to the birth of the second child for families of type 3. The latter is, in fact, the distribution of a "double" interval which, of course, would be expected to be appreciably longer than the corresponding distribution for a single interval. The observed distribution should therefore be bi-modal and its components resolvable by fitting a weighted mixture of two distributions describing in turn the expected distributions for the interval from marriage to the first child for families of type 2 and the interval from marriage to the second child for families of type 3. More specifically, if $f_{21}(x)$ represents the expected distribution of the interval from marriage to the first child for families of type 2 and $F_3(x)$ represents the probability density function for the distribution of the interval from marriage to a second child for families of type 3 then the expected probability density function for the interval from marriage to the child present for families with one child absent is given by

$$\frac{p_2}{p_2 + p_3} f_{21}(x) + \frac{p_3}{p_2 + p_3} F_3(x)$$

Given a theoretical distributional form for birth intervals, i.e. for $f_{21}(x)$ and $F_3(x)$, we can use standard statistical procedures, such as maximum likelihood, to fit this expected mixed distribution to the observed distribution. This will give estimates of the proportions p_2 and p_3 and of the parameters defining the distributions $f_{21}(x)$ and $F_3(x)$. We can then ask the question as to whether these distributions differ significantly from the corresponding distributions observed for completed families (type 1), and so assess biases introduced by ignoring incomplete families. It is anticipated that some general two parameter distribution, for example, the gamma distribution or if necessary a three parameter distribution, possibly a modified gamma distribution, may turn out to be a suitable analytical form for fitting birth interval distributions. It will in any case be important to choose the most appropriate theoretical distribution for fitting the observed birth interval distributions (see below).

The general approach outlined above can easily be extended to larger families. The eight types of families for three children ever born are given in Table II. We observe data for completed families of type 1; for families with one child missing, namely the combination of families of types 2, 3 and 4; for families with 2 children missing, corresponding to the combination of families of types 5, 6 and 7; and fin-

ally the proportion p_8 of families with all three children missing. For families with one child missing there are two observed interval distributions, namely the interval from marriage to the first child present, and the interval from the first child present to the second child present. If we write $f_{31}(x)$, $f_{41}(x)$ and $F_2(x)$ for the probability density functions of the interval from marriage to the first child for families of type 3 and type 4 and from marriage to the second child for families of type 2, respectively, then the expected probability density function for the distribution of the interval from marriage to the first child present for families with one child missing will be

$$\frac{p_2}{p_2 + p_3 + p_4} F_2(x) + \frac{p_3}{p_2 + p_3 + p_4} f_{31}(x) + \frac{p_4}{p_2 + p_3 + p_4} f_{41}(x)$$

This is a weighted sum of the distributions of two single intervals and one double interval. If we make the simplifying assumption that the expected distribution functions of the two single intervals are identical, this problem reduces to the one described above for families with two children ever born and one child missing. An exactly analogous procedure applies to the resolution of the distribution of the interval from the first child present to the second child present for families with onechild missing. For families with two children missing, there is a single interval observed, namely that from marriage to the child which is present. The expected distribution is now a composite of three distributions: one for a single interval, one for a double interval, and the third for a triple interval. These are respectively the distribution from marriage to the first child for families of type 7, from marriage to the second child for families of type 6 and from marriage to the third child for families of type 5. Adequate resolution of this observed distribution would then require the fitting of a mixture of three distributions, which is likely to be the limit for this statistical procedure. Families with four children ever born will provide the following observed distributions:

1. All intervals for completed families
2. Three bimodal distributions for families with one child missing
3. Two trimodal distributions for families with two children missing
4. One quadrimodal distribution for families with three children missing, i.e., only one child present.

Useful information may still be extractable from families with one or at most two children missing. However, the hope of extracting useful information where more children are missing from the family is clearly very limited.

Illegitimacy has not been taken into account in these procedures. It can in any case not be resolved unless illegitimate children are specifically identified. Illegitimacy must be considered as a factor possibly modifying birth interval distributions for given categories according to the preponderence of illegitimacy in the particular category.

A serious limitation of this approach is the possibility of resolving mixed distributions given limited numbers of observations. Experience only will show how satisfactory the method will be for any given level of cross classification. A program for fitting mixtures of normal distributions by maximum likelihood has already been written, and some experience been gained with this general statistical problem. It may be expected that the substitution of another distribution for the normal distribution will not lead to any major change in the program or the general approach to the problem of fitting mixed distributions.

The gamma distribution gives a very poor fit to data from the August 1959 CPS on the intervals from marriage to first birth and a somewhat better, but still inadequate, fit to subsequent intervals, The main reason for the poor fit to the first interval appears to be the inability of the gamma distribution to take account of the large mode at 9 - 10 months together with the considerable number of births occurring at much longer intervals. It is, moreover, difficult if not impossible to attach any specific biological significance to the parameters of the gamma distribution when used in this context. Unfortunately, no other simple (as opposed to compound) analytical distribution appears to be better suited to fitting the entire observed birth interval distribution.

As has been pointed out by Perrin, Sheps and others, theoretical models for birth intervals lead to the expectation that birth interval distributions will be compound. For the interval from marriage to first birth there are at least three qualitatively distinguishable components:

1. Births before 9 months, representing mainly premarital conceptions.
2. Births in the interval immediately following the first nine months, representing mainly post-marital conceptions in the absence of birth control.
3. Later births reflecting the heterogeneous effects of birth control.

In the absence of birth control, assuming a constant probability, p, of conception per month, the probability of conception in the r^{th} month following marriage (and so birth in the r + 9th month) is well known to be pq^r, where $q = 1 - p$. When p varies from family to family, a reasonable approximation to this theoretical distribution is generally obtained by using the mean value of p as the parameter for the geometric distribution. Data from the August 1959 CPS on the 9th to the 14th or 15th months of the interval from marriage to first birth fit a geometric distribution very well. Furthermore, the proportion of births falling in this category (No. 2 above) can also be estimated reasonably accurately. Since, however, the 1960 census data are collected only by quarter, they will give somewhat poorer resolution by this method of analysis, but still hopefully will lead to meaningful values. A further distribution is needed to fit the tail of the observed distribution represented by the third category of births following marriage.

For the second and subsequent birth intervals, premarital conceptions are no longer relevant, but there is the extra complication of the distribution of the length of the post-partum sterile period. There is no doubt that the single interval can itself best be fitted by a mixture of at least two distributions. These complications in choosing appropriate distributional forms for birth intervals aggravate still further the problems of dealing with data from families with children missing from the household at the time of the census. However, we are hopeful that at least in some of the simpler cases, and for minimal cross-classifications, some useful information can be obtained using the procedures outlined above. These will first be tested on the August 1959 and June 1965 current population surveys for which at least in some cases the actual distributions corresponding to the missing children are known. In cases where the allocation procedures corresponding to the missing children are known. In cases where the allocation procedures cannot be satisfactorily applied, only data from the complete families will be used for analysis. Our experience with these general problems should undoubtedly contribute substantially to the design and analysis of future large scale surveys for studies in genetic demography.

TABLE I

Families with two children ever born

Family Type	1st Child	2nd Child	Proportion of Families of given type
1	+	+	p_1
2	+	0	p_2
3	0	+	p_3
4	0	0	p_4
			1

+ = child present

0 = child absent

TABLE 2

Families with three children ever born

Family type	1st child	2nd child	3rd child	Proportion
1	+	+	+	p_1
2	0	+	+	p_2
3	+	0	+	p_3
4	+	+	0	p_4
5	0	0	+	p_5
6	0	+	0	p_6
7	+	0	0	p_7
8	0	0	0	p_8

Continuation page

Dr. Bodmer is co-investigator with Drs. Karlin and McGregor of the Stanford Mathematics Department on a research grant (GM 10452) entitled "Stochastic Models in Medicine and Biology" (renewal from May 1, 1966 pending under title "Mathematical Models in Genetics and Population Biology") which supports some of the theoretical and model building (as opposed to data analysis) aspects of the work described above. Dr. John Sved, who has been working with Dr. Bodmer on models for the ascertainment biases and birth interval distributions is supported under this grant. (GM 10452).

Publications:

Bodmer, W. F., 1965. A program for genetic demography based on data from large-scale social surveys. Eugenics Quarterly 12:85-89.

Bodmer, W. F. and L. L. Cavalli-Sforza, 1965. Perspectives in genetic demography. Proc. of the 1965 World Population Conference (in press).

SECTION II - PRIVILEGED COMMUNICATION

3. BIOGRAPHICAL SKETCHES

(Give the following information for EACH key staff member, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)

NAME	TITLE	BIRTHDATE (Mo., Day, Yr.)

PLACE OF BIRTH (City, State, Country)	PRESENT NATIONALITY (If non-U.S. citizen, indicate visa status)	SEX
		☐ Male ☐ Female

EDUCATION (Begin with baccalaureate training and include postdoctoral)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED

HONORS

MAJOR RESEARCH INTEREST

RELATIONSHIP TO PROPOSED PROJECT

RESEARCH AND/OR PROFESSIONAL EXPERIENCE (Start with present position; list ALL experience relevant to project.)

See attached material.

JOSHUA LEDERBERG

Department of Genetics
Stanford University School of Medicine
Palo Alto, California

Born: May 23, 1925, Montclair, New Jersey

Education:

1938-41	Stuyvesant High School (New York City)
1941-44	B.A., Columbia College
1944-46	Enrolled as medical student, Columbia University, College of Physicians and Surgeons
1946-47	Ph.D., Yale University

Experience:

1945-46	Research assistant in Zoology (with Professor F. J. Ryan), Columbia University
1946-47	Research Fellow of the Jane Coffin Childs Fund for Medical Research at Yale University (with Professor E. L. Tatum)
1947-59	Professor of Genetics; 1957-59, Chairman, Department of Medical Genetics, University of Wisconsin
1959-	Professor of Genetics (also Biology); Executive Head, Department of Genetics, Stanford University
1962-	Director, Kennedy Laboratories for Molecular Medicine, Stanford University

Visiting Appointments:

1950	Visiting Professor of Bacteriology, University of California, Berkeley
1957	Fulbright Visiting Professor of Bacteriology, Melbourne University (Australia)
1962	Lecturer, Japan Society for the Promotion of Science

Special Field: Genetics, Chemistry and Evolution of Unicellular Organisms

Distinctions:

1957	National Academy of Sciences
1958	Nobel Prize (Medicine or Physiology) "for studies on organization of the genetic material in bacteria"

WALTER FRED BODMER

Born: Frankfurt am Main, Germany, January 10, 1936.

Nationality and Citizenship: British

Married Julia G. Pilkington (born July 31, 1934, Manchester, England)

Children: Mark William, born June 23, 1957
Helen Clare, born March 28, 1959
Charles Walter, born June 12, 1961

Education: B.A. (1956), Clare College, Cambridge University. Mathematics.
Ph.D. (1959), Department of Genetics, Cambridge University.
Population Genetics.

Appointments:

Research Fellow (1958-60), Official Fellow (1961), Clare College, Cambridge.

Demonstrator (1960-61), Department of Genetics, Cambridge University

Fellow, Visiting Assistant Professor (1961-62); Assistant Professor (July, 1962 - August, 1968) Department of Genetics, Stanford University School of Medicine, Palo Alto, California.

Scholarships, Honors:

General Certificate of Education (1952) in Mathematics and Theoretical Mechanics at Advanced and Scholarship levels; Physics at Advanced level; English, French, German and Latin at Ordinary level.

Awarded State Scholarship 1952.

Major Scholarship in Mathematics to Clare College, Cambridge University, 1952.

Undergraduate at Clare College, Cambridge, 1953-56.

Wrangler (1st class honors) in Part II of Mathematics Tripos, 1955.

Obtained honors in Part III of Mathematics Tripos, 1956, having taken courses in Genetics, Statistics and Numerical Analysis.

Awarded Owst Prize by Clare College for performance in Part III, 1956.

Agricultural Research Council doing research in genetics under Professor Sir Ronald Fisher, F.R.S., and Dr. A.R.G. Owen at the Department of Genetics, University of Cambridge, 1956-58.

Elected to a Research Fellowship by competition at Clare College, 1958.

Obtained Ph.D. 1959 (Short title of thesis: The Study of Population Genetics and Gene Effects).

Summer, 1959, worked under Professor Pontecorvo in the Genetics Department, University of Glasgow, Scotland. Subsequently started microbiological work on Neurospora and Aspergillus at Department of Genetics, Cambridge.

Director of Studies for Clare College in Mathematics and Statistics for Scientists, 1959-61.

July 1961-April 1962, Postdoctoral Research Fellow, Department of Genetics, Stanford University.

INSTITUT NATIONAL D'ÉTUDES DÉMOGRAPHIQUES

1 – Name : J A C Q U A R D Albert, Marie, Joseph (Male)

2 – Curriculum vitae

– Born : December 23 – 1925 at LYON (France) Present Nationality: French.

– Education

Degrees : 1948 : Ecole Polytechnique
1950 : Institut de Statistiques – Université de Paris
1965 : Institut de Démographie – Université de Paris

– occupations :

1951-58 : Organization Department of the State Tobacco Monopoly
1959-61 : Deputy general Secretary of State Tobacco Monopoly
1962-64 : Deputy Director of the Equipment Department, Ministry of Public Health
1965 : Research worker, National Institute of Demographic Studies

SECTION II - PRIVILEGED COMMUNICATION

4. DETAILED BUDGET FOR FIRST 12-MONTH PERIOD (DIRECT COSTS ONLY)	FROM	THROUGH

DESCRIPTION (Itemize)			AMOUNT REQUESTED (Omit Cents)		
PERSONNEL					
NAME	TITLE OF POSITION	TIME OR EFFORT %/HRS.	SALARY	FRINGE BENEFITS	TOTAL
J. Lederberg	Professor	15			
W. Bodmer	Asst. Professor	15			
A. Jacquard Ph. D.	Res. Associate	100	13.000.-	1.222.-	14.222.-
2 Computer Programmers	at 9.000.-	100	18.000.-	1.692.-	19.692.-
					33.914.-
CONSULTANT SERVICES					
EQUIPMENT *Depending on progress of plans for time-sharing computer, part of this amount may be requested instead for purchase or lease of terminal console equipment. (See listing under "Computer Time")					
SUPPLIES Tapes and other data processing supplies					3.000.-
TRAVEL DOMESTIC					
TRAVEL FOREIGN					
HOSPITALIZATION (Study patients)					
OUTPATIENT OR SUBJECT COSTS (Study patients)					
ALTERATIONS AND RENOVATIONS					
PUBLICATION COSTS Publication, photography, reproduction costs					500.-
ALL OTHER EXPENSES Computer time *(See note above under "Equipment")					15.000.-
Rental office space					1.200.-
Reimbursement of costs to other data sources (State of Calif., office of Vital Statistics, etc.)					5.000.-
Census Bureau - Contract reimbursement					25.000.-
TOTAL (Enter on Page 1, Item 5) →					$ 83.614.-

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SECTION II - PRIVILEGED COMMUNICATION

5. BUDGET ESTIMATES FOR ALL YEARS OF SUPPORT REQUESTED FROM PUBLIC HEALTH SERVICE (DIRECT COSTS ONLY - OMIT CENTS)

DESCRIPTION	1ST PERIOD (SAME AS DETAILED BUDGET)	ADDITIONAL YEARS SUPPORT REQUESTED (This application only)					
		2ND YEAR	3RD YEAR	4TH YEAR	5TH YEAR	6TH YEAR	7TH YEAR
PERSONNEL (Salaries, fringe benefits, etc.)	33.914.-	35.610.-*	37.390.-*				
CONSULTANT SERVICES (Include fees, travel, etc.)							
EQUIPMENT							
SUPPLIES	3.000.-	3.000.-	3.000.-				
TRAVEL — DOMESTIC							
TRAVEL — FOREIGN							
HOSPITALIZATION (Study patients)							
OUTPATIENT OR SUBJECT COSTS (Study patients)							
ALTERATIONS AND RENOVATIONS							
PUBLICATION COSTS	500.-	500.-	500.-				
ALL OTHER EXPENSES	46.200.-	46.200.-	46.200.-				
TOTALS	83.614.-	85.310.-	87.090.-				

TOTAL FOR ENTIRE PROPOSED PROJECT PERIOD (Enter on Page 1, Item 4) ⟶ $ 256.014.-

REMARKS (Justify continuing funds where the need may not be apparent)

*Same personnel as first year, but includes a 5% increase in salary each year.

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6. RESEARCH SUPPORT

List all other research support of the principal investigator, including requests now being considered as well as any proposals which the principal investigator plans to submit to the Public Health Service or other granting agencies, regardless of relevance to this application.

To be included also are current or pending contracts, Fellowship Awards, Research Career Awards, and Training Grants. Include support for this project received from own organization. Amounts shown should reflect total funds awarded or pending over the entire grant periods indicated in the final column.

Use blank continuation pages, if necessary, and follow the same format.

A. PUBLIC HEALTH SERVICE SUPPORT

GRANT NUMBER (If designated)	TITLE OF PROJECT	PERCENT TIME/EFFORT ON PROJECT	TOTAL AMOUNT	TOTAL PERIOD OF SUPPORT WITH DATES
(1) ACTIVE OR APPROVED				
5TI GM 295	Training Program in Genetics		$460,600	7/1/64 to 6/30/69
AI-5160	Genetics of bacteria		253,348	9/1/63 to 8/31/68
NB-04270	Molecular Neurobiology		453,183	12/1/62 to 11/30/67
(2) APPLICATIONS PENDING DECISION OR PLANNED				
FR 00311	Advanced Computer for Medical Research		2,763,407	4/1/66 to 3/31/71

B. ALL OTHER RESEARCH SUPPORT

SOURCE AND PROJECT NO. (If designated)	TITLE OF PROJECT	PERCENT TIME/EFFORT ON PROJECT	TOTAL AMOUNT	TOTAL PERIOD OF SUPPORT WITH DATES
(1) ACTIVE OR APPROVED				
NSF GB-4430	Program in Genetics & Molecular Biology		$ 65,200	10/15/65 to 10/14/66
Kennedy Foundation	Molecular Neurobiology		100,000	1/31/63 to 1967
NASA NsG 81-60	Cytochemical studies of planetary micro-organisms; medical instrumentation		349,899	4/1/65 to 3/31/66
Air Force AF 49(638)-1599	Molecular Biology Applications of Mass Spectrometry		75,564	7/1/65 to 12/31/66
(2) APPLICATIONS PENDING DECISION OR PLANNED				
NASA	Computer Control of External Devices and an Automated Biological Laboratory		1,196,854	First year

NOTE: Most of the projects listed are cooperative programs involving a number of staff members.